Electronic Cigarette Use Is Not Associated with COVID-19 Diagnosis

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Abstract

This analysis tested the hypothesis that current e-cigarette use was associated with an increased risk of SARS-CoV-2 infection in patients seeking medical care. E-cigarette and conventional cigarette use were ascertained using a novel electronic health record tool, and COVID-19 diagnosis was ascertained by a validated institutional registry. Logistic regression models were fit to assess whether current e-cigarette use was associated with an increased risk of COVID-19 diagnosis. A total of 69,264 patients who were over the age of 12 years, smoked cigarettes or vaped, and were sought medical care at Mayo Clinic between September 15, 2019 and November 30, 2020 were included. The average age was 51.5 years, 62.1% were females and 86.3% were white; 11.1% were currently smoking cigarettes or using e-cigarettes and 5.1% tested positive for SARS-CoV-2. Patients who used only e-cigarettes were not more likely to have a COVID-19 diagnosis (OR 0.93 [0.69-1.25], $P = .628$), whereas those who used only cigarettes had a decreased risk (OR 0.43 [0.35-0.53], $P < .001$). The OR for dual users fell between these 2 values (OR 0.67 [0.49-0.92], $P = .013$). Although e-cigarettes have the well-documented potential for harm, they do not appear to increase susceptibility to SARS-CoV-2 infection. This result suggests the hypothesis that any beneficial effects of conventional cigarette smoking on susceptibility are not mediated by nicotine.

Introduction

The impact of tobacco use on SARS-CoV-2 infection risk and COVID-19 severity remains unclear. A meta-analysis found that compared with never smokers, current cigarette smokers appear to be at reduced risk of SARS-CoV-2 infection.[1] Another systematic review and meta-analysis found that both current and former smoking significantly increased the risk of severe COVID-19 and death.[2] However, little is known about how electronic (e-) cigarette use might affect risk. E-cigarettes can be associated with inflammation and lung disease, as well as disruptions of lung immunity; both of these factors could increase susceptibility to symptomatic disease.[3] In one report, e-cigarette use in adolescents was associated with an increase in the risk of SARS-CoV-2 infection.[4] Another study found that SARS-CoV-2 infection rates were higher in U.S. states with a higher prevalence of e-cigarette use, but this is at best indirect evidence.[5] Factors complicating the study of how e-cigarette use may affect SARS-CoV-2 risk include inconsistent ascertainment of e-cigarette use in medical records, and the fact that many who use e-cigarettes also use other forms of tobacco. The aim of this study was to test the hypothesis that current e-cigarette use is associated with an increased risk of COVID-19 diagnosis in patients seeking medical care.

Methods

This retrospective study was reviewed by The Institutional Review Board (IRB) and determined to be exempt under section 45 CFR 46.101, item 2.

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Study Population

Beginning September 15, 2019, patients were screened for e-cigarette and conventional cigarette use during ambulatory appointments at a national multisite medical practice. Screening utilized a novel electronic health record documentation as previously described.[6] As part of routine clinical care during ambulatory appointments, clinicians ascertain e-cigarette use history from patients and document the information as structured data in the electronic health record (EHR). This documentation framework was implemented in EHR as a quality improvement initiative for our health system since September 2019.

The diagnosis of COVID-19 within this period was ascertained using COVID-19 registry data as previously described.[7] All patients with current or former history of SARS-CoV-2 infection (a positive SARS-CoV-2 test or active infection record in EHR or a diagnosis of COVID-19 on the problem list of the EHR) are included in this validated registry.[7]

Data Analysis

Patient demographics, tobacco use status, and COVID-19 test status were abstracted from the EHR. Current e-cigarette or conventional cigarette use within the last 30 days was queried during each medical visit. For those patients diagnosed with COVID-19, tobacco use status was defined according to the current status at the time of diagnosis. For those not diagnosed with COVID-19, tobacco use status was defined according to the current status noted at the time of their last medical visit during the study period. Data are summarized using mean ± SD for continuous variables and frequency counts and percentages for categorical variables. Two logistic regression models were fit to assess whether current e-cigarette use was associated with an increased risk of COVID-19 diagnosis. For both models, COVID-19 diagnosis was the dependent variable. One model included e-cigarette and smoking status as separate variables, and the other model included a single variable defining current inhaled tobacco use (e-cigarettes only, cigarettes only, dual use, none) Covariates in both models included age (modeled as a continuous variable using a restricted cubic spline with 4 knots), sex, race/ethnicity and Institutional practice site. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

From September 15, 2019 to November 30, 2020, 78 547 patients were screened for e-cigarette and conventional cigarette use during ambulatory appointments at our medical facility. After removing patients <12 years old and those not consenting for research use of their medical records, 69 264 patients were analyzed. Of these patients, 1888 (2.7%) reported current e-cigarette use and 1669 (2.4%) reported former use. Compared with never users of e-cigarettes, current and former users were more likely to be younger ($P < .001$) and current users were more likely to be male ($P < .001$) (Table 1). The majority of current e-cigarette users (55.9%) were also current users of conventional cigarettes, as were many (31.0%) former e-cigarette users (Table 1). COVID-19 was diagnosed in 3567 (5.1%) patients.

In the first logistic regression model that included e-cigarette and conventional cigarette use as separate variables, current or former e-cigarette use was not associated with COVID-19 diagnosis (odds ratio [OR] 1.15, 95% confidence interval [CI] 0.93, 1.43 for current use, OR 1.01 [95% CI 0.81, 1.26] for former use, Table 2). Current, but not former, smokers were less likely to have a COVID-19 diagnosis compared to never smokers (OR 0.47 [95% CI 0.41, 0.54], $P < .001$). In the second logistic regression model when inhaled tobacco use was included as a single variable, patients who used only e-cigarettes were not more likely to have a COVID-19 diagnosis (OR 0.93 [95% CI 0.69, 1.25], $P = .628$), whereas those who used only cigarettes had a decreased risk (OR 0.43 [95% CI 0.35, 0.53], $P < .001$). The OR for dual users fell between these 2 values (OR 0.67 [95% CI 0.49, 0.92], $P = .013$).

Discussion

This analysis affirms prior studies that conventional cigarette smokers are underrepresented in the population of patients diagnosed with COVID-19.[1] As previously discussed the potential for confounding and the limitations of observational cohort studies preclude causal inferences. There is a paucity of evidence regarding association of vaping and COVID-19.[8] In contrast to the few prior studies that explored the association of e-cigarette use and COVID-19,[4,5] we find no evidence that current or former e-cigarette users are more likely to be diagnosed, although our study design differed substantially, making direct comparisons problematic. For example, a cross sectional online survey study used a convenience sample cohort of adolescents and young adults during early period (May 2020) of the COVID-19 pandemic and found both dual use and e-cigarette use were associated with the risk of infection,[4] although some aspects of the study were criticized.[9] However, similar to our findings, another cross sectional online study from the United Kingdom (conducted in May-June 2020) found no difference in self-reported diagnosed/suspected COVID-19 between never, current and former e-cigarette users.[10] Compared with these previous investigations, our study analyzed a clinical cohort (ie, patient seeking medical care) and used self-reported e-cigarette use data that were confirmed and documented in an EHR

Table 1. Patient Characteristics According to e-Cigarette Status.

Characteristic	All patients (N = 69 264)	Current e-cigarette user (N = 1888)	Former e-cigarette user (N = 1669)	Never e-cigarette user (N = 65 707)
Age, years; mean ± SD	51.5 ± 19.7	35.5 ± 16.0	39.1 ± 17.9	52.2 ± 19.6
12-19; n (%)	3323 (4.8)	220 (11.7)	150 (9.0)	2953 (4.5)
20-29; n (%)	8863 (12.8)	685 (36.3)	523 (31.3)	7655 (11.7)
30-39; n (%)	9890 (14.3)	337 (17.8)	316 (18.9)	9237 (14.1)
40-49; n (%)	8546 (12.3)	234 (12.4)	193 (11.6)	8119 (12.4)
50-59; n (%);	11 141 (16.1)	201 (10.6)	186 (11.1)	10 754 (16.4)
60-69; n (%)	13 294 (19.2)	152 (8.1)	192 (11.5)	12 950 (19.7)
70-79; n (%)	9421 (13.6)	55 (2.9)	84 (5.0)	9282 (14.1)
≥80; n (%)	4757 (6.9)	4 (0.2)	25 (1.5)	4757 (7.2)
Sex, n (%)				
Female	43 040 (62.1)	1040 (55.1)	1031 (61.8)	40 969 (62.4)
Male	26 224 (37.9)	848 (44.9)	638 (38.2)	24 738 (37.6)
Race/ethnicity, n (%)				
White, non-Hispanic/Latino	59 741 (86.3)	1600 (84.8)	1430 (85.7)	56 711 (86.3)
White, Hispanic/Latino	1962 (2.8)	64 (3.4)	51 (3.1)	1847 (2.8)
Black/African American	2231 (3.2)	61 (3.2)	47 (2.8)	2123 (3.2)
Asian/Native/Hawaiian/ Pacific islander	1502 (2.2)	26 (1.4)	23 (1.4)	1453 (2.2)
Other/multiracial	2293 (3.3)	79 (4.2)	82 (4.9)	2132 (3.2)
Unknown	1535 (2.2)	58 (3.1)	36 (2.2)	1441 (2.2)
Smoking status, n (%)				
Current	7679 (11.1)	1055 (55.9)	518 (31.0)	6106 (9.3)
Former	19 346 (27.9)	592 (31.4)	910 (54.5)	17 844 (27.2)
Never	42 239 (61.0)	241 (12.8)	241 (14.4)	41 757 (63.5)

Table 2. Association between Tobacco Use Status and COVID-19 Diagnosis.

Characteristic	N	COVID-19 diagnosis n (%)	OR (95% CI)	P
Model 1[a]				
E-cigarette status				
Current	1888	102 (5.4)	1.15 (0.93, 1.43)	.190
Former	1669	94 (5.6)	1.01 (0.81, 1.26)	.924
Never	65 707	3371 (5.1)	1.00 (reference)	
Cigarette smoking status				
Current	7679	236 (3.1)	0.47 (0.41, 0.54)	<.001
Former	19 346	938 (4.8)	1.01 (0.93, 1.10)	.862
Never	42 239	2393 (5.7)	1.00 (reference)	
Model 2[b]				
Current use of inhaled tobacco				
E-cigarettes only	833	50 (6.0)	0.93 (0.69, 1.25)	.628
Cigarettes only	6624	184 (2.8)	0.43 (0.35, 0.53)	<.001
Dual use	1055	52 (4.9)	0.67 (0.49, 0.92)	.013
None	60 752	3281 (5.4)	1.00 (reference)	

[a]Model 1 included e-cigarette status (current, former, never) as a variable and cigarette smoking status (current, former, never) as separate variables.
[b]Model 2 included current use of inhaled tobacco (e-cigarettes only, cigarettes only, dual use, and no current use) as a single variable. Both models included covariates for age (modeled as a continuous variable using a restricted cubic spline with 4 knots), sex, race/ethnicity, and region. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

by a clinician.[6] Also, COVID-19 diagnosis in our study was confirmed using a diagnostic PCR test.[7]

This analysis is subject to the limitations common to observational cohort studies, for example, inclusion of some, but likely not all, confounding variables (ie, related both to COVID-19 risk and e-cigarette use). Study participants were a convenience sample who presented for outpatient care to Mayo Clinic's ambulatory clinics, a sample that may not be entirely representative of the population of e-cigarette users in the United States.[11] Also, case numbers were insufficient to analyze how e-cigarette use might influence the severity and outcomes of COVD-19. Given the deleterious effects of e-cigarette use on lung function,[12] it is possible that even if e-cigarette use does not increase the risk of developing infection, it could still increase the severity of disease, as may be the case for conventional cigarettes.[2]

Although e-cigarettes have the well-documented potential for harm,[13,14] and the COVID-19 pandemic presents an opportunity to reduce e-cigarette use,[15-17] our study found that such use does not appear to increase susceptibility to SARS-CoV-2 infection among patients seeking medical care. This result suggests the hypothesis that any effects of conventional cigarette smoking on susceptibility are not mediated by nicotine. Future work should evaluate whether e-cigarette use could moderate COVID-19 outcomes.[18]

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Authors' Contributions

All the authors participated in the study concept and design, analysis and interpretation of data, drafting and revising the paper, and have seen and approved the final version of the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics and Consent to Participate

In accordance with the Declaration of Helsinki, this study was reviewed and approved by The Mayo Clinic Institutional Review Board (IRB). The IRB approved informed consent waiver.

Ethical Standards

This study was determined to be EXEMPT under 45 CFR 46.101, item 2 by The Mayo Clinic Institutional Review Board which had ethical oversight for this study. In addition, the authors assert that all procedures contributing to this work comply with the ethical standards of the Institutional Review Board guidelines on human experimentation in accordance with the Declaration of Helsinki of 1975, as revised in 2008.

Availability of Data and Materials

All data supporting the study findings are contained within this manuscript

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