



Incidence and determinants of high-sensitivity troponin and natriuretic peptides elevation at admission in hospitalized COVID-19 pneumonia patients

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Received: 25 June 2020 / Accepted: 5 September 2020 / Published online: 28 September 2020
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Abstract

Background Myocardial involvement in the course of coronavirus disease 2019 (COVID-19) pneumonia has been reported, though not fully characterized yet. The aim of the present study is to undertake a joint evaluation of hs-Troponin and natriuretic peptides (NP) in patients hospitalized for COVID-19 pneumonia.

Methods In this multicenter observational study, we analyzed data from $n = 111$ patients. Cardiac biomarkers subgroups were identified according to values beyond reference range.

Results Increased hs-Troponin and NP were found in 38 and 56% of the cases, respectively. As compared to those with normal cardiac biomarkers, these patients were older, had higher prevalence of cardiovascular diseases (CVD) and had more severe COVID-19 pneumonia by higher CRP and D-dimer and lower PaO₂/FIO₂. Two-dimensional echocardiography performed in a subset of patients ($n = 24$) showed significantly reduced left ventricular ejection fraction in patients with elevated NP ($p = 0.02$), whereas right ventricular systolic function (tricuspid annular plane systolic excursion) was significantly reduced both in patients with high hs-Troponin and NP ($p = 0.022$ and $p = 0.03$, respectively). Both hs-Troponin and NP were higher in patients with in-hospital mortality ($p = 0.001$ and $p = 0.002$, respectively). On multivariable analysis, independent associations were found of hs-Troponin with age, PaO₂/FIO₂ and D-dimer ($B = 0.419$, $p = 0.001$; $B = -0.212$, $p = 0.013$; and $B = 0.179$, $p = 0.037$, respectively) and of NP with age and previous CVD ($B = 0.480$, $p < 0.001$; and $B = 0.253$, $p = 0.001$, respectively).

Conclusions Myocardial involvement at admission is common in COVID-19 pneumonia. Independent associations of hs-Troponin with markers of disease severity and of NP with underlying CVD might point toward existing different mechanisms leading to their elevation in this setting.

Keywords COVID-19 · Hs-troponin · Natriuretic peptide · D-dimer · PaO₂/FIO₂

Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory infection caused by a novel type of betacoronavirus, 2019-nCoV, later renamed severe acute respiratory syndrome

coronavirus 2 (SARS-CoV-2) [1], that emerged in China and later spread worldwide leading to a global pandemic. In some countries, this required the creation of dedicated multidisciplinary “COVID units” for the management of affected patients [2–4]. COVID-19 is a highly contagious infection [5], associated with a significant rate of severe interstitial pneumonia and related complications including respiratory failure, thrombosis, multiorgan failure and death [6]. Systemic implications include, among others, coagulopathy with increased D-dimer levels [7, 8], marker of more severe disease affecting prognosis [9]. Several reports also described the common occurrence of myocardial involvement in patients affected by COVID-19, as

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s11739-020-02498-7>) contains supplementary material, which is available to authorized users.

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revealed by detection of increased levels of high-sensitivity troponin (hs-Troponin) [10, 11] and natriuretic peptides (NP) [12] which both showed to have prognostic relevance [10, 13–15]. Reasons for myocardial injury in this setting span from cytokine or hypoxia-related injury to myocarditis and myocardial infarction [16–19]. A full understanding of mechanisms leading to myocardial involvement in the course of COVID-19 pneumonia might help gaining insights into disease pathogenesis and aid daily clinical management in these patients, in which downstream testing is usually complex and constitutes a risk for the safety of both patients and healthcare personnel [20]. Hence, the aim of the present study is to undertake a joint assessment of hs-Troponin and NP value at admission in a cohort of consecutively hospitalized COVID-19 pneumonia patients, in order to describe the incidence and the determinants of their rise.

Methods

This is a multicenter observational study on COVID-19 pneumonia patients ($n = 118$) consecutively admitted to dedicated medical units at Madre Giuseppina Vannini Hospital, Rome, Italy ($n = 39$, admission time between 1 and 30 April) and St. Andrea Hospital-Sapienza University of Rome, Italy ($n = 79$, admission time between 15 March and 30 April). Clinical care within these units, recently established in order to provide dedicated assistance to COVID-19 patients, was managed by full-time dedicated internal medicine or cardiology specialists.

Diagnosis of COVID-19 infection was confirmed before admission by means of nasopharyngeal swab and subsequent quantitative real-time reverse transcriptase polymerase chain reaction (qRT-PCR) [6], while pulmonary involvement was demonstrated in all patients by means of chest computed tomography. Symptoms at presentation and clinical history were assessed by the accepting physician. History of previous cardiovascular disease (CVD) was defined by the presence of either atrial fibrillation, coronary artery disease, heart failure or stroke. All patients underwent blood gas analysis, routine blood examination and 12-lead ECG within 24 h upon admission. Patients ($n = 7$) who did not have timely recorded blood gas analysis and assessment of either hs-Troponin or NP were excluded from the analysis. The final sample size consisted of $n = 111$ patients of whom $n = 103$ had hs-Troponin and $n = 82$ had natriuretic peptide evaluation. No routine withdrawal of any previous treatment with cardiovascular drug was undertaken, while we recorded the presence of ongoing treatment with angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). Blood gas examination was performed with standard commercially available machines. Arterial oxygen concentration (PaO₂) was normalized to the

fractional volume of the inspired oxygen to calculate the PaO₂/FIO₂ ratio. Venous blood samples were analyzed by standard techniques within 2 h from collection. Hs-Troponin T (normal value < 14 pg/ml) and N-terminal-pro-natriuretic peptide (NT-pro-BNP) were evaluated at Madre Giuseppina Vannini Hospital. Hs-Troponin I (normal value < 35 pg/ml) and B-type natriuretic peptide (BNP) were evaluated at St. Andrea Hospital. D-dimer results were reported as fibrinogen equivalent units [21]. In order to provide unified analysis of different NPs at our institutions, we referred to specific upper range for normality (URN) as suggested by guidelines (NT-pro-BNP: 300 pg/ml; BNP: 100 pg/ml) [22]. We then reported data from our population as factor of URN increase as described in [23]. Data regarding hs-Troponin, NP, D-dimer and C-reactive protein (CRP) were all log₁₀ transformed to yield approximately normal distribution when performing analysis of relationships as well as multivariable analysis. Outcome data are updated at May 31, 2020.

All analysis was performed using SPSS software 25 (SPSS Inc., Chicago, IL). Data are presented as mean \pm standard deviation, counts (percentages) or median (interquartile range, IQR), as appropriate. Comparisons between groups were performed using Chi-squared test, Fisher's exact test, Student t-test for independent samples or Mann–Whitney U test as appropriate. Analysis of relationships was performed using bivariate correlation and providing corresponding Pearson's or Spearman correlation coefficients as appropriate. Log-transformed values for serum biomarkers (hs-Troponin, NP, D-dimer, CRP) were used. Multivariable linear regression was performed to investigate factors independently associated with hs-Troponin and NP, and using age, hemoglobin, creatinine, history of previous CVD, PaO₂/FIO₂ and CRP and D-dimer as independent variables. All tests were two-tailed, and p value of < 0.05 was considered statistically significant. All patients provided informed consent for the use of their record for research purpose, and the study complied with the content of the Declaration of Helsinki. This study received the approval from Sapienza University Ethic Committee no. CE_5773_2020.

Results

Baseline characteristics

Baseline clinical and demographic findings in $n = 111$ patients included in the study are summarized in Table 1. Mean age was 72 ± 17 years and 46% were male. Comorbidities were common in our population, more than half of the patients had known hypertension, approximately one-third had preexisting CVD, and 22% were taking an ACE inhibitor or ARB before hospital admission. Venous

Table 1 Characteristics of study population overall and according to cardiac biomarkers levels at admission

Variable	Overall (n = 111)	Hs-Troponin (n = 103)			Natriuretic peptide (n = 82)		
		Hs-Troponin ≤ URN (n = 64)	Hs-Troponin > URN (n = 39)	P	NP ≤ URN (n = 36)	NP > URN (n = 46)	P
Age	72 ± 17	66 ± 17	79 ± 13	<0.001	61 ± 17	81 ± 9	<0.001
Sex (male)	51 (46%)	28 (44%)	19 (49%)	0.623	21 (58%)	21 (46%)	0.254
Coexistent conditions							
Hypertension	62 (56%)	32 (50%)	26 (67%)	0.098	15 (42%)	31 (67%)	0.02
Dyslipidemia	15 (14%)	8 (12%)	6 (15%)	0.679	2 (6%)	9 (20%)	0.065
Diabetes	21 (19%)	12 (19%)	8 (20%)	0.826	6 (17%)	9 (20%)	0.736
Previous CVD	35 (31%)	13 (20%)	18 (46%)	0.006	4 (11%)	26 (56%)	<0.001
Atrial fibrillation	21 (19%)	6 (9%)	12 (31%)	0.006	1 (3%)	17 (37%)	<0.001
Coronary artery disease	12 (11%)	5 (8%)	7 (18%)	0.120	0 (0%)	11 (24%)	0.002
Heart failure	8 (7%)	1 (2%)	5 (13%)	0.028	0 (0%)	7 (100%)	0.016
Stroke	8 (7%)	3 (5%)	4 (10%)	0.422	3 (8%)	5 (11%)	> 0.99
CKD	7 (6%)	2 (3%)	5 (13%)	0.101	0 (0%)	6 (13%)	0.024
COPD	26 (23%)	18 (28%)	6 (15%)	0.138	6 (17%)	10 (22%)	0.565
Cancer	8 (7%)	6 (9%)	1 (3%)	0.249	1 (3%)	5 (11%)	0.223
Autoimmune disease	6 (5%)	4 (6%)	2 (5%)	> 0.99	4 (11%)	2 (4%)	0.397
ACE inhibitor/ARB therapy	24 (22%)	12 (19%)	9 (23%)	0.597	8 (22%)	13 (28%)	0.534
Laboratory tests							
Hb (g/dl)	11.8 ± 2	12.1 ± 2	11.6 ± 2	0.181	12.7 ± 2	11.2 ± 1.7	0.002
WBC (per µL)	7839 ± 4777	8147 ± 5430	7880 ± 3546	0.786	6876 ± 3187	8132 ± 6201	0.274
Neutrophil (per µL)	4857 ± 3034	4597 ± 2746	5582 ± 3412	0.148	3705 ± 1972	4719 ± 2909	0.141
Lymphocyte (per µL)	1402 ± 1196	1575 ± 1415	1220 ± 836	0.192	1473 ± 887	990 ± 550	0.011
Creatinine (mg/dl)	1.13 ± 1	0.96 ± 0.9	1.43 ± 1.9	0.025	0.78 ± 0.2	1.51 ± 1.4	0.002
ALT (U/L)	32 ± 52	26 ± 13	45 ± 87	0.098	25 ± 15	41 ± 80	0.238
AST (U/L)	30 ± 39	26 ± 18	42 ± 65	0.083	24 ± 12	38 ± 60	0.294
CRP (mg/dl)	4.8 (1.3, 9)	4 (1.1, 7.4)	9 (1.3, 14.3)	0.042	2.6 (0.6, 6.9)	5.3 (2.2, 11.4)	0.011
D-dimer (ng/ml FEU)	566 (293, 1554)	442 (244, 778)	1269 (560, 2759)	<0.001	338 (248, 1058)	990 (463, 2054)	0.004
Hs-Troponin (pg/ml)	17 (5, 47)	6.8 (4, 15)	60 (35, 94)	NA	6.2 (4, 16)	37.6 (19, 82)	<0.001
Hs-Troponin > URN	39/103 (38%)	0 (0%)	39 (100%)	NA	6 (18%)	27 (64%)	<0.001
Hs-Troponin (> 3 × URN)	17/103 (16%)	0 (0%)	17 (43%)	NA	0 (0%)	16 (42%)	<0.001
NP (factor × URN)	1.35 (0.35, 3.56)	0.7 (0.1, 1.8)	3 (1.3, 15)	0.003	0.3 (0.1, 0.6)	3.3 (1.8, 15)	NA
NP > URN	46/82 (56%)	15/42 (36%)	27/33 (82%)	<0.001	0 (0%)	46 (100%)	NA
Blood gas analysis							
pH	7.44 ± 0.08	7.43 ± 0.07	7.46 ± 0.08	0.045	7.45 ± 0.07	7.44 ± 0.08	0.571
pO ₂ (mmHg)	75 ± 22	75 ± 20	75 ± 24	0.856	74 ± 19	76 ± 21	0.630
pCO ₂ (mmHg)	38 ± 7	39 ± 6	37 ± 7	0.108	39 ± 6	38 ± 7	0.375
PaO ₂ /FIO ₂	308 ± 99	325 ± 97	276 ± 92	0.012	342 ± 91	293 ± 100	0.024
Echocardiographic findings*							
LVEF (%)	55 (50, 60)	60 (53, 60)	55 (40, 55)	0.112	60 (55, 60)	55 (40, 55)	0.01
TAPSE (mm)	21 (19, 23)	23 (22, 24)	20 (18, 22)	0.022	22 (20, 24)	19 (17, 22)	0.03
In-hospital outcome							
In-hospital death	23 (21%)	7 (11%)	12 (31%)	0.012	5 (14%)	15 (33%)	0.05

Bold values indicates $p < 0.05$

NP Natriuretic peptide, URN upper reference of normality, CVD cardiovascular disease, CKD chronic kidney disease, COPD chronic obstructive pulmonary disease, ACE angiotensin-converting enzyme, ARB angiotensin receptor blocker, Hb hemoglobin, WBC white blood cells, AST aspartate transaminase, ALT alanine transaminase, CRP C-reactive protein, FEU fibrinogen equivalent unit, LVEF left ventricular ejection fraction, TAPSE tricuspid annular plane systolic excursion, NA not applicable

*Available in 24 out of 111 patients

blood samples analysis revealed increase of median CRP and D-dimer. We detected raised troponin (identified by value > URN) in 38% of the cases, whereas in 16% of the patients the increase was beyond three times the respective URN. NP values were elevated in 56% of the cases. On blood gas analysis, mean PaO₂ was 75 ± 22 mmHg and mean PaO₂/FIO₂ 308 ± 99. In-hospital mortality rate in our population was 21% (*n* = 23).

Characteristics of population according to cardiac biomarkers

On subgroups analysis, patients who had raised hs-Troponin at admission were older, with higher prevalence of previous CVD (46% vs 20%) and NP beyond URN (82% vs 36%), higher CRP (9 (1.3, 14.3) mg/dl vs 4 (1.1, 7.4) mg/dl) and creatinine (1.43 ± 1.9 mg/dl vs 0.96 ± 0.9 mg/dl) values, whereas they had lower PaO₂/FIO₂ (276 ± 92 vs 325 ± 97) as compared to those with normal hs-Troponin. Of note, D-dimer was significantly increased in patients with high hs-Troponin at admission (1269 (560, 2759) ng/ml vs 442 (244, 778) ng/ml). These findings were similarly represented in patients with NP beyond cut-off levels. D-dimer was significantly elevated in patients with high hs-Troponin, irrespective of whether they had normal or high NP (Fig. 1). Rate of (ACE) inhibitor or ARB intake before hospital admission was similar between cardiac biomarkers subgroups. Both patients with hs-Troponin and NP beyond normal values experienced higher rate of in-hospital mortality (31% vs 11%, *p* = 0.012, and 33% vs 14%, *p* = 0.05, respectively). In patients with worse in-hospital outcome, we detected higher levels of both hs-Troponin and NP (*p* = 0.001 and *p* = 0.002, respectively, depicted in Fig. 2).

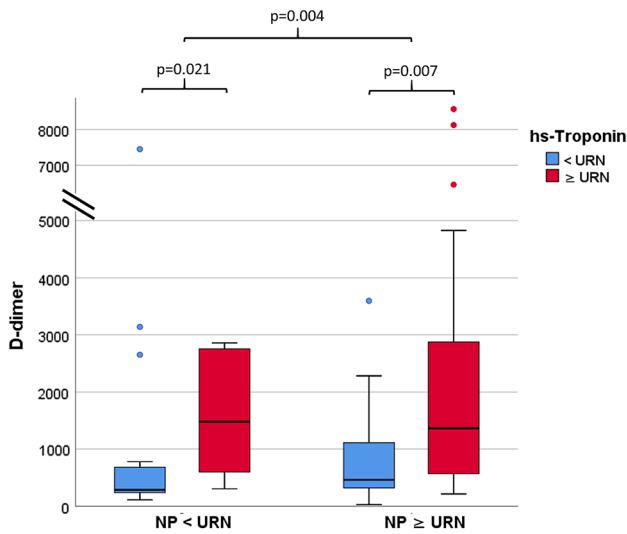


Fig. 1 Boxplot shows significantly higher D-dimer values in patients with hs-Troponin beyond URN, both in patients with normal (*p* = 0.021) and elevated (*p* = 0.007) NP

Echocardiographic findings

Transthoracic echocardiography was performed in 24 patients (22%) within the overall population. Median left ventricular ejection fraction (LVEF) and tricuspid annular plane systolic excursion (TAPSE) were 55% (50, 60) and 21 mm (19, 23), respectively. LVEF was significantly lower in patients with elevated NP, but not in those with elevated

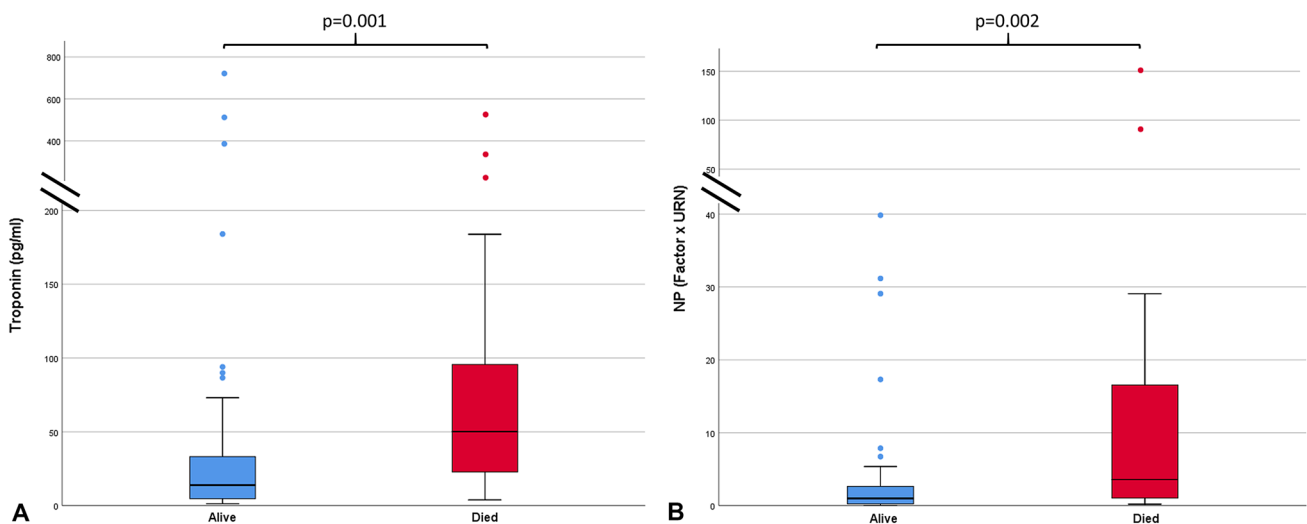


Fig. 2 Boxplots showing significantly higher cardiac biomarkers levels in patients with poor in-hospital outcome. Hs-Troponin (a) and NP (b) with *p* = 0.001 and *p* = 0.002, respectively

hs-Troponin ($p=0.02$ and $p=0.112$, respectively). TAPSE was significantly lower in both groups of elevated cardiac biomarkers (hs-Troponin: 20 mm (18, 22) vs 23 mm (22, 24), $p=0.022$; NP: 19 mm (17, 22) vs 22 mm (20, 24), $p=0.03$).

Analysis of relationships

Analysis of relationships results are summarized in Table 2. We observed a significant and close correlation between hs-Troponin and NP values ($r=-0.730$, $p<0.001$; Supplementary Fig. 1). Both hs-Troponin and NP were associated with age ($r=0.484$ and $r=0.696$, respectively, both $p<0.001$) and history of previous CVD ($r=0.332$ and $r=0.489$ with $p=0.001$ and $p<0.001$, respectively), as well as with hemoglobin and creatinine levels. Moreover, we detected significant associations between both cardiac biomarkers on one side and indexes of COVID-19 pneumonia severity on the other (depicted in Fig. 3). These relationships were significant for hs-Troponin (CRP: $r=0.396$, $p<0.001$; D-dimer: $r=0.366$, $p<0.001$; PaO₂/FIO₂: $r=-0.411$, $p<0.001$) as well as NP (CRP: $r=0.293$, $p=0.008$; D-dimer: $r=0.358$, $p=0.001$; PaO₂/FIO₂: $r=-0.347$, $p=0.001$).

On multivariable analysis (Table 3) including age, creatinine, hemoglobin, CRP, D-dimer and PaO₂/FIO₂, we observed independent associations between hs-Troponin and age ($B=0.419$, $p=0.001$), PaO₂/FIO₂ ($B=-0.212$,

$p=0.013$) and D-dimer ($B=0.179$, $p=0.037$), whereas NP remained associated with age ($B=0.480$, $p<0.001$) and history of previous CVD ($B=0.253$, $p=0.001$).

Discussion

Results from our multicenter observational study highlight the common occurrence of myocardial involvement in patients with COVID-19 pneumonia. Cardiac biomarkers increase was associated with both patients' preexisting conditions and markers of COVID-19 disease severity, as well as worse in-hospital outcome. Moreover, we described significant independent correlations between hs-Troponin and PaO₂/FIO₂ and D-dimer on one side and between NP and history of CVD on the other. Increasing age remained an independent determinant of both cardiac biomarkers increase.

Incidence

In our analysis, more than one-third of patients had increased hs-Troponin level, though an elevation that exceeded more than three times the URN was observed only in 16% of the population, while NP elevation beyond URN was present in more than a half of our sample. Though multiple studies described lower incidence of myocardial injury in patients with COVID-19 pneumonia [6, 24], our findings are in keeping with what observed by others [12, 25], likely in relation to older age and higher prevalence of comorbidities in these cohorts. Results from our population could be related to the peculiar epidemiology of COVID-19 pneumonia in Lazio region during the index period, which was in several cases related to clusters within nursing homes and rehabilitation clinics (partial nationwide data available at [26]). This highlights the heterogeneity of COVID-19 populations described by different studies, which in turn might explain existing differences in terms of patients' characteristics and outcomes [6, 12].

Potential mechanisms underlying myocardial involvement

We observed hs-Troponin and NP to be associated with both preexisting factors leading to higher vulnerability of myocardium (age, anemia, renal failure, previous CVD) as well as markers of COVID-19 pneumonia disease severity (D-dimer [9], CRP [24] and PaO₂/FIO₂ [27]). This result reiterates the view of myocardial injury in the course of COVID-19 pneumonia as mainly caused by virus independent factors, including higher myocardial oxygen consumption, increased inflammatory driver and hypoxemia and favored by underlying comorbidities such as heart

Table 2 Bivariate correlations of hs-Troponin and NP with patients' characteristics and laboratory results

Variable	Troponin (Log10)		NP (Log10 (factor × URN))	
	R	P	R	P
Age	0.484	< 0.001	0.696	< 0.001
Sex (male)	0.012	0.907	- 0.180	0.106
Previous CVD	0.332	0.001	0.489	< 0.001
ACE inhibitor/ARB therapy	0.021	0.833	0.156	0.162
Creatinine (mg/dl)	0.288	0.003	0.244	0.027
Hb (g/dl)	- 0.213	0.031	- 0.412	< 0.001
CRP (Log10)	0.396	< 0.001	0.293	0.008
D-dimer (Log10)	0.366	< 0.001	0.358	0.001
Hs-Troponin (Log10)	NA	NA	0.730	< 0.001
NP factor x URN (log10)	0.730	< 0.001	NA	NA
pH	0.063	0.535	- 0.040	0.728
pO ₂	0.030	0.766	- 0.086	0.443
pCO ₂	- 0.059	0.560	- 0.049	0.667
PaO ₂ /FIO ₂	- 0.411	< 0.001	- 0.347	0.001

Pearson's and Spearman (rho) coefficient, as appropriate for the type of the data; p value <0.05 was considered significant. Bold values indicates $p < 0.05$

NP Natriuretic peptide, CVD cardiovascular disease, ACE angiotensin-converting enzyme, ARB angiotensin receptor blocker, Hb hemoglobin, CRP C-reactive protein, NA not applicable

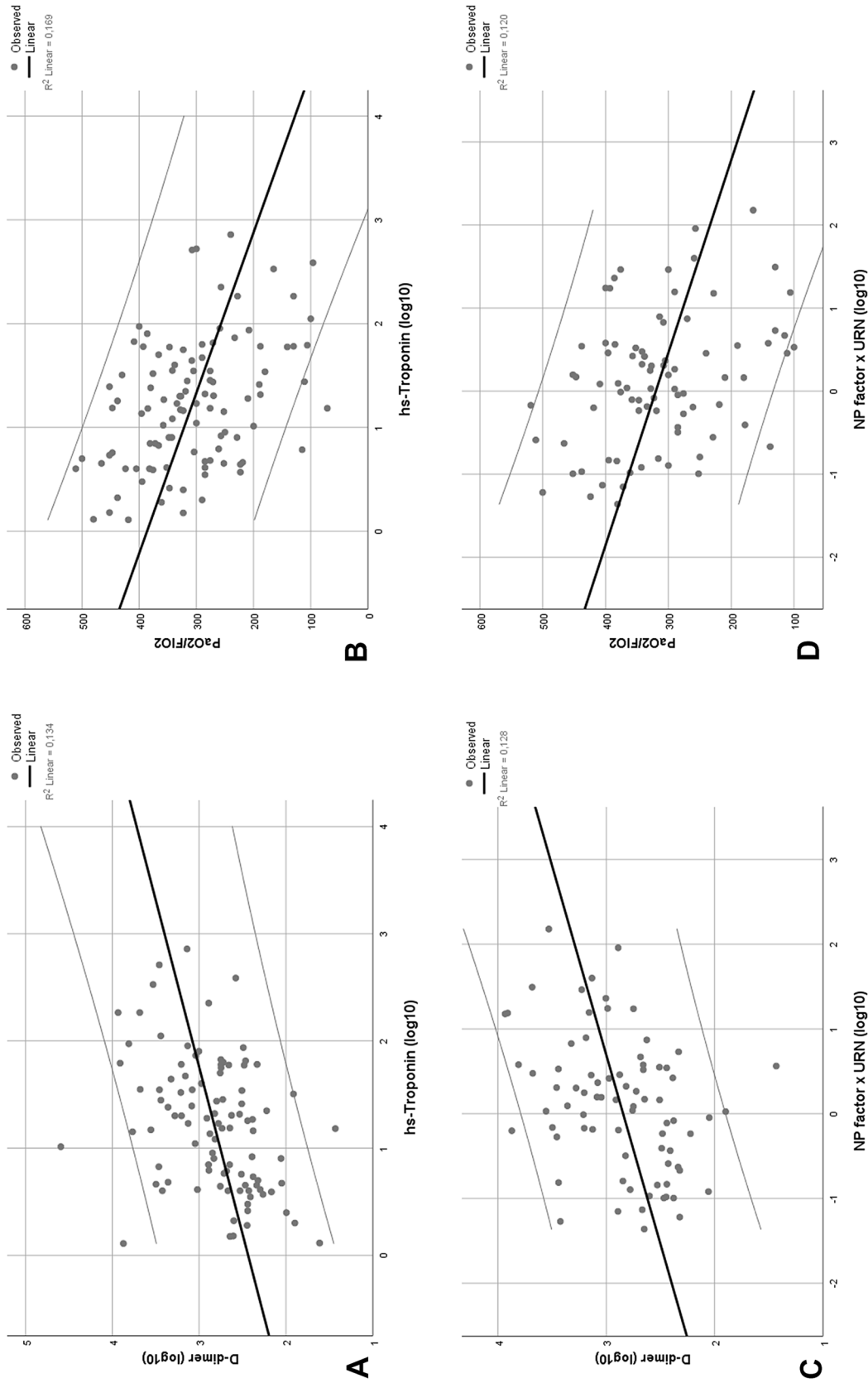


Fig. 3 Scatter plots showing correlations between hs-Troponin with D-dimer (a) and PaO2/FIO2 (b) with $r = 0.366$, $p < 0.001$ and $r = -0.411$, respectively, both $p < 0.001$, as well as between NP with D-dimer (c) and PaO2/FIO2 (d) with $r = 0.358$ and $r = -0.347$, respectively, both $p = 0.001$

Table 3 Multivariable linear regression of predictive associations with hs-Troponin and NP

Hs-Troponin (Log10)		NP (Log10 (factor × URN))					
Adj-R2	Variable	Beta	<i>P</i>	Adj-R2	Variable	Beta	<i>P</i>
0.335	Age	0.419	0.001	0.442	Age	0.480	< 0.001
	PaO ₂ /FIO ₂	− 0.212	0.013		Previous CVD	0.253	0.001
	D-dimer (Log10)	0.179	0.037				

Independent variables included in both models: age, hemoglobin, creatinine, history of previous CVD, PaO₂/FIO₂ and CRP and D-dimer. Bold values indicates *p* < 0.05

NP Natriuretic peptide, CVD cardiovascular disease, Hb hemoglobin, CRP C-reactive protein

failure [18]. Of note, in the course of COVID-19 pneumonia [13, 16, 17], these factors have been described as potential drivers of both hs-Troponin and NP increase, which, as expected, had parallel trend in our population.

Notwithstanding, results from our study might point toward some existing differences in mechanisms leading to hs-Troponin and NP elevation in COVID-19 pneumonia. Indeed, we observed an independent association between both D-dimer and PaO₂/FIO₂ with hs-Troponin, but not with NP. Interestingly, significantly elevated D-dimer concentration has been reported in COVID-19 patients with myocardial injury [10], but not in those with preexisting CVD [12]. Conversely, history of previous CVD was independently associated only with NP increase in our cohort, suggesting that preexisting underlying conditions such as heart failure and atrial fibrillation might be the major determinants of NP rather than hs-Troponin increase in these patients.

Reasons for reported findings cannot be discerned from data from our study as correlations we observed do not promptly imply the existence of any causative link. However, several hypotheses could be made to explain our observations. PaO₂/FIO₂ ratio is a key parameter for defining acute respiratory distress syndrome [28] and in patients with COVID-19 pneumonia has been used as marker of disease severity [27] as well as end point in studies testing novel treatments [29]. Additionally, PaO₂/FIO₂ may decrease with higher oxygen consumption and lower cardiac output [30]: both elements can contribute to myocardial injury. High D-dimer is commonly found in patients with COVID-19 pneumonia [7], albeit not necessarily representing the occurrence of pulmonary embolism but inflammation, hypoxia and disseminated intravascular coagulation [9, 31], factors that can be all related to myocardial injury [11]. Furthermore, thrombosis of small vessels within lung and kidney has been reported by multiple studies (reviewed in [32, 33]), possibly favored by coexistent endotheliitis found in several organs, including the heart [34]. In this context, microvascular thrombosis in coronary vessels [35, 36] is an adjunctive potential mechanism consistent with our results, already anecdotally reported [37].

Clinical implications

Our findings could potentially carry clinical implications. The therapeutic management of COVID-19 pneumonia is currently based on supportive therapy and experimental approaches [38, 39]. To provide a reliable discrimination of phenotypes within COVID-19 population could be helpful in order to plan targeted treatment [40], as hypothesized for patients with marked D-dimer elevation who might require higher anticoagulant dosage administration [41]. Based on our results, it is tempting to speculate whether increase of hs-Troponin might help identifying the subset of patients with higher systemic inflammatory response to COVID-19 infection, whereas NP the subgroup those in which preexisting CVD contributes more to the severe clinical course [12]. Finally, irrespective of the underlying mechanisms and in accordance with previous studies [10, 13], we observed higher in-hospital mortality in patients with either high hs-Troponin or NP within our population, strengthening the hypothesis that cardiac biomarkers assessment might provide useful information to aid COVID-19 pneumonia risk stratification.

Limitations

The present study should be read in light of several limitations. Though presenting a timely report regarding an ongoing medical emergency, the sample size is small, and results should be interpreted as hypothesis generating only, in need of further studies to ascertain the existence of any cause–effect relationship regarding the observed associations. Enrollment took place including patients consecutively admitted to medical units dedicated to COVID-19 assistance. However, it cannot be excluded that patients (especially males [42]) who were more severely affected when presenting to the emergency department were sent directly to intensive care units, thus being missed in our analysis. Due to safety reasons, and according to current specific guidelines [20], transthoracic echocardiography was performed only in a subset of patients within the whole population; hence, we could not provide comprehensive data

regarding echocardiographic findings; notwithstanding, our results are in line with previous research linking right ventricular dysfunction to increased levels of cardiac biomarkers in COVID-19 pneumonia [43]. Individuals affected by COVID-19 represent a heterogeneous group of patients, in which the time and location of data collection may lead to significant variation among different samples; hence, our results cannot be immediately translated to study populations characterized by largely different demographic and clinical characteristics.

Conclusions

Cardiac biomarkers elevation was common in our cohort of patients with COVID-19 pneumonia and associated with worse prognosis. Independent association of hs-Troponin with PaO₂/FIO₂ and D-dimer on one side, and of NP with history of CVD on the other, would require further studies to fully assess whether these biomarkers could effectively contribute to a reliable differentiation of phenotypes and subsequent treatment guidance in COVID-19 pneumonia patients.

Data availability Data will be made available upon request.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethics approval This study received the approval from Sapienza University Ethic Committee no. CE_5773_2020.

Consent to participate All patients provided informed consent for the use of their record for research purpose.

Consent for publication All authors have participated in the work and have reviewed and agree with article contents.

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