risk adults living with such workers. One limitation is that the study’s prepandemic data do not reflect current employment levels, changes in ability to WAH, or local infection rates. Additionally, risk factors were reported by MEPS participants rather than measured by medical professionals, likely causing an underestimate of risk. Policy makers seeking to make efficient and equitable decisions about reopening the economy and about vaccine distribution should consider the health risks not only of workers, but also of those with whom they live.

Thomas M. Selden, PhD
Terecia A. Berdahl, PhD

Author Affiliations: Center for Financing, Access and Cost Trends, Agency for Healthcare Research and Quality, Rockville, Maryland.

Accepted for Publication: September 13, 2020.

Published Online: November 9, 2020. doi:10.1001/jamainternmed.2020.6249

Corresponding Author: Thomas M. Selden, PhD, Center for Financing, Access and Cost Trends, Agency for Healthcare Research and Quality, 5600 Fishers Ln, Rockville, MD 20857 (thomas.selden@ahrq.hhs.gov).

Author Contributions: Drs Selden and Berdahl had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: All authors.

Administrative, technical, or material support: Berdahl.

Conflicts of Interest Disclosures: None reported.

Funding/Support: There was no external funding associated with this research; it was conducted by Selden and Berdahl as employees of AHRQ as part of AHRQ’s intramural research program.

Role of the Funder/Sponsor: Drs Selden and Berdahl are employees of the US AHRQ. Aside from the internal peer review process, AHRQ had no role in designing and conducting the study; collecting, managing, analyzing and interpreting the data; preparing, reviewing or approving the manuscript; or the decision to submit the manuscript for publication.

Disclaimer: The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the views of the US Department of Health and Human Services or AHRQ.

Additional Contributions: Joel Cohen, PhD, David Meyers, MD, and G. Edward Miller, PhD, provided comments on early versions of the draft. Drs Cohen, Meyers, and Miller work for AHRQ and received no compensation.


Supplemental content

Diaphragm Pathology in Critically Ill Patients With COVID-19 and Postmortem Findings From 3 Medical Centers

Extrapulmonary manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are now widely recognized and have important clinical implications.1,2 To our knowledge, the association of SARS-CoV-2 with the respiratory muscles has not been studied. This is surprising, as the respiratory muscles drive alveolar ventilation and their weakness results in acute respiratory failure. In critically ill patients undergoing ventilation, respiratory muscle weakness prolongs mechanical ventilation and increases mortality.3 The aim of this study was to investigate the association of severe coronavirus disease 2019 (COVID-19) with the respiratory muscles in critically ill patients and compare the findings with those obtained from non-COVID-19 critically ill patients.

Methods | Our study focused on the diaphragm, the main muscle of respiration. Consecutive diaphragm muscle specimens were collected during autopsy from the corpses of 26 patients who had been critically ill with COVID-19 in 3 academic medical centers in the Netherlands (referred to as COVID-19-intensive care unit [ICU]) in April and May 2020. As a control group, autopsies diaphragm specimens were collected from corpses of 8 patients who had been critically ill without COVID-19 (referred to as control-ICU). Specimens from the left midcostal diaphragm were used for analyses. Methodological details are described in the eMethods and eTables 2 and 3 in the Supplement. This study was approved by the medical ethical committee at Amsterdam UMC, and written informed consent was provided by the decedents’ next of kin. Data were analyzed using SPSS, version 22 (IBM), and visualized with GraphPad Prism, version 7.0 (GraphPad). Statistical significance was set at P < .05.

Results | The median age of COVID-19–ICU patients was 71 years (interquartile range, 61-74 years), and 21 (81%) were men. Twenty-four patients (92.3%) received invasive mechanical ventilation for a median of 12 days (interquartile range, 6-25 days). The number of days receiving invasive mechanical ventilation and ICU length of stay were comparable between COVID-19–ICU and control-ICU patients. COVID-19–ICU patients had higher body mass index (calculated as weight in kilograms divided by height in meters squared) and were less likely to be treated with steroids (Table). No patients in either group had preexisting neuromuscular disease.

We report angiotensin-converting enzyme 2 (ACE-2) in the diaphragm of COVID-19–ICU and control-ICU patients (Figure, A). The ACE-2 predominantly localizes at the myofiber membrane (Figure, A), providing an entry point for SARS-CoV-2 to infect diaphragm myofibers. Evidence for SARS-CoV-2 viral RNA in the diaphragm was found in 4 patients (15.4%; Figure, B). Further analyses, for which we applied RNA in situ hybridization, indicated that viral RNA localized inside diaphragm myofibers (Figure, B). The RNA sequencing analyses showed...
that 315 genes were upregulated and 281 were downregulated in the diaphragm of COVID-19–ICU patients compared with control-ICU patients. Subsequent analyses of all upregulated and downregulated genes revealed activation of fibrosis pathways (fibroblast growth factor signaling). In line with these findings, epimysial and perimysial fibrosis was more than 2-fold higher in the diaphragms of COVID-19–ICU patients compared with control-ICU patients (Figure, C).

**Discussion** | In this study, we provide unique evidence for ACE-2 expression in the human diaphragm and SARS-CoV-2 viral infiltration in the diaphragm of a subset of COVID-19–ICU patients. In COVID-19–ICU patients, we reported increased expression of genes involved in fibrosis and histological evidence for the development of fibrosis in the diaphragm. This myopathic phenotype was distinctly different from that of control-ICU patients, with comparable duration of mechanical ventilation and ICU length of stay.6,5 It remains to be established whether diaphragm myopathy is a direct effect of SARS-CoV-2. Only 3 patients in the control-ICU group (37.5%) had viral lung disease, and the association of viral pneumonia with diaphragm muscles is unknown. We hypothesize that severe diaphragm myopathy associated with COVID-19, as described in this study, may lead to diaphragm weakness and

**Table. Summary of the Demographic and Clinical Characteristics of the Study Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>COVID-19–ICU (n = 26)</th>
<th>Control-ICU (n = 8)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), y</td>
<td>71 (61-74)</td>
<td>66 (64-68)</td>
<td>.44</td>
</tr>
<tr>
<td>Sex, No. (%), male</td>
<td>21 (81)</td>
<td>6 (75)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>28 (4)</td>
<td>25 (4)</td>
<td>.02</td>
</tr>
<tr>
<td>Duration of ICU stay, median (IQR), d</td>
<td>13 (8-25)</td>
<td>12 (9-12)</td>
<td>.35</td>
</tr>
<tr>
<td>Duration of IMV, median (IQR), d</td>
<td>12 (6-25)</td>
<td>10 (6-12)</td>
<td>.25</td>
</tr>
<tr>
<td>Duration of NMB administration, median (IQR), h</td>
<td>0 (0-100)</td>
<td>84 (0-240)</td>
<td>.45</td>
</tr>
<tr>
<td>Systemic steroid administration, No. (%)</td>
<td>11 (44)</td>
<td>7 (88)</td>
<td>.05</td>
</tr>
<tr>
<td>Maximum CRP level, median (IQR), mg/dL</td>
<td>33.1 (25.9-39.4)</td>
<td>32.1 (27.6-45.3)</td>
<td>.72</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ICU, intensive care unit; IMV, invasive mechanical ventilation; IQR, interquartile range; NMB, neuromuscular blocking agents.

SIC conversion factor: To convert CRP to milligrams per liter, multiply by 10.

**Figure. Angiotensin-Converting Enzyme 2 (ACE-2). SARS-CoV-2, and Fibrosis in the Diaphragms of Patients With COVID-19**

A, Left panel: ACE-2 mRNA in diaphragm specimens determined by quantitative polymerase chain reaction (qPCR) and normalized to housekeeping gene TBP. Right panel: α-ACE-2 antibody localization with fluorescein microscopy on diaphragm cross-sections; the arrowheads show membrane and cytosolic localization (bar = 50 μm). B, Left panel: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA, determined by qPCR and normalized to housekeeping gene TBP, is detected in the diaphragm of 4 coronavirus disease 2019 (COVID-19)–intensive care unit (ICU) patients (patients 7, 9, 33, and 36). Right panel: in situ hybridization using RNAscope on patient #7 shows intramyofiber SARS-CoV-2 virus particles (red dots, indicated with arrowheads); a myofiber edge is highlighted with dashed line (bar = 30 μm). C, Left panels: representative images of picrosirius red-stained diaphragm cross-sections to highlight fibrosis; patients #22 and 3a are shown (bar = 100 μm). Right panel: quantification of the amount of fibrosis.
might contribute to ventilator weaning failure, persistent dyspnea, and fatigue in patients with COVID-19 who survive their ICU stay.6

Zhonghua Shi, MD
Heder J. de Vries, MD
Alexander P. J. Vlaar, MD, PhD
Johannes van der Hoeven, MD, PhD
Reinier A. Boon, PhD
Leo M. A. Heunks, MD, PhD
Coen A. C. Ottenheijm, PhD
for the Dutch COVID-19 Diaphragm Investigators

Author Affiliations: Physiology, Amsterdam UMC (location VUmc), Amsterdam, the Netherlands (Shi, Boon, Ottenheijm); Intensive Care Medicine, Amsterdam UMC (location VUmc), Amsterdam, the Netherlands (de Vries, Heunks); Critical Care Medicine, Beijing Tiantan Hospital, Capital Medical University, Beijing, China (Shi); Intensive Care Medicine, Amsterdam UMC (location AMC), Amsterdam, the Netherlands (Vlaar); Intensive Care Medicine, Radboudumc, Nijmegen, the Netherlands (van der Hoeven); Cellular and Molecular Medicine, University of Arizona, Tucson, Arizona (Ottenheijm).

Group Information: The Dutch COVID-19 Diaphragm Investigators are listed at the end of the article.

Accepted for Publication: September 10, 2020.


Corresponding Author: Coen Ottenheijm, PhD, Department of Physiology, Amsterdam UMC, De Boelelaan 1108, 1081 HZ Amsterdam, The Netherlands (c.ottenheijm@amsterdamumc.nl).

Author Contributions: Dr Ottenheijm had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Shi, Boon, Heunks, Ottenheijm. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Shi, Heunks, Ottenheijm. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Shi, de Vries, Ottenheijm. Administrative, technical, or material support: Ottenheijm. Supervision: Vlaar, Boon, Heunks, Ottenheijm.

Conflict of Interest Disclosures: Dr de Vries reported grants from Amsterdam Cardiovascular Sciences during the conduct of the study and personal fees from a Dutch ultrasound center outside the submitted work. Dr Heunks reported personal fees from Getinge and grants from Liberate Medical outside the submitted work. No other disclosures were reported.

Dutch COVID-19 Diaphragm Investigators: Bernadette Schuurink, MD, PhD, Eva Roos, MD, PhD, Hans W.M. Niessen, MD, PhD, Sylvia Bogaards, BSc, Stefan Conijn, BSc, Yezsamin L. Onderwater, MSc, Pedro Espinosa, MSc, Ankie van Bergen, BSc, Diewertje I. Bink, MSc, Marloes van den Berg, MD (Amsterdam UMC, location VUmc), and Benno Kusters, MD, PhD (Radboudumc).

Funding/Support: The research reported in this work was supported by a grant from the National Institutes of Health/Heart Lung and Blood Institute (ROIHL12500 to Dr Ottenheijm).

Role of the Funder/Sponsor: The National Institutes of Health/Heart Lung and Blood Institute had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Results | Of the total 220 unique guests speaking on COVID-19 content, 66 (30.0%) were women (Table 1). Women

Diversity and Representation of Physicians During the COVID-19 News Cycle

Although 41% of medical school faculty are women,1 women appear underrepresented as authors of coronavirus disease 2019 (COVID-19) pandemic-related publications2 and as leaders of the US response.3 Given the news media’s longstanding role in shaping public consciousness,4 we sought to investigate whose voices are being broadcast. Because cable news provides extended segments that frequently include expert interviews (unlike shorter network nightly news broadcasts), we investigated the diversity of speakers who discussed COVID-19 and other content on cable news programs.

Methods | From May 18 to June 19, 2020, we analyzed prime-time programming on 3 popular American cable news networks: Fox News Network, CNN, and MSNBC. The primetime slot, defined as 8 to 11 PM Eastern/Pacific Time, was chosen to sample programming with the highest ratings. The investigators filed the study plan with the University of Michigan Institutional Review Board, which does not regulate studies of this nature that use publicly available data.

The observation window began with the country’s early state reopenings, extended throughout the national protests over police brutality, and ended with President Trump’s controversial campaign rally in Tulsa, Oklahoma. We recorded the name, gender, given job title, degree, speaking time, and interview content (COVID-19 related vs unrelated) for every guest interviewed on a primetime show. A guest was defined as any nonanchor individual speaking on-air. Network employees, contributors, and correspondents were included. To avoid duplication, clips of past interviews shared on-air were excluded. Because some videos were not uploaded to public archives, speaking time was not recorded for a small subset of interviews (5%).

Data were analyzed both across and among networks. We also evaluated physician speakers (including MD/PhDs) and nonphysician PhD speakers separately. For comparisons of proportions, the Fisher exact test statistics were used. For comparison of average speaking times, network summaries were compared using the F statistic (analysis of variance). To compare average speaking time between COVID-19 content and other content (regardless of network), we used the Wilcoxon rank-sum test statistic. All summaries and statistics were calculated using the SAS, version 9.4 (SAS Institute), and P values less than .05 were considered statistically significant.

Results | Of the total 220 unique guests speaking on COVID-19 content, 66 (30.0%) were women (Table 1). Women