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Letter to the Editor

Lung mechanics during recovery of a non-invasively ventilated patient with severe COVID-19 pneumonia

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To the Editor,

An unvaccinated woman in her mid-60s was admitted to the COVID unit of Semmelweis University, Budapest, due to respiratory failure secondary to bilateral pneumonia. The patient had been suffering from weakness, coughing, nausea, fever, and progressive dyspnea consistent with general symptoms of COVID-19 for three weeks prior to hospitalization (Grant et al., 2020). A rapid test at admission confirmed SARS-CoV-2 infection. The initial CT image, taken on the 2nd day of hospitalization, demonstrated considerable lung involvement (50–75% on the right and 25–50% on the left) with wide-spread consolidation, occasional ground-glass opacity and airway dilation (Fig. 1A) similar to previous findings (Parekh et al., 2020), and, in particular, to the rapid onset post-infection bronchiectasis reported recently (Gilmartin et al., 2022). Despite supportive treatment, the patient continued to show signs of progressive dyspnea weeks after hospitalization and was admitted to the intensive care unit (ICU) on day 25 with an estimated alveolar-arterial (A-a) gradient of 530 mmHg and the repeat CT scan showing nearly 100% involvement of the lung (Fig. 1B), consistent with severe COVID-19. The patient was given remdesivir therapy combined with dexamethasone and placed on pressure controlled non-invasive ventilation (NIV) with an initial fractional inspired oxygen (F_iO_2) of 100% tapered to 65%, a positive end-expiratory pressure (PEEP) of 8 cmH_2O, and an inspiratory peak airway pressure (IPAP) of 24 cmH_2O. Despite initial substantial dyspnea and O_2 desaturation upon physical activity, dexmedetomidine sedation allowed good tolerance of NIV therapy with relatively stable vitals.

On day 35, the patient was moved from the ICU to the Long-Term Ventilation and Weaning Unit, where NIV was continued with an FiO_2 of 50%, a PEEP of 6 cmH_2O and an IPAP range of 24–30 cmH_2O. Persisting dependence on NIV and particularly high driving pressures to counteract increased work of breathing (WOB) prompted advanced respiratory monitoring by staff, which included measurements of airway pressure and flow, as well as gastric and esophageal pressures. Transpulmonary pressure (P_{tp}) was calculated as the difference between airway and esophageal pressures, and volume (V) was obtained by integration of flow. Despite considerable ventilator support, the patient produced remarkable respiratory efforts ($P_{tp} > 40$ cmH_2O), explaining her severe dyspnea and fatigue. Raising IPAP to 35 cmH_2O matched the patient-initiated tidal volumes, lowering maximum inspiratory effort, and WOB. This setting allowed stability in the coming weeks, during which minor improvements in lung mechanics were observed, steroid dose was gradually reduced and weaning from NIV and rehabilitation could be started. The patient was discharged on day 95.

Fig. 1E shows a series of maximal spontaneous P_{tp}-V loops obtained between the 36th and 301st days. During maximum efforts, changes in P_{tp} ranged between 70 and 80 cmH_2O. Although the patient was no longer in the acute phase, on day 36, the maximum effort resulted in an inhaled volume of only 0.66 L and the P_{tp}-V loop showed negligible hysteresis. This highly abnormal mechanical behavior was accompanied by an A-a gradient of 143.4 mmHg. No evidence of noticeable recruitment of collapsed regions is seen on the P_{tp}-V loop (massive alveolar opening would result in dynamic instabilities which would generate a sudden large increase in inhaled volume in a narrow range of pressure) (Alencar et al., 2002). Additionally, the spontaneous tidal volume of the patient (~0.5 L) was barely smaller than that during maximum effort, indicating minimal reserve. Such stiff lung behavior is consistent with pulmonary fibrosing alveolitis (Thompson and Colebatch, 1989) driven by profibrotic macrophage-induced collagen deposition in the alveoli (Wendisch et al., 2021). By day 67, the maximum lung volume gradually increased, reaching a value of 1.03 L. The corresponding CT on day 69 (Fig. 1C) demonstrates substantial improvements with most ground glass opacities cleared up, although some dilated airways can still be seen. By day 148 the maximum inhaled volume was 1.66 L with an A-a gradient of 60.1 mmHg. At a recent follow-up visit on day 301, the P_{tp}-V curve displayed a very significant change: a maximum effort of $P_{tp} < 50$ cmH_2O produced a V of 2.11 L. This near healthy lung mechanical behavior was supported by a near normal CT image (Fig. 1D).

The P_{tp}-V loops during spontaneous tidal breathing were also recorded (not shown), which were helpful in setting the NIV parameters. First, the lack of recruitment and reserve capacity between day 36 and 67 suggested no advantage of applying a high PEEP, which would have only stiffened the lung without improving gas exchange. Second, by examining the compliance of the lung, defined as the local slope of the P_{tp}-V relation, the conventional low tidal volume approach would not

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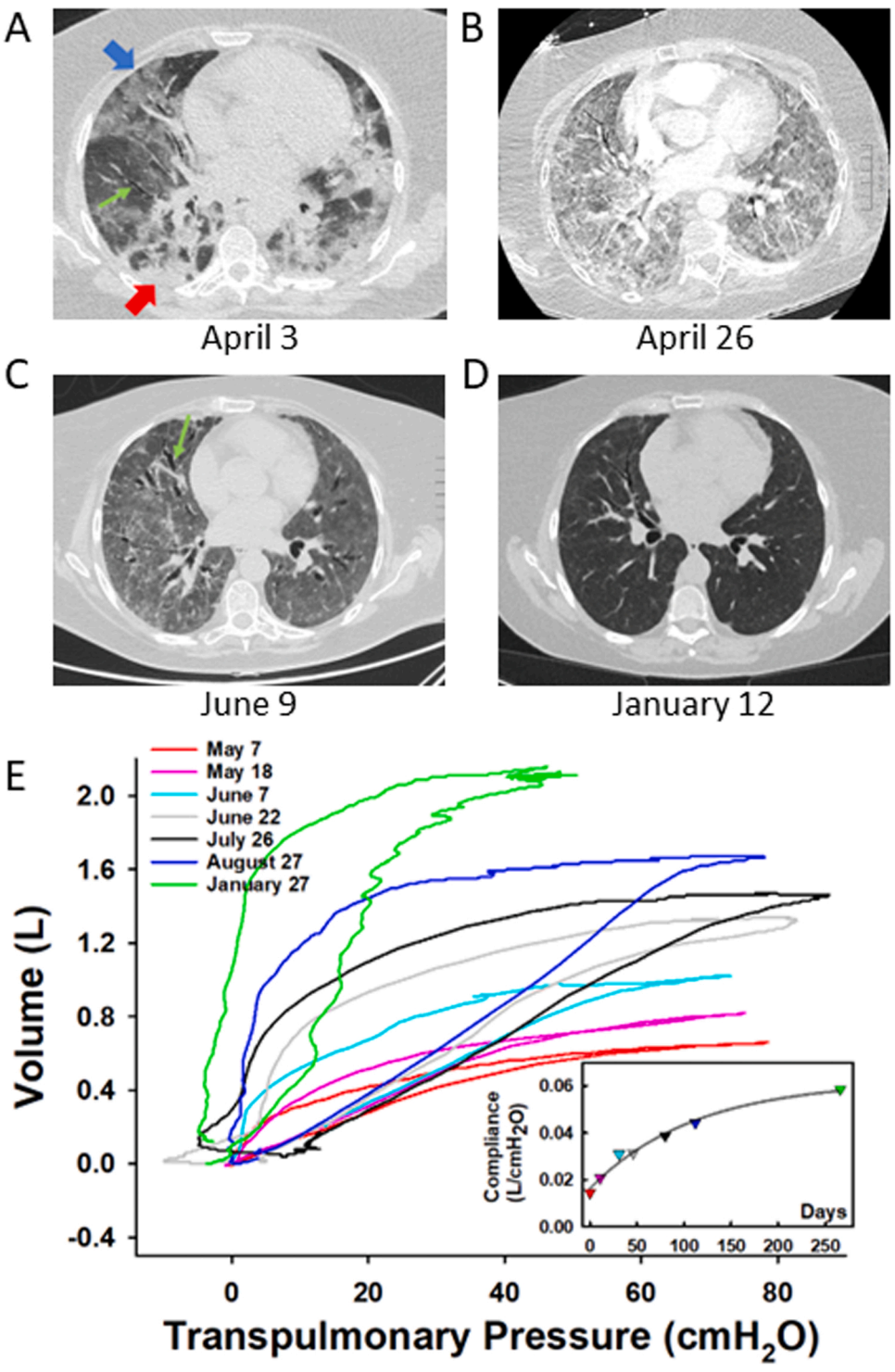

Fig. 1. CT images and lung mechanics of a female patient with COVID-19. (A) Image taken at the time of hospital admission (Day 1). Red, blue and green arrows mark regions of consolidation, ground-glass opacity, and airway dilation, respectively. (B) The patient was moved to the ICU (Day 25). The corresponding CT image (using contrast) shows massive bi-lateral ground-glass opacity throughout the lung. (C) The image on Day 69 shows substantial improvement in ground-glass opacity compared to the image on Day 25. (D) Nearly normal CT image 7 months later (Day 301). (E) Transpulmonary pressure-lung volume curves during the recovery of the patient post COVID-19 infection. Different colors correspond to measurements taken on different dates. Inset: Dynamic lung compliance during spontaneous breathing (triangles) and a nonlinear regression (solid line) as a function of the number of days from hospital admission.

have provided acceptable ventilation and oxygenation and would have increased pathological patient effort, possibly promoting P-SILI (Brochard et al., 2017). The dynamic lung compliance (C_{dyn}) was obtained during spontaneous breathing as the ratio of the volume inhaled and the pressure swing between end-inspiration and end-expiration. The time course of C_{dyn} (inset, Fig. 1E) reveals a substantial increase (3.6-fold between day 36 and 301). The improvements in lung elastic behavior were also accompanied by a gradual but substantial increase in the hysteresis loop of the P_{tp}-V curve, suggesting a stronger contribution of active surface tension to lung mechanics (Smith and Stamenovic, 1986). These results uniquely demonstrate how lung structure on CT images and lung function from the P_{tp}-V curves evolve during the ten-month long recovery of this patient.

In conclusion, the conventional protective ventilation protocol in acute respiratory distress syndrome is to apply high PEEP and low tidal volume to maintain an open lung without overstretching the tissues (Amato et al., 1998, Girard and Bernard, 2007). The effects of high PEEP on lung physiology are complex (Cronin et al., 2021) and may not be beneficial in COVID-19 patients (Bhatt et al., 2021). The case reported here demonstrates that application of higher PEEP or invasive ventilation enforcing lung protective parameters would not have been feasible in the recovery phase because even the small tidal volumes require large

P_{tp} changes. The tailored NIV application guided by lung mechanics helped optimize patient WOB and minimize further lung injury avoiding possible complications due to long-term invasive treatment. This in turn resulted in a well-tolerated long-term NIV treatment allowing lung healing while stimulating spontaneous breathing during the recovery of the patient from an extreme case of severe COVID-19 pneumonia.

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Competing interests

The authors have no competing interests to disclose.

Consent for publication

Written informed consent for publication of the clinical details and images was obtained from the patient.

Author contributions

AL designed and carried out measurements and wrote the manuscript; SB, EP, LV and JG interpreted data and took part in writing the manuscript; BS analyzed data and wrote the manuscript. All authors approved the final version of the manuscript.

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