Association of Smoking and Cumulative Pack-Year Exposure With COVID-19 Outcomes in the Cleveland Clinic COVID-19 Registry

There is limited and contradictory evidence on the association of smoking status with adverse outcomes of severe acute respiratory syndrome coronavirus 2 infection.1,3 Furthermore, current smoking status does not encompass the cumulative effect of smoking. To our knowledge, no studies have assessed the cumulative effect of smoking over time, as measured by pack-years, though a single study of coronavirus disease 2019 (COVID-19) in a small cohort of 102 patients with lung cancer found that the patients with severe outcomes had a higher average pack-year history (30 vs 20 years).4 We hypothesize that there is an adverse association of cumulative smoking exposure, as measured by pack-years, with outcomes of patients with COVID-19.

Methods | The Cleveland Clinic initiated a COVID-19 registry starting on March 8, 2020, that includes all patients tested for COVID-19 within the Cleveland Clinic Health system in Ohio and Florida. Basic demographic information was collected during testing, including age, height, weight, self-reported gender, self-reported race, and select comorbidities. Additional data on comorbidities, medications, and outcomes were extracted from patient electronic medical records.5 The Cleveland Clinic Institutional Review Board approved this study and waived the need for patient informed consent owing to use of deidentified database information on study participants.

Results | Of the 7102 patients included in the cohort, 6020 (84.8%) were never smokers, 172 (2.4%) were current smokers, and 910 (12.8%) were former smokers. All demographics are summarized in Table 1, and the results of logistic regression analyses are summarized in Table 2. The findings showed a dose-response association between pack-years and adverse COVID-19 outcomes. Patients who smoked more than 30 pack-years had a 2.25 times higher odds of hospitalization (95% CI, 1.76-2.88), and these heavy smokers were 1.89 times more likely to die following a COVID-19 diagnosis (95% CI, 1.29-2.76) when compared with never smokers. The association between cumulative smoking and adverse COVID-19 outcomes is likely mediated in part by comorbidities. The odds ratios for all adverse outcomes were attenuated in the mediation models. There was no evidence of effect modification by smoking status; similar odds ratios were seen in both current and former smokers.

Discussion | The results of this study suggest that cumulative exposure to cigarette smoke is an independent risk factor for hospital admission and death from COVID-19. Smoking is imperfectly classified in patient electronic medical records, and
Table 1. Demographics of Patients Who Tested Positive for COVID-19 Within the Cleveland Clinic Health System

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Smokers, No. (%)</th>
<th>0-10 Pack-years (n = 341)</th>
<th>10-30 Pack-years (n = 341)</th>
<th>&gt;30 Pack-years (n = 341)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female</td>
<td>3683 (61.2)</td>
<td>212 (53.0)</td>
<td>145 (42.5)</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Black</td>
<td>1911 (31.7)</td>
<td>100 (25.0)</td>
<td>125 (36.7)</td>
<td></td>
<td>78 (22.9)</td>
</tr>
<tr>
<td>White</td>
<td>3370 (56.0)</td>
<td>277 (69.3)</td>
<td>132 (33.0)</td>
<td></td>
<td>245 (71.9)</td>
</tr>
<tr>
<td>Other</td>
<td>424 (7.0)</td>
<td>42 (11.8)</td>
<td>7 (2.0)</td>
<td></td>
<td>7 (2.0)</td>
</tr>
<tr>
<td>BMI score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Underweight (&lt;18.5)</td>
<td>41 (0.7)</td>
<td>11 (2.8)</td>
<td>3 (0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (18.5-24.9)</td>
<td>682 (11.3)</td>
<td>48 (12.0)</td>
<td>66 (19.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight (25.0-29.9)</td>
<td>1081 (18.0)</td>
<td>92 (23.0)</td>
<td>85 (24.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese (&gt;30.0)</td>
<td>1632 (27.1)</td>
<td>132 (33.0)</td>
<td>125 (36.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pack-years, mean (SD)</td>
<td>0 a</td>
<td>5.3 (3.4)</td>
<td>20.8 (5.8)</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Current smokers</td>
<td>0 a</td>
<td>49 (14.4)</td>
<td>67 (16.8)</td>
<td></td>
<td>56 (16.4)</td>
</tr>
<tr>
<td>Received flu shot this year</td>
<td>1742 (45.6)</td>
<td>253 (63.3)</td>
<td>259 (76.0)</td>
<td></td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; NSAID, nonsteroidal anti-inflammatory drug.

Table 2. Logistic Regression Models for COVID-19 Outcomes by Smoking Status Among the Cohort

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
</tr>
<tr>
<td>Hospitalization given a positive COVID-19 test</td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>0-10 Pack-years</td>
<td>1.41 (1.10-1.81)</td>
</tr>
<tr>
<td>10-30 Pack-years</td>
<td>2.48 (2.01-3.07)</td>
</tr>
<tr>
<td>&gt;30 Pack-years</td>
<td>4.65 (3.72-5.82)</td>
</tr>
<tr>
<td>ICU admission given a positive COVID-19 test and hospitalization</td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>0-10 Pack-years</td>
<td>1.33 (0.84-2.08)</td>
</tr>
<tr>
<td>10-30 Pack-years</td>
<td>1.74 (1.23-2.45)</td>
</tr>
<tr>
<td>&gt;30 Pack-years</td>
<td>2.11 (1.54-2.89)</td>
</tr>
<tr>
<td>Death given a positive COVID-19 test</td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>0-10 Pack-years</td>
<td>2.38 (1.50-3.80)</td>
</tr>
<tr>
<td>10-30 Pack-years</td>
<td>3.40 (2.31-5.02)</td>
</tr>
<tr>
<td>&gt;30 Pack-years</td>
<td>6.11 (4.33-8.61)</td>
</tr>
</tbody>
</table>

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit.

*Angiotensin receptor blockers and oral or inhaled corticosteroids.

bCoronary artery disease, chronic obstructive pulmonary disease or emphysema, hypertension, and diabetes.
former smokers are potentially classified as never smokers, while pack-years may be underrecorded. However, this misclassification is likely to bias the present results toward the null, which would underestimate the association of cigarette smoking on adverse COVID-19 outcomes. The limitations on who has access to care at tertiary medical centers in the United States prevent generalizability to the whole population. The patients with complete data in this study are likely to be wealthier and have more consistent access to health care, as pack-years of smoking was typically collected during previous visits to the Cleveland Clinic. Nevertheless, we have demonstrated in this single central registry of patients who tested positive for COVID-19 that increased cumulative smoking was associated with a higher risk of hospitalization and mortality from COVID-19 in a dose-dependent manner.

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Author Contributions: Ms Lowe had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

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Drafting of the manuscript: Lowe, Hatipoğlu, Attaway.

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

Statistical analysis: Lowe, Zein, Attaway.

Administrative, technical, or material support: Hatipoğlu, Supervision: Zein, Hatipoğlu, Attaway.

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State Legislation Related to Abortion Services, January 2017 to November 2020

The 1973 US Supreme Court decision, Roe v Wade, simultaneously established the constitutional right to abortion and provided states with regulatory power over access to reproductive health services. Since Roe v Wade, the Supreme Court has heard 43 cases related to abortion, nearly all from states that have restricted access. To understand trends in abortion policies among states, we analyzed enacted legislation between January 2017 and November 2020.

Methods | We collected legislation through NexisUni, a database of legislation across all states, searching bill text for these keywords: abortion, abortion services, abortion provider, and abortion funding. The inclusion criteria were: (1) enacted legislation, (2) 2017 to 2020 legislative sessions, and (3) legislation substantively related to abortion policy. After identifying 736 pieces of legislation, we confirmed the relevance of each bill to abortion services and discarded unrelated legislation.

The final sample included 256 enacted laws from 45 states; a member of the research team (E.B.G.) coded each law, using inductive and deductive coding techniques. Prior to coding any legislation, we developed an initial set of anticipated codes, related to clinicians, patients, and financing of the procedure. After reading the bills, we expanded the codebook to reflect the nuances of policies. Subsequently, we combined previously distinct codes into parent categories to identify themes (Table 1 and Table 2). The University of Utah institutional review board deemed the study exempt from approval; the data were publicly available and there were no human participants.

Results | During the study period, 35 states enacted 227 laws restricting access to abortion services (median of 4 laws; range, 1-20) (Table 1). Seven states—Arkansas, Indiana, Kentucky, Louisiana, Missouri, Ohio, and Utah—accounted for 119 (52.4%) of the laws. By comparison, 12 states and Washington, DC, enacted 29 laws expanding access to abortion services (median of 2 laws; range, 1-7) (Table 2). Two states (Illinois and Maryland) enacted laws that restricted and expanded access in various respects. Of the laws, 86 established restrictions for physicians, advanced clinicians, or facilities that provide abortions, typically involving medical records, required clinical specifications, available emergency services, and licensing as hospitals or surgical centers. In addition, 69 laws established restrictions on patients, for example by extending waiting periods for abortions to 24 or 72 hours or requiring patients to view information modules to dissuade them from having an abortion. Another 48 laws restricted state funding or insurance coverage of abortion services or established tax credits for dona-