Acute cor pulmonale in Covid-19 related acute respiratory distress syndrome

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Right ventricle (RV) dysfunction is a frequent complication of acute respiratory distress syndrome (ARDS). Its more severe presentation, acute cor pulmonale (ACP), is defined at echocardiography as a dilated RV (end-diastolic RV/left ventricle area ratio > 0.6) associated with the presence of septal dyskinesia. The prevalence of ACP in non-Covid-19 related ARDS (NC-ARDS) has been evaluated to be 22% [95% confidence interval (CI) 19–25%] during the first 72 h of protective mechanical ventilation [1]. A clinical risk score has been proposed to select NC-ARDS patients at risk of ACP, including four variables: pneumonia as a cause of ARDS, elevated driving pressure, severe hypoxemia and severe hypercapnia [1]. RV dysfunction has been also reported in the setting of COVID-19-related ARDS (C-ARDS) [2], but the prevalence of ACP and the validity of ACP risk score in C-ARDS patients are still unknown. We performed an observational study in the medical ICU of Henri Mondor University Hospital (Créteil, France), from March 9th 2020 to March 9th 2021 to assess the prevalence and predictors of ACP in C-ARDS.

Continuous data are expressed as the mean ± standard deviation or median [25th–75th percentiles] and were compared using the Student t test or Mann–Whitney U test, as appropriate. Categorical variables, expressed as number and percentages, were evaluated using the chi-square test or Fisher’s exact test. To evaluate independent factors associated with ACP, significant or marginally significant (p < 0.10) bivariate risk factors (using the above-mentioned tests) were examined using univariate and multivariable backward stepwise logistic regression analysis. Coefficients were computed by the method of maximum likelihood. The calibrations of model was assessed by the Hosmer–Lemeshow goodness-of-fit statistic and discrimination by the area under the receiver operating characteristics curve.

Among 282 Covid-19 patients admitted in our ICU during the study period, 175 were intubated and ventilated for C-ARDS. Fifty-eight C-ARDS patients were excluded because they had no available echocardiographic data obtained within 72 h of initiation of invasive mechanical ventilation and the remaining 117 patients were included. In our cohort, the observed prevalence of ACP (44/117, 38%, 95% confidence interval 0.29–0.47) was higher than previously described for NC-ARDS. C-ARDS patients with ACP were less likely to have diabetes or chronic kidney disease (Table 1). They were not more likely to have a thorax computed tomography angiogram performed but, if they did have the exam, they were significantly more likely to present a pulmonary embolism (Table 1). On the contrary, there was no significant association between the presence of ACP and the ACP risk score or its components (Table 1). In multivariable analysis, pulmonary embolism was the only factor associated with ACP (Table 2). Including the ACP risk score in the model yielded similar results. Patients with ACP had a trend towards more extracorporeal membrane oxygenation and required tracheostomy more frequently, but had a similar mortality than their counterparts (Table 1).

Our study suggests that ACP is more prevalent in C-ARDS than previously reported in NC-ARDS, and is rather driven by pulmonary vascular obstruction in
|                          | N patients with data | All patients (n = 117) | No ACP (n = 73) | ACP (n = 44) | p value |
|--------------------------|---------------------|------------------------|----------------|--------------|---------|
| **Patient characteristics** |                     |                        |                |              |         |
| Age (years)              | 117                 | 62.0 ± 10.3            | 63.2 ± 9.9     | 60.2 ± 10.9  | 0.132   |
| Male gender              | 117                 | 94 (80%)               | 60 (82%)       | 34 (77%)     | 0.517   |
| Body mass index (kg/m²)  | 113                 | 29.06 ± 5.69           | 28.27 ± 5.69   | 30.34 ± 5.50 | 0.061   |
| SAPS II                  | 116                 | 36 [28–46]             | 37 [30–47]     | 34 [27–46]   | 0.249   |
| SOFA score (Day 1)       | 117                 | 5 [4–8.5]              | 5 [4–9]        | 5 [4–8]      | 0.503   |
| **Medical history**      |                     |                        |                |              |         |
| Diabetes                 | 117                 | 47 (40%)               | 36 (49%)       | 11 (25%)     | 0.009   |
| Arterial Hypertension    | 117                 | 69 (59%)               | 47 (64%)       | 22 (50%)     | 0.125   |
| Heart failure (NYHA III-IV) | 117          | 9 (8%)                 | 8 (11%)        | 1 (2%)       | 0.150   |
| Chronic kidney disease   | 117                 | 19 (16%)               | 17 (23%)       | 2 (5%)       | 0.008   |
| Chronic obstructive pulmonary disease | 117 | 11 (9%) | 7 (10%) | 4 (9%) | 0.929 |
| **Respiratory parameters** |                     |                        |                |              |         |
| pH                       | 112                 | 7.36 [7.31–7.41]       | 7.36 [7.31–7.42] | 7.38 [7.33–7.41] | 0.366   |
| PaCO₂ (mmHg)             | 112                 | 42 [38–47]             | 42 [38–47]     | 44 [39–48]   | 0.313   |
| P/F ratio                | 116                 | 132 [95–177]           | 135 [96–175]   | 129 [91–189] | 0.869   |
| PEEP (cmH₂O)             | 110                 | 11 [9–12]              | 11 [8.75–12]   | 11.5 [9–12]  | 0.869   |
| Driving Pressure (cmH₂O) | 100                 | 12 [10–15]             | 13 [11–15]     | 12 [10–14]   | 0.108   |
| Tidal Volume (mL/kg)     | 86                  | 6.0 [5.7–6.4]          | 6.1 [5.9–6.4]  | 5.9 [5.6–6.5] | 0.37    |
| Respiratory Rate (/min)  | 83                  | 30 [26–32]             | 28 [25–32]     | 30 [28–34]   | 0.126   |
| Respiratory-system compliance (mL/cmH₂O) | 102 | 35 [28–40] | 34 [27–40] | 37 [29–44] | 0.089 |
| **ARDS ACP risk score**  |                     |                        |                |              |         |
| Pneumonia as cause of ARDS | 117           | 117 (100%)             | 73 (100%)      | 44 (100%)    | > 0.99  |
| Driving pressure ≥ 18 cmH₂O | 100              | 11 (9%)                | 9 (12%)        | 2 (5%)       | 0.192   |
| P/F < 150                | 116                 | 77 (66%)               | 46 (63%)       | 31 (70%)     | 0.468   |
| PaCO₂ ≥ 48 mmHg          | 112                 | 27 (23%)               | 16 (22%)       | 11 (25%)     | 0.773   |
| Total ACP risk score (0–4) | 97             | 2 [1–2.5]              | 2 [1, 2]       | 2 [1–3]      | 0.978   |
| **Laboratory data**      |                     |                        |                |              |         |
| Platelets (10⁹/L)        | 115                 | 244 [182–303]          | 244 [182–298]  | 243 [189–312] | 0.92    |
| Fibrinogen (g/L)         | 94                  | 6.82 ± 1.72            | 6.95 ± 1.65    | 6.62 ± 1.83  | 0.379   |
| D-dimer (ng/mL)          | 84                  | 1948 [1140–4205]       | 1948 [1249–2956] | 2335 [1006–8660] | 0.551  |
| **CT-scan data**         |                     |                        |                |              |         |
| Thorax CT angiography*** | 117                 | 81 (69%)               | 54 (74%)       | 27 (61%)     | 0.431   |
| Pulmonary embolism       | 81                  | 9 (8%)                 | 2 (3%)         | 7 (16%)      | 0.007   |
| **ICU and outcome data**** |                     |                        |                |              |         |
| Prone position           | 117                 | 107 (91%)              | 64 (88%)       | 43 (98%)     | 0.087   |
| Shock                    | 117                 | 91 (78%)               | 55 (75%)       | 36 (82%)     | 0.414   |
| Nitrous oxide use        | 117                 | 26 (22%)               | 14 (19%)       | 12 (27%)     | 0.308   |
| Tracheotomy              | 117                 | 19 (16%)               | 8 (11%)        | 11 (25%)     | 0.046   |
| VV-ECMO                  | 117                 | 22 (19%)               | 10 (14%)       | 12 (27%)     | 0.069   |
| Ventilation days (survivors) | 71          | 17 [10–38]             | 15 [8–34]      | 22 [11–42]   | 0.395   |
| Ventilator-free days at D28 | 115            | 0 [0–13]               | 0 [0–15]       | 0 [0–13]     | 0.516   |
| D28 all-cause mortality  | 117                 | 44 (38%)               | 29 (40%)       | 15 (34%)     | 0.542   |

ACP: Acute cor pulmonale; CT: Computed Tomography Scan; NYHA: New York Heart Association; PEEP: Positive End-Expiratory Pressure; SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; VV-ECMO: Veno-Venous ExtraCorporeal Membrane Oxygenation

*Data obtained at the time of echocardiographic evaluation; **Data obtained within 48 h (either before or after) of the echocardiographic evaluation; ***CT scan was performed a median of 2 [0–4] days before the echocardiographic evaluation; **** Data regarding the totality of ICU stay.
this group of patients than classical risk factors favoring vascular constriction/compression (hypoxemia, hypercapnia and driving pressure). Widespread pulmonary thrombosis with microangiopathy is a characteristic histological feature of C-ARDS [3, 4]. Pulmonary embolism is reported in up to 24% of critically-ill patients with C-ARDS [5]. Our data suggests that the presence of ACP may prompt the search of pulmonary embolism by a CT-scan in C-ARDS patients.

In conclusion, ACP seems more frequent and more related to pulmonary embolism in C-ARDS as compared to NC-ARDS. These observations need to be confirmed in larger studies.

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**Authors’ contributions**

All authors were involved in study conception and design. PM, FB and AMD conceived the study. PC, PM, FB and TD collected data. PC and AMD performed statistical analyses. PC and AMD wrote the original draft of the manuscript. All authors were involved in interpreting data and reviewing the final manuscript.

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**Availability of data and materials**

The dataset used during the current study is available from the corresponding author upon reasonable request.

**Declarations**

**Ethics approval and consent to participate**

This study was performed in accordance with the Helsinki Declaration and was approved by the ethics commission of the French Intensive Care Society. Due to the observational nature of the study, patient consent waived as per the French law.

**Consent for publication**

Not applicable.

**Competing interests**

Authors declare no competing interest for this work.

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