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LETTER

Comparison of radiographic pneumothorax and pneumomediastinum in COVID-19 vs. non-COVID-19 acute respiratory distress syndrome

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Dear Editor,

Pneumothorax and pneumomediastinum may complicate acute respiratory distress syndrome (ARDS). Early studies in ARDS caused by coronavirus disease 2019 (COVID-19) suggested increased pneumothorax incidence but lacked relevant controls [1, 2]. We investigated whether COVID-19 ARDS is associated with more radiographic pneumothorax and/or pneumomediastinum than pre-pandemic ARDS and whether pneumothorax/pneumomediastinum in COVID-19 ARDS is associated with worse outcomes or differing treatments.

This retrospective cohort study included adult ARDS patients admitted between 2017 and 2021 to a 23-hospital system in the Intermountain West. We abstracted data from the electronic health record and used natural language processing to identify radiographic pneumothorax and/or pneumomediastinum [3, 4]. We performed bivariate and adjusted analyses to compare patients with pre-pandemic ARDS (2017–2020) to patients with a positive SARS-CoV-2 polymerase chain reaction (PCR) result proximate to ARDS (2020–2021) (see also Supplemental Methods).

Comparing 2,211 patients with COVID-19 ARDS and 5522 with pre-pandemic ARDS (Table 1 and Supplemental Fig. 1), unadjusted incidence of pneumothorax/pneumomediastinum was similar (24% vs. 22.5%, $p<0.148$). After adjustment, pneumothorax/pneumomediastinum risk was significantly higher in COVID-19 vs. pre-pandemic ARDS (adjusted odds ratio 1.31, 95% CI 1.13–1.52, $p<0.001$). COVID-19 ARDS patients had significantly higher rates of pneumomediastinum but not pneumothorax in unadjusted and adjusted analyses (Table 1 and Supplemental Table 2). Compared to COVID-19 ARDS, chest tube placement for pre-pandemic pneumothorax patients was more frequent (52.1% vs. 38.2%, $p<0.001$), occurred earlier (− 0.4 vs. 1.3 days, $p<0.001$) and remained in place longer (9.9 days vs. 7 days, $p<0.001$).

Mortality rates in COVID-19 ARDS were higher than pre-pandemic ARDS (39.4% vs. 28.5% $p<0.001$). Among COVID-19 ARDS patients, we observed higher 30-day mortality rates with pneumothorax/pneumomediastinum (49.5% vs. 36.2%, $p<0.001$), while we observed a lower mortality in pre-pandemic ARDS patients with pneumothorax/pneumomediastinum (24.8% vs. 29.5%, $p<0.001$). Adjusted analyses yielded similar results (Supplemental Table 3).

Prior to pneumothorax/pneumomediastinum, both COVID-19 and pre-pandemic ARDS cohorts had similar receipt of invasive mechanical ventilation (77% vs. 74%, $p=0.17$). COVID-19 patients received higher maximum PEEP (16 vs. 10 mmHg, $p<0.001$). The median duration of invasive ventilation prior to pneumothorax/pneumomediastinum was much longer in the COVID-19 patients (2 vs. 0.3 days, $p<0.001$; Supplemental Fig. 2), as was time from admission until pneumothorax/pneumomediastinum (7.3 vs. 1.3 days, $p<0.001$).

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Study strengths include comparison of large, multihospital COVID-19 and control ARDS cohorts. Limitations include the possibility of unmeasured confounding and potentially counting radiographic pneumothorax/pneumomediastinum events that were "clinically insignificant" or not due to acute lung injury. We note a substantially higher rate of pneumothorax/pneumomediastinum compared with other published cohorts (Supplemental Table 5). Our detection is more sensitive than clinically reported as all events are included, not just pneumothorax/pneumomediastinum > 2 cm or presence in clinical notes, which may limit generalizability. The relationships between radiographic and clinically significant pneumothorax/pneumomediastinum, pneumothorax/pneumomediastinum risk factors (including use of guideline-endorsed "high positive end-expiratory pressure (PEEP)" ventilation [5]), and pneumothorax management warrant further study.

In conclusion, COVID-19 ARDS patients experienced similar rates of radiographic pneumothorax but more pneumomediastinum. Chest tubes were used less frequently and placed later in COVID-19 ARDS than in pre-pandemic ARDS. Radiographic pneumothorax/

Table 1 Summary demographic and outcome data presented as n (%) or median [IQR]

	Overall		*p*	No pneumothorax or pneumomediastinum		Pneumothorax and/or pneumomediastinum		*p*
	COVID-19	Prepandemic		COVID-19	Prepandemic	COVID-19	Prepandemic	
n	2211	5522		1680	4282	531	1240	
Female	810 (36.6)	2377 (43)	< 0.001	641 (38.2)	1913 (44.7)	169 (31.8)	464 (37.4)	< 0.001
Age	61 [49, 70]	63 [51, 74]	< 0.001	61 [49, 71]	64 [52, 74]	61 [49, 69]	61 [46, 71]	< 0.001
ARDS Qualifying Diagnostic Group (more than one category possible)								
Trauma	130 (5.9)	1199 (21.7)	< 0.001	89 (5.3)	742 (17.3)	41 (7.7)	457 (36.9)	< 0.001
Pneumonia	2132 (96.4)	2689 (48.7)	< 0.001	1621 (96.5)	2124 (49.6)	511 (96.2)	565 (45.6)	< 0.001
Sepsis	37 (1.7)	1208 (21.9)	< 0.001	26 (1.5)	985 (23)	11 (2.1)	223 (18)	< 0.001
Aspiration	95 (4.3)	1390 (25.2)	< 0.001	70 (4.2)	1123 (26.2)	25 (4.7)	267 (21.5)	< 0.001
Shock	228 (10.3)	787 (14.3)	< 0.001	155 (9.2)	505 (11.8)	73 (13.7)	282 (22.7)	< 0.001
Acute pancreatitis	16 (0.7)	144 (2.6)	< 0.001	11 (0.7)	115 (2.7)	5 (0.9)	29 (2.3)	< 0.001
Overdose	15 (0.7)	336 (6.1)	< 0.001	14 (0.8)	288 (6.7)	1 (0.2)	48 (3.9)	< 0.001
Worst ARDS severity (first 7 days)								
Mild	38 (1.7)	955 (17.3)	< 0.001	32 (1.9)	794 (18.5)	6 (1.1)	161 (13)	< 0.001
Moderate	232 (10.5)	2581 (46.7)		194 (11.5)	2045 (47.8)	38 (7.2)	536 (43.2)	
Severe	1941 (87.8)	1986 (36)		1454 (86.5)	1443 (33.7)	487 (91.7)	543 (43.8)	
Hospital Day 1 Lowest P/F Ratio	78.1 [61.7, 118.9]	148.6 [96.7, 204.8]	< 0.001	79.4 [62.9, 124.1]	148.4 [96.8, 203.5]	74.4 [60.8, 101.5]	149.2 [96.2, 212.9]	< 0.001
Hospital day 1 SOFA Score	6 [4, 9]	8 [5, 11]	< 0.001	6 [4, 9]	8 [5, 11]	7 [4, 10]	8 [5, 11]	< 0.001
BMI	32.8 [28.4, 38.9]	28.9 [24.3, 35.4]	< 0.001	33.5 [28.5, 40.1]	29.2 [24.4, 35.9]	31.5 [27.5, 35.8]	28 [23.9, 34]	< 0.001
Weighted (von Walraven) Elixhauser comorbidity score	15 [7, 25]	23 [13, 32]	< 0.001	15 [6.5, 24]	23 [14, 32]	17 [10, 26]	22 [12, 32]	< 0.001
Days from admission until endotracheal Intubation	0.8 [0, 3.9]	0.1 [0, 1.3]	< 0.001	0.7 [0, 3.3]	0.1 [0, 1.1]	1.2 [0, 5.3]	0.3 [0, 1.8]	< 0.001
Maximum respiratory support on hospital day 1								
FiO_2	100 [66, 100]	76.5 [50, 100]	< 0.001	100 [66, 100]	74 [50, 100]	100 [70, 100]	81 [40, 100]	< 0.001
PEEP	14 [10, 18]	8 [7, 10]	< 0.001	14 [10, 18]	8 [7, 12]	15 [12, 18]	8 [7, 10]	< 0.001
Plateau pressure	29 [25, 32]	22 [18, 26]	< 0.001	29 [25, 32]	22 [18, 26]	29 [26, 33]	21 [17, 26]	< 0.001
Peak inspiratory pressure	31 [21, 36]	26 [20, 32]	< 0.001	30 [21, 36]	25 [19, 32]	33 [23, 37]	27 [21, 33]	< 0.001
Positive pressure ventilation	1281 (58)	4189 (76)	< 0.001	970 (57.8)	3306 (77.3)	311 (58.6)	883 (71.4)	< 0.001

Table 1 (continued)

	Overall		*p*	No pneumothorax or pneumomediastinum		Pneumothorax and/or pneumomediastinum		*p*
	COVID-19	Prepandemic		COVID-19	Prepandemic	COVID-19	Prepandemic	
Invasive mechanical ventilation	872 (39.5)	2902 (52.6)	< 0.001	639 (38.1)	2194 (51.3)	233 (43.9)	708 (57.3)	< 0.001
Outcomes								
Pneumomediastinum	288 (13)	188 (3.4)	< 0.001			288 (54.2)	188 (15.2)	< 0.001
Pneumothorax	448 (20.3)	1201 (21.7)	0.158			448 (84.4)	1201 (96.9)	< 0.001
Pneumothorax or pneumomediastinum	531 (24)	1240 (22.5)	0.148					
Days from admission until pneumothorax or pneumomediastinum	7.3 [2.9, 12.6]	1.3 [0.1, 5.1]	< 0.001			7.3 [2.9, 12.6]	1.3 [0.1, 5.1]	< 0.001
Hospital Length of Stay (days)	14.5 [9.5, 23.7]	9.2 [5.3, 15.4]	< 0.001	13.1 [8.9, 21]	8.3 [4.9, 13.6]	20.8 [12.8, 33.4]	13.9 [8.4, 21]	< 0.001
30 Day Mortality	871 (39.4)	1572 (28.5)	< 0.001	608 (36.2)	1265 (29.5)	263 (49.5)	307 (24.8)	< 0.001
ICU Length of Stay	10.4 [6, 18.4]	4.9 [2.5, 9.9]	< 0.001	9 [5.2, 15.2]	4.3 [2.2, 8.6]	17.1 [10.1, 27.3]	7.9 [4, 14.4]	< 0.001
Management of pneumothorax and/or pneumomediastinum								
Chest tube placed						203 (38.2)	646 (52.1)	< 0.001
Days from admission until chest tube placement						8.6 [3.9, 15.9]	0.9 [0.2, 3.8]	< 0.001
Duration of chest tube (days)						9.9 [4.9, 17]	7 [4.1, 11.5]	< 0.001
Treatment occurring prior to pneumothorax/pneumomediastinum								
Nasal canula utilized						228 (44)	598 (56.5)	< 0.001
High-flow nasal canula utilized						402 (77.6)	179 (16.9)	< 0.001
Non-invasive ventilation utilized						251 (48.5)	368 (34.8)	< 0.001
Invasive ventilation utilized						400 (77.2)	783 (74)	< 0.001
Positive pressure ventilation						481 (92.9)	918 (86.8)	< 0.001
Nasal canula days						0 [0, 0.9]	0.2 [0, 2]	< 0.001
High-flow nasal canula						0.6 [0, 3.5]	0 [0, 0]	< 0.001
Non-invasive ventilation						0 [0, 0.7]	0 [0, 0.3]	< 0.001
Invasive ventilation days						2 [0, 8.4]	0.3 [0, 2.6]	< 0.001
Maximum FiO_2						100 [100, 100]	100 [65.5, 100]	< 0.001
Maximum PEEP						16 [14, 20]	10 [8, 12]	< 0.001
Maximum plateau pressure						34 [30, 40]	24 [19, 30]	< 0.001
Maximum peak inspiratory pressure						38 [28, 45]	29 [23, 36]	< 0.001

pneumomediastinum in COVID-19 ARDS patients is associated with an increased mortality.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1007/s00134-022-06816-9.

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Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Daniel Knox. The first draft of the manuscript was written by Alex Brunhoeber and Daniel Knox and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability
To protect patient privacy and comply with relevant regulations, identified data are unavailable. Requests for deidentified data from qualified researchers with appropriate ethics board approvals and relevant data use agreements will be processed by the Intermountain Office of Research, officeofresearch@imail.org.

Declarations

Conflicts of interest
SMB chairs a DSMB for Hamilton Ventilators and has received research funding from National Institutes of Health, Department of Defense, and Centers for Disease Control and Prevention. IDP reports grant support from NIH, Centers from Disease Control and Prevention, Intermountain Research and Medical Foundation, and Janssen Pharmaceuticals, and payments to his institution for trial enrollment from Asahi Kasei Pharma and Regeneron. Otherwise no conflicts for any other authors.

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References

1. Belletti A, Todaro G, Valsecchi G et al (2021) Barotrauma in Coronavirus Disease 2019 patients undergoing invasive mechanical ventilation: a systematic literature review. Crit Care Med. https://doi.org/10.1097/CCM.0000000000005283
2. Shrestha DB, Sedhai YR, Budhathoki P et al (2022) Pulmonary barotrauma in COVID-19: a systematic review and meta-analysis. Ann Med Surg 73:103221. https://doi.org/10.1016/j.amsu.2021.103221
3. Afshar M, Joyce C, Oakey A et al (2018) A computable phenotype for acute respiratory distress syndrome using natural language processing and machine learning. AMIA Annu Symp Proc AMIA Symp 2018:157–165
4. Mayampurath A, Churpek MM, Su X et al (2020) External validation of an acute respiratory distress syndrome prediction model using radiology reports. Crit Care Med 48:e791–e798. https://doi.org/10.1097/CCM.0000000000004468
5. Fan E, Del Sorbo L, Goligher EC et al (2017) An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 195:1253–1263. https://doi.org/10.1164/rccm.201703-0548ST