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Hospitalizations and Deaths Associated with EVALI

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Abstract

BACKGROUND—As of January 7, 2020, a total of 2558 hospitalized patients with nonfatal cases and 60 patients with fatal cases of e-cigarette, or vaping, product use–associated lung injury (EVALI) had been reported to the Centers for Disease Control and Prevention (CDC).

METHODS—In a national study, we compared the characteristics of patients with fatal cases of EVALI with those of patients with nonfatal cases to improve the ability of clinicians to identify patients at increased risk for death from the condition. Health departments reported cases of EVALI to the CDC and included, when available, data from medical-record abstractions and patient interviews. Analyses included all the patients with fatal or nonfatal cases of EVALI that were reported to the CDC as of January 7, 2020. We also present three case reports of patients who died from EVALI to illustrate the clinical characteristics common among such patients.

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RESULTS—Most of the patients with fatal or nonfatal cases of EVALI were male (32 of 60 [53%] and 1666 of 2498 [67%], respectively). The proportion of patients with fatal or nonfatal cases was higher among those who were non-Hispanic white (39 of 49 [80%] and 1104 of 1818 [61%], respectively) than among those in other race or ethnic groups. The proportion of patients with fatal cases was higher among those 35 years of age or older (44 of 60 [73%]) than among those younger than 35 years, but the proportion with nonfatal cases was lower among those 35 years of age or older (551 of 2514 [22%]). Among the patients who had an available medical history, a higher proportion of those with fatal cases than those with nonfatal cases had a history of asthma (13 of 57 [23%] vs. 102 of 1297 [8%]), cardiac disease (26 of 55 [47%] vs. 115 of 1169 [10%]), or a mental health condition (32 of 49 [65%] vs. 575 of 1398 [41%]). A total of 26 of 50 patients (52%) with fatal cases had obesity. Half the patients with fatal cases (25 of 54 [46%]) were seen in an outpatient setting before hospitalization or death.

CONCLUSIONS—Chronic conditions, including cardiac and respiratory diseases and mental health conditions, were common among hospitalized patients with EVALI.

E-cigarette, or vaping, products were introduced into the U.S. market in 2007, and after their introduction, sales rose rapidly.[1] The aerosols generated by these products typically contain nicotine, flavorings, and additives[2] and can deliver other substances, such as tetrahydrocannabinol (THC), the main psycho-active component in cannabis, and cannabidiol.[3,4] Because solvents and other constituents generally differ between nicotine- and THC-containing products,[5] dual users of nicotine and THC are potentially exposed to a greater variety of constituents. Few regulations exist to control the quality and composition of the ingredients used in e-cigarettes and e-liquids, including solvents.[6]

Since August 2019, the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration, state and local health departments, and others have been investigating a national outbreak of e-cigarette, or vaping, product use–associated lung injury (EVALI).[7] Most of the patients with EVALI reported using THC-containing products and were hospitalized; many received critical care and respiratory support.[8,9] Vitamin E acetate, an additive sometimes used in THC-containing products,[10] is strongly linked to the EVALI outbreak; however, evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC-containing or non–THC-containing products.[11]

The clinical presentations and outcomes of survivors of EVALI have been described,[8,12–18] but data from patients who died are limited. Moritz et al. reported that the median age of the patients who survived EVALI was 23 years, as compared with 45 years among those who died.[13] National studies are lacking to describe in detail the demographic and clinical characteristics and substance use history of patients with fatal cases of EVALI or to compare such data with data from patients with nonfatal cases. We conducted a national study to compare e-cigarette, or vaping, product use, medical history, and clinical course between patients with fatal cases of EVALI and those who were hospitalized for the condition but survived in order to improve the ability of clinicians to recognize the clinical characteristics that may be associated with an increased risk of death. We also present three case reports of

patients who died from EVALI to illustrate the clinical characteristics common among such patients.

METHODS

STUDY OVERSIGHT

This investigation was reviewed in accordance with CDC procedures for protection of human research participants and was considered non-research public health surveillance activity intended for use in disease control or to inform policy during an emergency response. Details regarding the author contributions to the study are provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.

CASE DEFINITIONS

State health departments, a Council of State and Territorial Epidemiologists Task Force, and the CDC developed and disseminated EVALI surveillance case definitions and data-collection tools beginning in August 2019.[7,19,20] For this analysis, a fatal case of EVALI was defined as a confirmed or probable[12] case of EVALI (as determined with the use of the primary or out-of-hospital case definitions shown in Tables S1 and S2 in the Supplementary Appendix) in a patient who died as of January 4, 2020, and whose death was reported to the CDC as of January 7, 2020. A nonfatal case of EVALI was defined as a confirmed or probable case of EVALI in a hospitalized patient who had not died and whose case was reported to the CDC as of January 7, 2020.

DATA COLLECTION

Health departments from 50 states, the District of Columbia, and two U.S. territories (Puerto Rico and the Virgin Islands) voluntarily reported cases of EVALI in hospitalized patients to the CDC and, when available, included data from medical-record abstractions and patient interviews. Proxies were interviewed if patients were too ill or had died. The CDC received data on patients hospitalized for EVALI through a standardized national case-report form. Medical records were the primary data source for the variables included in the standardized form for both fatal and nonfatal cases; patient interviews were used for nonfatal cases and proxy interviews for fatal cases when data from the medical-record abstraction were missing. Individual state health authorities determined the methods and procedures used for data collection (such as those to be used for the incorporation of data from proxy interviews), which resulted in variations in data completeness. Data on fatal cases were supplemented with data abstracted from medical-record review, which included additional variables such as body-mass index and initial vital signs and laboratory results that were not available for nonfatal cases. Imaging reports were reviewed by two investigators.

ANALYSES

The results of the descriptive analyses are presented as proportions for categorical variables and medians and ranges for continuous variables. Differences are not reported with P values or confidence intervals because this study describes the entire population of patients with fatal or nonfatal cases of EVALI reported as of January 7, 2020. Analyses were completed with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

RESULTS OF THE NATIONAL STUDY

As of January 7, 2020, a total of 2558 nonfatal cases of EVALI in hospitalized patients from 50 states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands and 60 fatal cases in patients from 27 states and the District of Columbia were reported to the CDC. The demographic characteristics and substance use histories of these patients are provided in Table 1. Among the patients with available data on sex, 32 of 60 (53%) of those with fatal cases and 1666 of 2498 (67%) of those with nonfatal cases were male. The median age was 51 years (range, 15 to 75) among patients with fatal cases and 24 years (range, 13 to 85) among those with nonfatal cases. Among the patients with available data on race and ethnic group, 39 of 49 (80%) of those with fatal cases and 1104 of 1818 (61%) of those with nonfatal cases were non-Hispanic white.

Among the patients with available data on e-cigarette, or vaping, product use (45 patients with fatal cases and 2021 with nonfatal cases), 30 (67%) and 1593 (79%), respectively, reported nonexclusive use of THC-containing products; 25 (56%) and 1109 (55%), respectively, reported nonexclusive use of nicotine-containing products; 12 (27%) and 803 (40%), respectively, reported using both THC-containing and nicotine-containing products; and 2 (4%) and 122 (6%), respectively, reported using neither (Table 1). Among the patients with available data on combustible tobacco use, 44 of 56 (79%) of those with fatal cases and 439 of 1327 (33%) of those with nonfatal cases were current or former smokers.

The medical histories of the patients with fatal or nonfatal cases of EVALI who had available data are provided in Table 2. The patients with fatal cases were more likely than those with nonfatal cases to have a history of any respiratory disease (25 of 57 [44%] vs. 371 of 1429 [26%]), cardiac disease (26 of 55 [47%] vs. 115 of 1169 [10%]), and any mental health condition (32 of 49 [65%] vs. 575 of 1398 [41%]). A total of 26 of 50 patients (52%) with fatal cases had obesity.

The clinical characteristics of the hospitalized patients with fatal or nonfatal cases of EVALI who had available data are provided in Table 3 (full details are provided in Table S3). Approximately half the hospitalized patients with fatal cases (25 of 54 [46%]) and 479 of 2320 (21%) of those with nonfatal cases had presented initially in an outpatient setting (e.g., primary care physician location, urgent care center, or emergency department) without being admitted for EVALI-related symptoms. Among the hospitalized patients with fatal cases, 40 of 55 (73%) had hypoxia, 25 of 54 (46%) had tachycardia, and 26 of 52 (50%) had tachypnea at the time of admission to the hospital. The laboratory values at the initial admission showed that 37 of 52 patients (71%) with fatal cases had leukocytosis (white-cell counts >11,000 per cubic millimeter) and 29 of 45 (64%) had neutrophil predominance (white-cell count with >80% neutrophils). Most of the patients with fatal cases (93%) died in the hospital. Radiologic findings are provided in Table S4.

CASE REPORTS OF THREE PATIENTS WHO DIED FROM EVALI

Case 1: Multiple Preexisting Medical Conditions—A patient with coexisting asthma, chronic obstructive pulmonary disease, morbid obesity, preexisting heart failure, and

reported use of THC-, cannabidiol-, and nicotine-containing e-cigarette, or vaping, products was admitted to the hospital 8 days after the onset of symptoms because of severe respiratory distress. Treatment with broad-spectrum antibiotics, diuretics, bronchodilators, systemic glucocorticoids, and bilevel positive airway pressure was initiated. Within 48 hours, acute respiratory distress syndrome developed, and the patient underwent intubation and mechanical ventilation. Evaluation and treatment decisions were complicated by respiratory failure and multiple chronic conditions. The provision of adequate oxygenation and ventilation remained difficult even though the patient was in a prone position. The patient died on hospital day 21. The full case report is provided in the Supplementary Appendix.

Case 2: Recrudescence of Symptoms—A patient visited two different health facilities 2 days after the onset of illness and was discharged home with a prescription for antibiotics and antiemetics for presumed community-acquired pneumonia. Three days later, the patient visited a different health facility and was admitted; treatments with bronchodilators and broad-spectrum antibiotics were initiated. The patient reported using nicotine-containing, but not THC-containing, e-cigarette, or vaping, products. The patient had increasing respiratory distress and fever (to a temperature of 38.9°C), which led to the initiation of systemic glucocorticoids on hospital day 3. On hospital day 5, the patient was discharged home with prescriptions for levofloxacin and a glucocorticoid on a tapering schedule.

Two days after discharge, the patient's family reported that nausea, vomiting, and malaise recurred, and they found the patient to be unresponsive. Despite resuscitation efforts and readmission, the patient died a few hours later. According to the family report, the patient had used THC-containing products (Dank Vapes and Maui Wowi). Residue on the product cartridges tested positive for THC and vitamin E acetate. The full case report is provided in the Supplementary Appendix.

Case 3: No Glucocorticoids during Initial Hospitalization—A patient visited an outpatient facility the day after the onset of symptoms and was treated for viral gastroenteritis and sent home. This patient presented again with headache, nausea, vomiting, and diarrhea on day 6 of illness and was admitted to the hospital for dehydration. A chest radiograph on hospital day 4 showed prominent bilateral interstitial markings. The patient reported using nicotine-containing e-cigarette, or vaping, products, received treatment with azithromycin, and was transferred to the intensive care unit because of respiratory distress.

On hospital day 15, the patient was discharged home with instructions to abstain from using such products. During an interview with public health department staff, the patient reported having used the THC-containing product Dank Vapes. On day 24, because of continued respiratory compromise, the patient was readmitted to the hospital to undergo intubation and mechanical ventilation. Treatment with systemic glucocorticoids was initiated. On day 40, the patient underwent extracorporeal membrane oxygenation. On day 41, the patient had severe hypotension and cardiac arrest and died. The products submitted for testing after death included a THC-containing product, which was found to contain castor oil (no vitamin E acetate). The full case report is provided in the Supplementary Appendix.

DISCUSSION

This study assesses the clinical characteristics of hospitalized patients with fatal or nonfatal cases of EVALI. Consistent with the findings in previous reports,[12,13,15,17] most of the patients with fatal cases reported using THC-containing e-cigarette, or vaping, products. Nearly one third of the patients with fatal cases reported nicotine use only, and almost one quarter reported dual use, which suggests that other causal mechanisms may need to be considered. The median age was higher among the patients with fatal cases than among those with nonfatal cases, and the proportion of patients who had chronic medical conditions or were current or former combustible tobacco smokers was higher among those with fatal cases. Some patients with fatal cases had initially reported gastrointestinal symptoms (e.g., diarrhea and nausea), although such symptoms were reported more frequently among patients with nonfatal cases. Clinicians should consider EVALI in patients who present primarily with constitutional symptoms, gastrointestinal symptoms, or both.[21]

More than half the patients with fatal cases (63%) received a diagnosis of acute respiratory distress syndrome, which can lead to life-threatening acute hypoxemic respiratory failure.[22] Patients with EVALI who have multiple chronic conditions may be at higher risk for acute respiratory distress syndrome and its complications. Because traditional mechanical ventilation can worsen lung injury in patients with acute lung injury or acute respiratory distress syndrome, which would then increase the risk of nonpulmonary organ or system failure,[23] clinicians should consider evidence-based principles regarding the management of acute respiratory distress syndrome when treating patients with severe cases of EVALI.[24]

A higher proportion of hospitalized patients with fatal cases than those with nonfatal cases had cardiac disease, asthma, or chronic obstructive pulmonary disease. Cardiac or respiratory conditions in patients who use e-cigarette, or vaping, products may complicate assessment, radiologic interpretations, and management, particularly if the exposure history is incomplete. Patients may withhold medically relevant information because they fear being judged negatively by their clinical provider, they do not want to hear how harmful their behavior was, or they are embarrassed.[25] Cases 2 and 3 show how incomplete exposure history may delay treatment. Illegality of THC use can contribute to an incomplete exposure history, which reinforces the need for empathetic, nonjudgmental communication between the clinician and patient (or proxy) in a confidential setting.

Two thirds of patients with fatal cases (65%) had a known mental health condition — a higher percentage than that among patients with nonfatal cases (41%) and the U.S. general population (19%).[26] Patients, particularly former smokers, with mental health conditions are more likely to report lifetime and current e-cigarette, or vaping, product use.[27] The prevalence of mental health conditions is higher among persons reporting concurrent use of cannabis and conventional cigarettes.[28] Addressing underlying mental health conditions among patients with EVALI is an important component of hospital care, discharge planning, and postdischarge follow-up care.[29]

In the current study, the percentage of patients who had obesity was higher among those with fatal cases (52%) than in the general population (40%). Data on body weight

were not available for the patients with nonfatal cases. Obesity, a major risk factor for respiratory diseases,[30–33] can lead to changes in pulmonary physiologic variables, complicate respiratory disease, and present challenges in achieving adequate mechanical ventilation.[30–32,34] More studies are warranted to determine if there is an association between obesity and development of EVALI and whether obesity contributes to the severity of EVALI outcomes.

In outpatient settings, when symptoms are attributable to infections, glucocorticoid use is cautioned[9]; limited research suggests that glucocorticoids may be beneficial in the treatment of EVALI.[8,15,29,35] Glucocorticoid administration may be warranted in severely ill patients when it is considered safe and feasible, after ruling out any life-threatening infections, such as influenza. Among the patients with fatal cases who had available data, the time from the onset of symptoms to glucocorticoid administration varied widely, and coadministration with antibiotics was frequently observed. Few patients with fatal cases had reported improvement with glucocorticoids; administering glucocorticoids too late in the clinical course may partially explain this finding. Glucocorticoid administration has been attributed to rapid clinical improvement, including improvement in oxygenation.[21,36] Glucocorticoid administration is recommended if there is no improvement with antibiotics, respiratory support, or both, and the dosing and duration should be determined on a case-by-case basis.[36] Current interim clinical guidance from the CDC provides more details on glucocorticoid administration.[29]

The data in our study have limitations. We counted any patient with EVALI who died as a fatal case, although many patients had preexisting medical conditions that may have contributed to death. Preexisting medical conditions may have influenced hospitalization; however, a previous report noted that as of November 5, 2019, nonhospitalized patients with EVALI were similar to hospitalized patients with EVALI and composed only 5% of all cases.[9] If death takes place outside a hospital, it may be difficult to attribute the cause of death to EVALI, so some fatal cases may have been missed. Many patients were either too ill to interview or died before they could be interviewed, so some data are subject to limitations of reporting by proxies. More in-depth data collection and follow-up were used for patients with fatal cases but not for those with nonfatal cases; this could account for some reported differences. We did not compare data on glucocorticoid use between patients with fatal cases and those with nonfatal cases because of limited information from those with nonfatal cases. Misclassification of substance use could have occurred, and ascertainment bias may have been present in the reporting of substance use between the patients with fatal cases and those with nonfatal cases because more proxy interviews were performed for the patients who died.

About half the patients in this series were seen at least once in an outpatient setting before their final hospital admission; earlier diagnosis and appropriate treatment may have improved outcomes.[15,35] Eight patients had been discharged from a hospital before they died, which suggests that there may be opportunities to review stability before discharge, to tailor messaging and interventions more toward the avoidance of e-cigarette, or vaping, products, to communicate the importance of adherence to a glucocorticoid-tapering

schedule, to enhance coordinated postdischarge care, and to identify worsening symptoms with timely follow-up after discharge.[29]

Chronic conditions, such as asthma, chronic obstructive pulmonary disease, cardiac disease, and any mental health condition, were common among hospitalized patients with EVALI. Clinicians and public health practitioners should ensure an accurate and timely assessment of exposures and cessation of those exposures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Office on Smoking and Health. E-cigarette use among youth and young adults: a report of the Surgeon General. Atlanta: National Center for Chronic Disease Prevention and Health Promotion, 2016.
2. Grana R, Benowitz N, Glantz SA. E-cigarettes: a scientific review. Circulation 2014; 129: 1972–86. [PubMed: 24821826]
3. Morean ME, Lipshie N, Josephson M, Foster D. Predictors of adult e-cigarette users vaporizing cannabis using e-cigarettes and vape-pens. Subst Use Misuse 2017; 52: 974–81. [PubMed: 28323498]
4. Giroud C, de Cesare M, Berthet A, Varlet V, Concha-Lozano N, Favrat B. E-cigarettes: a review of new trends in cannabis use. Int J Environ Res Public Health 2015; 12: 9988–10008. [PubMed: 26308021]
5. Thanavala Y, Goniewicz ML. Vaping-induced severe respiratory disease outbreak: what went wrong? Lancet Respir Med 2019; 7: 1014–5. [PubMed: 32944502]
6. Parraga G, Morissette MC. E-cigarettes: what evidence links vaping to acute lung injury and respiratory failure? Can J Respir Crit Care Sleep Med 2020; 4: 48–54.
7. Outbreak of lung injury associated with e-cigarette use, or vaping. Atlanta: Centers for Disease Control and Prevention, 2019 (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html).
8. Layden JE, Ghinai I, Pray I, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin — final report. N Engl J Med 2020;382: 903–16. [PubMed: 31491072]
9. Chatham-Stephens K, Roguski K, Jang Y, et al. Characteristics of hospitalized and nonhospitalized patients in a nationwide outbreak of e-cigarette, or vaping, product use–associated lung injury — United States, November 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 1076–80. [PubMed: 31751326]
10. Taylor J, Wiens T, Peterson J, et al. Characteristics of e-cigarette, or vaping, products used by patients with associated lung injury and products seized by law enforcement — Minnesota, 2018 and 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 1096–100. [PubMed: 31774740]
11. Krishnasamy VP, Hallowell BD, Ko JY, et al. Update: characteristics of a nation-wide outbreak of e-cigarette, or vaping, product use–associated lung injury — United States, August 2019–January 2020. MMWR Morb Mortal Wkly Rep 2020; 69: 90–4. [PubMed: 31971931]
12. Perrine CG, Pickens CM, Boehmer TK, et al. Characteristics of a multistate outbreak of lung injury associated with e-cigarette use, or vaping — United States, 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 860–4. [PubMed: 31581168]

13. Moritz ED, Zapata LB, Lekiachvili A, et al. Update: characteristics of patients in a national outbreak of e-cigarette, or vaping, product use-associated lung injuries — United States, October 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 985–9. [PubMed: 31671085]
14. Navon L, Jones CM, Ghinai I, et al. Risk factors for e-cigarette, or vaping, product use–associated lung injury (EVALI) among adults who use e-cigarette, or vaping, products — Illinois, July–October 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 1034–9.
15. Siegel DA, Jatlaoui TC, Koumans EH, et al. Update: interim guidance for health care providers evaluating and caring for patients with suspected e-cigarette, or vaping, product use associated lung injury — United States, October 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 919–27. [PubMed: 31633675]
16. Davidson K, Brancato A, Heetderks P, et al. Outbreak of electronic-cigarette–associated acute lipoid pneumonia — North Carolina, July–August 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 784–6. [PubMed: 31513559]
17. Ghinai I, Pray IW, Navon L, et al. E-cigarette product use, or vaping, among persons with associated lung injury — Illinois and Wisconsin, April–September 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 865–9. [PubMed: 31581166]
18. Lewis N, McCaffrey K, Sage K, et al. E-cigarette use, or vaping, practices and characteristics among persons with associated lung injury — Utah, April–October 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 953–6. [PubMed: 31647788]
19. 2019 Lung injury surveillance case definition for out-of-hospital deaths (CDC) — October 4, 2019. Atlanta: Centers for Disease Control and Prevention, 2019 (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/assets/2019-Lung-Injury-Surveillance-Case-Definition-Out-of-Hospital-508.pdf).
20. 2019 Lung injury surveillance primary case definitions, September 18, 2019. Atlanta: Centers for Disease Control and Prevention, 2019 (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/assets/2019-Lung-Injury-Surveillance-Case-Definition-508.pdf).
21. Blagev DP, Harris D, Dunn AC, Guidry DW, Grissom CK, Lanspa MJ. Clinical presentation, treatment, and short-term outcomes of lung injury associated with e-cigarettes or vaping: a prospective observational cohort study. Lancet 2019; 394: 2073–83. [PubMed: 31711629]
22. Howell MD, Davis AM. Management of ARDS in adults. JAMA 2018; 319: 711–2. [PubMed: 29466577]
23. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342: 1301–8. [PubMed: 10793162]
24. Griffiths MJD, McAuley DF, Perkins GD, et al. Guidelines on the management of acute respiratory distress syndrome. BMJ Open Respir Res 2019; 6(1): e000420.
25. Levy AG, Scherer AM, Zikmund-Fisher BJ, Larkin K, Barnes GD, Fagerlin A. Prevalence of and factors associated with patient nondisclosure of medically relevant information to clinicians. JAMA Netw Open 2018; 1: e185293. [PubMed: 30646397]
26. Office of Science Policy, Planning, and Communications. Mental illness. Bethesda, MD: National Institute of Mental Health, 2019 (https://www.nimh.nih.gov/health/statistics/mental-illness.shtml).
27. Spears CA, Jones DM, Weaver SR, Pechacek TF, Eriksen MP. Use of electronic nicotine delivery systems among adults with mental health conditions, 2015. Int J Environ Res Public Health 2016; 14(1): 10.
28. Peters EN, Schwartz RP, Wang S, O'Grady KE, Blanco C. Psychiatric, psychosocial, and physical health correlates of co-occurring cannabis use disorders and nicotine dependence. Drug Alcohol Depend 2014; 134: 228–34. [PubMed: 24183498]
29. Evans ME, Twentyman E, Click ES, et al. Update: interim guidance for health care professionals evaluating and caring for patients with suspected e-cigarette, or vaping, product use-associated lung injury and for reducing the risk for rehospitalization and death following hospital discharge — United States, December 2019. MMWR Morb Mortal Wkly Rep 2020; 68: 1189–94. [PubMed: 31895915]
30. Zammit C, Liddicoat H, Moonsie I, Makker H. Obesity and respiratory diseases. Int J Gen Med 2010; 3: 335–43. [PubMed: 21116339]

31. Peters U, Suratt BT, Bates JHT, Dixon AE. Beyond BMI: obesity and lung disease. Chest 2018; 153: 702–9. [PubMed: 28728934]

32. Suratt BT, Ubags NDJ, Rastogi D, et al. An official American Thoracic Society Workshop report: obesity and metabolism: an emerging frontier in lung health and disease. Ann Am Thorac Soc 2017; 14: 1050–9. [PubMed: 28570148]

33. Franssen FME. Overweight and obesity are risk factors for COPD misdiagnosis and overtreatment. Chest 2014; 146: 1426–8. [PubMed: 25451339]

34. Fernandez-Bustamante A, Hashimoto S, Serpa Neto A, Moine P, Vidal Melo MF, Repine JE. Perioperative lung protective ventilation in obese patients. BMC Anesthesiol 2015; 15: 56. [PubMed: 25907273]

35. Jatlaoui TC, Wiltz JL, Kabbani S, et al. Update: interim guidance for health care providers for managing patients with suspected e-cigarette, or vaping, product use–associated lung injury — United States, November 2019. MMWR Morb Mortal Wkly Rep 2019; 68: 1081–6. [PubMed: 31751322]

36. Kalininskiy A, Bach CT, Nacca NE, et al. E-cigarette, or vaping, product use associated lung injury (EVALI): case series and diagnostic approach. Lancet Respir Med 2019; 7: 1017–26. [PubMed: 31711871]

Table 1.

Case Status, Demographic Characteristics, and Substance Use History of Patients with Fatal or Nonfatal Cases of EVALI.[*]

Variable	Patients with Fatal Cases	Patients with Nonfatal Cases
Case status		
Confirmed — no./total no. (%)	34/60 (57)	1344/2558 (53)
Probable — no./total no. (%)	26/60 (43)	1214/2558 (47)
Demographic characteristics		
Sex — no./total no. (%)		
Male	32/60 (53)	1666/2498 (67)
Female	28/60 (47)	832/2498 (33)
Age group — no./total no. (%)		
<35 yr	16/60 (27)	1963/2514 (78)
≥35 yr	44/60 (73)	551/2514 (22)
Median age (range) — yr	51 (15–75)	24 (13–85)
Male	48 (15–73)	23 (13–77)
Female	52 (18–75)	25 (13–85)
Race and ethnic group — no./total no. (%)[†]		
White, non-Hispanic	39/49 (80)	1104/1818 (61)
Other	10/49 (20)	714/1818 (39)
Substance use history		
Substances used in e-cigarette, or vaping, products in the 3 mo before illness onset — no./total no. (%)[‡]		
THC-containing products[§]		
Nonexclusive use	30/45 (67)	1593/2021 (79)
Exclusive use	18/45 (40)	669/2021 (33)
Frequency of THC-containing product use		
Daily	7/10 (70)	641/862 (74)
A few times per week	1/10 (10)	121/862 (14)
A few times per month	0	49/862 (6)
Monthly or less	2/10 (20)	51/862 (6)
Nicotine-containing products[¶]		
Nonexclusive use	25/45 (56)	1109/2021 (55)

Variable	Patients with Fatal Cases	Patients with Nonfatal Cases
Exclusive use	13/45 (29)	279/2021 (14)
Frequency of nicotine-containing product use		
Daily	12/14 (86)	569/670 (85)
A few times per week	1/14 (7)	56/670 (8)
A few times per month	0	22/670 (3)
Monthly or less	1/14 (7)	23/670 (3)
Use of both THC- and nicotine-containing products	12/45 (27)	803/2021 (40)
Use of neither THC- nor nicotine-containing products	2/45 (4)	122/2021 (6)
Other substances used — no./total no. (%)		
Combustible marijuana[//]	14/30 (47)	566/1137 (50)
Combustible tobacco	44/56 (79)	439/1327 (33)
Former use	22/56 (39)	NA
Current use	22/56 (39)	NA
Other substance abuse	3/45 (7)	NA

[*] The values shown are based on available data. EVALI denotes e-cigarette, or vaping, product use–associated lung injury, NA data not available, and THC tetrahydrocannabinol.

[†] Race and ethnic group were reported by the patient (or proxy) during the interview or were abstracted from the medical record. “Other” race and ethnic group includes black or African American, non-Hispanic; American Indian or Alaska Native, non-Hispanic; Asian, native Hawaiian, or other Pacific Islander, non-Hispanic; other, non-Hispanic; and Hispanic. The data were combined to protect patient identity.

[‡] Data are reported for the patients who had available data on both THC-containing and nicotine-containing product use.

[§] Patients with nonexclusive use were those who reported using THC-containing products and other e-cigarette, or vaping, products, and patients with exclusive use were those who reported using THC-containing products but did not report the use of any nicotine-containing products.

[¶] Patients with nonexclusive use were those who reported using nicotine-containing products and other e-cigarette, or vaping, products, and patients with exclusive use were those who reported using nicotine-containing products but did not report the use of any THC-containing products.

[//] Combustible marijuana use included both current and former use.

Table 2.

Medical and Mental Health Conditions in Fatal or Nonfatal Cases of EVALI.

Medical History	Patients with Fatal Cases	Patients with Nonfatal Cases
	no./total no. with data (%)	
Any preexisting medical condition*	44/58 (76)	NA
Any chronic respiratory disease†	25/57 (44)	371/1429 (26)
History of asthma	13/57 (23)	102/1297 (8)
History of chronic obstructive pulmonary disease	12/57 (21)	25/1297 (2)
Any cardiac disease‡	26/55 (47)	115/1169 (10)
Hypertension	25/55 (45)	NA
Heart failure	4/57 (7)	NA
Myocardial infarction	1/57 (2)	NA
Any mental health condition§	32/49 (65)	575/1398 (41)
Depression	22/52 (42)	375/1183 (32)
Anxiety	14/51 (27)	434/1189 (37)
Overweight¶	9/50 (18)	NA
Obese‖	26/50 (52)	NA

*Any preexisting medical condition includes any cardiac disease, any chronic respiratory disease, or obesity.

†Any chronic respiratory disease includes asthma, bronchiectasis, chronic obstructive pulmonary disease, cystic fibrosis, pneumonitis, or other lung conditions.

‡Any cardiac disease includes heart failure, hypertension, myocardial infarction, or other cardiac conditions.

§Any mental health condition includes anxiety, attention deficit–hyperactivity disorder, bipolar disorder, depression, post-traumatic stress disorder, or other mental health conditions, with the exclusion of history of substance use.

¶Overweight was defined as a body-mass index (the weight in kilograms divided by the square of the height in meters) between 25.0 and 29.9.

‖Obesity was defined as a body-mass index of 30.0 or higher.

Table 3.

Clinical Course, Initial Vital Signs, and Initial Laboratory Results in Hospitalized Patients with Fatal or Nonfatal Cases of EVALI.*

Variable	Patients with Fatal Cases†	Patients with Nonfatal Cases
	no./total no. with data (%)	
Clinical course		
Presented initially in an outpatient setting without being admitted for symptoms‡	25/54 (46)	479/2320 (21)
Reported any respiratory symptoms§	55/56 (98)	1707/1779 (96)
Reported any gastrointestinal symptoms¶	26/49 (53)	1343/1681 (80)
Admitted to an ICU‖	52/57 (91)	638/1504 (42)
Received ventilatory support with CPAP or BiPAP	32/56 (57)	179/1068 (17)
Underwent endotracheal intubation**	47/58 (81)	131/755 (17)
Received antibiotics	57/57 (100)	1154/1183 (98)
Received glucocorticoids	45/58 (78)	1252/1419 (88)
Location of death		
Hospital, ICU, or ED	56/60 (93)	—
Other	4/60 (7)††	—
Initial vital signs		
Oxygen saturation <95% while breathing ambient air	40/55 (73)	NA
Tachycardia, heart rate >100 beats/min	25/54 (46)	NA
Tachypnea, respiratory rate >20 breaths/min	26/52 (50)	NA
Evidence of hypotension, SBP <90 mm Hg or DBP <60 mm Hg	12/54 (22)	NA
Body temperature ≥38°C	11/53 (21)	NA
Initial laboratory results ‡‡		
White-cell count >11,000/mm^3	37/52 (71)	NA
White-cell count with >80% neutrophils	29/45 (64)	NA
White-cell count with >10% lymphocytes	15/44 (34)	NA
Aspartate aminotransferase level, alanine aminotransferase level, or both		
>35 U/liter	36/49 (73)	NA
>105 U/liter	16/49 (33)	NA

[*] Full details of the clinical characteristics are provided in Table S3. BiPAP denotes bilevel positive airway pressure, CPAP continuous positive airway pressure, DBP diastolic blood pressure, ED emergency department, ICU intensive care unit, NA data not available, and SBP systolic blood pressure.

[†] One out-of-hospital death occurred, and this patient was not included in the denominator for the following variables: admitted to an ICU, received ventilatory support with CPAP or BiPAP, underwent endotracheal intubation, received antibiotics, received glucocorticoids, all the initial vital signs, and all the initial laboratory results.

[‡] Outpatient settings included, for example, primary care physician locations, urgent care centers, and EDs.

[§] Respiratory symptoms included chest pain (and pleuritic chest pain), congestion, cough (and productive cough), difficulty breathing, hemoptysis, shortness of breath, sneezing, sore throat, runny nose, and wheezing.

[¶] Gastrointestinal symptoms included abdominal pain, diarrhea, nausea, and vomiting.

[‖] Three patients with fatal cases were not admitted to the ICU at the first hospital admission but were later admitted to the ICU at readmission.

[**] Four patients with fatal cases did not undergo intubation at the first hospital admission but underwent intubation on readmission. Two patients with fatal cases declined intubation.

[††] Three patients were admitted to the hospital, had confirmed cases of EVALI, and died in a location other than the hospital. One patient was never admitted and died in an out-of-hospital setting..

[‡‡] The normal range for white-cell count is 4500 to 11,000 cells per cubic millimeter; for aspartate aminotransferase level, 10 to 30 U per liter; and for alanine aminotransferase level, 10 to 40 U per liter.