Early echocardiographic findings in patients hospitalized for COVID-19 pneumonia: a prospective, single center study

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Abstract
Background Cardiac dysfunction, mainly assessed by biomarker alterations, has been described in COVID-19 infection. However, there are still areas of uncertainty regarding its effective role in disease evolution. Aim of this study was to evaluate early echocardiographic parameters in COVID pneumonia and their association with severity disease and prognosis.

Methods An echocardiographic examination was performed within 72 h from admission in 64 consecutive patients hospitalized for COVID-19 pneumonia in our medium-intensity care unit, from March 30th to May 15th 2020. Six patients were excluded for inadequate acoustic window.

Results Fifty-eight consecutive patients were finally enrolled, with a median age of 58 years. Twenty-two (38%) were classifiable as severe COVID-19 disease. Eight out of 58 patients experienced adverse evolution (six died, two were admitted to ICU and received mechanical ventilation), all of them in the severe pneumonia group. Severe pneumonia patients showed higher troponin, IL-6 and d-Dimer values. No significant new onset alterations of left and right ventricular systolic function parameters were observed. Patients with severe pneumonia showed higher mean estimated systolic pulmonary artery pressure (sPAP) (30.7 ± 5.2 mmHg vs 26.2 ± 4.3 mmHg, \( p = 0.006 \)), even if in the normality range values. No differences in echocardiographic parameters were retrieved in patients with adverse events with respect to those with favorable clinical course.

Conclusion A mild sPAP increase in severe pneumonia patients with respect to those with milder disease was the only significant finding at early echocardiographic examination, without other signs of new onset major cardiac dysfunction. Future studies are needed to deepen the knowledge regarding minor cardiac functional perturbation in the evolution of a complex systemic disorder, in which the respiratory involvement appears as the main character, at least in non-ICU patients.

Keywords Echocardiography · COVID-19 · Cardiac dysfunction · Systolic pulmonary artery pressure

Background
The global pandemic of the novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began in China in December 2019 and spread globally a few months later [1]. Although it seems to spare the cardiovascular system as the primary site of infection, there is increasing evidence linking COVID-19 with cardiovascular morbidity [2]. A discrete prevalence of cardiac damage, defined by troponin elevation independently from electrocardiographic and echocardiographic findings, has been reported in patients hospitalized for COVID infection, with significant correlation with mortality [3–5]. Several pathways have been proposed for cardiovascular involvement during COVID illness. Firstly, direct heart involvement has been described, with a
clinical damage could be mediated by systemic cytokine toxicity during the hyperinflammation stage, inducing an increase in troponin values [4, 8]. However, troponin elevation in COVID-19 patients could represent the consequence of a more severe systemic disease, not necessarily being indicative of primary cardiac dysfunction [4, 9]. Finally, the strict heart–lung interaction should be considered, in particular in the setting of the most severe cases of COVID pneumonia, where a right ventricle (RV) dysfunction has been reported [10]. This condition is mainly described in ICU patients with advanced stages of the disease, when substantial alterations of heart–lung interaction have already occurred, both due to disease itself and to mechanical ventilation consequences.

Although there is increasing evidence of cardiovascular involvement during COVID disease, there are still areas of uncertainty regarding its effective role in determining disease evolution, in particular in the early phases of the disease course. In this regard, the aim of this study was to evaluate the eventual presence of early cardiac dysfunction and its prognostic role by means of echocardiography in consecutive COVID pneumonia patients, hospitalized in a medium-intensity care department.

Methods

Study design and participants

We performed a prospective study at the Internal Medicine Department of Luigi Sacco University Hospital (Milan, Italy) from March 30th to May 15th, 2020. Our Institution is one of the major regional tertiary teaching hospitals that managed COVID-19 patients, and the Milan Hub for Infectious Diseases. The Internal Medicine Department was commuted into a COVID-19 medium-intensity care unit for the whole duration of the emergency [11]. The level of intensity of care of this department ranged from low-flow oxygen delivery to non-invasive ventilation. All adult patients (> 18 years old) admitted to our medical ward for COVID pneumonia were considered eligible. The following conditions were considered exclusion criteria: pregnancy, absence of consent to participate in the study or a non-interpretable echocardiographic examination as defined below.

The study protocol complied with the Declaration of Helsinki. The study was approved by the local Ethics Committee and informed consent was obtained.

Data collection

All patients enrolled in the study were admitted from the Emergency Department (ED) to the ward with a diagnosis of COVID pneumonia based on a positive nasopharyngeal swab and the presence of pulmonary infiltrate at chest X-ray or computed tomography scan. Accurate past medical history was obtained together with data about pre-existing cardiovascular morbidity and ongoing treatment. Previous echocardiographic data were registered if available. Time from symptoms onset was also examined.

All patients received the following tests at admission: arterial blood gas analysis, 12 leads EKG, complete blood panel including high sensitivity Troponin T (hs-TnT), D-Dimer and Interleukin-6 (IL-6). Values were considered normal if the following were met: hs-TnT ≤ 15 mg/L, D-Dimer < 500 mcg/L, IL-6 < 7 ng/L.

The partial arterial oxygen pressure to fractional inspired oxygen ratio (P/F) was calculated for each patient.

Adverse outcomes were death and/or intubation during hospitalization.

Echocardiographic examination and image interpretation

The echocardiographic examination was performed within 72 h from admission. If the patient was on CPAP ventilation therapy, the echocardiographic examination was performed during brief 30 min “CPAP free” windows, when standard oxygen therapy (through high flow cannula, reservoir or Venturi mask) was administered. This protocol allowed to avoid the effect of positive end expiratory pressure itself on right ventricle function and pressure. Examinations were performed at bedside using a Philips CX-50 portable device by operators (FC; EC, MD, AL; DT) with minimum level-2 echocardiography competence (proficiency defined according to ACC/ASE societies) [12]. Each examination was subsequently interpreted off-line by level-3 echocardiography competence cardiologists (SD, AM) blinded to clinical information, using TomTec® analysis software. The examination interpretation was further supervised by a third experienced echocardiographist (AB) to promote measurement standardization. The echocardiographic examination was performed by operators protected by suitable personal protective equipment [13]. COVID-19 infections in operators were regularly assessed on a clinical basis; at the end of the study period serology was performed in all operators involved in the image acquisition.

Measures were defined according to the latest European and American Echocardiography Society guidelines [14, 15]. Briefly, left ventricle (LV) function was considered normal if the ejection fraction (EF) was > 52% for males and > 54% for females. Ejection fraction was evaluated by the Simpson biplane method. Left ventricle mass was estimated by the linear method; relative wall thickness was also calculated. For right ventricular (RV) function the adopted normal cutoff values were: fractional area change (FAC) > 35%; Tricuspid Annular Plane Systolic Excursion
or more comorbidities. Among the comorbidities, the most
patients (36%) were women. Thirty patients (52%) had one
was used to measure Pulmonary Artery Acceleration Time
sniff, as suggested by guidelines [15]. Pulse wave Doppler
inferior vena cava collapsibility index was evaluated with a
assessed among groups by the
ables with non-normal distribution. Categorical data were
bution, while the Mann–Whitney test was used for vari-
parameters (Hs-TnT,
for skewed distributions. Independent Student T-test was
and without adverse outcomes.
parameters (Hs-TnT, d-Dimer, IL-6) with main LV and RV func-
tional parameters.
Data were expressed as percentages, mean and standard
deviations (SD), or median with interquartile range (IQR) for
used to compare continuous variables with normal distribu-
tion, while the Mann–Whitney test was used for vari-
ables with non-normal distribution. Categorical data were
assessed among groups by the $\chi^2$ test or the Fisher exact test,
as appropriate.

Aim of the study and statistical analysis
The primary endpoint was to describe echocardiographic
characteristics of our cohort of patients hospitalized for
COVID pneumonia. Two subgroups of patients will be con-
sidered for a better disease characterization: those patients
with mild to moderate respiratory involvement and those
classifiable with severe disease according to the NIH clas-
ification for COVID disease, relying on respiratory failure
severity [16].
The secondary endpoint was to evaluate the impact of
echocardiographic findings, clinical and laboratory variables
on prognosis comparing two groups of patients, those with
and without adverse outcomes.
The following correlations were made: laboratory param-
eters (Hs-TnT, d-Dimer, IL-6) with main LV and RV func-
tional parameters.

Laboratory results
Cardiac troponin T and d-Dimer were elevated in 19 (33%)
and in 32 (56%) patients respectively. Median IL-6 values
were 25 (9.5–97.0) ng/L. Hs-TnT positivity was found in 12
out of 20 (62%) of severe pneumonia patients vs seven out
of 34 (21%) of non-severe patients, $p$: 0.003. d-Dimer positivity
was found in 17 out of 22 (77%) of severe pneumonia patients
vs 15 out of 35 (45%) in non-severe patients, $p$: 0.011. Of notice, we performed compre-
sive ultrasound of inferior leg proximal veins in all patients,
as part of local practice for COVID-19 in-patients, and we
found one deep vein thrombosis case. This patient belonged
to the severe pneumonia group and showed a d-Dimer
value $> 500$.

Results
Demographic and clinical characteristics
Sixty-four consecutive patients diagnosed as having COVID-
19 pneumonia were eligible for the study. Six patients were
excluded because of a poor acoustic window. The demo-
graphic and clinical characteristics are summarized in
Table 1.
The median age was 58.5 years (IQR 46–75) and 21
patients (36%) were women. Thirty patients (52%) had one
or more comorbidities. Among the comorbidities, the most
represented were hypertension in 21 patients (36%) and dia-
abetes mellitus in eight patients (13%).
The median duration of symptoms before hospital admis-
sion was 6 days (IQR 3–10). The median time from admis-
sion to discharge or event occurrence was 9 days (IQR
6–15.5). Twenty-two of 58 patients (38%) were attributed
to the severe pneumonia group, 15 of them were treated with
Continuous Positive Airway Pressure (CPAP) with a PEEP
range of 7.5–12 cmH2O.
Compared with those with milder disease, the severely
affected patients were older [68 years (IQR 57–78.3) vs
51.5 years (IQR 40–70.5), $p$: 0.006], while no signifi-
cant differences were observed in gender and comorbid-
ities, except for diabetes mellitus, that was more frequent in
the severe pneumonia subgroup [6/22 (27%) vs 2/36 (6%);
$p$: 0.044].
Pathological EKG findings were documented in eight out
of 57 patients (14%), with no significant differences in the
two severity subgroups of patients and in those who reached
the composite outcome. Among patients with EKG alter-
ations, only one received a diagnosis of unstable angina upon
further evaluation, due to stressor-related exacerbations of
an already known cardiac ischemic disease.
Three patients were diagnosed as having non-massive
pulmonary embolism, two of them with severe respira-
tory failure accordingly to NIH classification. All of them
survived.
Eight out of 58 (14%) patients reached the composite
outcome (six died, two were admitted to ICU and received
mechanical ventilation), all of them in the severe pneumonia
group.
The patients who reached the composite event were
older [77.5 years (IQR 66.3–82) vs 57 years (IQR 43–72),
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TAPSE > 17 mm, Tissue Doppler-derived right ventricular
systolic excursion velocity ($S'$) > 9.5 cm/s. Systolic Pulmo-
mary Artery Pressure (sPAP) was calculated adding right
atrioventricular gradient (estimated by tricuspid regurgita-
tion continuous wave Doppler) and central venous pressure
(estimated from inferior vena cava expiratory diameter and
collapsibility index), with normal value $\leq 35$ mmHg. The
inferior vena cava collapsibility index was evaluated with a
sniff, as suggested by guidelines [15]. Pulse wave Doppler
was used to measure Pulmonary Artery Acceleration Time
(pACT, normal value $< 105$ ms). Finally, the presence or
absence of pericardial effusion was reported.
Median IL-6 values were higher in the more severely affected group of patients: 116 (IQR 7.5–247.5) ng/L vs 14 (IQR 5.25–29.0) ng/L, \( p < 0.001 \).

Similar laboratory differences observed in severe vs non-severe pneumonia patients were observed when patients who experienced an adverse outcome were compared with those with an uneventful clinical course (Table 1).

### Echocardiographic characteristics

The echocardiographic characteristics of the population are summarized in Table 2. Median time from admission to echocardiographic examination was 2 days (IQR 1–2). In non-invasively ventilated patients, time range between CPAP support interruption and echocardiography performance was 10–15 min.

Considering the entire population as a whole, no significant alterations of right ventricular systolic function parameters were observed, with measured values of tricuspid annulus peak systolic excursion (TAPSE), RV fractional area change (FAC) and RV S’ falling within the normal range of healthy subjects. The same findings were seen when evaluating the right ventricular basal diameter and the right ventricle/left ventricle ratio. The only patient presenting with right ventricular systolic dysfunction had a pre-existing chronic cor pulmonale. Of notice, patients with pulmonary embolism presented normal echocardiographic findings.

When comparing the patients presenting with severe pneumonia, mean estimated Pulmonary Artery Systolic Pressure (sPAP) values resulted higher in severely affected patients (30.7 ± 5.2 mmHg vs 26.2 ± 4.3 mmHg respectively, \( p = 0.006 \) (Table 2).

Reduced left ventricular EF was identified in four patients; in three of them this condition was pre-existing, while in one patient it was related to the acute coronary syndrome. All these patients belonged to the non-severe pneumonia group. No significant differences in left side chamber dimensions and function were identified when comparing the severe vs non-severe pneumonia patients or those that reached the composite event vs those with an uneventful clinical course. Notably, relative wall thickness was significantly higher in severe pneumonia patients with a tendency

### Table 1  Clinical and laboratory characteristics in the study population, in the subgroups of severe vs non-severe pneumonia and in patients who experienced adverse outcome during hospitalization vs patients who didn’t experienced adverse events

| Clinical and laboratory characteristics | All patients \((n = 58)\) | Severe pneumonia \((n = 36)\) | Yes \((n = 22)\) | \( p \) value | Adverse outcome \((n = 50)\) | Yes \((n = 8)\) | \( p \) value |
|----------------------------------------|-----------------|-----------------|-----------|------------|-----------------|-----------|------------|
| Age, years\(^a\)                       | 58.5 (46–75)    | 51.5 (40–70.5)  | 68 (57–78.25) | 0.006 57.0 (43–72) | 77.5 (66.25–82) | 0.005 |
| Female sex, \(n (%)\)                  | 21 (36)         | 14 (39)         | 7 (32)    | 0.587 17 (34)   | 4 (50)     | 0.443     |
| Arterial hypertension, \(n (%)\)       | 21 (36)         | 10 (28)         | 11 (50)   | 0.088 15 (30)   | 6 (75)     | 0.021     |
| Coronary artery disease, \(n (%)\)    | 2 (3)           | 0 (0)           | 2 (9)     | 0.140 1 (2)     | 1 (12)     | 0.259     |
| Heart failure, \(n (%)\)              | 3 (5)           | 2 (6)           | 1 (4)     | 1.000 3 (6)     | 0 (0)      | 1.000     |
| Chronic obstructive lung disease, \(n (%)\) | 3 (5)         | 2 (6)           | 1 (4)     | 1.000 3 (6)     | 0 (0)      | 1.000     |
| Diabetes Mellitus, \(n (%)\)          | 8 (13)          | 2 (6)           | 6 (27)    | 0.044 7 (14)    | 1 (12)     | 1.000     |
| Atrial fibrillation, \(n (%)\)        | 6 (10)          | 2 (6)           | 4 (18)    | 0.187 4 (8)     | 2 (25)     | 0.189     |
| ECG alterations, \(n (%)\)            | 8/57 (14)       | 5/36 (14)       | 3/21 (14) | 1.000 7/50 (14) | 1/7 (14)   | 1.000     |
| Troponin T (ng/L)\(^a\)               | 8.5 (5.75–21.5) | 6.5 (4.75–11.75)| 17.5 (10.25–41.5) | <0.001 7.0 (5.0–16.0) | 21 (16.5–38.5) | 0.002     |
| Troponin T positivity (> 15 ng/L)      | 19/54 (33)      | 7/34 (21)       | 12/20 (60) | 0.003 12/46 (26) | 7/8 (87)   | 0.002     |
| d-Dimer (mcg/L)\(^a\)                 | 630 (367.5–1262.0) | 444 (327–851) | 1152 (582–3646) | 0.002 441 (348–851) | 3940 (1167.75–17,450.75) | 0.001     |
| d-dimer positivity (> 500 mcg/L)       | 32/57 (56)      | 15/35 (43)      | 17/22 (77) | 0.011 24/49 (49) | 8/18 (100) | 0.007     |
| Interleukin-6 (ng/L)\(^a\)            | 25 (9.5–97.0)   | 14 (5.25–29.0)  | 116 (37.5–247.5) | <0.001 18 (7.0–46.0) | 237 (153.0–354.0) | <0.001     |
| P/F\(^b\)                             | 305 ± 142       | 402.91 ± 75.73  | 153.86 ± 68.08 | <0.001 340.04 ± 121.38 | 95.25 ± 40.90 | <0.001     |
| CPAP, \(n (%)\)                       | 15 (26)         | 0 (0)           | 15 (68)   | <0.001 9 (18)   | 6 (75)     | 0.003     |

\(^a\)Data reported as median (IQR)

\(^b\)Data reported as mean ± SD
Table 2  Echocardiographic characteristics in the study population, in the subgroups of severe vs non-severe pneumonia and in patients who experienced adverse outcome during hospitalization vs patients who didn’t experienced adverse events

| Echocardiographic characteristics | All patients | Severe pneumonia | Adverse outcome | $p$ value |
|----------------------------------|--------------|-----------------|----------------|-----------|
| Left atrial indexed volume (mL/m²) | 32.7 ± 13.7  | 32.6 ± 13.2  | 33.1 ± 14.8  | 0.887  |
| Left atrial indexed volume > 34 mL/m², n (%) | 20/56 (36%)  | 15/35 (43%)  | 5/21 (24%)  | 0.150 |
| Septal thickness (mm) | 10.7 ± 1.9  | 10.3 ± 1.94 | 11.35 ± 1.76  | 0.051  |
| Left ventricular end diastolic diameter (mm) | 43.8 ± 4.2  | 44.33 ± 4.30 | 42.75 ± 3.92  | 0.178 |
| Indexed left ventricular mass (g/m²) | 85.6 ± 24.2  | 83.6 ± 24.6 | 89.1 ± 23.6  | 0.417 |
| Relative wall thickness | 0.45 ± 0.09 | 0.43 ± 0.10 | 0.48 ± 0.07 | 0.021 |

| Left ventricular geometry | | | | |
|----------------------------|-----------------|-----------------|---------------|-----------|
| Normal                     | 31 (54%)        | 23 (64%)        | 8 (36%)       | 0.181    |
| Concentric remodelling     | 15 (26%)        | 7 (19%)         | 8 (36%)       | 0.150    |
| Concentric hypertrophy     | 10 (17%)        | 6 (17%)         | 4 (19%)       | 0.150    |
| Eccentric hypertrophy      | 0 (0%)          | 0 (0%)          | 0 (0%)        | 0.150    |
| Not evaluable              | 2 (3%)          | 0 (0%)          | 2 (9%)        | 0.150    |
| Ejection fraction (%)      | 64.41 ± 7.55   | 63.31 ± 8.94   | 66.29 ± 3.73  | 0.086    |
| Reduced ejection fraction, n (%) | 4/57 (7) | 4/36 (11) | 0/21 (0) | 0.285 |
| E/A ratio                  | 1.08 ± 0.48    | 1.05 ± 0.37    | 1.13 ± 0.63   | 0.606    |
| Lateral E/E’ ratio         | 6.68 ± 2.16    | 6.64 ± 2.07    | 6.91 ± 2.42   | 0.695    |
| Septal E/E’ ratio          | 8.85 ± 2.75    | 8.05 ± 2.04    | 10.02 ± 3.40  | 0.064    |
| E deceleration time, msec  | 187.25 ± 50.81 | 195.53 ± 49.23 | 174.06 ± 51.72 | 0.139 |

| Diastolic function, n (%) | | | | |
|----------------------------|-----------------|-----------------|---------------|-----------|
| Normal                     | 38 (66%)        | 24 (67%)        | 14 (63%)      | 0.709    |
| Grade I dysfunction        | 10 (17%)        | 7 (19%)         | 3 (14%)       | 0.914    |
| Grade II dysfunction       | 1 (2%)          | 1 (3%)          | 0 (0%)        | 0.150    |
| Grade III dysfunction      | 1 (2%)          | 0 (0%)          | 1 (5%)        | 0.150    |
| Not evaluable              | 8 (13%)         | 4 (11%)         | 4 (18%)       | 0.150    |
| Right atrial volume (mL)   | 46.60 ± 23.48   | 46.86 ± 23.61   | 46.11 ± 23.91 | 0.914 |
| Right ventricular basal diameter (mm) | 36.58 ± 6.14 | 36.69 ± 6.25 | 36.40 ± 6.09 | 0.870 |
| Ventricular basal diameters right/left ratio | 0.81 ± 0.11 | 0.80 ± 0.12 | 0.84 ± 0.10 | 0.160 |
| Fractional area change (%) | 47.57 ± 6.84 | 47.71 ± 7.38 | 47.32 ± 5.91 | 0.840 |
| Tricuspid annular plane systolic excursion (mm) | 22.94 ± 3.37 | 23.06 ± 3.51 | 22.74 ± 3.21 | 0.742 |
| Right ventricular S’ (cm/sec) | 0.14 ± 0.03 | 0.13 ± 0.03 | 0.15 ± 0.02 | 0.078 |
| Right ventricular systolic dysfunction, n (%) | 1/55 (2) | 1/35 (3) | 0/15 (0) | 1.000 |
| Inferior vena cava inspiratory diameter (mm) | 14.5 ± 4.2  | 13.96 ± 4.27  | 15.40 ± 4.03  | 0.298 |
| Inferior vena cava collapsibility (%) | 44.8 ± 13.0 | 45.23 ± 14.97 | 44.07 ± 9.99 | 0.795 |
| Pulmonary artery systolic pressure (mm Hg) | 27.9 ± 5.09 | 26.24 ± 4.34 | 30.67 ± 5.16 | 0.006 |
| Pulmonary artery systolic pressure > 35 mmHg, n (%) | 4/40 (10) | 1/25 (4) | 3/15 (20) | 0.139 |
| Pericardial effusion, n (%) | 0/58 (0) | 0/36 (0) | 0/22 (0) | NS |

*pData reported as mean ± SD*
to a higher prevalence of concentric remodeling (0.48 ± 0.07 vs 0.43 ± 0.10, p = 0.021).

In addition, we found that IL-6 and D-dimer positivity was associated with higher values of sPAP (24.6 ± 2.3 vs 28.9 ± 5.0 mmHg, p = 0.003, and 26.1 ± 4.3 vs 29.3 ± 5.3, p = 0.048, respectively). No other significant correlations between biomarkers and principal LV and RV function parameters were observed.

Finally, we did not register any COVID-19 infections among the five operators directly involved in echocardiography acquisition. In particular, we did not record any symptomatic infection during the study period, nor any possible asymptomatic infection at serological screening performed at the end of the study.

Discussion

COVID-19, in particular in the severe form, is a complex disease characterized by systemic involvement, in which the temporal cascade and the effective role of single organ damage is still poorly understood.

Our prospective study showed the absence of early significant major myocardial dysfunction in a cohort of patients admitted to a middle intensity care department. In particular, in both mild/moderate and severe pneumonia patients we did not find new onset LV dysfunction (with the exception of the patient with acute coronary syndrome evidence) or significant RV impairment, showing just a mild -but significant- increase in sPAP in the more compromised group. These observations are apparently in contrast with previous data [17, 18]. We think that our results have to be interpreted taking into account some methodological differences with respect to previous studies. Argulian et al. described RV dilation in about 30% of COVID patients [17]. Differently from our study, in which echocardiography was performed in consecutive COVID pneumonia patients, these Authors analyzed the results of “clinically indicated” echocardiographic examinations, thus considering a selected population. In that study, roughly one third of the patients were invasively ventilated, while this subset of patient was not included in our population, as we focused on early cardiac dysfunction before the eventual onset of mechanical ventilation. A high percentage of ICU, mechanically ventilated patients was also present in a recent study in which a frequent LV systolic dysfunction was described [18]. The absence of new onset LV dysfunction in our cohort is in line with data reported by Yuman Li et al., where a smaller percentage of intubated patients was enrolled [19]. On the other hand, the same Authors reported a positive correlation between lower values of RV systolic function parameters and worse prognosis, although the considered cut-off values for RV parameters were largely within the normal range even in the adverse event group [19]. It is important to underline that, differently from previous studies, we assessed an early evaluation of cardiac involvement, performing echocardiographic examinations within 72 h from admission. The absence of significant pathological findings even in the most severely compromised patients, seem not to indicate the heart as one of the target organs at least in this phase of the illness. Nevertheless, we cannot exclude that subtle functional modification could have some relevance. In these perspectives, even cardiac parameters in the lower range of normality shown in some studies could represent the signal of a reduced functional reserve, possibly playing a role in the later complex development of the systemic response to the virus-triggered cascade. The detection of a higher sPAP in our more severely affected patients could be part of this picture, in particular reflecting an early pulmonary vascular perturbation, not unexpected in a condition of overt lung involvement. Of notice, sPAP elevation after 2 months from discharge was shown in up to 8% of patients with moderate COVID disease [20].

Elevated serum hs-TnT levels were observed in one third of our cohort, with a significant difference between survivors and non-survivors, in line with previous reports [3, 4, 21]. In our population this biomarker was related to adverse events in the absence of an association with electrocardiographic or echocardiographic changes. This observation could confirm the hypothesis that troponin elevation mainly represents a warning sign of systemic involvement rather than a proper marker of cardiac injury [4, 22]. On the other hand, a more specific role of increased troponin as a sign of subclinical cardiac dysfunction has to be kept in consideration.

Our results confirm the important association between outcomes and clinical parameters like age, history of hypertension, P/F and biomarkers [23]. Interestingly, echocardiography parameters potentially related to preexisting hypertensive cardiomyopathy, like relative wall thickness and concentric remodeling, were more frequent in severely affected patients.

IL-6 was significantly related to lung involvement and death, confirming the role of severe inflammation in the disease course, according to previous literature [24]. Similarly, D-Dimer elevation was associated with disease severity and prognosis. This association could reflect the role of hypercoagulability that has extensively been highlighted in COVID disease [25]. Moreover, the IL-6 and D-Dimer significant correlation with sPAP value may reflect the detrimental role of cytokinin storm in heart–lung interaction.

The limit of our study is related to the restricted number of enrolled patients, which did not allow us to further investigate the prognostic characteristics within the severe pneumonia group. Moreover, the enrollment of patients in a middle intensity department excludes patients with critical illness at presentation. Nevertheless, our event rate in the
severe form of the disease was fairly high (36%), reflecting a severe subsequent evolution in a part of our population, in line with the described natural history of COVID pneumonia. The strength of our study was the prospective and consecutive enrollment of patients that avoided the possible selection bias potentially affecting previous studies that enrolled patients with echocardiography performed for cardiological concerns. Moreover, we focused on the early phase of the disease, before eventual overt hemodynamic compromise and mechanical ventilation onset.

In conclusion, a mildly increased sPAP in severe COVID-19 pneumonia patients with respect to those with milder disease was the only significant finding at early echocardiographic examination. We did not find early new onset major COVID-related myocardial dysfunction, as evaluated by routinely performed echocardiographic parameters, in our cohort of consecutive patients hospitalized in a medium intensity care department. Echocardiography remains an irreplaceable tool to detect major cardiac complications, like acute coronary syndrome or myocarditis, and to assess pre-existing cardiovascular impairment, in particular in comorbid populations [26]. Moreover, the possibility to perform bedside examination without evidence of an increased risk for properly protected operators, make echocardiography suitable for the non-invasive hemodynamic monitoring, without displacing COVID infected patients. Future studies with repeated measurements, in particular during the detrimental phase of the disease, and post-discharge follow-up are needed to deepen the knowledge regarding the timing and possible complementary role of cardiac function reserve alterations in the evolution of a complex systemic disorder in which respiratory involvement appears as the main character, at least in non-ICU patients.

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Declarations

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

Human and animal rights The study protocol complied with the Declaration of Helsinki.

Informed consent The study was approved by the local Ethics Committee and informed consent was obtained.

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