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CLINICAL RESEARCH
Interventional cardiology

Prognosis after switching to electronic cigarettes following percutaneous coronary intervention: a Korean nationwide study

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Abstract

Background and Aims Despite the increasing popularity of electronic cigarettes (E-cigarettes), the prognostic impact of switching to E-cigarettes in smokers with coronary artery disease who have undergone percutaneous coronary intervention (PCI) remains unclear.

Methods Using a nationwide cohort from the Korean National Health Insurance database, 17 973 adults (≥20 years) identified as smokers (based on a health screening examination within 3 years before PCI) who underwent health screening within 3 years after PCI were enrolled to determine changes in smoking habits. Patients were classified as continued combustible cigarette users, successful quitters, or switchers to E-cigarettes. The group switching to E-cigarettes was further divided into dual users (using both combustible and E-cigarettes) and those exclusively using E-cigarettes. Primary outcomes included major adverse cardiac events (MACEs), a composite of all-cause death, spontaneous myocardial infarction, and repeat revascularization.

Results Among the total population, 8951 patients (49.8%) continued using combustible cigarettes, 1694 (9.4%) were switched to E-cigarettes, and 7328 (40.7%) successfully quit smoking after PCI. During a median follow-up of 2.4 years, the cumulative incidence of MACE was lower among E-cigarette switchers (10%) or quitters (13.4%) than among continued combustible cigarette users (17%). When continued combustible cigarette users were used as the reference, the multivariable-adjusted hazard ratios with 95% confidence intervals for MACE were 0.82 (0.69–0.98) for switchers to E-cigarettes and 0.87 (0.79–0.96) for successful quitters. Compared with dual users, entirely switching to E-cigarettes was associated with a significantly lower MACE risk (hazard ratio 0.71; 95% confidence interval 0.51–0.99).

Conclusions Among smokers who underwent PCI for coronary artery disease, switching to E-cigarette use (particularly complete transition) or quitting smoking was associated with reduced MACE risk than with continued combustible cigarette use.

Clinical Trial Registration ClinicalTrials.gov NCT06338761

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Structured Graphical Abstract

Key Question

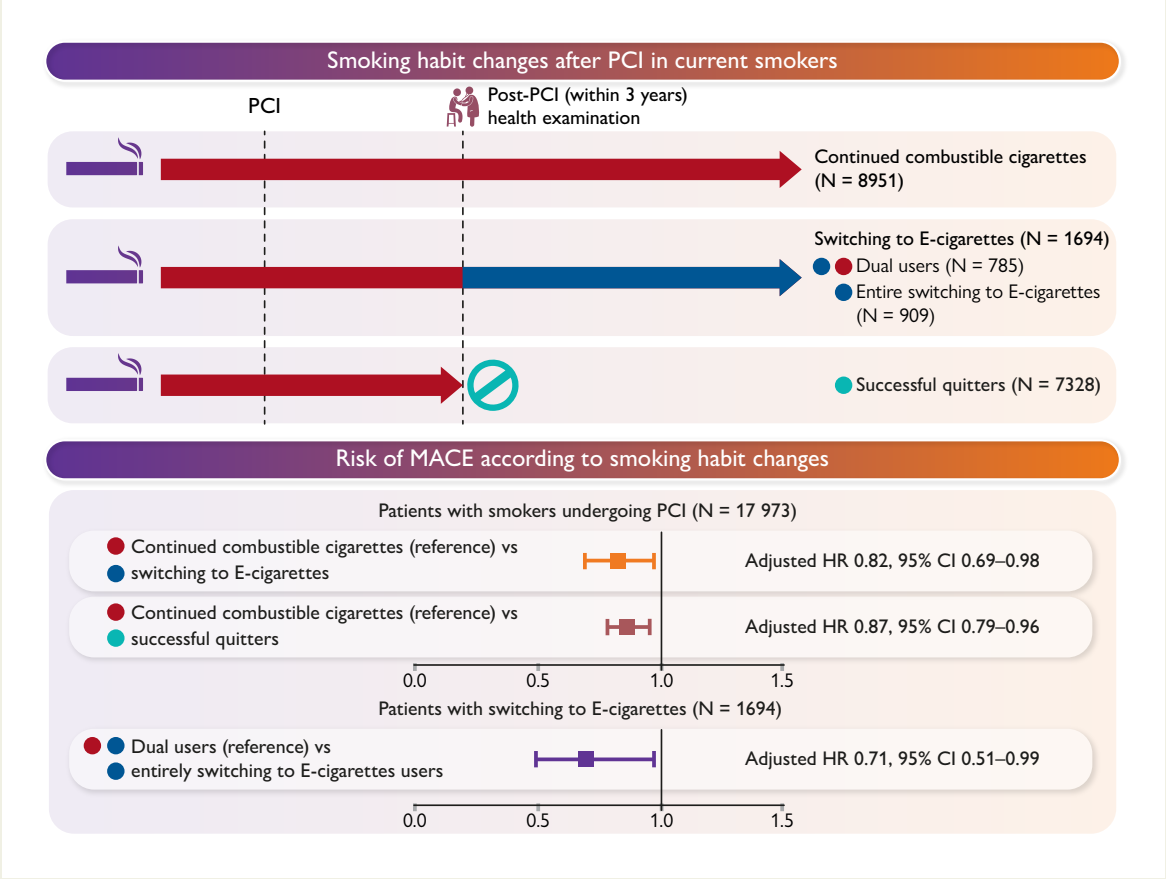
What is the prognosis of current tobacco smokers switching to electronic cigarettes (E-cigarettes) after percutaneous coronary intervention (PCI)?

Key Finding

Switching to E-cigarettes or quitting smoking was associated with a significantly lower risk of major adverse cardiac events (MACE) than continued combustible cigarette use. Compared to dual users, entirely switching to E-cigarettes was associated with a significantly lower MACE risk.

Take Home Message

Although the best strategy for smokers undergoing PCI is to stop smoking, switching to E-cigarettes may be worth considering for patients unable to quit tobacco smoking.



Main findings on the switching to electronic cigarettes or quitting smoking and their association with major adverse cardiac events in smokers with coronary artery disease who underwent percutaneous coronary intervention from the Korean National Health Insurance Service claim database on 17 973 patients. CI, confidence interval; E-cigarette; electronic cigarette; HR, hazard ratio; MACE, major adverse cardiac event; PCI, percutaneous coronary intervention

Keywords Electronic cigarettes • Combustible cigarettes • Tobacco cessation • Percutaneous coronary intervention • Cardiovascular event

Introduction

Tobacco smoking is one of the major risk factors for various chronic diseases, including multiple pulmonary and cardiovascular diseases.[1] Most of the harm caused by tobacco smoking comes from exposure to the combustion products of cigarettes such as tar and carbon monoxide, and sustained use of cigarettes is driven by nicotine addiction.[2] In this regard, electronic cigarettes (E-cigarettes), which eliminate the need for the combustion of tobacco, have been advocated as a less harmful alternative for nicotine delivery and have become a very popular smoking cessation aid worldwide.[3–5] However, many constituents of E-cigarette aerosols, including propylene glycol and vegetable glycerin, and flavourings, typically with nicotine and particulate matter, have raised concerns about substantial toxicity inducing inflammation and oxidative stress.[6–8] Therefore, there is debate on whether switching from combustible cigarettes to E-cigarettes benefits or harms smoker's health. However, substantial evidence shows E-cigarettes can help quit combustible cigarettes.[9–11]

Recently, several studies have reported that E-cigarette users have a significantly higher risk of future myocardial infarction (MI) or cardiovascular disease than non-smokers or quitters but a lower risk than combustible cigarette users.[12–14] However, because previous studies have primarily focused on the general healthy population, these results cannot be extrapolated to patients with already proven atherosclerotic cardiovascular disease (ASCVD), such as those undergoing percutaneous coronary intervention (PCI) for coronary artery disease (CAD). Several studies have consistently shown that endothelial function and vascular stiffness were significantly improved in participants who switched from smoking to using E-cigarettes compared with those who continued to smoke[15,16]; however, data regarding the impact of such transitions on clinical outcomes in current smoker patients with CAD who have undergone PCI are lacking.

Therefore, this study aimed to address this gap in knowledge by evaluating the prognostic implications of smoking habit changes (continued combustible cigarette use, switching to E-cigarette use, or quitting) among CAD patients with a current smoking status following PCI.

Methods

Data sources

We used a nationwide database provided by the National Health Insurance Service (NHIS), the sole provider of universal healthcare coverage in South Korea. The NHIS database includes socio-demographic details, reimbursement claims with the International Classification of Diseases, 10th revision (ICD-10) codes, and death information for the entire South Korean population.[17] Additionally, NHIS provides routine biennial health examinations to all Korean adults, during which clinical and biochemical measurements and questionnaire-based lifestyle information are collected.[18] Health examination facilities are designated and overseen for quality control according to relevant national laws and regulations. Further details of the NHIS database and health examinations are described elsewhere.[19] This study complied with the Declaration of Helsinki, and the study protocol was approved by the Institutional Review Board of Samsung Medical Center, Seoul, Korea (SMC-2024-02-035). Written informed consent was waived because this was a retrospective study using de-identified administrative data.

Study population

Between 1 January 2018 and 31 December 2021, a total of 216 566 adults aged ≥20 years underwent PCI. Among the 146 616 patients who underwent health screening 3 years prior to the PCI, 38 716 (26.4%) were smokers. Of the participants, 22 787 underwent a health assessment within 3 years after PCI. The period of 3 years was chosen *a priori* based on previous literature as well as the anticipated sample size and follow-up duration.[20,21] The study index date was defined as the date of the health screening visit within 3 years of PCI (see Supplementary data online, *Figure S1*). We excluded patients with a history of cancer (ICD-10, C codes) or ischaemic stroke (ICD-10, I63, I64, and G45) before the study index date ($N = 1489$). We also excluded participants who newly developed acute MI, underwent additional PCI, or underwent coronary artery bypass grafting (CABG) from the index PCI date to the study index date ($N = 4145$) to reduce the impact of additional events on smoking habit changes before health screening after PCI. To minimize potential reverse causality, participants who died within the first 3 months of follow-up from the index date ($N = 267$) were also excluded. Given that study participants could meet more than one exclusion criteria, 4814 patients were excluded and resulting in a final sample size of 17 973 (*Figure 1*).

Assessment of smoking habits

All participants were smokers within 3 years prior to PCI (Exam 1). Changes in smoking status were assessed using a self-reported questionnaire during the last examination within 3 years before PCI (Exam 1) and the first examination within 3 years after PCI (Exam 2).

The questionnaire asked participants whether they had ever smoked five or more packs of combustible cigarettes in their lifetime and, if so, whether they were currently smoking. For the E-cigarette question, participants were asked how often they had used E-cigarettes in the past month, using a scale from 'never' to 'at least once a month' to 'daily'. Participants who did not use E-cigarettes and continued to use combustible cigarettes were classified as continued combustible cigarette users, whereas those who reported being past smokers without using both combustible and E-cigarettes were considered successful quitters. Participants who used E-cigarettes were classified as switching to E-cigarette users. Among these populations, those who also used combustible cigarettes were classified as dual users, and those who quit combustible smoking but used E-cigarettes were classified as entirely switching to E-cigarette users. The observed changes in smoking habits were considered to have occurred after PCI.

Outcomes

The primary outcome was major adverse cardiac events (MACEs). Major adverse cardiac event was defined as the composite of all-cause death, spontaneous MI, and repeat revascularization. Vital status was obtained from death certificates collected by Statistics Korea at the Ministry of Strategy and Finance of South Korea.[22] Cause-specific deaths were classified into cardiovascular disease (ICD-10, I codes), cancer (ICD-10, C codes), and pulmonary disease (ICD-10, J codes). Spontaneous MI was defined as the presence of the diagnostic codes ICD-10, I21, or I22 in the primary position during hospitalization with procedure codes for PCI or CABG (see Supplementary data online, *Table S1*). In a validation study, the accuracy of MI diagnosis in the Korean NHIS data was 93%.[23] Repeat revascularization was defined as the presence of a procedure code for PCI or CABG after the study index date. Participants were followed up from the index date until the occurrence of an outcome event, death, or 31 December 2022, whichever occurred first.

Covariables

Information on smoking duration and intensity (number of packs smoked per day) was obtained from Exam 1. Follow-up smoking intensity was obtained from Exam 2 for continued combustible cigarette users or dual users only. The Charlson Comorbidity Index was calculated using insurance claims data during a 1-year look-back period from the study index date.[24] Data on age, residence area, alcohol consumption, physical activity, body mass index, blood pressure, fasting glucose, and total, HDL, and LDL cholesterol levels were collected in Exam 2. Information on PCI, including clinical presentation and medication use at discharge, was also collected from the claims data.

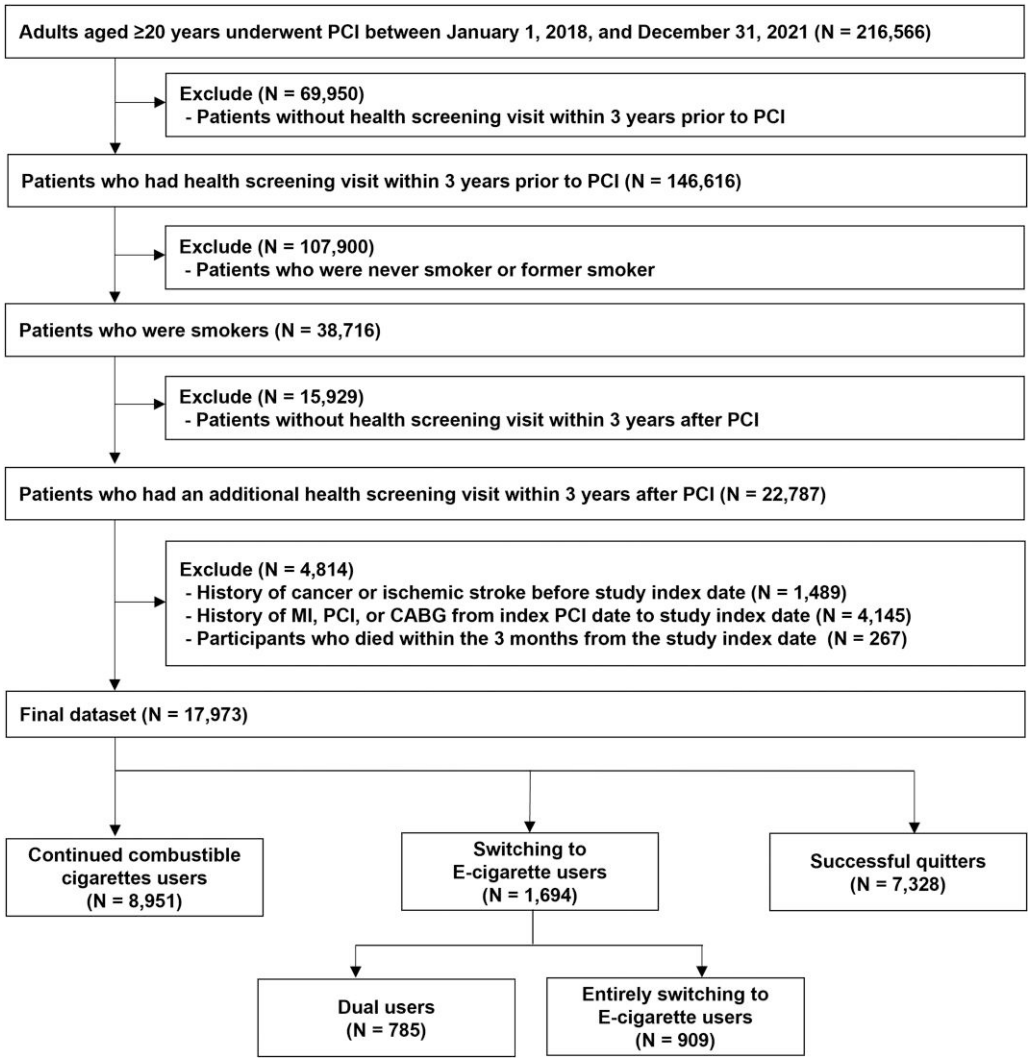


Figure 1 Study flowchart. CABG, coronary artery bypass grafting; E-cigarette, electronic cigarette; MI, myocardial infarction; PCI, percutaneous coronary intervention

Statistical analysis

Baseline characteristics were reported as means ± standard deviations, medians (interquartile range), or numbers (%), as appropriate. Incidence rates were calculated as the number of events per 100 person-years of follow-up. Hazard ratios (HRs) and the corresponding 95% confidence intervals (CIs) of the outcomes for each group were calculated using Cox proportional hazards models. Models were adjusted for age, sex, clinical presentation, smoking pack-years prior to PCI, prior comorbidities, body mass index, and years from PCI to the health screening exam. Covariables were selected *a priori* based on their possible associations with smoking habits and outcomes. For cause-specific death, MI, and revascularization, we calculated the sub-HR using the Fine–Gray regression model to account for the competing risks of other causes of death.[25] We performed subgroup analysis by age (≤55, 56–64, 65–70, and ≥71 years), sex (male vs. female), residential area (rural vs. metropolitan), smoking pack years before PCI (<30 packs/year vs. ≥30 packs/year), obesity (non-obese vs. obese), clinical presentation (non-MI vs. MI), diabetes mellitus (no vs. yes), hypertension (no vs. yes) and dyslipidaemia (no vs. yes). The proportionality of hazards was confirmed by visual inspection of log-minus-log plots and Schoenfeld residuals. We also performed a sensitivity analysis, using smoking status at the last visit within 3 years after PCI to minimize the potential bias from further changes in smoking habits.

All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

Of the 17 973 patients who were smokers before PCI (mean age, 60.4 years; 97.1% male), 8951 (49.8%) were continued combustible cigarette users, 1694 (9.4%) were switching to E-cigarette users, and 7328 (40.8%) were successful quitters following PCI. Compared with continued combustible cigarette users, switching to E-cigarette users were more likely to be younger. Switching to E-cigarette users and successful quitters were more likely to present with MI at the time of PCI than continued combustible cigarette users after PCI (*Table 1*). However, the three groups had similar Charlson Comorbidity Index scores, and

Table 1 Baseline characteristics

	Continued combustible cigarette users (*N* = 8951)	Switching to E-cigarette users (*N* = 1694)	Successful quitters (*N* = 7328)	*P*-value
Age, years	61.56 (9.35)	52.90 (8.87)	60.43 (9.83)	<.01
Sex, male	8701 (97.2)	1672 (98.7)	7071 (96.5)	<.01
Body mass index, kg/m^2	24.99 (3.24)	26.44 (3.41)	25.47 (3.13)	<.01
Residential area, metropolitan	5165 (57.7)	1109 (65.5)	4318 (58.9)	<.01
Clinical presentation				<.01
MI	4118 (46.0)	887 (52.4)	4064 (55.5)	
Angina	4833 (54.0)	807 (47.6)	3264 (44.5)	
Prior comorbidities				
Charlson Comorbidity Index	2.6 (1.8)	2.6 (1.7)	2.4 (1.6)	.05
Diabetes mellitus	4422 (49.4)	597 (35.2)	3026 (41.3)	<.01
Hypertension	5480 (61.2)	796 (47.0)	3911 (53.4)	<.01
Dyslipidaemia	6474 (72.3)	1077 (63.6)	4846 (66.1)	<.01
Medication at discharge				
Aspirin	8491 (94.9)	1629 (96.2)	7036 (96.0)	<.01
P2Y12 inhibitor	8179 (91.4)	1580 (93.3)	6774 (92.4)	.01
Clopidogrel	4564 (51.0)	732 (43.2)	3328 (45.4)	
Ticagrelor	3002 (33.5)	694 (41.0)	2888 (39.4)	
Prasugrel	613 (6.8)	154 (9.1)	558 (7.6)	
Beta-blocker	5262 (58.8)	1026 (60.6)	4442 (60.6)	<.01
ARB	3190 (35.6)	584 (34.5)	2456 (33.5)	.48
ACE inhibitor	2111 (23.6)	446 (26.3)	1975 (27.0)	<.01
Statin	8308 (92.8)	1611 (95.1)	6928 (94.5)	<.01
Smoking habits				
Smoking pack year before PCI, ≥30 packs/year	3975 (44.4)	475 (28.0)	2184 (29.8)	<.01
Amount of combustible cigarettes before PCI, cigarettes/day	16.96 (7.46)	16.07 (6.52)	14.62 (7.12)	<.01
Amount of combustible cigarettes after PCI, cigarettes/day	14.84 (7.24)	2.96 (6.29)	0 (0.00)	<.01
% Change of continued combustible cigarettes	2.13 (127.62)	−81.76 (45.71)	−100 (0.00)	<.01
Years between PCI to Exam 2	1.1 (0.7)	0.9 (0.7)	0.9 (0.8)	<.01
Other habits in Exam 2				
Current drinker, yes	5123 (57.2)	1233 (72.8)	3853 (52.6)	<.01
Regular physical activity, yes	2579 (28.8)	474 (28.0)	2496 (34.1)	<.01
Laboratory findings in Exam 2				
Fasting glucose, mg/dL	115.2 (36.9)	113.8 (31.3)	113.4 (35.3)	<.01
Total cholesterol, mg/dL	142.1 (36.8)	141.8 (33.3)	139.3 (32.4)	<.01
HDL cholesterol, mg/dL	46.0 (11.5)	46.8 (11.2)	47.2 (14.4)	<.01
LDL cholesterol, mg/dL	67.5 (30.4)	67.2 (28.3)	65.7 (26.5)	.03

Continued

Table 1 *Continued*

	Continued combustible cigarette users (*N* = 8951)	Switching to E-cigarette users (*N* = 1694)	Successful quitters (*N* = 7328)	*P*-value
Vital sign in Exam 2				
Systolic blood pressure, mmHg	124.3 (14.9)	123.0 (13.0)	124.9 (14.6)	<.01
Diastolic blood pressure, mmHg	75.1 (10.2)	76.5 (9.6)	75.8 (9.9)	<.01

Values are presented as *n* (%), mean (SD), or median (IQR).
ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BMI, body mass index; E-cigarette, electronic cigarette; IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation.

>90% of the patients were discharged on aspirin, $P2Y_{12}$ inhibitors, and statin medications. The mean LDL cholesterol level was 66.3 mg/dL, and no significant differences in LDL cholesterol levels were observed among the three groups (*Table 1*).

Switching to E-cigarette users had a significantly lower smoking intensity of combustible cigarettes after PCI than the continued combustible cigarette users (continued combustible cigarette users vs. dual users, 14.84 vs. 6.39, cigarettes/day, $P < .01$).

Cardiovascular outcomes according to changes in smoking habits after percutaneous coronary intervention

During a median follow-up of 2.4 years (maximum of 4.5 years), a total of 1327 MACE occurred. The cumulative incidence of MACE was lower among switching to E-cigarette users (10.8%) or successful quitters (13.4%) than among continued combustible cigarette users (17%) (*Figure 2A*). When continued combustible cigarette users were set as a reference, multivariable-adjusted HRs (95% CIs) of MACE were 0.82 (0.69–0.98) for switching to E-cigarette users and 0.87 (0.79–0.96) for successful quitters (*Table 2*). No significant difference was observed in MACE risk between switching to E-cigarette users and successful quitters (adjusted HR 0.94; 95% CI 0.78–1.13). In subgroup analysis, risk reduction was consistently observed in all subgroups in the switching to E-cigarette user and successful quitter groups compared with the continued combustible cigarette user group (*Figure 3*).

Compared with the continued combustible cigarette users, switching to E-cigarette users exhibited a numerically lower risk of all-cause mortality (adjusted HR 0.64; 95% CI 0.41–0.99), spontaneous MI (adjusted HR 0.88; 95% CI 0.60–1.29), and repeat revascularization (adjusted HR 0.89; 95% CI 0.73–1.07), as did successful quitters (*Table 2*). Death from cardiovascular disease, cancer, and pulmonary disease were also numerically lower in the switching to E-cigarette user and successful quitter groups than in the continued combustible cigarette user group (*Table 2*). Even when death was considered as a competing risk, the results were similar. In the sensitivity analysis using smoking status at the last visit within 3 years after PCI, the results were consistent (see Supplementary data online, *Table S2*).

Cardiovascular outcomes according to the amount of continued combustible cigarettes in switching to electronic cigarette user

The baseline characteristics of dual users and entirely switching to E-cigarette users are presented in Supplementary data online, *Table S3*. Compared with entirely switching to E-cigarette users, dual users were more likely to be older and have more comorbidities, such as diabetes mellitus, hypertension, and dyslipidaemia, but were less likely to present MI. The total smoking pack years and number of combustible cigarettes per day before PCI were significantly higher in the dual user group than in the entirely switching to E-cigarette user group.

The cumulative incidence of MACE was lower among entirely switching to E-cigarette users (9.6%) than among dual users (12.2%) (*Figure 2B*). The multivariable-adjusted HR (95% CIs) for MACE was 0.71 (0.51–0.99) for entirely switching to E-cigarette users compared with those for dual users (*Table 3*).

Although there was no difference in spontaneous MI (adjusted HR 0.92; 95% CI 0.40–1.89), the risk of all-cause death (adjusted HR 0.74; 95% CI 0.31–1.76) and repeat revascularization (adjusted HR 0.73; 95% CI 0.51–1.03) were numerically lower in entirely switching to E-cigarette users than dual users (*Table 3*).

Discussion

In the present study, we evaluated the prognostic impact of smoking habit changes after PCI on clinical outcomes in smokers using a large-scale representative population database (*Structured Graphical Abstract*). Our principal findings are as follows. First, although successful quitting smoking after PCI was associated with a significantly lower risk of MACE than continued combustible cigarette use, only 40.7% of the patients quit smoking after PCI. Second, patients switching to E-cigarettes used markedly fewer combustible cigarettes than those who continued combustible cigarette use, which may have contributed to the reduced risk of MACE. Third, patients who completely switched to E-cigarettes after PCI had significantly lower risks of MACE than dual users.

The link between tobacco smoking and ASCVD has been substantiated by epidemiologic studies,[26] and various pathophysiological manifestations of tobacco combustion affected endothelial dysfunction, accelerated atherosclerosis progression, or increased thrombogenicity.[27] Previous clinical studies have shown that smoking cessation is associated with a significantly lower risk of cardiovascular events than continued smoking.[28,29] In agreement with these previous studies, we found that quitters after PCI had a significantly lower risk of MACE as well as all-cause mortality than those who continued to smoke combustible cigarettes. However, only 40% of the patients who smoked before PCI were able to quit smoking completely after PCI. Several previous studies that have investigated changes in smoking habits after the development of ASCVD from real-world data have also reported that <50% of patients quit smoking, even though smoking cessation resulted in an improved prognosis in all of these studies.[30–32] This means that nicotine addiction could be difficult to resolve, even in patients who have already suffered from ASCVD. Although current American and

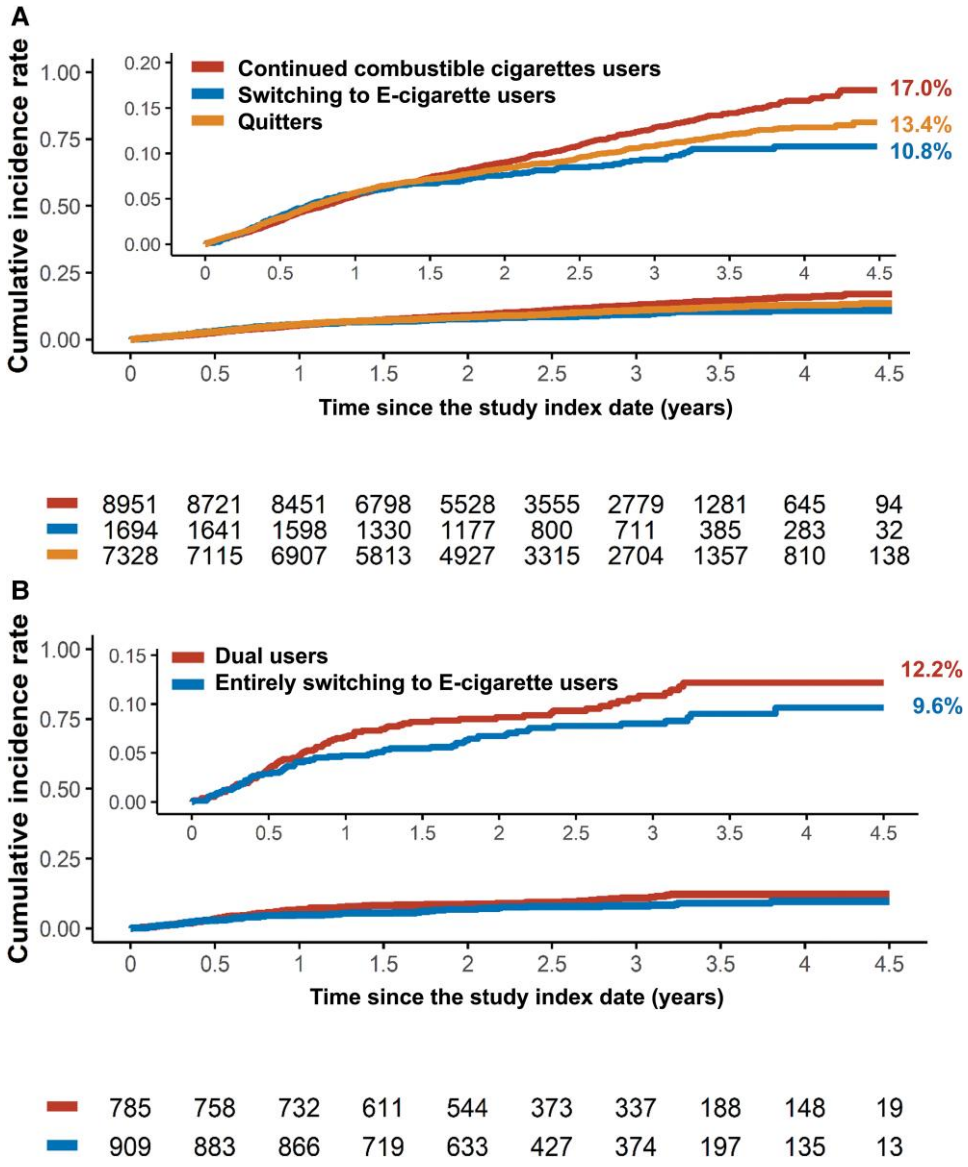


Figure 2 Cumulative incidence of clinical outcomes according to changes in smoking habits. Kaplan–Meier curves comparing major adverse cardiac event according to changes in smoking habits (*A*) and the amount of continued combustible cigarettes in switching to electronic cigarette users (*B*) among patients who were smokers and underwent percutaneous coronary intervention. E-cigarette, electronic cigarette; MACE, major adverse cardiac events; PCI, percutaneous coronary intervention

European guidelines recommend a combination of behavioural interventions with pharmacotherapy to maximize tobacco smoking cessation after PCI,[33,34] even the best methods have high rates of return to smoking within 1 year (72.8%).[35] Therefore, it is essential to provide more feasible guidance for patients.

A combination of behavioural support and pharmacological interventions, particularly using two forms of nicotine replacement therapy (NRT) and varenicline, is the most effective approach to smoking cessation.[36] Recently, however, E-cigarettes have become the most popular choice of support for smoking cessation, and by 2020, 27% of smokers made a cessation attempt, compared with 18% who used NRT.[36] We found that patients who used both combustible and E-cigarettes decreased the amount of combustible cigarettes they smoked compared with patients who continued to use combustible cigarettes. The current study demonstrated that switching to E-cigarettes was associated with a significantly lower risk of MACE than continued combustible cigarette use, similar to quitting smoking. This result supports the following statement from the American Heart Association: 'If a patient has failed initial treatment, has been intolerant to or refuses to use conventional smoking cessation medications, and wishes to use E-cigarettes to aid quitting, it is reasonable to support the attempt'.[37] Nevertheless, since E-cigarettes are addictive and data on the long-term effects of E-cigarettes on cardiovascular health are lacking, the European Society of Cardiology and European Association of Preventive Cardiology consistently recommend that E-cigarette should only be considered to aid tobacco cessation alongside a formal tobacco cessation programme.[38,39] Furthermore, considering that a previous study found that both smokers (combustible and E-cigarettes) had a higher risk of cardiovascular disease

Table 2 Comparison of clinical outcomes according to change in smoking habits

	Continued combustible cigarette users	Switching to E-cigarette users	Successful quitters
MACE[a]			
No of case (cumulative incidence %)	463 (17.0)	148 (10.8)	716 (13.4)
Crude HR (95% CI)	Reference	0.76 (0.64–0.91)	0.87 (0.79–0.96)
Adjusted HR[b] (95% CI)	Reference	0.82 (0.69–0.98)	0.87 (0.79–0.96)
All-cause death			
No of case (cumulative incidence %)	266 (6.4)	22 (2.1)	146 (4.1)
Crude HR (95% CI)	Reference	0.38 (0.25–0.59)	0.62 (0.51–0.77)
Adjusted HR[b] (95% CI)	Reference	0.64 (0.41–0.99)	0.65 (0.53–0.80)
Death from cardiovascular causes			
No of case (cumulative incidence %)	69 (2.0)	6 (0.5)	52 (1.6)
Crude HR (95% CI)	Reference	0.40 (0.17–0.92)	0.85 (0.59–1.22)
Adjusted HR[b] (95% CI)	Reference	0.63 (0.27–1.47)	0.88 (0.61–1.27)
SubHR[c] (95% CI)	Reference	0.63 (0.27–1.49)	0.88 (0.61–1.27)
Death from cancer			
No of case (cumulative incidence %)	90 (2.8)	7 (0.7)	39 (1.4)
Crude HR (95% CI)	Reference	0.36 (0.17–0.78)	0.49 (0.33–0.71)
Adjusted HR[b] (95% CI)	Reference	0.72 (0.33–1.57)	0.57 (0.39–0.84)
SubHR[c] (95% CI)	Reference	0.72 (0.33–1.60)	0.57 (0.40–0.85)
Death from pulmonary causes			
No of case (cumulative incidence %)	16 (0.5)	1 (0.2)	9 (0.2)
Crude HR (95% CI)	Reference	0.28 (0.04–2.13)	0.63 (0.28–1.41)
Adjusted HR[b] (95% CI)	Reference	0.76 (0.10–5.89)	0.64 (0.28–1.49)
SubHR[b] (95% CI)	Reference	0.76 (0.10–5.89)	0.64 (0.28–1.49)
Spontaneous myocardial infarction			
No of case (cumulative incidence %)	161 (3.1)	32 (2.6)	143 (2.7)
Crude HR (95% CI)	Reference	0.97 (0.87–1.43)	1.03 (0.83–1.30)
Adjusted HR[b] (95% CI)	Reference	0.88 (0.60–1.29)	0.92 (0.73–1.16)
SubHR[d] (95% CI)	Reference	0.88 (0.60–1.30)	0.93 (0.74–1.17)
Repeat revascularization			
No of case (cumulative incidence %)	727 (11.7)	132 (9.3)	596 (10.5)
Crude HR (95% CI)	Reference	0.91 (0.76–1.10)	0.97 (0.87–1.08)
Adjusted HR[b] (95% CI)	Reference	0.89 (0.73–1.07)	0.95 (0.85–1.06)
SubHR[d] (95% CI)	Reference	0.89 (0.73–1.07)	0.96 (0.85–1.07)

CI, confidence interval; E-cigarette; electronic cigarette; HR, hazard ratio; MACE, major adverse cardiac event; subHR, sub-distribution hazard ratio.
[a]Major adverse cardiac event was defined as the composite of all-cause death, spontaneous myocardial infarction, or repeat revascularization.
[b]Adjusted for age, sex, clinical presentation, prior comorbidities, body mass index, medication at discharge, smoking pack year before PCI, and years from PCI to health screening.
[c]Sub-hazard ratios were obtained using other causes of death as a competing risk.
[d]Sub-hazard ratios were obtained using all-cause death as a competing risk.

than those who smoked only combustible cigarettes if the participants did not reduce their use of combustible cigarettes,[40–42] it is important to somehow reduce the use of combustible cigarettes.

We found that even when patients switched entirely to E-cigarettes after PCI had a significantly lower risk of MACE than dual users. This is consistent with a recent review indicating that changing from

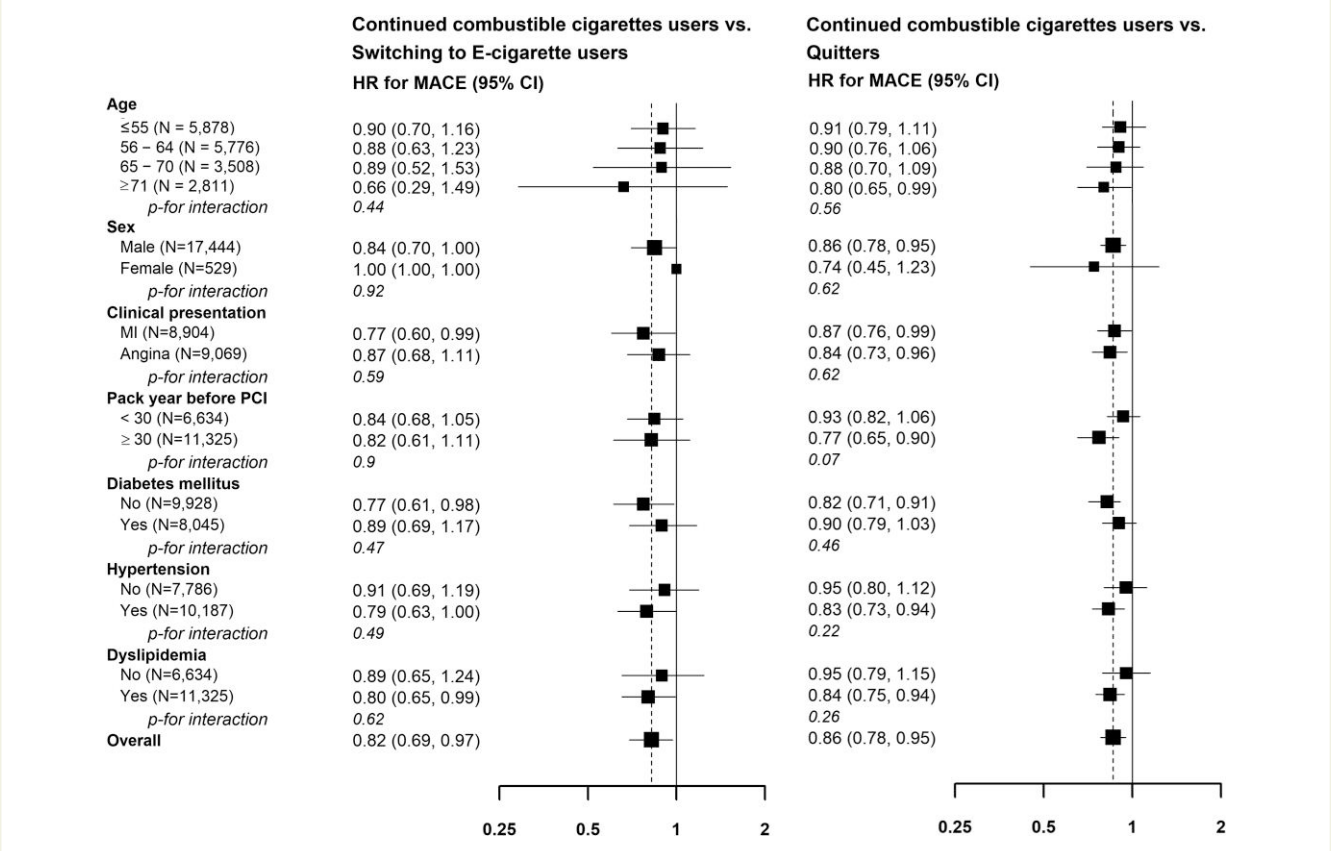


Figure 3 Subgroup analysis for major adverse cardiac events according to changes in smoking habits. Adjusted for age, sex, clinical presentation, prior comorbidities, body mass index, medication at discharge, smoking pack year before percutaneous coronary intervention, and years from percutaneous coronary intervention to health screening. Major adverse cardiac event was defined as the composite of all-cause death, spontaneous myocardial infarction, or repeat revascularization. CI, confidence interval; E-cigarette; electronic cigarette; HR, hazard ratio; MACE, major adverse cardiac event

combustible cigarettes to E-cigarettes might have health benefits.[43] A recent randomized controlled trial found that the endothelial function of venules and arteries of smokers who changed to E-cigarettes improved to the same extent as in the group of patients who quit smoking.[44] In a follow-up study, these positive effects were still present in both smaller and larger conduits for at least 6 months after changing to E-cigarettes.[16] Smooth muscle cell damage, caused by cigarettes (possibly via induction of a pro-inflammatory/matrix remodelling phenotype in smooth muscle cells),[45] reversed after changing to E-cigarettes, and this reversal could help reduce ASCVD risk. Conversely, Kuntic *et al.*[46] reported the association between E-cigarette exposure and increased vascular, cerebral, and pulmonary oxidative stress; thus, E-cigarettes have the potential to induce adverse cardiovascular and/or pulmonary events. In addition, acute E-cigarette smoking could increase blood pressure, cause endothelial dysfunction, and increase vascular and cerebral oxidative stress despite being less toxic than combustible cigarettes.[47] Taken together, based on the findings, the best lifestyle change for current smokers with proven CAD who have undergone PCI is to stop smoking without any nicotine supply; however, if this is not possible, it is worth considering switching to E-cigarettes. However, further well-designed studies are needed to understand the underlying mechanisms and determine the long-term effects of continued E-cigarette use on future cardiovascular outcomes in patients with CAD who have undergone PCI.

Limitations

This study had several limitations. First, we utilized retrospective data from a nationwide cohort, which has inherent limitations such as the possibility of unmeasured confounding factors influencing the findings and the inability to establish causality. Second, the reliance on self-reported smoking habits introduced the risk of recall bias and misclassification, potentially affecting the accuracy of our results. In particular, we cannot rule out the possibility that the smoking status of some patients may have changed after the health screening following PCI. However, the results of sensitivity analysis using smoking status at the last visit within 3 years after PCI were consistent. Third, the current study categorized patients based on broad smoking habit changes, including those entirely switching to E-cigarettes or using a combination of E-cigarettes and combustible cigarettes. However, E-cigarette products vary widely in composition and usage patterns, which can influence their impact on cardiovascular outcomes. Furthermore, we did not obtain information on the use of smoking cessation medications among successful quitters. Fourth, detailed information regarding PCI procedural data was not available because of the nature of the claims data set. Fifth, given that the majority of the current population was male, therefore, evaluating the implications of smoking habit changes on clinical outcomes among female smokers in this study was challenging.

Table 3 Comparison of clinical outcomes according to the amount of continued combustible cigarettes among switching to electronic cigarette users (*N* = 1694)

	Dual users	Entirely switching to E-cigarette users
MACE[a]		
No of case (cumulative incidence %)	79 (12.2)	69 (9.6)
Crude HR (95% CI)	Reference	0.75 (0.54–1.04)
Adjusted HR[b] (95% CI)	Reference	0.71 (0.51–0.99)
All-cause death		
No of case (cumulative incidence %)	12 (2.4)	10 (1.9)
Crude HR (95% CI)	Reference	0.74 (0.32–1.71)
Adjusted HR[b] (95% CI)	Reference	0.74 (0.31–1.76)
Death from cardiovascular causes		
No of case (cumulative incidence %)	2 (0.3)	4 (1.4)
Crude HR (95% CI)	Reference	1.73 (0.32–9.45)
Adjusted HR[b] (95% CI)	Reference	1.97 (0.35–11.10)
SubHR[c] (95% CI)	Reference	1.97 (0.45–8.60)
Death from cancer		
No of case (cumulative incidence %)	6 (1.0)	1 (0.5)
Crude HR (95% CI)	Reference	0.15 (0.02–1.23)
Adjusted HR[b] (95% CI)	Reference	0.13 (0.01–1.11)
SubHR[c] (95% CI)	Reference	0.13 (0.01–1.11)
Death from pulmonary causes		
No of case (cumulative incidence %)	1 (0.3)	0 (0)
Crude HR (95% CI)	Reference	NA
Adjusted HR[b] (95% CI)	Reference	NA
SubHR[c] (95% CI)	Reference	NA
Spontaneous myocardial infarction		
No of case (cumulative incidence %)	14 (2.7)	18 (2.4)
Crude HR (95% CI)	Reference	1.13 (0.56–2.28)
Adjusted HR[b] (95% CI)	Reference	0.92 (0.40–1.89)
SubHR[d] (95% CI)	Reference	0.92 (0.40–1.89)
Repeat revascularization		
No of case (cumulative incidence %)	69 (10.3)	63 (8.6)
Crude HR (95% CI)	Reference	0.79 (0.56–1.11)
Adjusted HR[b] (95% CI)	Reference	0.73 (0.51–1.03)
SubHR[d] (95% CI)	Reference	0.73 (0.51–1.03)

CI, confidence interval; E-cigarette; electronic cigarette; HR, hazard ratio; MACE, major adverse cardiac event; subHR, sub-distribution hazard ratio.
[a]Major adverse cardiac event was defined as the composite of all-cause death, spontaneous myocardial infarction, or repeat revascularization.
[b]Adjusted for age, sex, clinical presentation, prior comorbidity, body mass index, medication at discharge, smoking pack year before PCI, and years from PCI to health screening.
[c]Sub-hazard ratios were obtained using other causes of death as a competing risk.
[d]Sub-hazard ratios were obtained using all-cause death as a competing risk.

Conclusions

Among smokers with CAD undergoing PCI, switching to E-cigarettes was associated with a significantly lower risk of MACE than continued combustible cigarette use, similar to quitting smoking. Specifically, patients who completely switched to E-cigarettes experienced a greater reduction in the risk of MACE than dual users. These findings suggest that switching to E-cigarettes could be a viable alternative for patients who find it challenging to quit combustible cigarettes after PCI.

Supplementary data

Supplementary data are available at European Heart Journal online.

Declarations

Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

Data Availability

We used the claim data provided by the Korean National Health Insurance Service (K-NHIS) database. Data can only be accessed by visiting the K-NHIS datacentre, after approval from data access committee of K-NHIS. Those who want to access data set of this study should contact the corresponding authors (cardiokh@gmail.com), who will help with the process of contacting the K-NHIS.

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Ethical Approval

This study was approved by the Institutional Review Board of Samsung Medical Centre (IRB No. 2024-02-030), and informed consent was exempted because we only accessed de-identified data.

Pre-registered Clinical Trial Number

ClinicalTrials.gov: NCT06338761.

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