A pilot investigation of e-cigarette use and smoking behaviour among patients with chronic airway disease or respiratory symptoms

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Abstract

Background: This pilot study aimed to investigate the current status of e-cigarettes (ECs) use patterns among patients with chronic airway disease or chronic respiratory symptoms and the effects of ECs use on respiratory and mental health.

Methods: A cross-sectional survey was conducted at the outpatient clinic of eight teaching hospitals in South Korea between November 2019 and December 2019. All adult ECs users (19 years and above) who visited the outpatient clinic as a patient with chronic airway disease or chronic respiratory symptoms were eligible to participate in this study.

Results: A total of 51 subjects responded to the survey. Most of the participants were male (92.2%) and the mean age was 41.8 years. Dominant airway diseases were asthma and chronic obstructive pulmonary disease. Most of the subjects had a history of cigarette smoking, and 19 subjects were dual users of current cigarettes and ECs. Most of the subjects started ECs use due to health-related reasons. When comparing exclusive ECs users and dual users, St. George’s respiratory questionnaire (SGRQ) scores, the proportion of cases with moderate to severe depressive symptoms, and average Fagerstrom test for nicotine dependence scores for ECs were higher in dual users than exclusive ECs users (mean 4.64 vs. 2.38, \( p = 0.006 \)), respectively.

Conclusion: Most of the subjects started ECs use due to health concerns, but dual users have more respiratory symptoms and higher nicotine dependence in this pilot study. One hypothesis that comes from these results is that greater nicotine dependence may influence behaviours, habits, and views about ECs. These preliminary observations need confirmation in a large cohort.

Keywords
asthma, chronic obstructive lung disease, electronic nicotine delivery systems, nicotine dependence, respiratory symptoms
1 | BACKGROUND

The first e-cigarette (EC) was manufactured in 2003 by Hon Lik, a Chinese pharmacologist, with an intent to enable his father, who was a lung cancer patient and a heavy cigarette smoker, to quit smoking.1 Since the introduction of ECs into the Korean market, their prevalence has grown rapidly. After the introduction of IQOS in 2017, the market for cigarette type ECs has been estimated to be worth 1.67 billion (approximately 1.97 trillion won), and Korea is the world’s second-largest market after Japan.2

Even though a few studies have documented the usage trend of ECs in subjects with chronic airway disease, a recent study demonstrated an increase in the prevalence of ECs use from 5% to 12%–16% in chronic obstructive pulmonary disease (COPD) patients.3 Chronic airway disease is associated with cigarette smoking; ECs have been adopted by current conventional cigarettes (CCs) users as a safer alternative to deliver nicotine or a cessation device of CCs. However, the effects of ECs on CCs reduction and cessation are controversial.4,5 A recent meta-analysis demonstrated that ECs may interfere with the efforts imparted to quit cigarette smoking.6

Since the introduction of ECs, there has been an increase in the prevalence of ECs use and changes in the smoking pattern. The proportion of dual users (ECs and CCs) is constantly increasing in Korea.7 However, the current status of ECs use in patients with chronic airway disease in Korea is not well understood.

In our pilot study, we aimed to investigate the current status of ECs use patterns among patients with chronic airway disease or chronic respiratory symptoms and compare respiratory symptoms and mental health according to smoking behaviours including ECs use.

2 | MATERIALS AND METHODS

2.1 | Study population and data collection

This study was conducted between November 2019 and December 2019. A cross-sectional survey was conducted at the outpatient clinic of eight teaching hospitals in South Korea. All the adult ECs users (19 years and above) of both the genders who visited the respiratory outpatient clinic as a patient with chronic airway disease or chronic respiratory symptoms were eligible to participate in this study. EC user was defined as who used ECs on some days or every day in the past 30 days. The subjects who declined to participate in the study were the ones with cognitive impairment and/or could not complete the questionnaire and hence were excluded.

A total of 51 subjects responded to the survey, which included a questionnaire concerning the status of ECs use, perception of ECs, the motivation of selecting ECs, nicotine dependence, respiratory symptoms, modified Medical Research Council Dyspnea scale, asthma control test, COPD assessment test (CAT), EuroQol-5 dimension-5 level (EQ-5D-5L), St. George’s Respiratory Questionnaire-COPD (SGRQ-C), and Beck Depression Inventory (BDI).

2.2 | Questionnaires

The SGRQ is a disease-specific quality of life assessment tool that is validated in both asthma and COPD.8,9 In the current study, the COPD specific version (SGRQ-C) was used.10 The questionnaire consists of 76 items that are divided into three parts, measuring symptoms, activity limitation, and the social and emotional impact of the disease. Each score ranges from 0 (no impairment) to 100 (maximum perceived distress). Higher scores mean a poorer quality of life.

The CAT is a self-administered questionnaire that measures health-related quality of life. The total CAT score was calculated for each individual by summing the points for each variable. CAT scores range from 0 to 40, with a score of 0 indicating no impairment.

Depressive symptoms were assessed using the BDI, a 21-item self-report scale for assessing depressive symptoms. Total scores range from 0 to 63. In patients with medical illness, a score of 16 or higher indicates moderate to severe depressive symptoms.11

The Fagerström test for nicotine dependence (FTND) and its adapted versions for ECs were used to measure
nicotine dependence. The scores from each of the six questions of the FTND were summed and an overall total score for nicotine dependence was calculated. All the questionnaires were administered in-person to each of the participants.12,13

2.3 Statistical analysis

Baseline characteristics were given as percentages for categorical variables and as estimated means (± standard deviation) for continuous variables according to the smoking status. We compared clinical characteristics between exclusive ECs users and dual users. Categorical variables and continuous variables were compared using the chi-square test and Student’s t-test, respectively. A two-sided p value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows software (ver. 20.0; IBM Corp., Armonk, NY, USA).

3 RESULTS

3.1 Baseline characteristics

Of the 51 participants, 47 (92.2%) were male. The mean age of the participants was 41.8 ± 12.7 years. The 40s group had the highest rate (16, 31.4%) and the 70s group had the lowest rate (1, 2.0%) in the total population. The mean body mass index (BMI) was 25.2 kg/m². In the pulmonary function test, the mean value for predicted forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), and FEV₁/FVC was 84.8%, 88.3%, and 73.7%, respectively. Chronic airway disease included 11 cases of asthma (21.6%), six cases of COPD (11.8%), 39 cases of chronic bronchitis (76.5%), two cases of emphysema (3.9%), one case of bronchiectasis (2.0%), one case of chronic allergic rhinitis (2.0%), and one case of lung cancer (2.0%) (Table 1).

3.2 The current status of ECs uses

Of the 51 participants, 49 (96.1%) had a history of CCs use. Of these, 30 (61.2%) were currently smoking CCs. The mean pack years (Pys) was 18.3. Thirty-four (66.7%) participants reported current ECs use and 17 (33.3%) were former ECs users who have used ECs within 1 month. Nineteen (37.3%) were the current dual users (ECs and CCs).

The proportion of using the cigarette type of ECs was higher (33, 64.7%) than those using liquid type of ECs (22, 43.1%). There were four (7.8%) dual users for liquid- and cigarette-type ECs. The mean duration of liquid-type ECs use was 12.5 months. Of the liquid-type ECs users, 13 (59.1%) used flavoured e-liquids. The liquid-type ECs users smoked 11.2 times a day with 13.4 puff/frequency. In the case of cigarette-type ECs, the mean duration of ECs use was 23.4 months with 10.8 sticks a day.

After ECs use, 41.2% of CCs users demonstrated reduced consumption of CCs and the amount of reduction was 9.9 cigarettes. At the time of the survey, 39 (76.5%) participants answered to had a plan of smoking cessation, 26 (51.0%) had a plan of smoking cessation in a month, and 33 (64.7%) had a plan of smoking cessation in 6 months. In the past year, 23 (45.1%) participants tried smoking cessation attempts for more than 24 h and five (9.8%) participants used nicotine replacement therapy to quit smoking (Table 2).

After ECs use, the number of cigarettes decreased to an average of 10 cigarettes, but the increased number of ECs was 11 frequency/day for liquid type and 10 for stick type. If inhalation of 10 times of the liquid type of ECs (consuming about 0.04–0.05 g of liquid) is converted to one regular CC, the nicotine content in the smoke of a liquid type of ECs is 0.3–0.7 mg in terms of the amount of one CC, similar to the standard for CCs (0.01–0.7 mg). Also, nicotine content in cigarette type of ECs is 0.1–0.5 mg, which is similar to the content in CCs.14 Our results revealed that ECs only change the type of smoking behaviour from cigarettes to ECs without any reduction in the smoke arising from nicotine (Figure 1).

### TABLE 1 Baseline characteristics of patients with chronic airway disease using e-cigarettes (N = 51)

| Variable                      | Data                        |
|-------------------------------|-----------------------------|
| Sex, male                     | 47 (92.2)                   |
| Age, years                    | 41.8 ± 12.7                 |
| Body mass index, kg/m²        | 25.2 ± 3.6                  |
| Pulmonary function test       |                             |
| FEV₁/FVC                      | 73.8 ± 18.0                 |
| FVC % predicted               | 88.3 ± 22.0                 |
| FEV₁ % predicted              | 84.8 ± 25.4                 |
| Comorbidities                 |                             |
| Asthma                        | 11 (21.6)                   |
| COPD                          | 6 (11.8)                    |
| Chronic bronchitis            | 39 (76.5)                   |
| Lung emphysema                | 2 (3.9)                     |
| Bronchiectasis                | 1 (2.0)                     |
| Allergic rhinitis             | 1 (2.0)                     |
| Lung cancer                   | 1 (2.0)                     |

Note: Data are presented as number (%) or mean ± standard deviation.

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity.
In terms of odour, 26 (51.0%) participants thought that ECs had a smell, whereas 49.0% (n = 25) reported that ECs lacked any smell. About half of the participants reported that they could use ECs indoors (41.2%, n = 21), and 56.9% reported that they could not use ECs indoors (Figure 2).

### 3.4 The reasons to select ECs by patients with chronic airway disease

Most of the participants (80.4%, n = 41) selected ECs because ECs seemed to be less harmful than CCs, followed by “no tobacco odour” (78.4%, n = 40), “to help quit smoking” (45.0%, n = 23), “to reduce amounts of cigarette smoking” (37.2%, n = 19), “easy to smoke indoors” (31.4%, n = 16), “good flavour” (21.6%, n = 11), “easy to carry and use” (21.6%, n = 11), “advice by friends” (15.7%, n = 8), “tastes good” (11.7%, n = 6), “curiosity” (9.2%, n = 2), “looks great” (2.0%, n = 1), “cheaper than CCs” (2.0%, n = 1), “trendy” (2.0%, n = 1), and “easy to get” (2.0%, n = 1).

### 3.5 Attitudes, intentions, and restrictions related to ECs use

Table 3 shows the data regarding the attitudes and intentions to use ECs. The majority of the participants thought that ECs have fewer health risks than CCs (58.8%) but answered that ECs should be allowed where smoking is prohibited (33.3%). Only 7.8% of the participants believed that the Food and Drug Administration (FDA) should regulate the use of ECs.

Most of the participants reported that they planned to eventually quit the use of ECs and CCs (37.3%). Fewer participants reported that they were planning to use them as a complete replacement for CCs (27.5%) or they were planning to use ECs where they cannot use CCs (23.5%) or switching gradually from CCs to ECs (9.8%).

### 3.6 Respiratory symptoms and assessment of the quality of life

We surveyed the respiratory symptoms in EC users using questionnaires. About 70% of the EC users complained of cough and sputum. Fewer participants (11, 21.6%) reported that they had chest pain. Of these, half of the participants answered that they had cough or sputum for more than 1 month. Also, most of the participants had no
dyspnoea, but about 20% of participants had mild dyspnoea. EQ-5D-5L, which represents the participants’ quality of life, was 0.9 points, and the visual analogue scale rating was 70.9.

3.7 Comparison of clinical characteristics between exclusive EC users and dual users

We further compared the clinical characteristics of dual users and exclusive EC users. Age, BMI, total PYs of cigarettes, EQ-5D-5L index, pulmonary function test, comorbidities, and plan for smoking cessation were not different between the two groups. The total SGRQ was not different between the groups, but symptom SGRQ (42.2 ± 17.4 vs. 30.6 ± 17.40, p = 0.05) was higher in dual users. The mean BDI score (9.4 ± 8.2 vs. 4.2 ± 4.5, p = 0.016) and the proportion of cases with moderate to severe depressive symptoms (30.4% vs. 4.8%, p = 0.027) were higher in dual users than exclusive EC users (Table 4).

The average FTND score among the ECs users was 3.7 ± 2.9. The average FTND score among dual users was over twice as high compared with exclusive ECs users (mean 4.6 vs. 2.4, p = 0.006). Dual users were more likely to be difficult to refrain from the use of ECs in places where it was forbidden (50.0% vs. 4.8%, p = 0.001) and use ECs more frequently during the first hours after waking than during the rest of the day (46.4% vs. 9.5%, p = 0.006) (Table 5).

4 DISCUSSION

We investigated the clinical characteristics of adult EC users with chronic airway disease or chronic respiratory symptoms. Most of the participants were male, and dominant airway diseases were asthma and COPD. Most of the subjects had a history of CCs smoking, and 19 were dual users for current CCs and ECs. Most of the subjects started ECs use due to health-related problems (harm reduction, no foul odour, or for cigarette smoking cessation). A comparison between exclusive ECs users and
The attitude towards ECs and intention to use

| Variable                                      | Number (%) |
|-----------------------------------------------|------------|
| Attitude towards ECs (multiple choices)       |            |
| ECs have fewer health risks in comparison to regular cigarettes | 30 (58.8) |
| You should be able to use ECs in places where smoking is prohibited | 7 (13.7) |
| ECs have been shown to help smokers quit smoking | 8 (15.7) |
| ECs help people cut down on cigarettes or quit smoking | 17 (33.3) |
| The FDA should regulate the use of ECs         | 4 (7.8)    |
| Intention to use (multiple choices)            |            |
| I plan to eventually quit the use of ECs and CCs | 19 (37.3) |
| I plan to use them as a complete replacement for CCs | 14 (27.5) |
| I plan to use them when I cannot use cigarettes | 12 (23.5) |
| I plan to use them as a partial replacement for CCs | 6 (11.8) |
| I plan to gradually switch from CCs to ECs     | 5 (9.8)    |
| I plan to use them in addition to CCs          | 4 (7.8)    |
| I plan to just experiment with it—I have not yet made up my mind | 3 (5.9) |
| I just wanted to try something different and new | 3 (5.9) |

Abbreviations: CCs, conventional cigarettes; ECs, e-cigarettes; FDA, Food and Drug Administration.

The important finding of the current study was that nicotine dependence levels measured with FTND were higher in dual users than exclusive ECs users, respectively. In our study, about 35% of participants believed that ECs would help smokers quit smoking, and a quarter of participants intended to use ECs as a complete replacement for CCs. Previous research suggests that ECs have the potential to assist smokers to quit or reduce smoking. ECs deliver nicotine into the bloodstream and reduces tobacco withdrawal in a manner effective as nicotine replacement therapy. In a randomized controlled trial (RCT) that investigated the effectiveness of ECs versus nicotine patches for smoking cessation, abstinence rates at 6 months were 7.3% with ECs and 5.8% with nicotine patches and 4.1% with placebo ECs. Although the abstinence rate was higher in ECs users, the differences did not demonstrate a statistical significance. However, abstinence rates reported in the reported RCT were considerably lower in comparison with the abstinence rate of varenicline, which is widely used as a smoking cessation therapy. Continuous 1-year abstinence rate of varenicline ranged from 22% to 35%. In a meta-analysis that included 38 studies, ECs use was not associated with quitting compared with studies on only smokers interested in cigarette cessation.

ECs generate less tar and carcinogens than conventional cigarettes; therefore, ECs users believe that its use may reduce disease caused by harmful components. In our study, the majority of the participants answered that ECs have fewer health risks and are less harmful in comparison with regular cigarettes. The health effects of ECs are controversial. There is no doubt that the concentration of ingredients in ECs’ aerosol is lower than that of conventional cigarettes. The main ingredients in ECs liquids are the compounds that are used in pharmaceutical, cosmetic products, and food. However, there is a growing body of evidence on the association between ECs and acute lung injury. A total of 2807 electronic cigarettes or vaping product use-associated lung injury (EVALI) cases or deaths have been reported to the Center of Disease Control and Prevention (CDC) as of 18 February 2020. The FDA identified that vitamin E acetate is associated with EVALI. When inhaled, vitamin E acetate is incorporated into the phospholipids that are composed of surfactant, thereby increasing its permeability and resulting in function deterioration.

In the case of chronic airway disease, ECs use has been reported to be common in adults with or at risk for COPD and was associated with worse pulmonary-related health outcomes including lung function decline and exacerbations. It has been reported that ECs use is positively related to asthma and is associated with an increased risk of chronic bronchitis symptoms, such as chronic cough and phlegm in adolescents. These findings could be explained based on the theory that ECs vapour causes inhibition of cough reflex sensitivity. Chronic exposure to ECs vapour for 4 months did not induce pulmonary inflammation or emphysema but altered lung lipid homeostasis in alveolar macrophage and epithelial cells independent of the presence of nicotine in a murine model. Also, exposure to inhaled nicotine-containing ECs fluid triggered the effects associated with the development of COPD including cytokine expression, airway hyperreactivity, and lung tissue destruction.

The important finding of the current study was that nicotine dependence levels measured with FTND were higher in dual users than exclusive ECs users in adults with chronic airway disease or chronic respiratory symptoms. Also, ECs use increased proportionally to the reduction in the number of cigarettes for liquid type to 11 times and stick type to 10 sticks, which is approximately the same amount of nicotine in the Korean products. In line
with this finding, a recent study reported that ECs users are less dependent on nicotine than current cigarette smokers. Among healthy smokers, dual users consumed significantly fewer cigarettes but demonstrated no difference in cotinine levels, thereby suggesting that they supplemented their nicotine requirement by using ECs. Dual adult users with or at risk for COPD had higher nicotine dependence than those who smoked only CCs.

### TABLE 4
Comparison of symptoms and lung functions between exclusive ECs users and dual users

| Variable                          | Exclusive ECs users (n = 29) | Dual users (n = 19) | p value |
|-----------------------------------|-----------------------------|---------------------|---------|
| Age, years                        | 42.7 ± 10.4                 | 41.1 ± 14.3         | 0.643   |
| EQ-5D-5L, index                   | 0.9 ± 0.1                   | 0.9 ± 0.1           | 0.333   |
| Total SGRQ                        | 7.5 ± 6.8                   | 13.5 ± 12.2         | 0.091   |
| Symptom SGRQ                      | 30.6 ± 17.4                 | 42.2 ± 17.4         | 0.049   |
| Activity SGRQ                     | 1.7 ± 4.2                   | 10.0 ± 20.1         | 0.093   |
| Impact SGRQ                       | 3.9 ± 6.6                   | 5.8 ± 10.6          | 0.515   |
| BDI score, mean                   | 4.2 ± 4.5                   | 9.4 ± 8.2           | 0.016   |
| High BDI score ≥16                | 1 (3.4)                     | 7 (36.8)            | 0.027   |
| Reduction in cigarette amount after EC use | 11.9 ± 6.6                 | 7.8 ± 6.1           | 0.174   |
| PFT (post BD)                     |                            |                     |         |
| FVC, %                            | 94.6 ± 18.2                 | 89.5 ± 14.7         | 0.394   |
| FEV₁, %                           | 94.4 ± 20.6                 | 87.1 ± 19.3         | 0.322   |
| FEV₁/FVC                          | 77.7 ± 11.5                 | 78.4 ± 12.7         | 0.877   |

Note: Data are presented as mean ± standard deviation or number (%). Abbreviations: BMI, body mass index; BDI, Beck Depression Inventory; EC, e-cigarettes; EQ-5D-5L, EuroQol-5 dimension-5 level; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; PFT, pulmonary function test; SGRQ, St. George’s Respiratory Questionnaire.

### TABLE 5
Comparison of Fagerström test for nicotine dependence between exclusive ECs users and dual users

| Questions                                             | Exclusive ECs users | Dual users | p value |
|-------------------------------------------------------|---------------------|-----------|---------|
| How soon after waking up do you reach for an ECs?     |                     |           |         |
| Within 30 min                                         | 10 (34.4)           | 12 (63.2) | 0.191   |
| Do you find it difficult to refrain from the use of ECs in places where it is forbidden? |           |           |         |
| Yes                                                   | 1 (4.8)             | 14 (50.0) | 0.001   |
| Which ECs would you hate most to give up?             |                     |           |         |
| The first one in the morning                          | 2 (9.5)             | 6 (21.4)  | 0.265   |
| How many times a day do you use ECs?                  |                     |           |         |
| (Number of e-smoking sessions: one e-smoking session consist of 15 puffs or approximately 10 min of use) |           |           |         |
| 10 or less                                            | 8 (38.1)            | 8 (28.6)  | 0.337   |
| 11 to 20                                              | 13 (61.9)           | 16 (57.1) |         |
| 21–30                                                 | 0 (0.0)             | 2 (7.1)   |         |
| 31 or more                                            | 0 (0.0)             | 2 (7.1)   |         |
| Do you use ECs more frequently during the first hours after waking than during the rest of the day? |           |           |         |
| Yes                                                   | 2 (9.5)             | 13 (46.4) | 0.006   |
| Do you use ECs if you are so ill that you are in bed most of the day? |           |           |         |
| Yes                                                   | 5 (23.8)            | 13 (46.4) | 0.104   |
| FTND summary score                                    |                     |           |         |
| FTND (mean ± SD)                                      | 2.4 ± 1.8           | 4.6 ± 3.3 | 0.006   |

Note: Data are presented as number (%). Abbreviations: ECs, e-cigarettes; FTND, Fagerström test for nicotine dependence.
Multiple tobacco product users were associated with past quit attempts. Smokers with prior failed quitting may turn to other tobacco products to cut down on their cigarette consumption without complete cessation.\(^2\) A previous study demonstrated no significant decrease in cotinine levels from baseline to 1 or 2 months in regular smokers who initiated the use of ECs.\(^3\) Also, some ECs users can obtain a large amount of nicotine from ECs similar or higher levels observed in cigarette smokers.\(^3\) Higher levels of cotinine levels in dual users than exclusive users could be explained based on the concept that dual users cut some extent of their cigarette consumption after they start using ECs, but they supplement their nicotine through ECs use.

Cigarette smoking is known to be associated with higher levels of depressive symptoms and impairment of quality of life.\(^3\) Also, the ECs use is known to be associated with a history of clinical diagnosis of depression than never users.\(^3\) In a previous study, dual users had higher proportions of continuous depressive mood that lasted for > 2 weeks than cigarette only smokers. Park et al. showed that smokers with high psychological distress levels tended to be dual users than exclusive ECs users or exclusive cigarette users.\(^3\) In line with the previous studies, our results indicate that dual users had a higher mean BDI score and the proportion of participants with a BDI score of 16 or higher, which means moderate to severe depressive symptoms than exclusive ECs users. In Korea, the smoking pattern has changed from only users to dual and triple users.\(^7\) Therefore, cessation treatment and raising the importance of health concerns in case of dual users are needed.

This pilot has several limitations worth noting. First, a large number of subjects could not be recruited due to the relatively short registration period. Our study was too small to allow reliable comparisons between subgroups of patients. Further research is needed through large-scale recruitment in the future. Second, the inference of a causal relationship between ECs use and bronchitis symptoms, nicotine dependence, and depressive symptoms was limited because the cross-sectional nature of our study did not allow us to clarify the direction of the association. Because our study aimed to investigate the current status of ECs use patterns in patients with chronic airway disease and ECs users were registered, there was no need to include a control group to evaluate the influence of ECs.

## 5 | CONCLUSIONS

In conclusion, most of the ECs users had a history of CCs smoking and dual users for current CCs and ECs. Most of the subjects started ECs use due to health-related reasons and considered ECs as less harmful and intended to quit or reduce CCs use. But the use of ECs did not help in reducing the amount of nicotine. Dual users had higher symptom SGRQ, the proportion of cases with moderate to severe depressive symptoms, and average FTND scores for ECs than exclusive ECs users. One hypothesis that comes from these results is that greater nicotine dependence may influence behaviours, habits, and views about ECs. In the future, large-scale studies are needed to obtain more concrete evidence about the smoking behaviours and nicotine dependence according to ECs use in patients with chronic airway disease.

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## CONFLICT OF INTEREST

The authors declare that they have no competing interests.

## ETHICS STATEMENT

The survey was performed in accordance with the Declaration of Helsinki 7th version, and written informed consent was obtained from all the participants before completing the survey. The present study was approved by the Institutional Review Board (IRB) of the Kyung Hee University College of Medicine (IRB number: KHUH 2019-10-033-004).

## AUTHOR CONTRIBUTIONS

HSK, JWJ, JYK, and HSC contributed to protocol development, data analysis, and drafted the manuscript. HJP, DIP, and JSP contributed to study conception and participated in its coordination. JHP, SHL, and CEM contributed to data checking and information retrieval. HSK, JWJ, HJP, JYK, and HSC designed the study and contributed to the overall management of the study. All authors reviewed the manuscript and approved the final version of the manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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