IDCases 36 (2024) e01956

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

Secondary pneumomediastinum in COVID-19 patient: A case managed with VV-ECMO

Gianlorenzo Golino [a,b,*,1], Edoardo Forin [a,b], Elisa Boni [a,b], Marina Martin [a,b], Guido Perbellini [a,b], Veronica Rizzello [a,b], Anna Toniolo [a,b], Vinicio Danzi [a,b]

[a] Ospedale San Bortolo, Vicenza, Italy
[b] Department of Anesthesia and Intensive Care, Vicenza 36100, Italy

ARTICLE INFO

Keywords:
Pneumomediastinum
COVID-19
Extracorporeal membrane oxygenation
ECMO Macklin effect
Air leak
Mechanical power

ABSTRACT

Air leak syndrome, including pneumomediastinum (PM), pneumopericardium, pneumothorax, or subcutaneous emphysema, is primarily caused by chest trauma, cardiothoracic surgery, esophageal perforation, and mechanical ventilation. Secondary pneumomediastinum (SP) is a rare complication, with a much lower incidence reported in patients with coronavirus disease 2019 (COVID-19). Our patient was a 44-year-old nonsmoker male with a previous history of obesity (Body Mass Index [BMI] 35 kg/m^2), hyperthyroidism, hypokinetic cardiopathy and atrial fibrillation in treatment with flecainide, who presented to the emergency department with 6 days of fever, cough, dyspnea, and respiratory distress. The COVID-19 diagnosis was confirmed based on a polymerase chain reaction (PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). After initiation of mechanical ventilation, a chest computed tomography (CT) on the first day revealed bilateral multifocal ground-glass opacities, consolidation and an extensive SP and pneumoperitoneum. Our therapeutic strategy was initiation of veno-venous extracorporeal membrane oxygenation (VV-ECMO) as a bridge to recovery after positioning 2 drains (mediastinal and pleural), for both oxygenation and carbon dioxide clearance, to allow protective and ultra-protective ventilation to limit ventilator-induced lung injury (VILI) and the intensity of mechanical power for lung recovery. After another chest CT scan which showed a clear reduction of the PM, 2 pronation and neuromuscular relaxation cycles were also required, with improvement of gas exchange and respiratory mechanics. On the 15th day, lung function recovered and the patient was then weaned from VV-ECMO, and ultimately made a good recovery and was discharged. In conclusion, SP may be a reflection of extensive alveolar damage and should be considered as a potential predictive factor for adverse outcome in critically ill SARS-CoV2 patients.

Introduction

In December 2019, a novel respiratory virus that originated from Wuhan (China), later named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was found to be the cause of illness called coronavirus disease 2019 (COVID-19). It was recognised as a global public health emergency and SARS-CoV-2 was declared a pandemic on March 11th, 2020 [1].

Hypoxaemic respiratory failure leading to acute respiratory distress syndrome (ARDS) is the most frequent complication of COVID-19 [2]. The characteristic computed tomography (CT) scan findings of COVID-19 pneumonia are mainly bilateral, lower lobe, and peripheral distributed ground-glass opacities. Pneumothorax and pneumomediastinum (PM) are rare findings [3].

Invasive positive pressure ventilation (IPPV) and non invasive PPV are life-saving rescue treatments for COVID-19 ARDS. On the other hand, 1–2% of patients develop barotrauma while receiving PPV [4], due to increased intra-alveolar pressure, high tidal volume or intrinsic positive end-expiratory pressure (PEEPi), leading to dynamic hyperinflation [5].

Alveolar air leak, characterized by air passage into the mediastinum or pleural space via bronchovascular sheaths following ruptured alveoli, has been described in COVID-19 patients mostly after invasive ventilation [6].

* Correspondence to: San Bortolo Hospital, Vicenza, Italy.
E-mail address: gianlorenzo.golino@aulss8.veneto.it (G. Golino).
[1] Department of Anesthesia and Intensive Care, Viale F. Rodolfi, 37, Vicenza, 36100, Italy.

https://doi.org/10.1016/j.idcr.2024.e01956
Received 1 November 2023; Received in revised form 10 March 2024; Accepted 14 April 2024
Available online 15 April 2024

We present a case of a patient with COVID-19 pneumonia, who developed secondary pneumomediastinum (SP) and subcutaneous chest wall emphysema, successfully managed with veno-venous extracorporeal membrane oxygenation (VV-ECMO). In particular, we emphasize the importance of reducing mechanical power (MP) with initiation of veno-venous extracorporeal membrane oxygenation (VV-ECMO) as a bridge to recovery, for both oxygenation and carbon dioxide clearance, to allow protective and ultra-protective ventilation to limit ventilator-induced lung injury (VILI), as demonstrated by an International Multicenter Prospective Cohort Trial of Schmidt et al. [7].

Case presentation

A 44-year-old nonsmoker male with a previous history of obesity (body mass index [BMI] of 35 kg/m^2), hyperthyroidism, hypokinetic cardiopathy and atrial fibrillation which was treated with 2 electrical cardioversion, in treatment with flecainide. He presented to the emergency department with 6 days of fever, cough, dyspnea, and respiratory distress, and subsequently was transferred to the Intensive Care Unit (ICU) after 1 day on medical respiratory unit.

Laboratory parameters at admission to our unit were the following: leukocytes 9/nl, C-reactive protein (CRP) 29.6 mg/dl, procalcitonin (PCT) 0.97 ng/mL, lactic dehydrogenase LDH 565 U/l, and D-dimers 769 mg/l.

At the presentation, he was ill-appearing and suffering from respiratory distress with oxygen saturation of 80% on a non-rebreather mask at 12 L/min. His respiratory rate was 42 breaths/min, pulse rate was 110 beats/min, temperature 36.1 °C, and blood pressure 150/70 mmHg. After a trial of non-invasive ventilation for 3 h, the patient's respiratory distress worsened requiring intubation with mechanical ventilation (MV) settled in Pressure Regulated Volume Control (PRVC).

On examination, course bilateral respiratory sounds alongside chest wall crepitation and subcutaneous emphysema were detected. The initial chest X-ray revealed bilateral air space consolidation opacities and PM. After 24 h management with amoxicillin/clavulanic acid was empirically started and intravenous methylprednisolone (40 mg every 12 h).

The patient underwent cervical, chest and abdominal angio-TC scan, that demonstrated bilateral multifocal ground-glass opacities and consolidation, extensive SP, free air in the abdomen and right-sided subcutaneous emphysema extending from mid-chest up to cervical region (Fig. 1).

After multidisciplinary evaluation with general and cardiac surgeons, on the 3th day it was decided to place 2 chest drains in the operative room (mediastinal and pleural) with aspiration treatment.

Due to refractory hypoxemia, he was deemed a candidate for VV-ECMO as a bridge to recovery.

VV-ECMO cannulation was done on day 4 percutaneously under echocardiography guidance by a cardiovascular surgeon wearing full personal protective equipment. Blood drainage was achieved with a large cannula (25 Fr multi-stage Maquet inflow) inserted into the common femoral vein, and returned through the right internal jugular vein (22 Fr Euroset outflow cannula).

Pump speed was adjusted to obtain optimal blood-oxygen saturation. Cannula positioning was verified by cardiac ultrasonography and chest X-ray. Platelets, D-dimer, fibrinogen, prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR) and antithrombin were monitored daily. We titrated anticoagulation of VV-ECMO with unfractionated heparin on aPTT time and thromboelastography R-time.

The hemoglobin threshold for red blood cell transfusion was < 8 g/dL (or ≤ 9 g/dL when hypoxaemia persisted); platelet transfusions were discouraged except for severe thrombocytopenia ($<50 \times 10^9$ cells per L) or thrombocytopenia of more than 100×10^9 cells per L with bleeding.

We also perform a bronchoscopy to exclude a possible undiagnosed tracheal damage. To enhance protection against ventilator-induced lung injury (VILI), protective and ultraprotective MV on VV-ECMO was used, by targeting lower MP delivered to the lungs and lower tidal volume, respiratory rate, and airway and driving pressures.

After another chest CT scan (Fig. 1) which showed a clear reduction

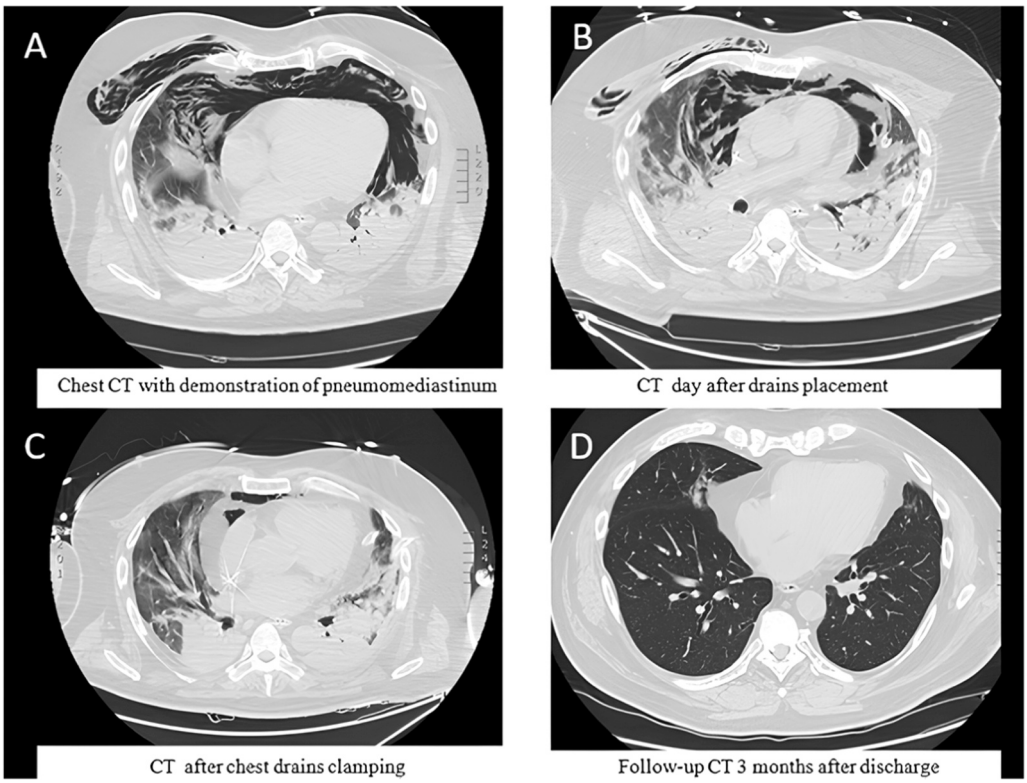

Fig. 1. A. Chest CT with demonstration of PM. B. CT on the day after drains placement. C. CT after chest drains clamping. D. Follow-up CT 3 months after discharge.

of the PM, 2 pronation and neuromuscular relaxation cycles were also required, with improvement of gas exchange and respiratory mechanics. Drains were clamped on the 11th and removed on the 13th day.

VV-ECMO weaning was started on the 11th day after ECMO initiation because chest X-ray findings and the patient's respiratory parameters progressively improved. The extracorporeal blood flow (BF) was reduced to 1.4 L/min, and the sweep gas flow (SGF) was reduced to 0 L/min (Fraction of inspired oxygen [FiO2] 0.21), while the ventilator was set at PRVC mode with FiO2 0.5, positive end-expiratory pressure (PEEP) 12 cmH_2O and Respiratory Rate (RR) 12/min. We confirmed if the patient could maintain oxygenation and ventilation for 5 h. Decannulation was performed on the 12th day after VV-ECMO initiation.

Thereafter, the patient was successfully extubated on the 20th and transferred to the medical respiratory unit on 22th day for respiratory improvement.

Three months after discharge the CT's follow-up showed an absent consolidation and no PM/subcutaneous emphysema (Fig. 1).

Discussion

PM, a disease defined by the presence of air in the mediastinum, was first reported in 1819 by Laennec and since 1939 when Hammaan described different causes of spontaneous pneumomediastinum [8] several classifications were created.

Kouritas et al., in 2015, classified PM in primary (spontaneous) and secondary (iatrogenic, traumatic, non-traumatic) [9]. Primary PM is common in young adults without a previous history of invasive procedures or trauma, but is a rare diagnosis; men represent 76% of the cases [9,10]. SP counts barotrauma as one of the causes, in particular for patients with severe acute respiratory syndrome and in those needing MV [8].

In 1944 Macklin described a pathophysiological mechanism, known as Macklin Effect: the rupture of the alveolar tree with increased intra alveolar pressure (cough, vomiting, vigorous activity, shouting or inhalation of an illicit drugs) leading to rupture of the alveoli and releasing of air that dissects the peribronchovascular sheath into the mediastinum [11], and finally pulmonary interstitial emphysema.

It has been estimated that only about 1% to 2% of COVID-19 patients develop pneumothorax [4]. Although pneumothorax is a known complication of COVID-19 patients necessitating MV, only a few cases of spontaneous pneumothorax and PM have been described during the coronavirus pandemic, as uncommon, life-threatening presentations of the disease [12].

CT is the gold standard for the diagnostic algorithm of these conditions, as it shows high sensitivity and a high negative predictive value [13].

In literature there is another case of pneumothorax and PM managed successfully with VV-ECMO implantation [14].

Our patient with COVID-19 ARDS complicated by SP, likely had increased intrathoracic pressure generated from MV compounded with fragile alveolar walls due to diffuse alveolar cell damage from SARS-CoV-2 preference to infect alveolar type II cells [15,16].

Furthermore, it has also been speculated that the use of steroids in the management of patients with COVID-19 ARDS, contributed to weakening the pulmonary interstitial tissue leading to alveolar air leakage [17].

Mediastinal and intrapleural chest drains were inserted for worsening PM and respiratory compromise.

According with Extracorporeal Membrane Oxygenation for COVID-19: Updated 2021 Guidelines from the Extracorporeal Life Support Organization (ELSO) [18], we evaluated indications and contraindications to VV-ECMO (Table 1). Our patient was affected by COVID-19 ARDS with a PaO2/FiO2 ratio < 150 complicated by PM (severe air leak syndrome, indication to start extracorporeal life support [ECLS]) with a Murray score of 11. There were no absolute contraindications to ECLS.

The significant treatment goals for patients with COVID-19 pneumonia-associated ARDS is to maintain blood oxygenation and carbon dioxide (CO2) removal; this must be done maintaining low airway plateau pressure to limit VILI.

Table 1
Indications/contraindications for adults VV-ECMO.

Indications	Contraindications (Relative)
Hypoxemic respiratory failure (PaO2/FiO2 <80 mmHg), after optimal medical management, including a trial of prone positioning.	Central nervous system hemorrhage
Hypercapnic respiratory failure (pH <7.25), despite optimal conventional mechanical ventilation (respiratory rate 35 bpm and plateau pressure [Pplat] $\leq$ 30 cmH_2O).	Significant central nervous system injury
Ventilatory support as a bridge to lung transplantation or primary graft dysfunction following lung transplant.	Irreversible central nervous system pathology
ARDS (viral/bacterial pneumonia, aspiration)	Systemic bleeding
Acute eosinophilic pneumonia	Contraindications to anticoagulation
Pulmonary hemorrhage	Immunosuppression
Severe asthma	Older age (increasing risk of death with increasing age, no threshold is established)
Thoracic trauma	Mechanical ventilation for more than 7 days with Pplat > 30 cmH_2O and FiO2 > 90%
Severe inhalational injury	
Large bronchopleural fistula or severe air leak syndrome	
Hypothermia < 28 °C	

Therefore, we immediately initiated VV-ECMO and switched to ultra protective ventilation. Although the timing for initiation of V-V ECMO in severe respiratory failure remains debatable, we decided to start promptly because a previous study observed that increased pre-ECMO ventilation duration is associated with worse outcomes [19].

Experimental and clinical data suggest that VILI may still occur despite lung-protective ventilation strategy [20–22] including low Vt (4–6 mL/kg) of predicted body weight (PBW), low plateau pressure (Pplat) below 28 cm H_2O and moderate positive end-expiratory pressure (PEEP). Prolonged and repeated prone position which is recommended in moderate to severe ARDS before VV-ECMO [23,24] mitigates VILI by promoting a more homogeneous distribution of total lung stress and strain [25] and by reducing biotrauma [26].

Prospective randomized studies have suggested a possible interest to target positive expiratory transpulmonary pressure (PL) by PEEP setting [27] and using an ultra-protective ventilation with both reduced tidal volume (Vt) and driving pressure [28,29]. Of note, retrospective data suggest a potential benefit of continuation or initiation of prone position in VV-ECMO patients [30,31].

More recently, the inspiratory flow and RR have also been recognized as possible factors promoting VILI [32–36]. To combine all these elements in a single physical variable, Gattinoni et al. proposed the concept of MP to estimate the contribution of the various ventilator-related causes of lung injury, defined as the amount of energy delivered to the respiratory system over time, which is the product of the absolute proximal airway pressure and related changes in volume and RR [37].

A ventilation strategy used in the ECMO arm of the EOLIA trial combined Pplat reduction $\leq$ 24 cmH_2O, driving pressure $\leq$ 14 cmH_2O while PEEP is maintained $\geq$ 10 cmH_2O [37]. Since this trial, physiological studies have suggested that decreasing the MP of MV during ECMO might be beneficial [21,30,38].

Our hypothesis was to perform an ultra-lung-protective ventilation strategy including a very reduced Vt (1–2 mL/kg of predicted body weight), a low RR (5–10 cycles/min) and the use of prone position to reduce MP and biotrauma and therefore enhance VILI prevention.

Table 2
PCV Pressure control ventilation, VCV Volume control ventilation, PRVC Pressure-regulated volume control, FiO2 Fraction of inspired oxygen, PIP Peak inspiratory pressure (cmH_2O), PEEP Positive end-expiratory pressure (cmH_2O), RR Respiratory rate (/min), TV Tidal volume (mL), PaO2 Partial pressure of oxygen in arterial blood (mmHg), PaCO2 Partial pressure of carbon dioxide in arterial blood (mmHg).

	Day 2	Chest Drains	ECMO start	Drains clamped	ECMO stop
Mode	VCV	PCV	PRVC	PRVC	PRVC
FiO2 (%)	0.75	0.9	0.5	0.5	0.5
PEEP	12	10	11	10	12
RR	20	20	16	16	12
TV	580	570	220	480	540
PIP/PS	30	28	24	26	27
pH	7.44	7.47	7.45	7.47	7.439
PaO2	68.8	68.5	91	110	131.1
PaCO2	42.4	43.4	45	30	39.4
SaO2 (%)	93.3	94.5	95.7	97.2	97.4

Table 2.

MP values were calculated as proposed by Chiumello et al.: 0.098·RR·Vt·[PIP − 0.5 (Pplat-PEEP)] for Volume Controlled Ventilation and 0.098·RR·Vt·[PEEP + pressure above PEEP] for Pressure Controlled Ventilation. In these equations, 0.098 is the conversion factor for converting from units of cmH_2O·L/min to J/min, unit of Vt is liter, and units of airway pressures and PEEP is cmH_2O [37].

As depicted in Fig. 2, this strategy has allowed us to reduce MP during the ICU stay, in order to prevent exacerbation of PM throughout the VV-ECMO period.

The energy required to move the lung from its functional residual capacity (FRC) to the end-inspiratory volume, is the sum of the static (due to PEEP) and the elastic component (due to Vt). In our patient with ECMO, we reduce mainly the elastic component with the protective and ultra-protective ventilation.

MP is a variable that can be included in any ventilator to guide the safety of MV, and including the effects of respiratory rate, flow and PEEP, gives a much more comprehensive view on the ventilator-related causes of VILI.

Conclusion

To the best of our knowledge, this is the first case reported in literature of COVID-19 pneumonia with worst Murray Score in an obese patient complicated with SP successfully managed with VV-ECMO, that was an effective method to allow protective and ultra-protective ventilation and reduce barotrauma and MP, in a bridge to recovery strategy.

Further research will be needed for studying the bedside calculation of MP, for a tailored approach to patients in severe respiratory failure.

Ethical approval

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient gave his consent for publication of the report.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

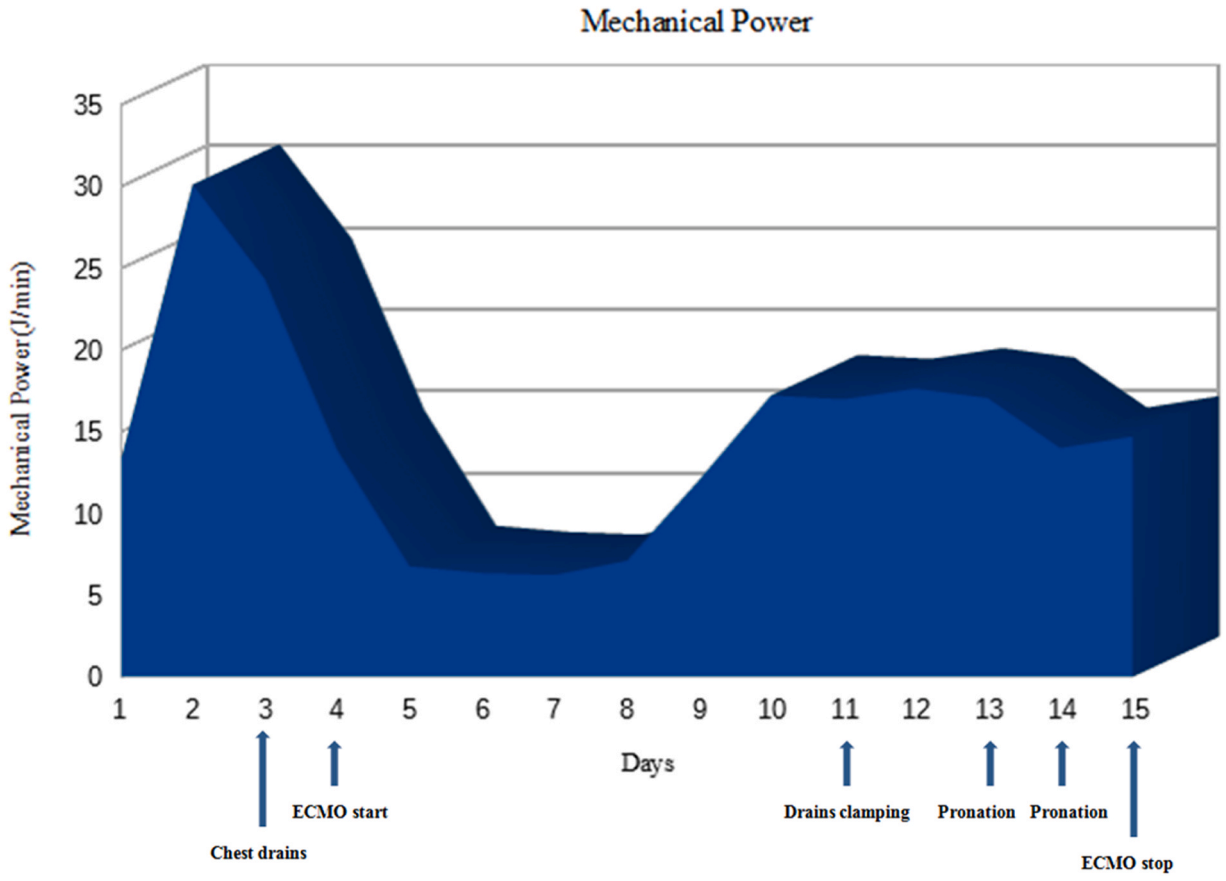

Fig. 2. Mechanical power calculated during ICU stay.

CRediT authorship contribution statement

Vinicio Danzi: Supervision, Validation. **Anna Toniolo:** Writing – review & editing. **Veronica Rizzello:** Writing – original draft, Writing – review & editing. **Guido Perbellini:** Conceptualization, Writing – review & editing. **Marina Martin:** Writing – review & editing. **Elisa Boni:** Writing – review & editing. **Edoardo Forin:** Writing – original draft, Writing – review & editing. **Gianlorenzo Golino:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors do not have any conflicts of interest to disclose.

Data Availability

Not applicable.

Acknowledgement

The authors thank all the members of the ECMO team of San Bortolo Hospital of Vicenza.

Authors' contributions

G. Golino wrote the first draft of the manuscript and provided revisions; V. Danzi critically revised the manuscript. All the authors read and approved the final version of the manuscript.

Author agreement statement

We the undersigned declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We understand that the Corresponding Author is the sole contact for the Editorial process. He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

References

[1] Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Bio-Med Atenei Parm 2020;91:157–60.
[2] Cascella M, et al. Features, Evaluation and Treatment Coronavirus (COVID-19). Treasure Island, FL: StatPearls; 2020.
[3] Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. Am J Roentgenol 2020;215:87–93.
[4] Wang W, et al. COVID-19 with spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema. J Travel Med 2020;27(5):taaa062. https://doi.org/10.1093/jtm/taaa062.
[5] Zhang XY, et al. Diagnosis and prognosis of spontaneous pneumomediastinum in eighteen children. Chin J Pediatr 2013;51:849–51.
[6] Martinelli AW, Ingle T, Newman J, Nadeem I, Jackson K, Lane ND, et al. COVID-19 and pneumothorax: a multicentre retrospective case series. Eur Respir J 2020;56 (5). https://doi.org/10.1183/13993003.02697-2020.
[7] Schmidt M, Pham T, Arcadipane A, Agerstrand C, Ohshimo S, Pellegrino V, et al. Mechanical ventilation management during extracorporeal membrane oxygenation for acute respiratory distress syndrome: an international multicenter prospective cohort. Am J Respir Crit Care Med 2019;200:1002–12.
[8] Mousa S, Edriss H. Pneumomediastinum secondary to invasive and non-invasive mechanical ventilation. Southwest Respir Crit Care Chron 2019;7:36–42.
[9] Kouritas VK, Papagiannopoulos K, Lazaridis G, et al. Pneumomediastinum. J Thorac Dis 2015;7:S44–9.
[10] Okada M, Adachi H, Shibuya Y, et al. Diagnosis and treatment of patients with spontaneous pneumomediastinum. Respir Invest 2014;52:36–40.
[11] Macklin MT, Macklin CC. Malignant interstitial emphysema of the lungs and mediastinum as an important occult complication in many respiratory diseases and other conditions: interpretation of the clinical literature in the light of laboratory experiment. Medicine 1944;23:281–358.
[12] Quincho-Lopez A, Quincho-Lopez DL, Hurtado-Medina FD. Case report: pneumothorax and pneumomediastinum as uncommon complications of COVID-19 pneumonia-literature review. Am J Trop Med Hyg 2020;103:1170–6.
[13] Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020;296:E32–40.
[14] Kohara J, Kai S, Hashimoto K, Takatani Y, Tanabe N, Hamada S, et al. Successful lung-protective ventilatory management during the VV-ECMO in a severe COVID-19 pneumonia patient with extensive pneumomediastinum and subcutaneous emphysema: a case report. JA Clin Rep 2022.
[15] Mason RJ. Pathogenesis of COVID-19 from a cell biologic perspective. Eur Respir J 2020;55(4):2000607. https://doi.org/10.1183/13993003.00607-2020.
[16] Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420–2. https://doi.org/10.1016/S2213-2600(20)30076-X.
[17] Hazariwala V, Hadid H, Kirsch D, Big C. Spontaneous pneumomediastinum, pneumopericardium, pneumothorax and subcutaneous emphysema in patients with COVID-19 pneumonia, a case report. J Cardiothorac Surg 2020;15(1):301. doi: 10.1186/s13019- 020- 01308- 7.
[18] Extracorporeal Life Support Organization: ECMO and ECLS > Resources > Guidelines. Available at: https://www.elso.org/ Resources/Guidelines.aspx. Accessed December 27, 2019.
[19] Liu X, et al. Survival predictors for severe ARDS patients treated with extracorporeal membrane oxygenation: a retrospective study in China. PLoS One 2016;11(6):e0158061.
[20] Frank JA, Gutierrez JA, Jones KD, Allen L, Dobbs L. Low tidal volume reduces epithelial and endothelial injury in acid-injured rat lungs. Am J Respir Crit Care Med 2002;165:242–9.
[21] Araos J, Alegria L, Garcia P, Cruces P, Soto D, Erranz B, et al. Near-apneic ventilation decreases lung injury and fibroproliferation in an acute respiratory distress syndrome model with extracorporeal membrane oxygenation. Am J Respir Crit Care Med 2019;199:603–12.
[22] Terragni PP, Rosboch G, et al. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med 2007;175:160–6.
[23] Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368:2159–68.
[24] Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. Mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2017;195:1253–63.
[25] Gattinoni L, Taccone P, Carlesso E, Marini JJ. Prone position in acute respiratory distress syndrome: rationale, indications, and limits. Am J Respir Crit Care Med 2013;188:1286–93.
[26] Papazian L, Gainnier M, et al. Comparison of prone positioning and high-frequency oscillatory ventilation in patients with acute respiratory distress syndrome. Crit Care Med 2005;33:2162–71.
[27] Wang R, Sun B, Li X, Tang X, He H, Li Y, et al. Mechanical ventilation strategy guided by transpulmonary pressure in severe acute respiratory distress syndrome treated with venovenous extracorporeal membrane oxygenation. Crit Care Med 2020;48:1280–8.
[28] Rozencwajg S, Guihot A, Franchineau G, Lescroat M, Bréchot N, Hékimian G, et al. Ultra-protective ventilation reduces biotrauma in patients on venovenous extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. Crit Care Med 2019;47:1505–12.
[29] Del Sorbo L, Goffi A, Tomlinson G, Pettenuzzo T, Facchin F, Vendramin A, et al. Effect of driving pressure change during extracorporeal membrane oxygenation in adults with acute respiratory distress syndrome: a randomized crossover physiologic study. Crit Care Med 2020;48:1771–8.
[30] Giani M, Rezoagli E, Guervilly C, Rilinger J, Duburcq T, Petit M, et al. Prone positioning during venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a pooled individual patient data analysis. Crit Care 2020;26:8. https:// doi. org/ 10. 1186/ s13054- 021- 03879-w. PMID: 34986 895; PMCID: PMC87 31201.
[31] Papazian L, Schmidt M, et al. Effect of prone positioning on survival in adult patients receiving venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis. Intensive Care Med 2022;48(3):270–80.
[32] Santer P, Wachtendorf LJ, et al. Mechanical power during general anesthesia and postoperative respiratory failure: a multicenter retrospective cohort study. Anesthesiology 2022;137:41–54.
[33] gurlu O, Küçük M, Bilgin M, Sizlan F, Yanarate¸s A, Eksert O, et al. A. Pressure-controlled vs. volume controlled ventilation during laparoscopic gynecologic surgery. J Minim Invasive Gynecol 2010;17:295–300.
[34] Lee JM, Lee SK, Rhim CC, Seo KH, Han M, Kim SY, et al. Comparison of volume-controlled, pressure-controlled, and pressure-controlled volume-guaranteed ventilation during robot-assisted laparoscopic gynecologic surgery in the Trendelenburg position. Int J Med Sci 2020;17:2728–34.
[35] Schick, Dusse V, Eckardt F, et al. Comparison of volume-guaranteed or -targeted, pressure-controlled ventilation with volume-controlled ventilation during elective surgery: a systematic review and meta-analysis. J Clin Med 2021;10:1276.
[36] Yao W, Yang M, Cheng Q, Shan S, Yang B, Han Q, et al. Effect of pressure-controlled ventilation-volume guaranteed on one-lung ventilation in elderly

patients undergoing thoracotomy. Med Sci Monit Int Med J Exp Clin Res 2020;26: e921417-1–921417-7.
[37] Chiumello D, Gotti M, Guanziroli M, Formenti P, Umbrello M, Pasticci I, et al. Bedside calculation of mechanical power during volume- and pressure-controlled mechanical ventilation. Crit Care 2020;24:417.
[38] https://clinicaltrials.gov/ct2/show/NCT04607551