Observational Study

Medicine

OPEN

The relationship between cardiological parameters and PCR in patients with coronavirus infection

A cross-sectional study

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Abstract

Cardiovascular injuries induced by SARS CoV-2 have been reported repeatedly in various studies. Therefore, it is necessary to understand cardiac complications at a low cost, quickly. This study aimed to determine the relationship between cardiological parameters and polymerase chain reaction (PCR) in patients with coronavirus infection. : Patients who were admitted to the emergency department due to the ongoing pandemic, all patients with similar symptoms to coronavirus disease 2019 infection were initially admitted to the respiratory emergency room and underwent subsequent evaluations to confirm or rule out SARS-COV2 infection symptoms were assessed for eligibility. Patient were categorized into 2 groups 1. Positive PCR and negative PCR groups. Binary logistic regression was performed to assess the effect of several factors on the likelihood of developing positive troponin, reduced ejection fraction (EF), and Positive brain natriuretic peptide (BNP). Among 195 patients included, 115 (58.9%) had positive PCR. Patient in the positive PCR and negative PCR were 58.04 ± 18.03 and 59.19 ± 15.38 years of age, respectively. Patients in the "positive PCR" were significantly less likely to have chronic kidney disease (6.69% vs 17.5%, *P* value: .022), consume calcium channel blockers (6.69% vs 18.75%, *P* value:0.012). At the univariable level, positive PCR was significantly associated with fewer odds for positive BNP (OR:0.46, *P* = .019); nevertheless, the association was no longer significant after adjusting for confounders (adjusted OR:0.56, *P* = .158). Unadjusted positive PCR results were not found to have a significant association with positive troponin or reduced EF. Likewise, multivariable regression revealed no association between positive PCR and positive troponin (aOR:1.28, *P* = .529) and reduced EF (aOR:0.65, *P* = .369). PCR positivity did not result in positive troponin and BNP and did not appear to decrease EF. In other words, serial troponin and BNP checks and initial echocardiography in coronavirus disease 2019 respiratory emergencies do not make significant differences in diagnostic and therapeutic management and inpatient outcomes of patients with positive or negative PCR and are not specific findings. Evidence suggests some coronavirus-induced cardiac complications will be manifested in the long term.

Abbreviations: BNP = brain natriuretic peptide, Ca = calcium, CMR = cardiovascular magnetic resonance imaging, COVID-19 = coronavirus disease 2019, EF = ejection fraction, HF = heart failure, ICU = intensive care unit, PAP = pulmonary artery pressure, PCR = polymerase chain reaction, PCT = procalcitonin.

Keywords: cardiac injury, emergency department, PCR, SARS-CoV-2, troponin

1. Introduction

Coronavirus disease 2019 (COVID-19) caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus, was first detected as a pandemic by the World Health Organization in early 2020, and has infected approximately 245 million people globally, killing over 5.5 million people between then and November 2021.[1] Because of the virus's high infectivity, ability to transmit while asymptomatic, low pathogenicity, and short incubation time, it propagated quickly across geographic borders, culminating in a pandemic. COVID-19 is primarily known for its respiratory involvement, which can range from flu-like symptoms like low-grade fever, dyspnea, cough and myalgia, to potentially fatal acute respiratory distress syndrome or fulminant pneumonia. However, it also has significant systemic effects,

The authors have no funding and conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Supplemental Digital Content is available for this article.

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How to cite this article: Majidi F, Mohagheghi Dare Ranj A, Jameie M, Jameie M, Mansouri P, Varpaei HA, Shirani S. The relationship between cardiological parameters and PCR in patients with coronavirus infection: A cross-sectional study. Medicine 2022;101:50(e31935).

Received: 3 June 2022 / Received in final form: 28 October 2022 / Accepted: 31 October 2022

http://dx.doi.org/10.1097/MD.0000000000031935

including cardiovascular involvement, multi-organ dysfunction, and high mortality rates.[2,3] COVID-19 has been related to a variety of cardiovascular involvement and complications, including cardiac injury, acute myocardial infarction, thromboembolic events, myocarditis, takotsubo cardiomyopathy, ventricular arrhythmia, acute heart failure and cardiogenic shock.[4]

Cardiac troponin is a myocardial damage marker, although it can also be elevated in several other disorders. According to a recent study, approximately 20% of COVID-19 patients suffered cardiac injury, which led to worse clinical outcomes than those who did not.[5,6] A retrospective single-center case investigation of 138 COVID-19 patients found that about 7% and 17% of patients suffered immediate cardiac injury and ventricular arrhythmia complications, respectively.[7] Therefore, its necessary to understand cardiac complications at low cost, and quickly in terms of prognostic values in patients who admitted to respiratory emergency department (COVID-19 suspected). We aimed to assess the relationship between cardiovascular parameters and polymerase chain reaction (PCR) in patients with COVID-19.

2. Materials and methods

2.1. Study settings

This cross-sectional study was conducted between February 2020 and June 2020 at Shariati Hospital Complex affiliated with Tehran University of Medical Sciences, Tehran, Iran. The study was approved by the ethic committee of the university (IR.TUMS.MEDICINE.REC.1399.343) in accordance with the declaration of Helsinki.[8] Written informed consent was obtained from the patients for participation and publication.

This study aimed to evaluate the association of positive results of polymerase chain reaction (PCR) for SARS-COV2 with 1. Positive troponin 2. Reduced ejection fraction 3. Elevated brain natriuretic peptide (BNP) among patients presenting to the emergency department due to the ongoing pandemic, all patients with similar symptoms to COVID-19 infection were initially admitted to the respiratory emergency room and underwent subsequent evaluations to confirm or rule out SARS-COV2 infection in a real-world setting.

2.2. Study population

Patients who were admitted to the emergency department due to the ongoing pandemic, all patients with similar symptoms to COVID-19 infection were initially admitted to the respiratory emergency room and underwent subsequent evaluations to confirm or rule out SARS-COV2 infection symptoms were assessed for eligibility. Patient were categorized into 2 groups 1. Positive PCR group 2. Negative PCR group. The former included various diseases presented at Table S1, Supplemental Digital Content, http://links.lww.com/MD/H988 in which SARS-COV2 was ruled out with 1 negative PCR and the presence of a more compatible alternative diagnosis. For the purpose of the study and due to the strong correlation of acute myocardial infarction (n = 6) with troponin and history of heart failure under traditional treatment (n = 8) with BNP, these 2 categories of patients were excluded from the final analyses. Moreover, those with following criteria were also excluded: patients who did not provide accurate information themselves or their companions. Consecutive data on 195 patients were gathered prospectively and entered for the analyses.

2.3. Study measures and variable definitions

The following data were assessed in the study: demographics; past medical history; past drug history; presenting symptoms; presenting vital signs; laboratory tests at admission; electrocardiogram at admission; echocardiogram at admission; in-hospital outcomes. The main variables of interest were assessed as follows. PCR test for SARS-COV2 was performed using TIB Molbiol kit and samples were gathered from both nasal and oral cavity. Troponin I was measured twice (at admission and 6 hours later), using ARCHITECT STAT High Sensitivity Troponin-I kit. The highest amount of troponin was entered in the analyses. Positive troponin was defined as troponin > 34.2 ng/L for males and > 15.6 ng/L for females). BNP was measure at admission using ARCHITECT BNP kit, and BNP ≥ 100 pg/mL was considered positive. Left ventricular Simpson biplane ejection fraction (EF), % was assessed by echocardiography, and reduced EF was defined as EF < 50. Other abnormal tests were defined as follows: c-reactive protein ≥ 6, aspartate transaminase ≥ 31 for females and ≥ 37 for males, alanine transaminase > 32, alkaline phosphatase > 136, albumin ≤ 3.5 (hypoalbuminemia), albumin ≥ 5 (hyperalbuminemia), sodium < 145 (hyponatremia), sodium ≥ 145 (hypernatremia), potassium < 3.5 (hypokalemia), potassium ≥ 5.5 (hyperkalemia), Ca < 8.5 (hypocalcemia), Ca ≥ 10.5 (hypercalcemia), magnesium < 1.8 (hypomagnesemia), magnesium ≥ 2.6 (hypermagnesemia), procalcitonin (PCT) ≤ 0.5 (low), PCT ≥ 2 (high), creatine phosphokinase ≥ 170, lactate dehydrogenase > 480, pulmonary artery pressure (PAP) ≥ 35.

2.4. Statistical analysis

Descriptive statistics for all variables were expressed using frequency and percentages for categorical variables and mean, Standard deviation, median, and interquartile range for continuous variables. Homogeneity between different groups was evaluated using the Chi-square test or Fisher exact test for qualitative variables and Student's *t* test or Wilcoxon rank-sum test for continuous variables.

Separate Binary logistic regression was performed to assess the effect of a number of factors on the likelihood of developing positive troponin, reduced EF, and Positive BNP. The model contained independent variables (Positive PCR, Age, Male, Hypertension, Diabetes, Hyperlipidemia, body mass index, Airway disease, Reduced EF, Elevated PAP, Diastolic dysfunction, valvular heart disease, white blood count, Leukopenia, Leukocytosis, Lymphocyte, Hemoglobin, Positive urine culture(U/C), c-reactive protein, creatine phosphokinase, lactate dehydrogenase, PCT, erythrocyte sedimentation rate, Ferritin, Sat O2 > 93%,Previous revascularization, Sinus rhythm, Corticosteroids). The variables that proved to be statistically significant in the univariable regression analyses with $P < .2$ were entered into a multivariable regression analysis as the initial risk factors. They were then analyzed by multivariable logistic regression to detect the independent risk factors of positive troponin, reduced EF, or Positive BNP. A 2-sided P value of .05 or lower was considered to be statistically significant. Statistical analyses were performed using Stata 16 (Stata Corp. 2019. Stata Statistical Software: Release 16. College Station, TX: Stata Corp LLC).

3. Results

3.1. Baseline characteristics

Among 195 patients included, 115 (58.9%) has positive PCR. Baseline characteristics of the 2 groups are presented in Table 1. Patient in the positive PCR and negative PCR were 58.04 ± 18.03 and 59.19 ± 15.38 years of age, respectively, with almost equal sex distribution between males and females. The 2 groups were comparable regarding various baseline and para-clinical characteristics except the following. Patients in the "positive PCR" were significantly less likely to have chronic kidney disease (6.69% vs 17.5%, P value: .022), consume Ca

Table 1

Baseline characteristics of the study cohort.

	Negative PCR (n = 80)	Positive PCR (n = 115)	*P* value
Demographics			
Male	39 (48.75%)	62 (53.91%)	.478
Age (continuous)	58.04 ± 18.03	59.19 ± 15.38	.632
Age (categorical)			.772
<50	22 (27.50%)	27 (23.48%)	
50–70	43 (53.75%)	63 (54.78%)	
>70	15 (18.75%)	25 (21.74%)	
Past medical history			
Hypertension	30 (37.50%)	50 (43.48%)	.404
Diabetes mellitus	24 (30.00%)	40 (34.78%)	.484
Hyperlipidemia	3 (3.75%)	5 (4.35%)	1.000
BMI	26.92 ± 3.18	27.48 ± 4.63	.356
Cerebrovascular accidents	2 (2.50%)	8 (6.96%)	.165
Airway disease	4 (5%)	4 (3.48%)	.719
Chronic kidney disease	14 (17.50%)	8 (6.96%)	.022
Cirrhosis	0	3 (2.61%)	.270
CABG	0	8 (6.96%)	.364
PCI	4 (5%)	9 (7.83%)	.565
Rheumatologic diseases	5 (6.25%)	4 (3.48%)	.491
Malignancy	15 (18.75%)	13 (11.30%)	.145
Chemotherapy	13 (16.25%)	10 (8.70%)	.108
Valve replacement	0	4 (3.4%)	.417
Past drug history			
ACEI	2 (2.50%)	9 (7.83%)	.205
ARB	20 (25%)	29 (25.22%)	.973
BB	16 (20%)	29 (25.22%)	.395
CCB	15 (18.75 %)	8 (6.96%)	.012
Statins	19 (23.75%)	29 (25.22%)	.815
Antiplatelet	21 (26.25%)	42 (36.52%)	.131
Anticoagulants	4 (5%)	7 (6.09%)	1
Diuretics	11 1(3.75%)	10 (8.70%)	.263
Nitrate	3 (3.75%)	3 (2.61%)	.691
Corticosteroids	6 (7.50%)	15 1(3.04%)	.219
Spray(bronchodilator)	3 (3.75 %)	4 (3.48%)	1
Presenting symptoms			
Asymptomatic	5 (6.25%)	7 (6.09%)	.963
Chest pain	9 (11.25%)	13 (11.30%)	.991
Dyspnea	49 (61.25%)	72 (62.61	.847
Palpitation	10 (12.50%)	5 (4.35%)	.036
Fever	21 (26.25%)	55 (47.83%)	.002
Chilling	13 (16.25 %)	24 (20.87%)	.418
Sore throat	4 (5%)	11 (9.57%)	.285
Cough	25 (31.25%)	55 (47.83%)	.021
Headaches	6 (7.50%)	4 (3.48%)	.322
Abdominal pain	10 (12.50%)	10 (8.70%)	.389
Myalgia	30 (37.50%)	31 (26.96%)	.118
Diarrhea	3 (3.75%)	3 (2.61%)	.691
Weakness	33 (41.25%)	43 (37.39%)	.587
Arthralgia	1 (1.25%)	2 (1.74%)	1
Presenting vital signs			
Temp (> 37.3)	11(13.75%)	32 (27.83%)	.020
O2sat (< 93)	52 (65%)	75 (65.22%)	.975
Respiratory rate	6 (7.50%)	9 (7.83%)	.933
Blood pressure			.087
BP < 100	13 (16.25%)	8 (6.96%)	
100 < BP < 140	49 (61.25%)	84 (73.04%)	
BP > 140	18 (22.50%)	23 (20%)	
Admission laboratory results			
Positive troponin I	26 (32.5%)	35 (30.43%)	.760
Elevated BNP	29 (36.25%)	25 (20.87%)	.018
BNP continuous, pg/mL	74.5 [30–281]	45 [25–91]	.006
ESR, mm/hr	50 [26–94]	53 [30–84]	.891
Elevated CRP	68 (85%)	105 (91.3%)	.171
CRP continuous, mg/L	67.5 [13.65–81.5]	71 [26.3–84]	.291
WBC, per microliter	8995 [5290–11700]	7700 [4980–12230]	.420
Lymphocyte%	19% [10–35]	15% [7–23]	.003
Neutrophil %	73% [55–83.5]	80% [71–87]	.001
Abnormal AST, U/L	39 (48.75%)	71 (61.74%)	.034
Abnormal ALT, U/L	23 (28.75%)	51 (44.35%)	.027

(*Continued*)

Table 1

(*Continued*)

	Negative PCR (n = 80)	Positive PCR (n = 115)	*P* value
Abnormal ALP, IU/L	60 (75%)	79 (68.70%)	.339
Albumin, g/dL			.010
Hypoalbuminemia	25 (31.25%)	17 (14.78%)	
Normal	49 (61.25%)	93 (80.87%)	
Hyperalbuminemia	6 (7.50%)	5 (4.35%)	
Sodium, mmol/L			.666
Hyponatremia	12(15%)	15(13.04%)	
Normonatremia	60 (75%)	92(80%)	
Hypernatremia	8(10%)	8(6.96%)	
Potassium, mmol/L			.273
Hypokalemia	5(6.25%)	4(3.48%)	
Normokalemia	67(83.75%)	105(91.30%)	
Hyperkalemia	8(10%)	6(5.22%)	
Calcium, mg/dL			.001
Hypocalcemia	24(30%)	65(56.52%)	
Normocalcemia	53(66.25 %)	47(40.87%)	
Hypercalcemia	3(3.75%)	3(2.61%)	
Magnesium, mg/dL			.917
Hypomagnesemia	31(38.75%)	42(36.52%)	
Normomagnesemia	47(58.75%)	70(60.87%)	
Hypermagnesemia	2(2.50%)	3(2.61%)	
PCT, ng/mL			.004
Low	57(71.25%)	103(89.57%)	
Moderate	11 (13.75 %)	5 (4.35%)	
High	12 (15%)	7(6.09%)	
Abnormal CPK	30(37.5%)	55(47.83%)	.153
CPK continuous, U/L	131 [60- 250]	155 [78- 310]	.163
LDH continuous, IU/L	575.5 [430- 756]	650 [467- 900]	.136
Abnormal LDH	54 (67.5%)	83 (72.17%)	.482
Positive UC†	6 (7.79%)	7 (6.86%)	.812
Positive BC†	3 (3.9%)	7 (6.86%)	.392
Hemoglobin, g/dL	11.08 ± 2.85	12.14 ± 2.41	.007
BUN, mg/dL	20.5 [15–33.95]	18 [13–26]	.052
Cr, mg/dL	1.09 [.865–1.795]	1 [.8–1.3]	.112
Ferritin, ng/mL	311.5 [145–600]	500 [221–870]	.010
PTT, s	25 [22–29]	26 [22–29.6]	.250
INR	1.2 [1–1.4]	1.2 [1–1.3]	.208
Admission electrocardiographic results			
Non-Sinus rhythm	10 (12.50%)	9 (7.83%)	.279
STT change	24 (30.77%)	34 (30.09%)	.920
Prolonged QT-interval	9 (11.25%)	7 (6.09%)	.196
Admission echocardiography results			
Simpson biplane EF, % continuous	51.75 ± 7.20	52.173 ± 7.13	.494
Reduced EF (< 50)	14 (17.50%)	17 (14.78%)	.610
Elevated PAP (PAP ≥ 35)	15 (18.75%)	30(26.09%)	.232
Hypokinesia			.222
GHK	12 (15%)	9 (7.83%)	
RWMA	4 (5%)	10 (8.70%)	
VHD	20 (25%)	24 (20.87%)	.497
Diastolic dysfunction	48 (60%)	70 (60.87%)	.903
DD grade			.644
No DD	32 (40%)	45 (39.13%)	
Grade 1	44 (55%)	64 (55.65%)	
Grade 2/3	4 (5%)	6 (5.21%)	

ACEI = angiotensin converting enzyme inhibitor, ALP = alkaline phosphates, ALT = alanine aminotransferase, ARB = angiotensin-receptor blocker, AST = aspartate aminotransferase, BB = beta-blocker, BC = blood culture, BMI = body mass index, BNP = brain natriuretic peptide, BUN = blood urea nitrogen, CABG = coronary artery bypass graft, CCB = calcium-channel blocker, ESR = erythrocyte sedimentation rate, CPK = creatinine phosphokinase, CRP = C-reactive protein, DD = diastolic dysfunction, EF = ejection fraction, GHK = global hypokinesia, RWMA = regional wall motion abnormality, INR = international normalized ratio, LDH = lactate dehydrogenase, PAP = pulmonary artery pressure, PCI = percutaneous coronary intervention, PCR = polymerase reactive chain, PCT = pro-calcitonin, PTT = partial thromboplastin time, UC = urine culture, VHD = valvular heart disease, WBC = white blood cells.

† Data of urine and blood culture were available for 77 PCR negative and 102 PCR positive patients.

channel blockers (6.69% vs 18.75%, *P* value: .012), present with palpitation (4.35% vs 12.5%, *P* value: .036), having moderate (4.35% vs 13.75%) or high pro-calcitonin (6.09% vs 15%, *P* value: .004), and having normal Ca ranges (40.87% vs 66.25%, *P* value: .001).By contrast, they were more likely to present with fever (47.83% vs 26.2%, *P* value: .036) and cough (47.83% vs 31.23%, *P* value: .021), having normal albumin ranges (80.87 % vs 61.25%, *P* value: .01) and abnormal liver enzymes. Furthermore, patients in the "positive PCR" groups had higher proportion of neutrophil count (80% vs 73%, *P* value: .001), lower proportion of lymphocyte count (15% vs 19%, *P* value: .003), and higher ferritin (500 vs. 311, *P* value: .010). Patients were also comparable regarding echocardiographic and electrocardiographic results.

3.2. In-hospital outcomes

Among patients with positive and negative PCR, 28.7% and 22.5% were diseased (Table 2), respectively (not significant). For the majority of both group of patients nasal/venturi masks were used as the main oxygenation therapy (73.7% in negative PCR and 71.3% in positive PCR, not significant), followed by intubation (21.25% and 23.48%) and noninvasive ventilation. Albeit not significant, patients with positive PCR had higher proportion of intensive care unit (ICU) admission (35.65% vs 26.25%) and ICU-stay < 14 days (6.96% vs 3.75%).

3.3. Main variables of interest and the association of positive PCR with these variables

Compared to patients with negative PCR, those with PCR-confirmed SARS-COV2 were significantly less likely to have BNP ≥ 100(20.87% vs 36.25%, *P* value:0.018). Furthermore, albeit not significant, the proportion of patients with positive troponin was a little less in this group (30.43% vs 32.5%, *P* value: .76) compared to patient with negative PCR (Table 1). The same result was applied to reduced EF as well (14.78% vs 17.5%, *P* value: 0.610). Table 3 represents the association of positive PCR with the aforementioned variables. At univariable level, positive PCR was significantly associated with less odds for positive BNP (OR:0.46, *P* value:0.019); nevertheless, the association was no longer significant after adjusting for confounders (adjusted OR:0.56, *P* value: .158). Unadjusted positive PCR was not found to have significant association with positive troponin or reduced EF. Likewise, multivariable regression revealed no association between positive PCR with positive troponin (aOR:1.28, *P* value:0.529) and reduced EF (aOR:0.65, *P* value: .369). Complete adjusted models are presented in Tables S2–S5, Supplemental Digital Content, http://links.lww.com/MD/H989.

4. Discussion

SARS CoV-2 can affect all vascular organs by targeting vascular endothelium.[9] Therefore, it is necessary to understand cardiac complications at a low cost, quickly, and without transferring the patient to other diagnostic units which increase the risk of contamination. Cardiovascular injuries induced by SARS CoV-2 have been reported repeatedly in various studies.[9,10] Studies have been conducted to investigate the mechanism of heart damage for the study of prognostic risk factors and outcomes, which in autopsy studies of deceased patients confirm the presence of the virus in myocardial cells, but the mechanism of COVID-related cardiac complications is not yet clear.[11,12]

It is noteworthy that most of the studies performed on people with COVID-19 were compared with healthy people. However, our main problem with COVID in the clinical settings is that people with COVID are referred to the emergency room that may diagnosed after examination for COVID 19, or they will be treated with other alternative diagnoses that justify the symptoms. Patients who are not diagnosed with COVID-19 infection are at risk of dealing with other real patients in the emergency department, even if they are genuinely not infected. It necessitates careful monitoring of their symptoms and disease progression. In this study, the baseline characteristics of the 2 groups were compared by considering COVID-19 as a multisystem disease. In PCR + (positive) patients, the probability of having chronic kidney disease and calcium-channel blocker consumption, higher heart rate, and the distribution of moderate and elevated procalcitonin levels and normal serum Ca level were lower. They were more likely to have a history of fever, Temperature (T) > 37.3, cough, normal serum albumin, and higher hemoglobin, and impaired aspartate transaminase, alanine transaminase, and left shift (higher neutrophils and lower lymphocytes) and high level of ferritin. Hypoalbuminemia is known[13] as a prognostic factor for mortality in acute and chronic heart failure, which was higher in the negative PCR patients. Low hemoglobin[13] levels are associated with severe symptoms of heart failure (HF), decreased exercise capacity and quality of life, and increased mortality, and are a known prognostic variable in acute and chronic HF. hemoglobin level was higher in the positive PCR patients. Renal failure[13] is also prognostic in patients with HF, which was more prevalent in the negative PCR patients. Electrolytes including sodium and potassium were checked at baseline and no significant difference was observed between the 2 groups due to the possible ACE-mediated direct damage mechanism.[14] Ferritin and left shift as inflammatory factors and fever were higher in the PCR + patients while elevated procalcitonin was lower this group. Due to the fact that the process of procalcitonin is important in the evaluation of clinical conditions, this variable is used to assess the response to treatment and therefore does not conflict with high ferritin, left shift, and fever. Evaluation of electrocardiogram rhythm at the patient's admission showed that there was no significant difference between the 2 groups in order to influence the positivity of troponin and BNP. Electrolytes including Ca and magnesium and QTc interval were measured as 1 of the underlying causes of arrhythmia during hospitalization as 1 of the in-hospital outcomes. Hypocalcemia was significantly higher in the PCR positive patients. Also, magnesium and prolonged QTc were

Table 2

In-hospital outcomes among the study cohort.

	Negative PCR (n = 80)	Positive PCR (n = 115)	*P* value
Mortality	18 (22.5%)	33 (28.70%)	.333
Hospitalization (d)			.557
<7	30 (37.5%)	37 (32.17%)	
7–14	30 (37.5%)	52 (45.22%)	
>14	20 (25%)	26 (22.61%)	
ICU admission	21 (26.25%)	41 (35.65%)	.165
ICU stay (d)			.550
No	59 (73.75%)	75 (65.22%)	
<7	9 (11.25%)	19 (16.52%)	
7–14	9 (11.25%)	13 (11.30%)	
>14	3 (3.75%)	8 (6.96%)	.550
Oxygen therapy			.930
Nasal or oral mask/ venture	59 (73.75%)	82 (71.3%)	
NIV	4 (5%)	6 (5.22%)	
Intubation	17 (21.25%)	27 (23.48%)	
Myocarditis	0	1 (0.87%)	.403
Cerebrovascular accidents	1 (1.25%)	0	.410
vasoconstrictor agents prescription	19 (23.75%)	33 (28.7%)	.442
Arrhythmia	13 (16.67%)	22 (19.13%)	.663

ICU = intensive-care unit, NIV = noninvasive ventilation, PCR = polymerase chain reaction.

Table 3

Unadjusted and risk-adjusted association of *positive PCR* with selected variable of interest.

	Unadjusted		Adjusted†	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Positive troponin	0.90 (0.49–1.67)	.76	1.28 (0.59–2.79)	.529
Reduced EF	0.81 (0.37–1.77)	.610	0.65 (0.25–1.65)	.369
Positive BNP	0.46 (0.24–0.87)	.019	0.56 (0.25–1.24)	.158

BNP = brain natriuretic peptide, CI = confidence interval, EF = ejection fraction, OR = odds ratio, PCR = polymerase chain reaction.
†Selected.

not significantly different. The arrhythmic outcomes (including atrial fibrillation, atrioventricular nodal reentrant tachycardia, nonsustained ventricular tachycardia, premature ventricular contraction, premature atrial contraction) were more prevalent in the positive PCR patients (not significant). According to the results, being positive PCR did not increase the chance of positive troponin, BNP, or reduced EF compared to the PCR negative patients, which can have different justifications. Early studies proposed that cardiac damage may be happen in different phases of COVID 19. They are the viral, pulmonary, inflammatory, and recovery phases, respectively, which damage the heart by different mechanisms, namely ACE2-mediated, myocardial cell hypoxia, systemic inflammation, and autoimmunity.[14–16] Assuming that patients present immediately after symptomatology, cardiac biomarkers are measured and echocardiography at the time of admission detects only viral lesions, whereas the severe phase of the disease occurs in the inflammatory phase. One study[17] showed that inflammatory involvement of the heart was reported in cardiovascular magnetic resonance imaging (CMR) 2 to 3 months after recovery from COVID 19 despite recovery and negative PCR, whereas this group had higher troponin and 2 to 3^{rds} of patients were treated on an outpatient basis.

It has been claimed that, in fact, cardiac involvement in different phases has caused reduced EF to be less common at the time of admission, and instead left ventricle diastolic dysfunction and right ventricle abnormality increase the risk of heart failure with preserved ejection fraction.[18] In a study,[19] the subclinical effects of COVID 19 were measured by global longitudinal strain, and even CMR-confirmed cardiac injury in the form of inflammation and scarring[20] in individuals who did not even have high troponin. It showed a mismatch between symptoms, serological and echocardiographic findings in different phases of disease.

Patients with negative PCR may be discharged on an outpatient basis due to the mildness of the disease. There is a hypothesis that some patients with heart damage referred to the health care system in the delayed phase of the disease (despite the negative PCR, cardiac damage and complications are evident). In-hospital mortality, total length of hospital stays between 7 and 14 days, ICU hospitalization and length of stay in ICU, Non-Invasive Ventilation, intubation rate and myocarditis, the need for vasoconstrictor and arrhythmia were higher in the PCR positive patient (not significant).

Because of the possibility of stable heart damage with different mechanisms even after the recovery phase and PCR negative of the patient and the duration of each of the known phases so far, cardiac and inflammatory biomarkers as well as echocardiography will have a variety of overlaps. This can make it difficult for the clinicians to make an accurate clinical judgment. Due to the uncertainty of the passage time of each phase, it seems that prolonging the follow-up to evaluate the long-term consequences, may be not a proper approach since it may results in loss of myocardial cells. There is the possibility of irreversible heart scarring, which is important to detect early.

4.1. Limitations

Due to fear of COVID19 transmission, patients did not return for additional imaging such as CMR, and cardiac damage was not fully assessed. Patients in the COVID19 emergency department do not have a good mental status for an accurate history of the onset of disease symptoms, and their companions are also affected by the condition, and these factors causes difficulty in determining the phase of the disease in symptomatic patients. Some patients left the hospital with personal consent, leading to incomplete follow-up of hospitalized patients and complications. Due to the lack of a non-portable and advanced echocardiography unit with global longitudinal strain facilities, it was not possible to evaluate right and left ventricular dysfunction at the subclinical level. Also, due to the limited time to perform echocardiography the examination of some echocardiographic parameters such as PAP was affected and led to underestimation. Patients with novel HF and a negative or slightly elevated troponin at baseline and global hypokinesia were not assessed for angiography due to non-emergency outcome, resulting in dilated cardiomyopathy and previous myocarditis with a less likely ischemic cardiomyopathy.

5. Conclusion

PCR positivity did not result in positive troponin and BNP and did not appear to decrease EF. In other words, serial troponin and BNP checks and initial echocardiography in COVID-19 respiratory emergencies do not make significant differences in diagnostic and therapeutic management and inpatient outcomes of patients with positive PCR and negative PCR and are not specific findings.

5.1. Suggestion

Due to the lack of clinical significance of cardiac involvement even with CMR, the Galectin 3 check appears to be one of the new tissue biomarkers produced by macrophages activated in response to tissue damage and is strongly associated with early detection of myocardial collagen formation and can predict the formation of fibrosis in seemingly healthy patients.[21] It is recommended that Galectin 3 be checked as a factor to diagnose adverse outcomes at admission so that timely diagnostic and therapeutic measures can be assigned to them.[22]

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