Original Article

Role of Troponin I and D-Dimer in Detection CVD in Coronavirus Patients

Ruqaya Yahya Abd AL-Shaheed[1,2], Huda Jameel Baker AL-Khilkhali[2]

[1]Department of Criminal Evidence, College of Science, University of Hilla, Babylon, [2]Faculty of Science, University of Kufa, Kufa, Iraq

Abstract

Background: The virus known as serious intense respiratory disease coronavirus 2 (SARS-CoV-2) is the source of the coronavirus infection, also known as COVID-19. Subsequently, the initial COVID-19 information in December 2019. **Objectives:** The present study aimed to the SARS-COV-2 detection strong positive and Study the virus effect on the heart. **Materials and Methods:** This is a case–control study design accompanied for dated from March to October 2022. Two case-control groups with 108 people each were enrolled in this study. The case group consisted of 54 patients with SARS-COV2 and CVD, all of whom were admitted to the intensive care unit (ICU) in Marjan, Babylon.There were 54 patients in the control group in this investigation. The group of control in this study comprised 54 issues. **Result:** The patient and control subjects' demographic characteristics. The study's findings show that, of the four age categories into which the samples were split, the largest percentage of patients with COVID-19 and CVD patients (48.1% and 66.7%, respectively) are in the age group of patients who are at least 66 years old. Furthermore, there is a notable difference in the mean D-dimer levels between patients with COVID-19 (1268.07±479 ng/ml) and control subjects (267.91±62.595 ng/ml). Although the mean D-dimer for CVD patients was significantly greater than that of the control group (1824.21±1634.92 ng/ml), it was still 1648.54±1428.63 ng/ml. In contrast to patients with COVID-19 alone, patients with cardiovascular disease have higher average D-dimer concentrations. The interpretation of these results may be due to the interaction between COVID-19 and cardiovascular illnesses on the rise in D-dimer levels. When the two factors are present in the same patient group, the raised D-dimer level in patients with COVID-19 and cardiovascular disease is increased. According to the current investigation, patients with COVID-19 and CVD had significantly higher mean troponin levels than control participants (1.734±1.506 ng/mL vs. 0.035±0.024 ng/mL, respectively). **Conclusion:** The study came to the conclusion that older people had a higher risk of cardiovascular disease and Covid disease. a significant proportion of Covid19 and CVD patients, and CVD patients only passed away in hospitals when they were monitored for the duration of this study. The study revealed highly statistically significant associations suggesting that patients with Covid and CVD group had significantly higher levels of dimer and troponin than individuals with CVD alone. Nonetheless, when it comes to troponin levels, patients with Covid19 only differ noticeably from healthy individuals.

Keywords: Coronavirus, Cardiovascular disease, Troponin I and D-dimer

Introduction

Concurrently, the primary case was identified in Wuhan, China, in December 2019. The severe acute respiratory disease caused by SARS-CoV-2 gave rise to the coronavirus syndrome 2019 (COVID-19) pandemic, which is spreading throughout the globe. A total of 25 million and/or above persons in further than 200 nations have stayed diseased, and above 840,000 individuals have death as an outcome, rendering to the Dashboard COVID-19 available on August 31, 2020, via "the Center for Systems Science and Engineering at Johns Hopkins University."[1]

A single-stranded, encapsulated, positive sense RNA virus (+ssRNA), coronavirus-2 causes severe acute respiratory illness. It is non-segmented. A cap structure assessed by a sequencing reader of around 70 bases, multiple open reading frames (ORFs) coding multiple proteins, a non-translated region including a poly-A sequence at the 3′

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Address for correspondence: Dr. Ruqaya Yahya Abd AL-Shaheed, Department of Criminal Evidence, College of Science, University of Hilla, Babylon, Iraq.
E-mail: huda.alkhilkhali@uokufa.edu.iq

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ends, and a gene size of sorts ranging from (27 to 32) kb at the 5′ ends.[2]

The SARS-CoV-2 medical demonstration begins 2 weeks after initial encounter; however, symptoms typically appear after around five days in 97.5% of cases, with symptoms starting within 11 days.[1] The prime cause of death due to COVID-19 is respiratory letdown; nevertheless, cardiac appearances might donate to general death and uniformly be the prime source of patients dead.[3]

Cardiac injury and fulminant myocarditis might result from the virus' direct impact on the cardiac cells as well as from the body's subsequent hyperimmune and systemic inflammatory reactions to the virus.[4] Higher mortality in COVID-19 patients has stayed related to rising ranks of inflammation indicators such as interleukin 6, creactive protein, D-dimer (LDH), and ferritin, presumably as a result of secondary hemophagocytic lymphohistiocytosis or cytokine storm.[3]

D-dimer is a thrombin and active coagulation-related indirect marker. It is a reflection of the endovascular thrombotic processes and is released when the fibrinolytic enzyme plasmin cleaves fibrin to break down clots.[5]

Troponins are proteomic structures complicated in flexible cardiac muscle and skeletal retrenchment.[6] Significance of troponin's role as a crucial risk assessor. Stating that there is a significant unfavorable prognosis rate for this biomarker in the COVID-19 environment.[7]

Elongated great ranks of cytokines, considered as the storm cytokine, might aggravate systemic immunity syndrome.[8] Patients with SARS-COV2 might progress austere difficulties owing to cytokine storms.[9]

Material and methods

The existing study, which was considered for case-control grouping, included 1800 subjects in the total sample, and the cohort included 54 subjects with SARS-COV2 and patients diagnosed with severe acute respiratory disease by a cardiovascular specialist. The syndrome caused by SARS-COV2 detected by reverase transcrptase polymerase chain reaction and other medical parameters and research laboratory tests was carried out at Al-Amal Hospital for Infectious Diseases and Al-Hakim Hospital in Al-Marjan Medical City in Babel Governorate, Najaf, Iraq, from March 2022 to October 2022. The group of control (appraisal group) in this study consisted of 54 issues separated into three groups (healthy individuals, SARS-CoV2 patients, and cardiovascular disease [CVD] patients.)

Samples of blood were engaged from coronavirus patients. Samples of blood were examined using (ELISA) for the detection of troponin I and D-dimer. For this determination, a 5-mL blood sample was kept in conventional tubes at 37°C for 30 min and then cooled for 15 min and centrifuged at 3000 revolutions per minute (rpm). Then, the clot was separated, then the residue was centrifugation for 10 min at 3000 rpm. The resulting serum was then aspirated using an automated mechanical pipette and transferred into two clean serological test tubes. Each tube was labeled, then stored at −20°C and snap-frozen for late serological testing of troponin I and D-dimer concentrations using enzyme linked immunosorbent assay kit (MELSIN, Changchun, China) equipment.

Ethical approval

The study was accompanied by rendering to moral ideologies. This was performed both verbally and analytically before sampling, with the patients' consent. The study protocol, subject statement, and consent form were reviewed via the Local Ethics Commission of the College of Science of Coffee University in accordance with Document No. 678 dated February 17, 2022, to obtain this approval.

Results

The samples were divided into four age groups, and the outcomes of this study are shown in Figure 1.

Figure 2 shows that dissemination of the sample and control groups rendered to sex. Figure 2 shows the result of this study.

Table 1 shows that the mean of D-Dimer for COVID-19 (CVD) and CVD patients is significantly higher than control issues.

Table 2 displays that the mean of troponin for COVID-19 (CVD) and with CVD patients is significantly higher than control subjects.

The result in Table 4 demonstrates that there is a significant association between death status and the study groups ($P = 0.011$).

Discussion

Figure 1 shows the highest percentage (48.1%, and 66.7%) of the COVID-19 and CVD patients, and patients with CVD belong to the age group (≥66 years), respectively. Additionally, the age group (≤ 46 years) had the highest percentage of COVID-19 patients (38.9%) and control subjects (66.7%), respectively. There is a greatly significant connection between age groups and the study groups (P <0.001). The mean of COVID-19 patients' age and CVD was 67.56 ± 12.53, and the mean age of patients with COVID-19 was 51.06 ± 21.87. The average age of patients with cardiovascular disease was 67.72±11.72, whereas the control group's mean age was 43.22±12.89. These results are consistent with the study by Boddington *et al*.,[10] which discovered that the uppermost proportion 34.6% of the COVID-19 patients belonged to the group of age (50–69 years). Also, the current study agreed with the study by

Yaghubi *et al*.,[11] who revealed that the mean of COVID-19 patients' age and CVD was 68.35±12.41. Although the study results prepared by[12] indicated that the mean age of patients with Covid-19 was 49.0 ± 19.6, these results also contradicted previous trainings,[13] which established that the mean age of COVID-19 patients was 41.17±15.11 years, and[14], which reported that the mean age of hospitalized patients with definite COVID-19 was 45 ± 18.01 years. The possible explanation for the discrepancy in the results may be owing to the variance in the study methodology, sampling size, and the groups studied.

The outcomes of the age study displayed an apparent increase in the older age groups in the patient groups, which may indicate that age is a dangerous feature for illness in cardiovascular. There are previous studies consistent with this interpretation, which reported that the patients were infected in various countries at various ages, whereas some were healthy, and others had chronic illnesses like hypertension, heart failure, kidney failure, and diabetes mellitus.[15]

The distribution of the study groups and control subjects by sex is shown in Figure 2. The results show that, in comparison to the control group, which had the lowest percentage of males (38.9%). These results agreed with the study by Meinie *et al*.[16] found that the highest percentage (59.2%) of SARS-COV2 patients were male. Also, Hernández-Garduño[17] reported that 58.7% of SARS-COV2 patients were male. Moreover, the results of this study supported those of Scully *et al*.,[18] who institute that the common of SARS-COV2 patients were male.

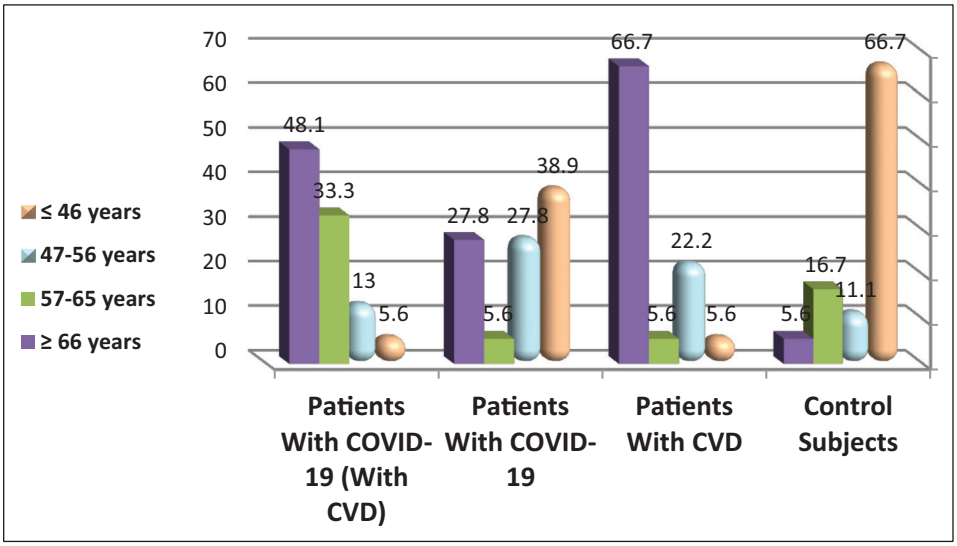

Figure 1: The dissemination of the sample and control groups rendering to age groups

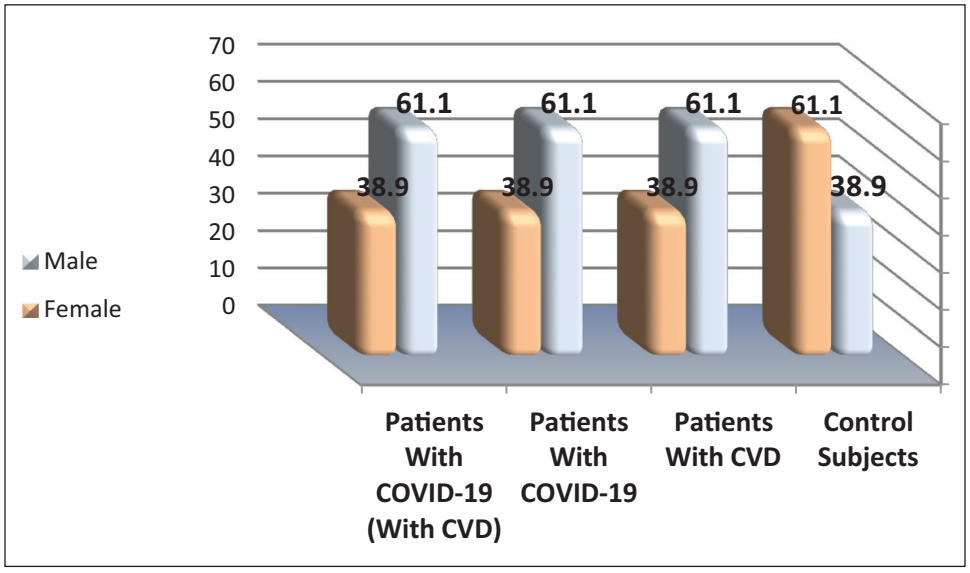

Figure 2: The distribution of the sample and control groups according to sex

Table 1: Level measurement of D-dimer in all samples (study) and control groups

D-Dimer	*N*	Mean ± SD (ng/mL)	Range (Min–Max)
COVID-19 patients (with CVD) (G1)	54	1824.21 ± 1634.92 a	328.31-8414.0
Patients with COVID-19 (G2)	18	1268.07 ± 479.81 a c	247.60-2174.0
Patients with CVD (G3)	18	1648.54 ± 1428.63 a c f	220.69-6285.0
Control subjects (G4)	18	267.91 ± 62.595 b e	176.92-449.0
Minimum significant variance (LSD)	**Absolute mean difference (AMD)**		
710.724	G1 vs. G2 = 556.14	AMD < LSD	*P* > 0.05 NS
	G1 vs. G3 = 175.67	AMD < LSD	*P* > 0.05 NS
	G1 vs. G4 = 1556.3	AMD > LSD	*P* < 0.05 HS
582.769	G2 vs. G3 = 380.47	AMD < LSD	*P* > 0.05 NS
	G2 vs. G4 = 1000.16	AMD > LSD	*P* < 0.05 HS
	G3 vs. G4 = 1380.63	AMD > LSD	*P* < 0.05 HS

SD: standard deviation

Dissimilar letters indicate the significant variance at $P < 0.05$

In Table 1, the mean of D-dimer for COVID-19 and CVD patients is significantly higher than control subjects (apparent healthy) (1824.21 ± 1634.92 ng/mL vs. 2t 67.91 ± 62.595 ng/mL) separately. Also, there is a significant variance among the mean of D-dimer for COVID-19 patients, which was 1268.07 ± 479 ng/mL compared with 267.91 ± 62.595 ng/mL for control issues. Also, there is a significant difference among the mean concentration of D-Dimer for COVID-19 patients was 1268.07±479 ng/ml compared to 267.91±62.595 ng/ml for (Apparent Healthy). While With a mean of 1648.54±1428.63 ng/ml, the D-Dimer for CVD patients is significantly higher than that of the seeming healthy (1824.21±1634.92 ng/ml).

When a blood clot is disintegrated via fibrinolysis, a minor protein portion called D-dimer is liberated into the blood.[19] The D-dimer concentration could be used to analyze thrombosis since it rises when the coagulation system is triggered through thrombosis or distributed intravascular coagulation (DIC). A great D-dimer rank might likewise indicate (DIC), pulmonary embolism, or deep vein thrombosis.[20] A great rank of D-dimer might aid in the initial medical analysis of COVID-19.[21] Also, the majority of patients in the SARS pandemic of 2003 had thrombocytopenia and high D-dimer levels.[22]

Therefore, this study is coordinated with the study outcomes accompanied via the study by Li *et al*.,[23] who revealed high D-dimer rank in CVD patients and COVID-19 paralleled to other comorbidities. The possible explanation of the raised D-dimer in COVID-19 and CVD patients is owing to several factors, including that COVID-19 is known to cause inflammation in the body, which could chief to an augmented danger of blood clots. Inflammation in the blood vessels can also cause damage to the vessel walls, which can trigger the formation of blood clots.[24]

In this study, COVID-19 patients have a great rank of d-dimer significantly higher than control issues. These results are dependable with the study by Paliogiannis *et al*.,[25] who reported that the concentrations of D-dimer were significantly higher in COVID-19 patients.

The scientific explanation for the high d-dimer in COVID-19 patients may be due to either COVID-19 can damage to the endothelial cells that line the blood vessels. This can chief to augmented clotting activity and the release of D-dimer into the bloodstream,[26] or COVID-19 can cause severe pneumonia, which can chief to a reduction in oxygen rank in the blood. This can source the body to release more D-dimer as it tries to break down blood clots to improve oxygenation.[27]

Also, the current results reveal that patients with CVD have a great rank of D-dimer significantly higher than control issues. These results are consistent with the study by Ford *et al*.,[28] who found that patients with CVD had elevated D-dimer rank.

In patients with CVD, upraised D-dimer concentration in cardiovascular patients is due to several explanations that have been discussed in previous studies, includes that patients with CVD are at higher danger of emerging blood clots (thrombosis), which can chief to D-dimer elevation. This is because when a clot forms, it triggers the body to break it down, releasing D-dimer into the bloodstream.[29] Also, patients with CVD may have reduced blood flow to various parts of the body, including the legs, which can cause the formation of blood clots. This can lead to D-dimer elevation as the body breaks down the clots.[30]

Although there were no significant variances in concentrations of D-dimer between cardiovascular and COVID-19 patients, and COVID-19 patients only, it is evident in this study that the average D-dimer concentration is higher in cardiovascular and COVID-19 patients than COVID-19 patients only. The interpretation of these results may be due to the scientific reasons mentioned above, which included the effect of CVDs on the rise of the dimer, and the effect of COVID-19 on its rise as well. The combination of the two causes in one group

of patients increases the D-dimer elevated in patients with cardiovascular and COVID-19.

Table 2 shows that the mean of troponin for COVID-19 and CVD patients is significantly higher than control subjects (1.734 ± 1.506 ng/mL vs. 0.035 ± 0.024 ng/mL) separately. Also, there is significant variance among patients with CVD and control issues, the mean of troponin in patients with CVD was 1.427 ± 1.813 ng/mL paralleled to 0.035 ± 0.024 ng/mL for control issues. *P* value >0.05 indicates that there are no significant differences between patients with COVID-19 and CVD, and patients with CVD alone. These outcomes are consistent with the training conclusions conducted via the study by Lala *et al*.,[31] which found that troponin I >0.09 ng/dL was significantly related to higher danger of death in patients with CVD and COVID-19 ($P < 0.001$). Another study by Guo *et al*.[32] revealed that patients with CVD were more possible to exhibit raise in troponin ranks paralleled with the patients without CVD (54.5% vs. 13.2%).

The high level of troponin may be due to several explanations, according to a study by Guo *et al*.,[32] which showed a substantial positive linear association, proposing that myocardial destruction might be strictly linked to inflammatory etiology throughout the progression of the illness. High doses of circulating cytokines also cause endothelial dysfunction, atherogenesis, and functional reprogramming of endothelial cells furthermore to their straight influence on cardiomyocytes. It is believed that endothelial cells are primarily responsible for the inflammatory reaction in viral infections.[32]

Patients with COVID-19 (with CVD) frequently have raised troponin ranks, which are strongly linked to catastrophic outcomes. This behavior might be explained by many mechanisms: microangiopathy, viral myocarditis, cytokine-driven cardiac destruction, and uncovered CAD.[33]

A possible explanation for the lack of statistically significant differences in the level of troponin between COVID-19 patients and healthy subjects is due to dividing the samples into four groups, including the group of COVID patients only, from which heart patients are excluded according to the groups classified in this study. Since the aforementioned group has no effects on the circulatory system, this division results in a drop in the level of troponin.

On the other hand, the study reveals, in Table 3, that there is a significant variance among the study groups and age groups according to troponin I ($P < 0.05$). This explains that patients with COVID-19 (with CVD) who are aged ≤46 years are higher significantly than patients

Table 2: Levels of troponin I in the group of the study and control

Troponin I	*N*	Mean ± SD (ng/mL)	Range (min–max)
COVID-19 patients (with CVD) (G1)	54	1.734 ± 1.506 a	0.05-4.50
Patients with COVID-19 (G2)	18	0.114 ± 0.113 b	0.02-0.36
Patients with CVD (G3)	18	1.427 ± 1.813 a	0.03-4.70
Control subjects (G4)	18	0.035 ± 0.024 b	0.01-0.08
Smallest significant variance (LSD)	**Absolute mean variance (AMD)**		
0.703	G1 vs. G2 = 1.620	AMD > LSD	*P* <0.05 HS
	G1 vs. G3 = 0.307	AMD < LSD	*P* >0.05 NS
	G1 vs. G4 = 1.699	AMD > LSD	*P* <0.05 HS
0.702	G2 vs. G3 = 1.314	AMD > LSD	*P* <0.05 HS
	G2 vs. G4 = 0.079	AMD < LSD	*P* >0.05 NS
	G3 vs. G4 = 1.392	AMD > LSD	*P* <0.05 HS

SD: standard deviation

The study reveals, in Table 3, that there is a significant variance among the study groups and age groups according to troponin I ($P < 0.05$)

Table 3: Relationship between the study groups and age groups according to troponin I

Troponin I	COVID-19 patients (with CVD)	COVID-19 patients	Patients with CVD	Control issues
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Age groups				
≤46 years	2.700 ± 1.967 an A	0.118 ± 0.0807 b A	4.500 ± 0.00 c A	0.032 ± 0.023 b A
47–56 years	1.047 ± 0.939 a B	0.980 ± 2.024 a B	2.212 ± 2.290 b B	0.035 ± 0.035 c A
57–65 years	1.507 ± 1.548 a BC	0.080 ± 0.00 b A	3.500 ± 0.00 c C	0.040 ± 0.036 b A
≥66 years	1.965 ± 1.523 a C	0.144 ± 0.255 b A	0.737 ± 1.289 b D	0.050 ± 0.00 b A
LSD	0.718			

Capital letters denote to compare between columns, and small letters denote to compare between rows.

Dissimilar letters represent the significant variance at $P < 0.05$

Table 4: The distribution of the COVID-19 patient according to death status

	Died				χ^2	*P* value
	Yes		No			
	No.	%	No.	%		
Groups						
With COVID-19(with CVD)	17	31.5%	37	68.5%	11.188	<0.001
With COVID-19	4	22.2%	14	77.8%		
With CVD	1	5.6%	17	94.4%		
Control subjects	0	0.0%	18	100.0%		

with COVID-19 and control subjects. Also, patients with COVID-19 (with CVD) aged ≥66 years are higher significantly than all the studied groups. As for patients with CVD, the results found that patients whose ages (≤46, 47–56, and 57–65 years) are higher significantly than all the studied groups.

The current outcomes approved with the training conclusions completed via the study by Zhang *et al*.,[34] which reported that older patients with CVD and COVID-19 have great rank of troponin.

Table 4 explains the uppermost death proportion (31.5%) of patients with COVID-19 and CVD, followed by 22.2% of patients with COVID-19 only. These results are dependable on the study by Luo *et al*.,[35] who revealed that CVDs are linked with an augmented danger for mortality. Rendering to a recent training by Zhao *et al*.,[36] the great majority of COVID-19 patients who passed away while receiving hospital treatment met the requirements for the analysis of disseminated intravascular coagulation. According to the results of the current investigation, COVID-19 patients' comorbidities enhanced their chance of dying.

Several earlier research demonstrated that people with COVID-19 may be more at risk for mortality if they also had diabetes mellitus and CVD.[37] From these results, we can summarize possible causes of death for patients with CVD and COVID, including patients with CVD may be more susceptible to ARDS due to preexisting lung damage or reduced lung function.[38] Furthermore, COVID-19 can rise the danger of blood clots, which can chief to heart spasm, stroke, or pulmonary embolism in patients with CVD.[39]

Conclusion

The study concluded that the elderly increased risk for COVID and CVD. At the same time, a high percentage of patients with COVID-19 and CVD, and patients with CVD only died in hospital when they followed up during this study. The study displayed that there are greatly statistically significant relationships that indicate that the rank of dimer and troponin is significantly higher in the group with COVID and CVD patients and patients with CVD only paralleled to healthy individuals. However, patients with COVID-19 only have no significant differences with people healthy regarding troponin levels.

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Conflicts of interest

There are no conflicts of interest.

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