

ORIGINAL RESEARCH

# Cardiovascular Risk Among Stroke Survivors With Combustible and Electronic Cigarettes: A Nationwide Study in Korean Men

Joonsang Yoo , MD, PhD; Jimin Jeon , MS; Minyoul Baik , MD; Yun Young Choi, MD; Jinkwon Kim , MD, PhD

**BACKGROUND:** Although use of electronic cigarettes (e-cigarettes) is increasing, its cardiovascular impact remains uncertain, especially among stroke survivors. We compared the incidence of major cardiovascular events in stroke survivors according to cigarette/e-cigarette use.

**METHODS:** We conducted a retrospective cohort study of Korean men with acute stroke who underwent national health check-ups within 3 years of the index stroke (2018–2022). The patients were categorized into 4 groups based on their cigarette/e-cigarette use status: nonusers, combustible cigarette users, dual users (both combustible cigarettes and e-cigarettes), and e-cigarette-only users. The primary outcome was a composite of recurrent stroke and myocardial infarction. Multivariable Cox models estimated hazard ratios (HRs) across groups.

**RESULTS:** Of the 115 240 men with stroke, 89 326 (77.5%) were nonusers, 23 688 (20.6%) were combustible cigarette users, 1498 (1.3%) were dual users, and 728 (0.7%) were e-cigarette-only users. During a mean follow-up of 2.61±1.46 years, 6722 patients suffered primary outcome events (ischemic stroke: 4799; hemorrhagic stroke: 1165; myocardial infarction: 758). Compared with nonusers, the risk of the primary outcome was higher in the combustible cigarette group (HR, 1.35 [95% CI, 1.27–1.43]) and dual users (HR, 1.27 [95% CI, 1.01–1.60]), whereas e-cigarette-only users showed a nonsignificant elevation (HR, 1.11 [95% CI, 0.77–1.59]).

**CONCLUSIONS:** Among Korean male stroke survivors, combustible cigarette use and dual use were associated with higher risk of recurrent stroke or myocardial infarction, whereas e-cigarette-only use was not significantly different from nonuse. Further research is warranted to clarify the long-term cardiovascular effects of e-cigarette use among stroke survivors.

**Key Words:** cardiovascular disease ■ electronic cigarettes ■ myocardial infarction ■ smoking ■ stroke

Smoking is a major modifiable risk factor for cardiovascular diseases and mortality, accounting for approximately 11% of global cardiovascular mortality.<sup>1</sup> In recent years, electronic cigarettes (e-cigarettes) have emerged as a potential alternative to conventional combustible cigarettes, with many individuals adopting them as a smoking cessation tool or harm-reduction strategy.<sup>2–4</sup> Unlike combustible

cigarettes, e-cigarettes eliminate the combustion process, thereby reducing exposure to certain toxins such as carbon monoxide and tar. However, these devices still deliver nicotine, ultrafine particles, and various chemical constituents that may adversely affect vascular function and contribute to inflammatory and prothrombotic states.<sup>5,6</sup> Although e-cigarettes may differ from conventional combustible cigarettes in terms

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This article was sent to Olufunmilayo H. Obisesan, MD, MPH, Assistant Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.125.044609>

For Sources of Funding and Disclosures, see page 7.

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## CLINICAL PERSPECTIVE

### What Is New?

- In a large-scale nationwide cohort of Korean male stroke survivors, both combustible cigarette use and dual use of combustible and electronic cigarettes were associated with a significantly increased risk of recurrent stroke or myocardial infarction compared with nonusers, whereas electronic cigarette-only use showed a nonsignificant elevation.

### What Are the Clinical Implications?

- Among stroke survivors, the use of combustible cigarette and dual use remain major risk factors for recurrent cardiovascular events.
- Although complete smoking cessation is the most appropriate choice, the risk for recurrent stroke and myocardial infarction associated with electronic-cigarette-only use appears lower than that of combustible cigarette or dual use in stroke survivors.

## Nonstandard Abbreviations and Acronyms

<b>e-cigarette</b>	electronic cigarette
<b>NHIS</b>	National Health Insurance Service

of nicotine content and exposure to specific chemicals, emerging evidence suggests that they may still pose substantial risks to vascular health, potentially comparable with or even worse than those of conventional combustible cigarettes.<sup>7,8</sup> Studies indicate that e-cigarette use can lead to endothelial dysfunction, oxidative stress, and inflammatory responses in the vasculature, which are also implicated in smoking-related vascular damage.<sup>9</sup> Nevertheless, findings across prior studies remain inconsistent, and the long-term cardiovascular consequences of e-cigarette use are not yet established.

Stroke remains one of the leading causes of death and disability, posing a serious global health challenge.<sup>10,11</sup> Although smoking is a well-established risk factor for recurrent cardiovascular events and death, persistent smoking is relatively common among stroke survivors.<sup>12</sup> Nevertheless, research focusing on e-cigarette use among stroke survivors remains limited, leaving a gap in our understanding of its impact on secondary cardiovascular prevention.<sup>13,14</sup> This gap in knowledge is particularly relevant for stroke survivors, a vulnerable group in whom even modest increases in cardiovascular risk may have major clinical

consequences. Given the growing popularity of e-cigarettes, there is an increasing need to clarify their long-term cardiovascular effects, which remain poorly understood and controversial. Accordingly, this study aimed to investigate the impact of e-cigarette use on cardiovascular events among patients who had experienced a stroke, using a nationwide health examination cohort database.

## METHODS

### Data Availability

The data set used in this study was provided by the National Health Insurance Service (NHIS) in South Korea (<https://nhiss.nhis.or.kr/bd/ab/bdaba000eng.do>) for research purposes related to this study (NHIS-2024-1-480). Therefore, public access to this data set is not available. To access the data, researchers must submit a completed application form, research proposal, and valid institutional review board-approval documents, all of which will be evaluated by the National Health Insurance Sharing Service's Inquiry Committee for Research Support.

### Data Source and Study Design

We conducted a retrospective cohort analysis using an anonymized nationwide health claims database provided by the NHIS. The NHIS is a single-payer system that provides health insurance to almost the entire Korean population.<sup>15</sup> The NHIS health claims database includes information on health care visits, diagnoses, procedures, and prescriptions for the Korean population. Diagnoses made during health care visits are recorded according to the *International Classification of Diseases, Tenth Revision (ICD-10)*. For health promotion and prevention, the NHIS offers a standardized national health examination free of charge every 2 years for Korean adults aged ≥40 years. The health examination contains questionnaires on various lifestyle factors, including smoking. Since 2018, the use of e-cigarettes has also been recorded. This study was approved by the institutional review board of Yongin Severance Hospital (approval number 9-2022-0194) with a waiver of informed consent, because it was a retrospective analysis of fully anonymized data.

### Study Population

We identified patients who underwent the national health examination between 2018 and 2022 and were diagnosed with acute stroke within the preceding 3 years of their examination. The index date for each participant was defined as the date of their national health examination. Acute stroke was defined as hospitalization with primary *ICD-10* diagnosis codes I60

to I63 (hemorrhagic stroke: I60–I62, ischemic stroke: I63) and confirmed by brain computed tomography or magnetic resonance imaging during admission.<sup>16</sup> Patients with missing data on cigarette/e-cigarette use status, other essential health examination variables (blood pressure, fasting glucose, body mass index, and serum creatinine), or key covariates (sex and age) were excluded. We also excluded women from the study because self-reported smoking rates in Korean women are low and unreliable, because they are more likely to underreport cigarette/e-cigarette use status due to social desirability bias.<sup>17–19</sup> Therefore, we included only men. In addition, we excluded patients with a follow-up of <30 days. This included patients who experienced a primary outcome (stroke or myocardial infarction [MI]), all-cause death, or were lost to follow-up due to emigration or a loss of eligibility for the NHIS within 30 days from the index date of health examination.

### Study Outcome

The primary outcome was defined as a composite of recurrent stroke and MI occurring after the index date. Secondary outcomes were the individual components of the primary outcomes (ischemic stroke, hemorrhagic stroke, and MI). Recurrent stroke was defined as hospitalization with a primary diagnosis of *ICD-10* codes I60 to I63, accompanied by brain computed tomography or magnetic resonance imaging during the admission, and either a hospital stay of  $\geq 3$  days or death within 3 days.<sup>20</sup> MI was defined as an admission with a primary diagnosis of *ICD-10* codes I21 or I22. The study participants were followed until the occurrence of the primary outcome, loss of eligibility, death, or December 31, 2022, whichever occurred first. The diagnostic accuracy of MI and stroke based on the NHIS claims data in Korea has been validated.<sup>20</sup>

### Cigarette/E-Cigarette Use Status and Covariates

From the index health examination, we collected demographic data (age, sex, and quartile of household income), laboratory test results, comorbidities (hypertension, diabetes, atrial fibrillation, chronic kidney disease, and coronary artery disease), and questionnaires for lifestyle (physical activity, alcohol consumption per week, and cigarette/e-cigarette use status). Based on the cigarette/e-cigarette use status questionnaire, individuals who reported current e-cigarette use were classified as either dual users (also reporting combustible cigarette use) or e-cigarette-only users. The remaining participants were classified as combustible cigarette users and nonusers. Hypertension was considered present if resting blood pressure was

$\geq 140/90$  mmHg, or if they self-reported a history of hypertension. Diabetes was defined as a fasting glucose level of  $\geq 7.0$  mmol/L or a self-reported history of diabetes. Atrial fibrillation was identified by the presence of *ICD-10* code I48 in the health claims data. Chronic kidney disease was identified by an estimated glomerular filtration rate of  $< 60$  mL/min per  $1.73$  m<sup>2</sup> or proteinuria of  $\geq 1+$  on a urine dipstick test. Coronary artery disease was identified by the main diagnosis of *ICD-10* codes I20 to I25 or claims for percutaneous coronary intervention and a coronary artery bypass graft. Physical activity was classified into 4 groups based on the total weekly metabolic equivalent of task minutes derived from the questionnaire (0, 1–499, 500–999, and  $\geq 1000$ ).<sup>21</sup> Alcohol consumption was categorized into 3 groups: no alcohol,  $< 2$  drinks per week, or  $\geq 2$  drinks per week.

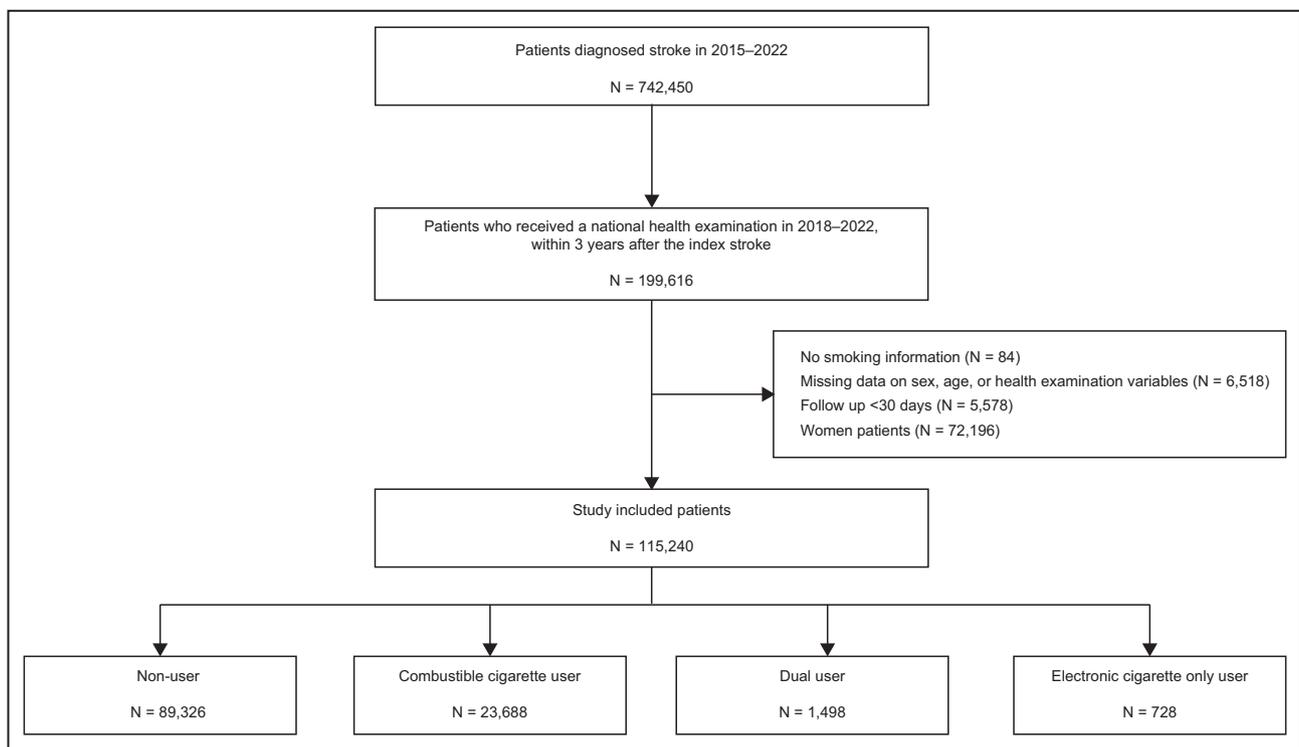
### Statistical Analysis

Continuous variables are presented as mean $\pm$ SD and categorical variables as number (%). Because the cohort comprises 4 smoking-status groups, baseline characteristics were compared across the 4 groups. For continuous variables, we used 1-way analysis of variance. For categorical variables, we used the  $\chi^2$  test. In general, e-cigarette users are relatively young and expected to have different baseline characteristics.<sup>22</sup> We conducted multivariable Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% CIs for the association between cigarette/e-cigarette use status and outcomes. Multivariable Cox models were adjusted for age, stroke type, period from stroke to health exam, household income, body mass index, hypertension, diabetes, atrial fibrillation, chronic kidney disease, coronary artery disease, physical activity, and alcohol consumption. As a secondary outcome analysis, we used cause-specific Cox regression models to estimate the HRs and 95% CIs for ischemic stroke, hemorrhagic stroke, and MI. The proportional hazard assumption in the Cox regression model was evaluated by calculating the Schoenfeld residuals and was not violated. All statistical analyses were performed using SAS (version 9.4) and the R software (version 4.3.0). All *P* values were 2-sided, and statistical significance was set at  $P < 0.05$ .

## RESULTS

### Study Populations

According to the inclusion and exclusion criteria (Figure), 115 240 men with stroke were included: 94 650 (82.1%) with ischemic stroke and 20 590 (17.9%) with hemorrhagic stroke. Health examinations were performed at a mean of 1.34 years after the acute



**Figure.** Flowchart with inclusion criteria.

stroke. In regard to cigarette/e-cigarette use status, 89 326 (77.5%) participants were nonusers, 23 688 (20.6%) were combustible cigarette users, 1498 (1.3%) dual users, and 728 (0.7%) were e-cigarette-only users (Table 1). The mean age was the highest among nonusers (65.64±11.92 years) and lowest among e-cigarette-only users (51.82±10.96 years,  $P<0.001$ ). In contrast, alcohol consumption was the lowest in nonusers and the highest in e-cigarette-only users.

### Primary Outcomes

During a mean follow-up of 2.61±1.46 years, 6722 patients experienced a primary outcome (ischemic stroke: 4799; hemorrhagic stroke: 1165; MI: 758). Compared with nonusers, combustible cigarette users (HR, 1.35 [95% CI, 1.27–1.43]) and dual users (HR, 1.27 [95% CI, 1.01–1.60]) had a higher hazard of the primary outcome, whereas e-cigarette-only users (HR, 1.11 [95% CI, 0.77–1.59]) had a slightly higher hazard that did not reach statistical significance (Table 2).

### Secondary Outcomes

In the secondary outcome analyses, the incidence of ischemic stroke was significantly higher among combustible cigarette users (HR, 1.37 [95% CI, 1.28–1.47]), whereas dual users (HR, 1.18 [95% CI, 0.89–1.58]) showed a nonsignificant trend toward elevated risk,

and e-cigarette-only users (HR, 1.01 [95% CI, 0.63–1.60]) showed similar risk compared with nonusers. For hemorrhagic stroke, the HRs were 1.11 (95% CI, 0.96–1.30) for combustible cigarette users, 1.06 (95% CI, 0.64–1.75) for dual users, and 1.30 (95% CI, 0.67–2.52) for e-cigarette-only users; none of these associations reached statistical significance. For MI, the HRs were 1.68 (95% CI, 1.42–2.00) for combustible cigarette users and 2.41 (95% CI, 1.38–4.22) for dual users, both statistically significant, whereas e-cigarette-only users had a slightly higher but nonsignificant risk (HR, 1.16 [95% CI, 0.37–3.62]).

### Subgroup Analyses

We performed subgroup analyses by age (<60 years, ≥60 years), stroke type (ischemic or hemorrhagic), and index year (before 2020, after 2020). No significant interaction was detected across the subgroups (Table S1). Compared with nonusers, combustible cigarette users and dual users aged <60 years showed higher hazard ratios for the primary outcome. No statistically significant associations were observed among e-cigarette-only users, and no significant interaction was detected across the subgroups. In contrast, no statistically significant associations were observed among e-cigarette-only users in any subgroup.

**Table 1. Baseline Characteristics of the Study Patients With Cigarette/Electronic Cigarette Use Status**

Variables	Total	Nonuser	Combustible cigarette user	Dual user	Electronic cigarette-only user
No.	115240	89326	23688	1498	728
Stroke type					
Ischemic stroke	94650 (82.13)	72846 (81.55)	20129 (84.98)	1142 (76.23)	533 (73.21)
Hemorrhagic stroke	20590 (17.87)	16480 (18.45)	3559 (15.02)	356 (23.77)	195 (26.79)
Age, y	64.40±11.87	65.64±11.92	60.91±10.30	51.73±10.54	52.01±11.78
Period from stroke to health exam, y	1.34±0.80	1.33±0.80	1.37±0.81	1.38±0.82	1.31±0.83
Household income					
Q1 (lowest)	30771 (26.70)	22145 (24.79)	8036 (33.92)	399 (26.64)	191 (26.24)
Q2	27505 (23.87)	20387 (22.82)	6558 (27.68)	400 (26.70)	160 (21.98)
Q3	31703 (27.51)	25130 (28.13)	5933 (25.05)	429 (28.64)	211 (28.98)
Q4 (highest)	25261 (21.92)	21664 (24.25)	3161 (13.34)	270 (18.02)	166 (22.80)
Body mass index, kg/m <sup>2</sup>	24.63±3.18	24.68±3.11	24.33±3.33	25.92±3.73	26.08±3.74
Hypertension	69452 (60.27)	54951 (61.52)	13300 (56.15)	795 (53.07)	406 (55.77)
Diabetes	36547 (31.71)	27556 (30.85)	8347 (35.24)	451 (30.11)	193 (26.51)
Atrial fibrillation	19309 (16.76)	16444 (18.41)	2674 (11.29)	132 (8.81)	59 (8.10)
Chronic kidney disease	20610 (17.88)	16490 (18.46)	3856 (16.28)	175 (11.68)	89 (12.23)
Coronary artery disease	14806 (12.85)	12007 (13.44)	2623 (11.07)	115 (7.68)	61 (8.38)
Physical activity, MET-min/wk					
0	50022 (43.41)	37341 (41.80)	11816 (49.88)	596 (39.79)	269 (36.95)
1–499	10974 (9.52)	8310 (9.30)	2367 (9.99)	207 (13.82)	90 (12.36)
500–999	12650 (10.98)	10028 (11.23)	2361 (9.97)	160 (10.68)	101 (13.87)
≥1000	41594 (36.09)	33647 (37.67)	7144 (30.16)	535 (35.71)	268 (36.81)
Alcohol consumption					
No	66983 (58.12)	56603 (63.37)	9769 (41.24)	367 (24.50)	244 (33.52)
<2/wk	27110 (23.52)	19664 (22.01)	6555 (27.67)	614 (40.99)	277 (38.05)
≥2/wk	21147 (18.35)	13059 (14.62)	7364 (31.09)	517 (34.51)	207 (28.43)

Data are presented as n (%) or mean±SD. MET indicates metabolic equivalent of task; and Q, quartile.

## DISCUSSION

In this retrospective nationwide cohort study of male stroke survivors, we evaluated the effects of e-cigarette and combustible cigarette use on the risk of recurrent

stroke or MI. Compared with nonusers, combustible cigarette users and dual users showed an increased risk of recurrent stroke and MI. In contrast, e-cigarette-only users demonstrated a numerically higher but nonsignificant hazard. These findings suggest that

**Table 2. Effect of Cigarette/E-Cigarette Use Status on Outcomes**

Variables	Adjusted hazard ratio [95% CI]*			
	Primary outcome†	Ischemic stroke	Hemorrhagic stroke	Myocardial infarction
No. of cases	6722	4799	1165	758
Cigarette/e-cigarette use status				
Nonuser	Reference	Reference	Reference	Reference
Combustible cigarette user	1.35 [1.27–1.43]	1.37 [1.28–1.47]	1.11 [0.96–1.30]	1.68 [1.42–2.00]
Dual user	1.27 [1.01–1.60]	1.18 [0.89–1.58]	1.06 [0.64–1.75]	2.41 [1.38–4.22]
E-cigarette-only user	1.11 [0.77–1.59]	1.01 [0.63–1.60]	1.30 [0.67–2.52]	1.16 [0.37–3.62]

E-cigarette indicates electronic cigarette.

\*Data are derived from multivariable Cox hazard regression models adjusted for age, stroke type, period from stroke to health exam, household income, body mass index, hypertension, diabetes, atrial fibrillation, chronic kidney disease, coronary artery disease, physical activity, and alcohol consumption.

†Composite of recurrent stroke and myocardial infarction.

combustible cigarette use and dual use remain major modifiable risk factors for recurrent stroke and MI among male stroke survivors, whereas the risk associated with e-cigarette-only use appears lower than that of combustible cigarette or dual use.

E-cigarettes have different characteristics from combustible cigarettes.<sup>2,3</sup> E-cigarettes do not involve combustion, thereby reducing the exposure to tar and carbon monoxide. However, they still contain nicotine and various chemical components that can adversely affect the cardiovascular system.<sup>6,9</sup> Nicotine can cause sympathetic overactivity, leading to increases in the heart rate, blood pressure, and arterial stiffness, all of which contribute to endothelial dysfunction and oxidative stress.<sup>5,6,9</sup> In addition, heating the carrier liquids (eg, propylene glycol and glycerin) can generate ultrafine particles and potentially harmful byproducts associated with inflammation and vascular injury.<sup>23–26</sup>

Several studies have reported that e-cigarette use also increase the risk of MI compared with nonusers, suggesting e-cigarette use is not completely risk free.<sup>27,28</sup> Meanwhile, in certain studies of patients undergoing percutaneous coronary intervention, switching from combustible cigarettes to e-cigarettes has shown reduced rates of major adverse cardiovascular events.<sup>4,29</sup> These findings suggest that although e-cigarettes still carry some cardiovascular risk compared with smoking cessation, their use may confer relative benefits compared with combustible cigarette use, especially for high-risk cardiovascular populations, as a less harmful alternative.

Currently, evidence on the association between e-cigarette use and stroke risk remains limited and largely inconclusive owing to insufficient data and inconsistent findings.<sup>30,31</sup> Some studies have suggested that e-cigarette use may not significantly alter cardiovascular risk, whereas others have highlighted that the high nicotine content in e-cigarettes can exacerbate vascular damage and accelerate atherosclerosis, including increases in the resting heart rate.<sup>32,33</sup> Certain preclinical studies indicate that e-cigarette exposure could compromise the blood–brain barrier and microvasculature, thereby raising the possibility of more severe ischemic brain injury.<sup>26,34</sup> A recent study using the National Health and Nutrition Examination Survey reported an increased stroke risk in e-cigarette users than nonusers, although the risk with e-cigarettes appeared lower than combustible cigarettes or dual use, reinforcing concerns that e-cigarettes may not be benign on stroke risk.<sup>35</sup> In a meta-analysis with 107 population-based epidemiological studies, the adjusted odds ratio (95% CI) for stroke with e-cigarette use compared with combustible cigarette use was 0.73 (0.47–1.13), and adjusted odds for stroke with e-cigarette use compared with nonuse of e-cigarettes was 1.32 (0.99–1.76).<sup>36</sup>

Among stroke survivors, evidence on the safety and effect of e-cigarettes remains limited and inconclusive.<sup>13,14,30,37</sup> Our data documented the clear harm from combustible smoking including dual use on recurrent risk in stroke survivors. As for e-cigarette-only users, we did not detect a statistically significant excess risk. However, the less risk relative to combustible smoking does not imply safety of e-cigarettes relative to non-smoking. Our results should not be interpreted as risk free for e-cigarette-only use in stroke survivors. Given the limited sample size and relatively short follow-up, potential excess risk associated with e-cigarette use may have been imprecisely estimated in this retrospective data set. From a secondary prevention standpoint, there is no doubt that complete cessation of smoking is the most appropriate choice for stroke survivors. Nevertheless, although e-cigarette use might be relatively less harmful than combustible smoking according to our study and prior reports, further research is warranted on their potential role as an alternative for those who have failed to complete smoking cessation, particularly in high-risk populations such as stroke survivors.

In the current study, dual use of combustible and e-cigarettes was 64% (1498/2326) among stroke survivors who smoke e-cigarettes. The dual users were at significantly increased risk of recurrent events, comparable with that of combustible users. Consistent with our data, many studies have shown that dual use of combustible cigarettes and e-cigarettes is associated with significant harm, in some cases exceeding that of exclusive combustible smoking.<sup>36,38</sup> The causes of e-cigarette use in dual users are varied, including attempts to quit smoking, avoiding public smoking bans, enjoying the flavors of e-cigarettes, social pressures to ban smoking, or a lack of harm perception with e-cigarettes.<sup>39</sup> Among dual users, one of the common causes is to quit or cut down on cigarette smoking.<sup>40</sup> However, there are complicating issues on whether e-cigarettes genuinely facilitate smoking cessation.<sup>31,41</sup> Although some recent clinical trials showed that use of e-cigarettes may be helpful for smoking cessation,<sup>42,43</sup> other studies reported that e-cigarette use was not effective<sup>44</sup> and actually lowers the rate of complete smoking cessation.<sup>45,46</sup> It remains unclear that dual use or use of e-cigarettes for the purpose of quitting smoking or reducing consumption of combustible cigarettes has the net effect on long-term smoking cessation and health outcomes. There are also concerns that dual users are exposed to an additional set of chemicals from both products, representing a wider range of toxins than either product alone, which may increase overall risk.<sup>36,40</sup> Consistent with our data and prior studies showing the harmful effect of dual use on cardiovascular risk compared with complete cessation, counseling to stroke survivors should prioritize

complete smoking cessation, rather than substitution or dual use.

This study has certain limitations. First, owing to the retrospective cohort design, the possibility of residual confounding factors could not be entirely ruled out despite adjustment for demographics, comorbidities, and lifestyle factors. Although our model incorporated several lifestyle factors, including physical activity and alcohol consumption, information on dietary habits, more detailed exercise patterns, and medication use was not incorporated. These unmeasured confounders may have influenced the observed associations. Also, we only included study participants with complete data on covariates. Because missing covariates may not have occurred at random, this could introduce potential bias. Patients with severe stroke sequelae might have limited access to cigarettes and are thus more likely to be classified as nonusers, potentially underestimating the true risk of smoking. Second, exposure characterization was limited because the national health examination database only captures the use of cigarettes and e-cigarettes but does not account for the use of other combustible products (eg, cigars, pipes, waterpipe) or noncombustible tobacco (eg, chewing tobacco, snuff, snus), which are uncommon in Korea. It also does not collect quantitative e-cigarette metrics such as nicotine concentration, vaping frequency, and device type. Given that the adverse cardiovascular effects of e-cigarettes may be dose-dependent, the absence of these exposure metrics limits our ability to assess potential dose–response relationships. Future studies incorporating more granular exposure data are warranted to clarify the cardiovascular impact of e-cigarette use among stroke survivors.<sup>35</sup> Third, the reliance on self-reported cigarette/e-cigarette use status may have introduced misclassification bias, and biochemical validation of smoking was not available in the national health examination database. Fourth, we assessed cigarette and e-cigarette use at a single time point after index stroke. Consequently, former users who quit before and after index stroke and never users were grouped together as nonusers in the analyses, although cardiovascular risk may remain elevated for some time after cessation. This limitation in classification could bias estimates toward the null or otherwise obscure true associations. In addition, cigarette and e-cigarette use may have changed during the follow-up, but this could not be accurately determined in our data set. Finally, although there were valid reasons, women were excluded and the study was limited to Korean stroke survivors who completed health checkups, which limits generalizability. Cultural and lifestyle factors may influence smoking behaviors and

cardiovascular risk and thereby should be taken into account when extrapolating these findings to women or individuals of different ethnic backgrounds.

Nonetheless, this study included patients with stroke from a nationwide cohort and accounted for multiple potential confounders, including income level, alcohol intake, physical activity, and comorbidities. Moreover, this study is noteworthy, because it provides real-world data focusing specifically on e-cigarette use in a high-risk stroke population, an area that has remained inconclusive in previous research. Future research should use prospective study designs with biochemical validation of cigarette/e-cigarette use status, collect more detailed e-cigarette exposure, and include more diverse populations beyond Korean male stroke survivors to improve generalizability of findings. These approaches would provide a more comprehensive understanding of the cardiovascular effects of e-cigarette use in high-risk populations including stroke survivors.

## CONCLUSIONS

In this nationwide cohort of Korean male stroke survivors, the use of combustible cigarette and dual use were associated with a significantly higher incidence of cardiovascular events compared with nonuse, whereas e-cigarette-only use showed slightly higher but non-significant risk. Therefore, active smoking cessation remains essential, and further research with longer follow-up and a larger cohort is warranted to clarify the long-term cardiovascular impact of e-cigarette use in stroke survivors.

## ARTICLE INFORMATION

Received October 8, 2025; accepted December 8, 2025.

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### Sources of Funding

This work was supported by a National Research Foundation of Korea grant funded by the Korea government (MSIT) (RS-2024-00345524).

### Disclosures

J.K. reports research grants from Chong Kun Dang Pharmaceutical and Myung In Pharmaceutical. The remaining authors have no disclosures to report.

### Supplemental Material

Table S1

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