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Title: Dissociation between the clinical course and chest imaging in severe COVID-19 pneumonia: a series of five cases.

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1 **Abstract:**

2 **Background:** Although an RT-PCR test is the “gold standard” tool for diagnosing an
3 infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), chest imaging
4 can be used to support a diagnosis of coronavirus disease 2019 (COVID-19) – albeit with
5 fairly low specificity. However, if the chest imaging findings do not faithfully reflect the
6 patient’s clinical course, one can question the rationale for relying on these imaging data in
7 the diagnosis of COVID-19.

8 **Aims:** To compare clinical courses with changes over time in chest imaging findings among
9 patients admitted to an ICU for severe COVID-19 pneumonia.

10 **Methods:** We retrospectively reviewed the medical charts of all adult patients admitted to our
11 intensive care unit (ICU) between March 1, 2020, and April 15, 2020, for a severe COVID-19
12 lung infection and who had a positive RT-PCR test. Changes in clinical, laboratory and
13 radiological variables were compared, and patients with discordant changes over time (e.g. a
14 clinical improvement with stable or worse radiological findings) were analyzed further.

15 **Results:** Of the 46 included patients, 5 showed an improvement in their clinical status but not
16 in their chest imaging findings. On admission to the ICU, three of the five were mechanically
17 ventilated and the two others received high-flow oxygen therapy or a non-rebreather mask.
18 Even though the five patients’ radiological findings worsened or remained stable, the mean \pm
19 standard deviation partial pressure of arterial oxygen to the fraction of inspired oxygen
20 ($\text{PaO}_2\text{:FiO}_2$) ratio increased significantly in all cases (from 113.2 ± 59.7 mmHg at admission
21 to 259.8 ± 59.7 mmHg at a follow-up evaluation; $p=0.043$).

22 **Interpretation:** Our results suggest that in cases of clinical improvement with worsened or
23 stable chest imaging variables, the $\text{PaO}_2\text{:FiO}_2$ ratio might be a good marker of the resolution
24 of COVID-19-specific pulmonary vascular insult.

- 25 **Keywords:** Acute vascular distress syndrome; Acute respiratory distress syndrome; COVID-
- 26 19; Critical care; Radiology and other imaging; Viral infection.

27 **List of abbreviations:**

28 AVDS: acute vascular distress syndrome

29 BMI: body mass index

30 CT: computed tomography

31 GGO: ground glass opacity

32 ICU: intensive care unit

33 PaO₂:FiO₂: ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen

34 RT-PCR: reverse-transcription polymerase chain reaction

35 **Introduction**

36

37 Since the start of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
38 outbreak in the Hubei province of China, more than 151 million people had been infected and
39 more than 3.1 million had died by the first week of May 2021 in the 213 countries, areas or
40 territories covered by the United Nations.¹ The pandemic of coronavirus 2019 disease
41 (COVID-19) hit France in late February 2020. Picardy was one of the country's most affected
42 regions, with an incidence of confirmed infection of over 10 per 100,000 people on March
43 11th, 2020.² The number of patients admitted to the intensive care units (ICUs) in our tertiary
44 hospital increased dramatically at this time, and forced us to reorganize our regional
45 resources.^{3,4} By April 21st, 2020, 81 COVID-19 patients had been admitted to our ICU.

46 Early diagnosis of COVID-19 is crucial for disease treatment and control, and the
47 detection of viral nucleic acid in a reverse-transcription polymerase chain reaction (RT-PCR)
48 test remains the gold standard diagnostic tool. However, it has been suggested that the RT-
49 PCR test's lack of sensitivity, insufficient stability and relatively long processing time weaken
50 our ability to control the COVID-19 pandemic.⁵ Moreover, RT-PCR assays for SARS-CoV-2
51 were not available in several countries during the epidemic period.⁶ In this context, chest
52 imaging can be used to support the diagnosis of COVID-19 pneumonia.^{7,8} There is currently
53 no consensus among the main radiology societies on the type of chest imaging to use in the
54 diagnosis of COVID-19 pneumonia. The British Society of Thoracic Imaging and the
55 Canadian Society of Radiologists suggested that a chest X-ray should be the first-line tool in
56 stable patients.^{9,10} Chest computed tomography (CT) is typically used to (i) assess patients
57 with comorbidities and/or a high risk of disease progression and (ii) screen for complications.
58 Chest CT can reveal early pneumonia with greater sensitivity than a chest X-ray. However,
59 the sensitivity and the specificity of CT are lower in non-pandemic areas.¹¹⁻¹³ Therefore, the

60 choice of the imaging modality depends on the judgment of clinical teams, the availability of
61 local resources, and the expertise of local radiologists.

62 Relative to RT-PCR, chest CT offers good sensitivity, positive predictive values and
63 negative predictive values, although the specificity is fairly low (97%, 65%, 83%, and 25%,
64 respectively).⁵ Nevertheless, the CT images used to diagnose COVID-19 pneumonia are not
65 specific for SARS-CoV-2 virus infections, which cannot easily be distinguished from cases of
66 viral pneumonitis due to influenza or other viruses. Despite this uncertainty, the imaging-
67 based diagnosis of COVID-19 pneumonia may still be valuable in an appropriate
68 epidemiologic context. However, if the clinical course differed from the change over time in
69 the concomitant imaging findings for PCR-confirmed COVID-19 pneumonia, one could
70 question the reliance on chest imaging when attributing pneumonia to the SARS-CoV-2 virus.

71 We therefore decided to compare clinical courses with changes over time in chest
72 imaging findings among patients admitted to an ICU for severe COVID-19 pneumonia.

73

74 **Methods**

75

76 This study was conducted in Amiens-Picardie University Medical Center (Amiens,
77 France). We retrospectively reviewed the medical charts of all adult patients with COVID-19
78 admitted to our ICU between March 1, 2020, and April 15, 2020. COVID-19 was diagnosed
79 on the basis of nasopharyngeal swab specimens that were positive in a SARS-CoV-2 RT-PCR
80 test. Severe COVID-19 pulmonary infection was defined as respiratory failure requiring
81 invasive mechanical ventilation or high-flow oxygen (through a high-flow nasal cannula or a
82 non-rebreather oxygen mask) upon admission to the ICU. We compared the clinical course
83 with the changes in chest imaging between admission and a follow-up evaluation. Patients

84 were classified into three categories (Figure 1): (i) those with clinical and radiological
85 improvement, (ii) those with clinical and radiological worsening, and (iii) those with a clinical
86 improvement but stable or worsening radiological findings. Clinical improvement was defined
87 as weaning off mechanical ventilation or a significant decrease in the inspired oxygen
88 fraction. Radiological improvement was defined as a decrease in the affected areas of the lung
89 and the absence of new lesions. Only the patients with clinical improvement but no
90 radiological improvement were selected for further analysis. The patients in this group were
91 further subdivided into those with stable radiological findings and those with worse
92 radiological findings. A radiologist with expertise in chest imaging analyzed the radiological
93 data and validated the radiological outcome. For patients assessed with chest CT, the
94 pneumonia extension was assessed according to the guidelines issued by the European
95 Society of Radiology and the European Society of Thoracic Imaging.¹⁴ For patients assessed
96 with chest X-rays, we used the scoring system described by Borghesi and Maroldi.¹⁵

97

98 *Variables assessed:*

99 The following data were obtained from the patients' medical charts: age, sex,
100 comorbidities, self-reported smoking status, and body mass index (BMI). Following
101 admission to the ICU, the results of arterial blood gas, ventilatory support mode and
102 concomitant thoracic imaging data were recorded. The time interval between symptom onset
103 and the initial evaluation was noted. The ratio of the partial pressure of arterial oxygen to the
104 fraction of inspired oxygen ($\text{PaO}_2:\text{FiO}_2$) was computed for each patient. These data were also
105 collected at the follow-up radiological evaluation (chest CT when it had been available for the
106 initial evaluation, or a chest X-ray). In patients to whom oxygen was delivered through nasal
107 prongs, the delivered FiO_2 was estimated using the equation published by Markovitz et al.
108 ($21\% + 2.5\%$ per L/min of additional oxygen).¹⁶ Wilcoxon's paired test was used to compare
109 the $\text{PaO}_2:\text{FiO}_2$ ratio at baseline and at follow-up.

110 *Ethical considerations:*

111 In line with the French legislation on non-interventional studies, our institutional review board
112 waived the need for written, informed consent. The study database was registered with the
113 French National Data Protection Commission (*Commission Nationale de l'Informatique et*
114 *des Libertés*, Paris, France; reference: PI2020_843_0026, March 19th, 2020). The patients and
115 their families were provided with verbal and written information on the study.

116

117 **Results**

118 Eighty-one patients with a positive SARS-CoV-2 RT-PCR test were admitted to our
119 ICU and included in the study. In line with our exclusion criteria, thirty-five patients were
120 excluded from the study (lack of radiological data at follow-up: n=22; non-severe COVID-19
121 pneumonia: n=7; COVID-19 without respiratory signs or symptoms: n=2; loss to follow-up:
122 n=4). Of the 46 patients with severe COVID-19 pneumonia, the change in radiological status
123 was assessed with a chest X-ray in 28 cases (60.9%) and with chest CT in 18 cases (39.1%).
124 Twenty-seven patients showed a clinical and radiological improvement, 14 had clinical and
125 radiological worsening, and 5 patients showed a discordant change (i.e. clinical improvement
126 in the absence of radiological improvement) and were analyzed further (Figure 1 and Table
127 1). The mean \pm standard deviation age of the study population was 65.0 ± 7.8 , and the mean
128 BMI was 31.6 ± 6.1 kg/m². Three patients presented at least one comorbidity, and only one
129 was a former smoker. The mean time from disease onset to ICU admission was 10.0 ± 6.1
130 days. At ICU admission, three patients were intubated and mechanically ventilated with a
131 lung-protective strategy, whereas the other two patients were given high-flow oxygen therapy
132 or a non-rebreather mask. The clinical course, blood gas levels, and chest imaging findings
133 were then evaluated between 9 and 28 days after admission.

134

135 *Cases presentation*

136 **Patient #1** was a 73-year-old man who required high-flow nasal oxygen therapy (flow
137 rate: 50 L/min; $\text{FiO}_2 = 100\%$), with a $\text{PaO}_2:\text{FiO}_2$ of 74. Mechanical ventilation was initiated
138 on day 3, and the patient underwent two prone-positioning sessions (each lasting at least 16
139 hours). Treatment with lopinavir/ritonavir (400/100 mg, twice daily) was initiated but was
140 withdrawn after 7 days because of overdosing. The clinical course was complicated by
141 ventilator-associated pneumonia (*Pseudomonas aeruginosa*) with concomitant pulmonary
142 mucormycosis. The patient was weaned off mechanical ventilation on day 22 and switched to
143 a Venturi oxygen mask (flow rate: 6 L/min; $\text{FiO}_2 = 30\%$); the $\text{PaO}_2:\text{FiO}_2$ was 353. He was
144 discharged to a pulmonary rehabilitation unit on day 43.

145 **Patient #2** was a 53-year-old man who initially received oxygen through a non-
146 rebreather mask (flow rate: 50 L/min; $\text{FiO}_2 = 100\%$), with a $\text{PaO}_2:\text{FiO}_2$ of 75. On day 2, the
147 blood gas profile worsened rapidly, and the patient was intubated, mechanically ventilated
148 with inhaled nitric oxide (10 ppm), and underwent two prone-positioning sessions (each
149 lasting at least 16 hours). The patient was given remdesivir (100 mg/day for 10 days) and was
150 weaned off mechanical ventilation on day 7. While breathing oxygen (4L/min) through nasal
151 prongs, the estimated $\text{PaO}_2:\text{FiO}_2$ was 256. The patient was discharged to home on day 16.

152 **Patient #3** was a 70-year-old man who required lung-protective mechanical
153 ventilation ($V_t = 420\text{ml}$; $F = 25.\text{min}^{-1}$), with a FiO_2 of 50%, a positive end-expiratory pressure
154 (PEEP) of 15 cmH_2O , and no inhaled nitric oxide. The $\text{PaO}_2:\text{FiO}_2$ ratio was 216. The patient
155 underwent eight prone-positioning sessions (each lasting at least 16 hours) and received
156 standard care (i.e. no specific antiviral agents were administered). Due to severe ICU-acquired
157 weakness, he was tracheotomized on day 27 and was switched from volume-controlled
158 ventilation to pressure support ventilation (pressure support = 8 cmH_2O , PEEP = 5 cmH_2O),

159 with a FiO_2 of 30%. The $\text{PaO}_2:\text{FiO}_2$ ratio increased to 250. The tracheostomy was closed on
160 day 40, and patient was discharged to a pulmonary rehabilitation unit on day 47.

161 **Patient #4** was a 62-year-old man who required lung-protective mechanical
162 ventilation ($V_t = 430\text{ml}$; $F = 30.\text{min}^{-1}$), with a FiO_2 of 80% FiO_2 , a PEEP of 15 cmH_2O , and
163 no inhaled nitric oxide. He underwent two prone-positioning sessions (each lasting at least 16
164 hours) and was given lopinavir/ritonavir (400/100 mg twice daily) for 10 days. The $\text{PaO}_2:\text{FiO}_2$
165 ratio was initially 87 and increased to 186 on day 9. At this time, the patient was switched to
166 pressure support ventilation (pressure support = 15 cmH_2O , PEEP = 12 cmH_2O), with a FiO_2
167 of 50%. He was weaned off mechanical ventilation on day 16 and discharged to a pulmonary
168 rehabilitation unit on day 18.

169 **Patient #5** was a 67-year-old man, who required venovenous extracorporeal
170 membrane oxygenation and lung-protective mechanical ventilation (peak inspiratory pressure
171 = 18 cmH_2O ; $F=20.\text{min}^{-1}$), with a FiO_2 of 60%, a PEEP of 12 cmH_2O , and inhaled nitric
172 oxide. The patient did not undergo any prone-positioning sessions. He was given
173 lopinavir/ritonavir (400/100 mg twice daily) for 10 days. Venovenous extracorporeal
174 membrane oxygenation was withdrawn on day 8. The $\text{PaO}_2:\text{FiO}_2$ was initially 114 and
175 increased to 254 on day 21. At this time, the patient was on pressure support ventilation
176 (pressure support = 18 cmH_2O , PEEP = 8 cmH_2O), with a FiO_2 of 50%. Due to severe ICU-
177 acquired weakness, the patient was tracheotomized on day 25 and was transferred to a general
178 hospital on day 27.

179
180 The radiological changes in the five patients between ICU admission and the follow-
181 up evaluation are shown in Table 1 and Figures 2 and 3. Despite the observed worsening or
182 stability of the radiological findings, the $\text{PaO}_2:\text{FiO}_2$ increased significantly in all five patients
183 ($p=0.043$). The mean $\text{PaO}_2:\text{FiO}_2$ ratio was 113.2 ± 59.7 mmHg at admission and 259.8 ± 59.7
184 mmHg at follow-up (Figure 4).

185

186 **Discussion:**

187 We observed statistically significant and clinically meaningful increases in PaO₂:FiO₂
188 in five ICU patients with severe COVID-19 pneumonia over a mean period of 18.0 ± 8.6
189 days, despite the lack of any improvement in the chest imaging. These observations suggest
190 that the radiographic and clinical courses can diverge in some confirmed cases of COVID-19,
191 and thus cast doubt on the reliability of chest imaging in the establishment of a firm diagnosis
192 of SARS-CoV-2 infection.

193 In their retrospective study of 81 hospitalized COVID-19 patients, Shi et al. reported
194 that the viral pneumonia manifested itself with typically abnormal chest CT findings - even in
195 asymptomatic individuals. A rapid progression from focal, unilateral ground-glass opacities
196 (GGOs) to diffuse, bilateral GGOs with consolidation can be observed within 1 to 3 weeks of
197 infection.¹⁷ Given that the imaging features of COVID-19 pneumonia can change rapidly, Pan
198 et al. distinguished four typical disease stages.^{18,19} According to this classification, the patients
199 in our series were admitted to the ICU at different disease stages: early-stage disease for
200 patient #1, progressive disease for patient #2; peak disease for patients #3 and #4, and
201 absorption-stage disease for patient #5. Hence, Pan et al.'s classification was not appropriate
202 for assessing the severity of COVID-19 pneumonia in our five patients.

203 Ai et al. reported that the specificity of chest CT for diagnosing COVID-19 infection
204 was as low as 25%.⁵ Indeed, the chest imaging features of COVID-19 pneumonia overlap
205 markedly with those of other types of viral pneumonia. Although GGOs are frequently
206 observed in *Adenoviridae*, *Herpesviridae* and *Picornaviridae* infections, consolidation is
207 reported with *Adenoviridae*, *Herpesviridae* and other emergent *Coronaviridae*.²⁰ In view of
208 this low specificity, the positive predictive value and the diagnostic accuracy are highly

209 dependent on the pre-test probability, which in turn is determined by the epidemiological
210 context. A recent meta-analysis by Kim et al. showed that in areas of low COVID-19
211 prevalence (range: 1%-22.9%), chest CT screening of patients with suspected disease had a
212 low positive predictive value (range: 1.5%-30.7%).¹³

213 Shi et al. described four radiological outcome patterns on follow-up CT scan: initial
214 progression to a peak level, followed by radiological improvement (46%); radiological
215 improvement (14%); unchanged radiological appearance (9%) and radiological deterioration
216 (32%).¹⁷ All our patients were reevaluated at the absorption stage, and our results are quite
217 similar to Shi et al.'s findings: we observed radiological improvement in 27 of the 46
218 evaluable patients (58.7%), an unchanged radiological appearance in two (4.3%), and
219 radiological deterioration in 17 (37.0%). Five of our 46 patients presented with a discordant
220 course (i.e. clinical improvement in the absence of radiological improvement). These results
221 are similar to those reported by Bruns et al. who observed a possible discordance between the
222 clinical course and radiological changes in patients with severe, community-acquired
223 pneumonia.²¹ The time to radiological resolution of the pneumonia appears to be correlated
224 with older age and the number of lobes involved.²² In these situations, however, the change in
225 the PaO₂:FiO₂ ratio is correlated with the radiological change.

226 Gattinoni et al. have described two time-dependent chronological phenotypes among
227 patients suffering from COVID-19 pneumonia.²³ The five cases reported here raise questions
228 about the mechanism of the increase in the PaO₂:FiO₂ ratio during COVID-19 pneumonia. In
229 fact, our observations suggest that the hypoxemia was due not only to lung parenchyma
230 lesions but also to another pathophysiological mechanism. The discordant changes observed
231 in our five patients (a dramatic increase in the PaO₂:FiO₂ ratio in the absence of a
232 radiological improvement) support our "intrapulmonary shunt" hypothesis. Indeed, we
233 recently hypothesized that all stages of COVID-19 are characterized by an elevated

234 pulmonary blood flow and an intrapulmonary right-to-left shunt – prompting us to introduce
235 the acronym AVDS for “acute vascular distress syndrome”.^{24,25}

236 Vascular abnormalities have been described by various researchers in histological or
237 radiological studies of patients with COVID-19 pneumonia.^{26–29} The vascular disorders
238 induced by COVID-19 may result in an intrapulmonary shunt, which is generally masked by
239 the diffuse damage to the lung parenchyma. In the study by Ai et al., 21 of the 601 patients
240 (3%) with a positive RT-PCR test had negative chest CT findings - suggesting that the
241 pulmonary vascular insult might be the only manifestation of the disease in some patients.⁵
242 These patients should not be considered as being asymptomatic, since their pulmonary
243 vascular insult might lead to an intrapulmonary shunt that can be only evidenced by contrast-
244 enhanced echocardiography.²⁵ One can assume that hypoxemia will decrease upon recovery
245 from the pulmonary vascular insult, regardless of the course of the lung’s parenchymal
246 lesions. The clear-cut PaO₂:FiO₂ ratio improvement observed in our five patients (despite
247 stable or worsening chest imaging results) argues in favor of this hypothesis.

248 Our study also had some limitations. Notably, the change in chest imaging findings
249 was assessed with CT in only 18 of the 46 patients. For patients assessed with a chest X-ray,
250 some radiological features (such as vascular enlargement and GGOs) may have been
251 misclassified.

252 **Conclusion:**

253 Our observation of five cases of significant clinical and blood gas improvements in
254 patients with stable or worsening radiological findings suggests that chest imaging is not a
255 reliable means of assessing the initial vascular damage and the likely outcome of some ICU
256 patients with severe COVID-19 disease. The PaO₂:FiO₂ ratio could then be considered as a

257 good marker of the resolution of the COVID-19-specific pulmonary vascular insult. Further
258 clinical studies will be useful to confirm this result.

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353

354 **Figure legends:**

355

356 **Figure 1:** Study flow chart

357

358 **Figure 2:** Changes in the chest CT findings (lung parenchyma window) between ICU
359 admission (A and B) and the follow-up evaluation (C and D) for patients #1 and #2.

360

- Patient #1: A and C; patient #2: B and D.

361

362 **Figure 3:** Changes in the chest X-ray findings between ICU admission (A, B, and C) and the
363 follow-up evaluation (D, E, and F) for patients #3, #4 and #5.

364

- Patient #3: A and D; patient #4: B and E; patient #5: C and F

365

366 **Figure 4:** Changes in the PaO₂:FiO₂ ratio between ICU admission and the follow-up
367 evaluation.

368 PaO₂:FiO₂ ratio data are presented for each patient at baseline (ICU admission) and at the
369 follow-up imaging evaluation.

370

371 **Table 1:** Characteristics of the five patients selected for analysis.

	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5
Gender	Male	Male	Male	Male	Male
Age	73	53	70	62	67
BMI	27.2	30.9	42.1	27.4	30.2
Comorbidities	Hypertension, diabetes	None	Hypertension, diabetes, coronary artery disease	Obstructive sleep apnea syndrome, coronary artery disease, prostate cancer	None
Tobacco	No	No	No	Ex-smoker	No
Initial evaluation					
Time since symptom onset (days)	3	5	13	11	18
Initial chest imaging[†]	Chest CT: bilateral GGOs (extension: 30%)	Chest CT: bilateral GGOs (extension: 30%)	Chest X-ray: bilateral infiltrates (extension: 2/18)	Chest X-ray: bilateral infiltrates (extension: 6/18)	Chest X-ray: bilateral infiltrates, consolidation (extension: 8/18)
Initial ventilation or oxygen therapy	HF oxygen: Flow rate: 50 FiO ₂ = 100%	Non-rebreather mask: Flow rate: 15 FiO ₂ = 100%	VCV: F=25; Vt = 420; PEEP = 15; FiO ₂ = 50%	VCV: F=30; Vt = 430; PEEP = 15; FiO ₂ = 80%	ECMO + PCV: F=20; PIP = 18; PEEP = 12; FiO ₂ = 60%;
PaO₂ (mmHg)	74.4	75.1	108	70.0	68.2
PaCO₂ (mmHg)	33.1	41.2	37.9	47.3	34.6
pH	7.48	7.41	7.32	7.35	7.47
PaO₂:FiO₂	74	75	216	87	114
Lactates (mmol:L)	3.1	1.8	2.1	1.6	2.4
Estimated GFR (ml/min)	102	143	17	84	113
CRP (mg:l)	397.1	175.2	163.1	357	329
Hemoglobin (g:dl)	11.4	12.0	11.8	11.8	10.9
Leukocyte count (10³/mm³)	7.2	10.3	7.1	7.0	7.1
Lymphocyte count (10³/mm³)	0.6	0.5	0.7	0.5	0.5
BNP (ng:L)	284	61	160	NA	NA
Therapy	Lopinavir - ritonavir	Remdesivir	No specific antiviral therapy	Lopinavir - ritonavir	Lopinavir - ritonavir
Second evaluation					
Time since first evaluation (days)	23	9	28	9	21

Follow-up chest imaging[†]	CT-scan: bilateral GGO, consolidation, (extension: 30%)	CT-scan: bilateral GGO, consolidation, (extension: 50%)	Chest x-ray: bilateral infiltrates, consolidation (extension: 8/18)	Chest x-ray: bilateral infiltrates, consolidation (extension: 7/18)	Chest x-ray: bilateral infiltrates, consolidation (extension: 8/18)
Ventilation / oxygen therapy*	Venturi oxygen mask: Flow rate: 6 FiO ₂ = 30%	Nasal prong: Flow rate: 4 FiO ₂ = 31%	PSV: PS = 8; PEEP = 5; FiO ₂ = 30%	PSV: PS = 15; PEEP = 12; FiO ₂ = 50%	PSV: PS = 18; PEEP = 8; FiO ₂ = 50%
PaO₂	106	79.7	74.5	92.9	127
PaCO₂	44	36.9	38.7	41.6	56.7
pH	7.38	7.44	7.43	7.42	7.35
PaO₂:FiO₂	353	256	250	186	254
Lactates (mmol:L)	1.4	1.3	2.1	2.9	1.5
Estimated GFR (ml/min)	41	49	118	90	137
CRP (mg:l)	94.3	NA	105.7	NA	105
Hb (g:dl)	7.2	10.4	8.4	10.9	9.5
Leukocyte count (10³/mm³)	5.4	8.0	7.1	14.9	16.6
Lymphocyte count (10³/mm³)	1.0	0.8	1.5	1.1	1.1

372

373 VCV: volume-controlled ventilation; ECMO: extracorporeal membrane oxygenation; PCV: pressure-controlled
374 ventilation; PIP: peak inspiratory pressure; PSV: pressure support ventilation; GFR: glomerular filtration rate;
375 CRP: C reactive protein; BNP: brain natriuretic peptide NA: not available

376 [†] For patients assessed with chest CT, our evaluation of the extension of pneumonia was based on the guidelines
377 issued by the European Society of Radiology and the European Society of Thoracic Imaging.¹⁴ For patients
378 assessed with a chest X-ray, we used the scoring system published by Borghesi et Maroldi.¹⁵

379 * In patients treated with oxygen via nasal prongs, we considered that the effective FiO₂ increased by 2.5% per
380 additional liter of oxygen flow.

381

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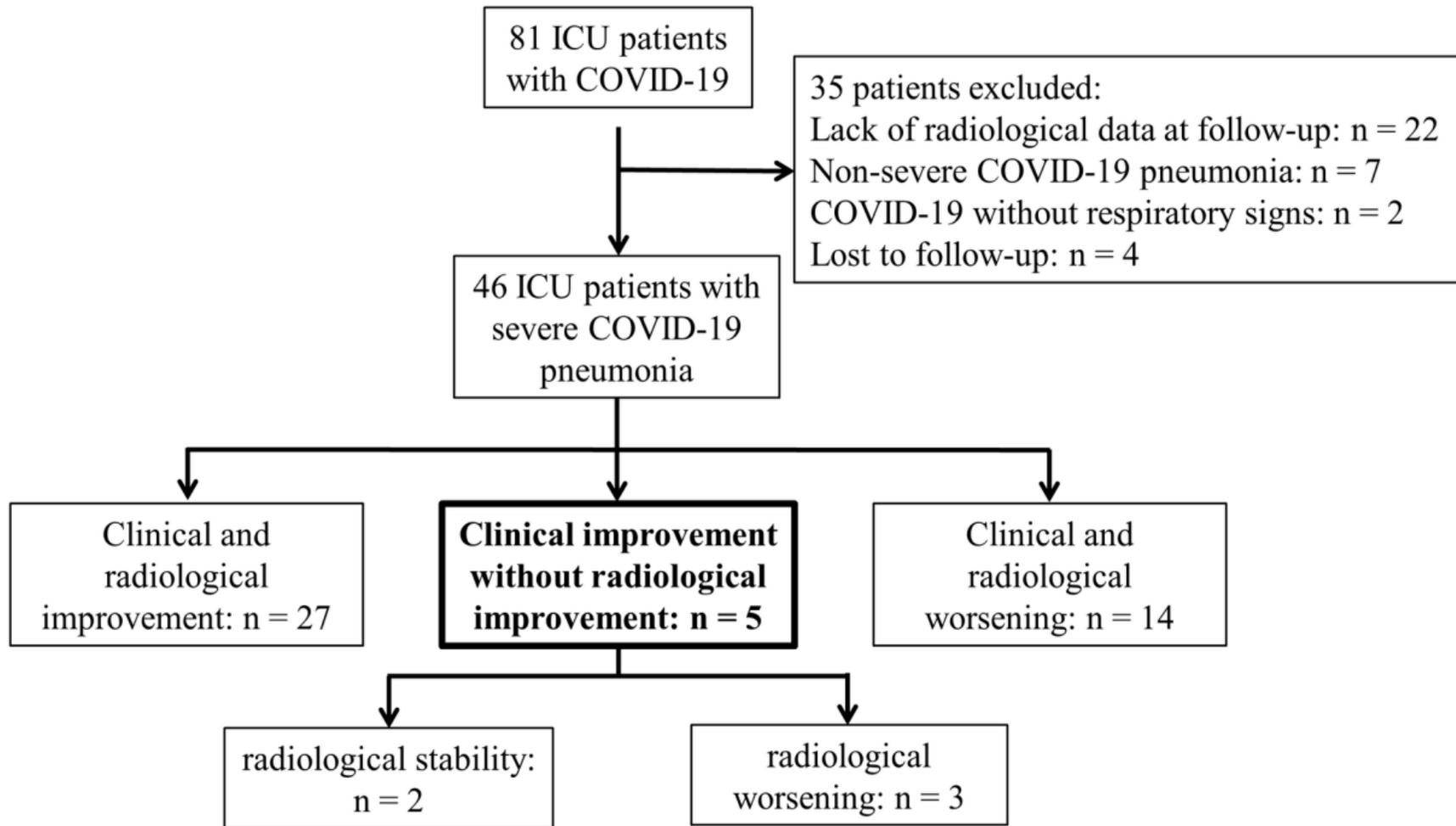
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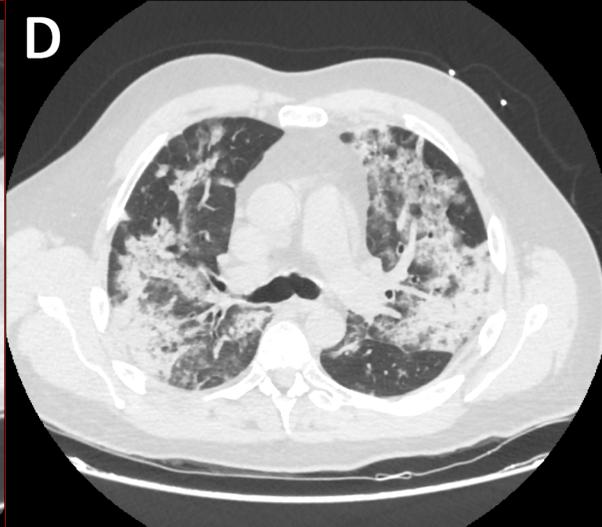
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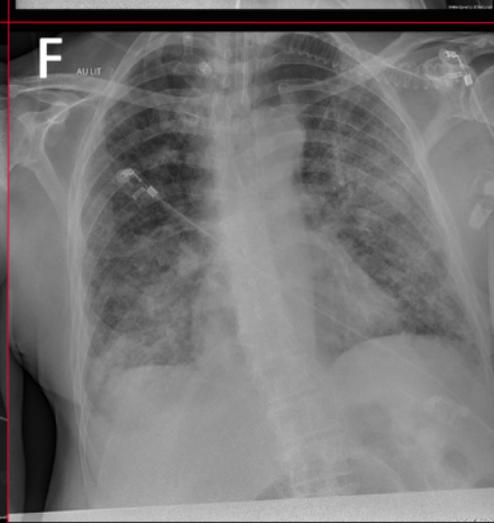
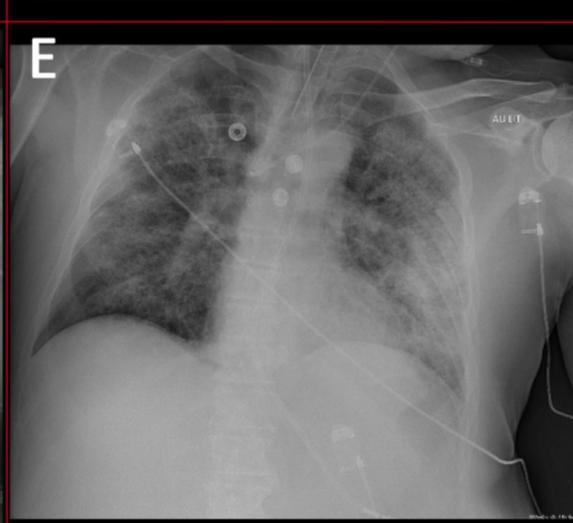
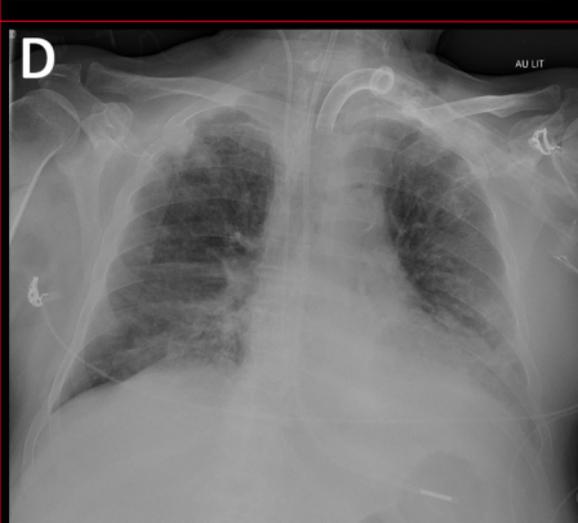
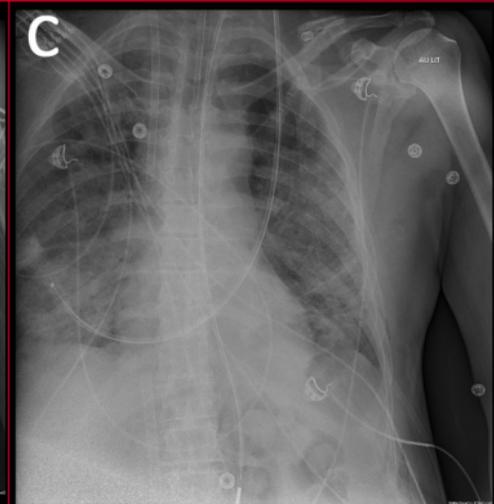
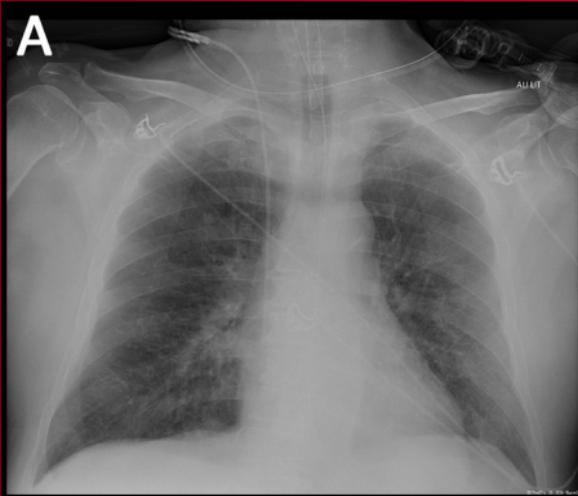
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A**B****C****D**



PaO₂:FiO₂

