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The Contribution of COVID-19 to Acute Respiratory Distress Syndrome-Related Mortality in the United States

Lavi Oud[a, c], John Garza[b]

To the Editor

Acute respiratory distress syndrome (ARDS) is the most common severe pulmonary complication of the coronavirus disease 2019 (COVID-19). Although considered earlier in the pandemic to represent a different clinical entity than non-COVID-19 ARDS [1], it is nevertheless estimated that ARDS is present in 75% of intensive care unit (ICU) patients with COVID-19 and in 90% of ICU non-survivors [2]. Importantly, autopsy data show that ARDS, as evidenced by findings of diffuse alveolar damage, is present either in all [3] or in the majority of decedents with COVID-19 [4].

The toll of pre-pandemic ARDS-related deaths in the United States was estimated at nearly 10,000/year [5]. With over 375,000 COVID-19-related deaths in the USA during the first year of the pandemic [6], the epidemiology of ARDS was likely transformed substantially [7]. Accurate accounting of the ARDS-related mortality burden during the COVID-19 pandemic can inform future preventive and interventional efforts, as well as health resource allocation. However, the impact of COVID-19 on ARDS-related mortality at a national level has not been quantified.

We used the National Center for Health Statistics (NCHS) Multiple Cause of Death data set, which is available through the Centers for Disease Control Wide-ranging Online Data for Epidemiological Research (CDC WONDER) website [8] to obtain mortality and population data. The mortality data in NCHS are based on information from all death certificates filed in the 50 states and the District of Columbia, and provides up to 20 causes of death in addition to an underlying cause of death. We have identified decedents with a diagnosis of ARDS

[a]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Texas Tech University Health Sciences Center at the Permian Basin, Odessa, TX, USA
[b]Department of Mathematics, The University of Texas of the Permian Basin, Odessa, TX, USA
[c]Corresponding Author: Lavi Oud, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Texas Tech University Health Sciences Center at the Permian Basin, Odessa, TX 79763, USA.
Email: lavi.oud@ttuhsc.edu

during 2015 - 2019, and with a diagnosis of COVID-19, ARDS, or both in 2020, listed among any of the 20 causes of death irrespective of the underlying cause of death, which could be ARDS, COVID-19, or other conditions (e.g., cardiovascular disease, etc.). ARDS and COVID-19 were identified by International Classification of Diseases, Tenth Revision, Clinical Modification codes J80 and J071, respectively. Negative binomial regression with log-link and robust standard errors was used on the 2015 - 2019 data to forecast the number of ARDS-related deaths in 2020. We then compared the number of observed vs. expected ARDS-related deaths in 2020. In addition, we examined the proportion of a diagnosis of COVID-19 among all decedents with a diagnosis of ARDS and reporting of a diagnosis of ARDS among all decedents with a diagnosis of COVID-19. We then repeated the later analysis within each of the Department of Health and Human Services (HHS) Regions. Data analysis was performed using R 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria).

The annual ARDS-related mortality and population data for 2015 - 2020 are detailed in Table 1. In 2020, there were 51,184 ARDS-related deaths, 384,536 COVID-19-related deaths, and 41,606 deaths with both in the USA. The predicted number of ARDS-related deaths for 2020 was 10,851 (95% confidence interval (CI) 9,714 - 12,120). The ratio of the observed vs. expected ARDS-related deaths was 4.71 (95% CI 4.62 - 4.82). A diagnosis of ARDS was reported in 10.8% of all COVID-19-related deaths, ranging from 8.2% (HHS regions 1 and 7) to 16.1% (HHS region 2). A diagnosis of COVID-19 was reported in 81.3% of ARDS-related deaths in 2020. The data on the proportion of a diagnosis of ARDS among decedents with COVID-19 within each HHS region are presented in Table 2.

Our study shows that the COVID-19 pandemic was associated with nearly five-fold rise in ARDS-related deaths in the USA during 2020, and a diagnosis of COVID-19 was present in over 80% of all ARDS-related deaths that year. This magnitude of change is unprecedented in ARDS epidemiology. Nevertheless, this dramatic change is likely a substantial underestimate of the actual contribution of COVID-19 to ARDS-related mortality in 2020. Although ARDS was present, as noted earlier, in the majority of decedents with COVID-19 in autopsy studies [3, 4], a diagnosis of ARDS was reported only in about 1 in 10 of death certificates of all COVID-19-related deaths.

The causes of the very low rate of death certificate-based ARDS diagnoses among COVID-19 decedents are unclear. However, this finding may reflect clinicians' uncertainties

Table 1. ARDS-Related Mortality and the United States Population, 2015 - 2020

Variable	Year					
	2015	**2016**	**2017**	**2018**	**2019**	**2020**
ARDS-related mortality	9,866	10,971	10,584	10,828	10,482	51,184
Population	321,418,820	323,127,513	325,719,178	327,167,434	328,239,523	329,484,123

ARDS: acute respiratory distress syndrome.

during the first year of the pandemic about the nature, care, and outcomes of an otherwise typical ARDS phenotype, when taking place in patients with COVID-19, especially given the uncertainties raised by thought leaders [1] and some differing features noted during the clinical course of affected patients, including among others higher frequency of pneumothorax and pneumomediastinum compared to ARDS in non-COVID-19 patients [9, 10]. The latter complications may have been driven by differential expression of pathways normally involved in lung regeneration and repair in patients with COVID-19 compared to those without this infection [11]. This hypothesis is supported by the nearly two-fold variation in the frequency of a diagnosis of ARDS among COVID-19-related deaths across HHS regions, possibly reflecting variation in practices of completing death certificates and their coding across regions.

This study is limited by the known inaccuracies of death certificates [12] and lack of data on potential differences in diagnostic processes and decision-making by clinicians during the first year of the pandemic compared to the pre-pandemic period, may have additionally affected the completion of death certificates. However, death certificate data represent the primary source for national and regional estimates of cause-specific mortality and this limitation of death certificates does not explain the observed trends from pre-pandemic to the pandemic period. In addition, our findings may not be generalizable to other countries and regions, especially those where the pandemic-induced strains on already limited healthcare resources may have reduced hospital access of patients in need and exacerbated scarcity of key diagnostic tools, all of which would have adversely affected accurate accounting of ARDS-related mortality among patients with and without COVID-19. Further studies are thus needed in other countries and regions, as well as in coming years in the USA to inform our understanding of the impact of COVID-19 on the ARDS-related mortality burden.

Acknowledgments

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Conflict of Interest

Table 2. Number and Percentage of Decedents With a Diagnosis of ARDS Among Decedents With COVID-19, Stratified by the Department of HHS Region

HHS region	Number (%) of ARDS diagnoses among decedents with COVID-19
HHS region #1 (CT, ME, MA, NH, RI, VT)[a]	1,613/19,725 (8.2)
HHS region #2 (NJ, NY)	9,112/56,707 (16.1)
HHS region #3 (DE, DC, MD, PA, VA, WV)	3,620/34,918 (10.4)
HHS region #4 (AL, FL, GA, KY, MS, NC, SC, TN)	6,406/70,574 (9.1)
HHS region #5 (IL, IN, MI, MN, OH, WI)	4,793/66,484 (7.2)
HHS region #6 (AR, LA, NM, OK, TX)	5,728/52,638 (10.9)
HHS region #7 (IA, KS, MO, NE)	1,510/18,521 (8.2)
HHS region #8 (CO, MT, ND, SD, UT, WY)	1,718/11,281 (15.2)
HHS region #9 (AZ, CA, HI, NV)	6,197/46,549 (13.3)
HHS region #10 (AK, ID, OR, WA)	909/7,139 (12.7)

[a]The parenthesized acronyms within each HHS region represent the states in that region. ARDS: acute respiratory distress syndrome; COVID-19: coronavirus disease 2019; HHS: Health and Human Services; AL: Alabama; AK: Alaska; AZ: Arizona; AR: Arkansas: CA: California; CO: Colorado; CT: Connecticut; DE: Delaware; FL: Florida; GA: Georgia; HI: Hawaii; ID: Idaho; IL: Illinois; IN: Indiana; IA: Iowa; KS: Kansas; KY: Kentucky; LA: Louisiana; ME: Maine; MD: Maryland; MA: Massachusetts; MI: Michigan; MN: Minnesota; MS: Mississippi; MO: Missouri; MT: Montana; NE: Nebraska; NV: Nevada; NH: New Hampshire; NJ: New Jersey; NM: New Mexico; NY: New York; NC: North Carolina; ND: North Dakota; OH: Ohio; OK: Oklahoma; OR: Oregon; PA: Pennsylvania; RI: Rhode Island; SC: South Carolina; SD: South Dakota; TN: Tennessee; TX: Texas; UT: Utah; VT: Vermont; VA: Virginia; WA: Washington; WV: West Virginia; WI: Wisconsin; WY: Wyoming; DC: District of Columbia.

Informed Consent

Not applicable.

Author Contributions

Lavi Oud has performed the design of work, acquisition of data, analysis and interpretation, composition, drafting, revising, editing, and final approval. John Garza has performed analysis and interpretation, revising, editing, and final approval.

Data Availability

The data used in this study are publicly available at: https://wonder.cdc.gov/controller/datarequest/D77

Abbreviations

COVID-19: coronavirus disease 2019; ARDS: acute respiratory distress syndrome; HHS: Health and Human Services; ICU: intensive care unit

References

1. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, Camporota L. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med. 2020;46(6):1099-1102. doi pubmed pmc
2. Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. Crit Care. 2020;24(1):516. doi pubmed pmc
3. Schaller T, Hirschbuhl K, Burkhardt K, Braun G, Trepel M, Markl B, Claus R. Postmortem examination of patients with COVID-19. JAMA. 2020;323(24):2518-2520. doi pubmed pmc
4. Elsoukkary SS, Mostyka M, Dillard A, Berman DR, Ma LX, Chadburn A, Yantiss RK, et al. Autopsy findings in 32 patients with COVID-19: a single-institution experience. Pathobiology. 2021;88(1):56-68. doi pubmed pmc
5. Cochi SE, Kempker JA, Annangi S, Kramer MR, Martin GS. Mortality trends of acute respiratory distress syndrome in the United States from 1999 to 2013. Ann Am Thorac Soc. 2016;13(10):1742-1751. doi pubmed pmc
6. Ahmad FB, Cisewski JA, Minino A, Anderson RN. Provisional mortality data - United States, 2020. MMWR Morb Mortal Wkly Rep. 2021;70(14):519-522. doi pubmed pmc
7. Hendrickson KW, Peltan ID, Brown SM. The epidemiology of acute respiratory distress syndrome before and after coronavirus disease 2019. Crit Care Clin. 2021;37(4):703-716. doi pubmed pmc
8. CDC Wonder. Centers for disease control and prevention. Available from: https://wonder.cdc.gov/mcd.html.
9. Lemmers DHL, Abu Hilal M, Bna C, Prezioso C, Cavallo E, Nencini N, Crisci S, et al. Pneumomediastinum and subcutaneous emphysema in COVID-19: barotrauma or lung frailty? ERJ Open Res. 2020;6(4):00385-2020. doi pubmed pmc
10. Belletti A, Palumbo D, Zangrillo A, Fominskiy EV, Franchini S, Dell'Acqua A, Marinosci A, et al. Predictors of pneumothorax/pneumomediastinum in mechanically ventilated COVID-19 patients. J Cardiothorac Vasc Anesth. 2021;35(12):3642-3651. doi pubmed pmc
11. Baratella E, Bussani R, Zanconati F, Marrocchio C, Fabiola G, Braga L, Maiocchi S, et al. Radiological-pathological signatures of patients with COVID-19-related pneumomediastinum: is there a role for the Sonic hedgehog and Wnt5a pathways? ERJ Open Res. 2021;7(3):00346-2021. doi pubmed pmc
12. McGivern L, Shulman L, Carney JK, Shapiro S, Bundock E. Death certification errors and the effect on mortality statistics. Public Health Rep. 2017;132(6):669-675. doi pubmed pmc