Severe organising pneumonia following COVID-19

István Vadász MD^{1,2,3}, Faeq Husain-Syed MD¹, Peter Dorfmüller MD, PhD^{2,3,4}, Fritz C. Roller MD⁵, Khodr Tello MD^{1,2,3}, Matthias Hecker MD, PhD^{1,2}, Rory E. Morty PhD^{1,2,3,6}, Stefan Gattenlöhner MD^{2,3,4}, Hans-Dieter Walmrath MD¹, Friedrich Grimminger MD, PhD^{1,2,3,7}, Susanne Herold MD, PhD^{1,2,3}, Werner Seeger MD^{1,2,3,6,7}

¹Department of Internal Medicine, University Hospital Giessen, Justus Liebig University Giessen, Klinikstrasse 33, 35392 Giessen, Germany

²Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Klinikstrasse 33, 35392 Giessen, Germany

³The Cardio-Pulmonary Institute (CPI), Aulweg 130, 35392 Giessen, Germany

⁴Institute of Pathology, University Hospital Giessen, Justus Liebig University Giessen, Langhansstrasse 10, 35392 Giessen, Germany

⁵Department of Radiology, University Hospital Giessen, Justus Liebig University Giessen, Klinikstrasse 33, 35392 Giessen, Germany

⁶Max Planck Institute for Heart and Lung Research, Department of Lung Development and Remodeling, Ludwigstrasse 43, 61231 Bad Nauheim, Germany

⁷Institute for Lung Health (ILH), Justus Liebig University Giessen, Klinikstrasse 33, 35392 Giessen, Germany

Correspondence to:

István Vadász, MD

Department of Internal Medicine, University Hospital Giessen, Justus Liebig University Giessen, Universities of Giessen and Marburg Lung Center, Member of the German Center for Lung Research and The Cardio-Pulmonary Institute

Klinikstrasse 33, 35392 Giessen, Germany

Tel: +49 641 985 42354, Fax: +49 641 985 42359

Email: istvan.vadasz@innere.med.uni-giessen.de

Supplementary material

Supplementary tables

Supplementary table 1: Characteristics of three patients diagnosed with organising pneumonia secondary to COVID-19.

	Patient 1	Patient 2	Patient 3
Demographics			
Sex	Male	Male	Male
Age, years	57	70	76
Body mass index, kg/m ²	29.4	23.2	24.7
Comorbidities	Hypertension, diabetes	Hypertension, COPD	Hypertension, diabetes, CAD
Laboratory findings			
White cell count, g/L	7.1	9.6	11.9
Total lymphocytes	1.54	0.87	0.36
Haemoglobin, g/dL	84	131	105
Platelet count, giga/L	316	233	287
Creatinine, mg/dL [†]	0.5	0.9	1.2
Urea, mg/dL‡	37	111	86
Lactate dehydrogenase, U/L	311	393	301
Alanine aminotransferase, U/L	104	81	38
Aspartate aminotransferase, U/L	44	108	56
Albumin, g/L	24.9	33.6	31.0
B-type natriuretic peptide, pg/mL	48	65	142
C-reactive protein, mg/L	71.1	58.1	212.4
Procalcitonin, μg/L	0.5	0.7	0.5
Interleukin-6, μg/L	74	334	280
Ferritin, µg/L	1588	524	1059
D-dimer, mg/L	3.1	4.3	0.69
Clinical characteristics			
SAPS II	37	39	57
SOFA score	7	6	7
V _T , mL/kg PBW			
24 h post-intubation	6.1	6.2	6.2
2 weeks post-intubation	6.3	5.9	5.8
At time point of OP diagnosis	5.6	6.1	5.4
2 weeks after CS initiation	6.2	SB	6.7
RR, breaths/min			
24 h post-intubation	26	20	15
2 weeks post-intubation	22	18	19
At time point of OP diagnosis	30	22	26
2 weeks after CS initiation	16	SB	15
P _{PLAT} , cmH ₂ O			

24 h post-intubation	28	25	24
2 weeks post-intubation	24	19	16
At time point of OP diagnosis	30	30	20
2 weeks after CS initiation	13	SB	14
PEEP, cmH ₂ O			
24 h post-intubation	12	11	12
2 weeks post-intubation	8	9	7
At time point of OP diagnosis	10	12	5
2 weeks after CS initiation	5	SB	5
Driving pressure, cmH ₂ O			
24 h post-intubation	18	14	12
2 weeks post-intubation	16	10	9
At time point of OP diagnosis	20	18	15
2 weeks after CS initiation	8	SB	9
Compliance, mL/mbar			
24 h post-intubation	38.4	42.7	41.2
2 weeks post-intubation	52.3	65.3	54.4
At time point of OP diagnosis	18.4	22.5	26.2
2 weeks after CS initiation	57.5	SB	55.6
PaO ₂ /FiO ₂ ratio			
24 h post-intubation	98.2	185.2	194.8
2 weeks post-intubation	175.5	261.1	240.0
At time point of OP diagnosis	153.3	197.7	208.3
2 weeks after CS initiation	308.2	385.7*	347.6
ARDS adjuvant therapy			
Prone positioning	Yes	Yes	Yes
Nitric oxide	Yes	No	Yes
ECCO ₂ R	Yes	No	No
LVEF, %	60	60	55

[†]To convert the values for serum creatinine to mg/dL, multiply by 88.4.

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CS, corticosteroid; ECCO₂R, extracorporeal carbon dioxide removal; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; LVEF, left ventricular ejection fraction; OP, organising pneumonia; PaO₂, arterial partial pressure of oxygen; PBW, predicted body weight; PEEP, positive end-expiratory pressure; P_{PLAT}, plateau pressure; RR, respiratory rate; SAPS, Simplified Acute Physiology Score; SB, spontaneously breathing; SOFA, Sequential Organ Failure Assessment

Legend to Supplementary figures

Supplementary figure 1: Initial and follow-up chest x-ray of a patient with severe

COVID-19. (A) Initial chest x-ray of a 57-year old male patient presenting with COVID-19 showing extensive ground-glass opacification in both lower lobes and the left midfield (black asterisk). A follow-up chest x-ray (B) three weeks later upon clinical deterioration and

[‡]To convert the value for urea to blood urea nitrogen, multiply by 0.467.

^{*}Spontaneously breathing at room air (FiO₂ 0.21%).

markedly decreasing pulmonary compliance showing extensive consolidations (black asterisk) in both lower lobes with positive bronchoaerogram and bronchiectasis (black arrow).

Supplementary figure 2: Histology of a transbronchial biopsy from the same patient upon pulmonary deterioration. HE stainings at a magnification of 40x and 200x are shown.

- (A) Overview of the pulmonary parenchyma with cell-rich interstitial infiltrate (thickening of alveolar septa) that is more prominent on the left side. Scale bar corresponds to 200 µm.
- (B) Interstitial inflammatory infiltrate, featuring mostly CD3+ lymphocytes (immunostainings not shown), but also scattered neutrophils (N) and eosinophils (E) with fibrinous leakage and bleeding into the alveoli (arrows). Scale bar corresponds to $50 \, \mu m$

Legend to Supplementary videos

Supplementary video 1: Colour-coded 3-D volume rendering technique (VRT) showing organising pneumonia following COVID-19. As shown in the transversal color-coded image, the blue coloured areas represent lung tissue with normal lung density on a Hounsfield unit scale, whereas green and red/white coloured areas represent lung tissue changes with increased density values due to ground-glass opacification and consolidations/fibrotic changes, respectively. The lower lobes show marked fibrotic pattern with extensive secondary volume loss.

Supplementary video 2: Follow-up colour-coded 3-D VRT showing partial recovery from organising pneumonia post COVID-19 upon corticosteroid therapy. Follow-up approximately eight weeks after initiation of corticosteroid therapy, showing partially recovery, suggesting less extensive opacification and consolidations.