

Underestimation of Smoking Rates in an East Asian Population with Crohn's Disease

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Background/Aims: The reported rates of current smoking at the time of Crohn's disease (CD) diagnosis tend to be low in East Asian studies. However, we hypothesized that East Asian patients may be reluctant to disclose their smoking history, likely because of the influence of the Confucian culture.

Methods: We prospectively re-evaluated the smoking status at diagnosis in 1,437 Korean CD patients whose smoking status had been reported in our previous study. **Results:** After re-evaluation, the current smokers at diagnosis increased from 388 patients (27.0%) to 445 patients (31.0%), indicating that 12.8% (57 of 445 patients) of the current smokers at diagnosis did not disclose their smoking status at their initial evaluation. The proportion of current smokers at diagnosis who had initially concealed their smoking status was significantly higher among the female patients (29.7%, 11/37) compared with the male patients (11.3%, 46/408) ($p < 0.005$) and among the patients who were ≤ 18 years old at diagnosis (56.4%, 22/39) compared with the patients > 18 years old at diagnosis (8.6%, 35/406) ($p < 0.001$). **Conclusions:** Subgroups of Korean CD patients, particularly young patients and female patients, are reluctant to disclose their smoking history. Therefore, the suggestion that smoking is not a risk factor for the development of CD in East Asians should be made with caution. (**Gut Liver 2017;11:73-78**)

Key Words: Crohn disease; Smoking; Age at diagnosis; Sex

INTRODUCTION

Smoking is one of the most well-defined environmental risk factors for the development and progression of Crohn's disease (CD).^{1,2} However, most previous studies reported low rates (8.3% to 16.6%) of current smoking at CD diagnosis in East Asian patients, thereby suggesting a different role of smoking in the development of CD in this population.³⁻⁸ In contrast to these studies, two recent studies from China and Japan have reported relatively high rates (47% and 38.5%, respectively) of current smoking at CD diagnosis.^{9,10} The reason for this big difference in the rate of current smoking at CD diagnosis has yet to be adequately explained.

We have prospectively maintained the Asan inflammatory bowel disease (IBD) registry since 1997 and reported the long-term prognosis of CD in 2,043 Korean CD patients who are enrolled in the registry.¹¹ In that study, the proportion of current smokers was 26.5% at CD diagnosis. Although this figure was higher than reported in most East Asian studies, we felt that the smoking rate of our study was probably underestimated because Korean patients may be reluctant to disclose their smoking history due to the influence of Confucian culture. Therefore, we performed our present study to re-evaluate the smoking rate in Korean patients with CD. For this purpose, we reinterviewed the CD patients whose smoking status at diagnosis had been evaluated and reported in our previous study.

MATERIALS AND METHODS

1. Study population

We prospectively re-evaluated smoking status at CD diagnosis

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in Korean patients who had been seen between June 1989 and December 2012 at the Asan Medical Center, a tertiary university hospital in Seoul, South Korea, and whose smoking status had been evaluated in our previous study on the long-term prognosis of CD (Fig. 1).¹¹ Re-evaluation was performed between January 1, 2015 and December 31, 2015. Among the 2,043 patients included in our previous study, 1,609 patients visited our outpatient clinic during the current study period. Of these 1,609 patients, smoking status at CD diagnosis was re-evaluated in 1,437 patients. The remaining 172 patients were excluded from this study because smoking history was not re-evaluated by attending physicians.

2. Study design

Baseline patient demographic and clinical information, including sex, date of birth, date of symptom onset, date of CD diagnosis, and smoking status at diagnosis, were retrieved from the Asan IBD registry. Smoking status at diagnosis was re-evaluated at least once during the study period. After explaining to the patients about the importance of reporting accurate information to physicians, patients were asked again about their smoking status at diagnosis. Moreover, this process was performed in the absence of family members, such as parents and

spouses, because patient responses might be influenced by their presence. The definition of smoking status at diagnosis in our current study did not differ from our previous study.^{11,12} Never smokers were defined as those who had a history of smoking fewer than 100 cigarettes in their entire life. Current smokers were defined as those who had a history of smoking at least 100 cigarettes in their entire life and had continued smoking within 6 months prior to CD diagnosis. Ex-smokers were defined as those who had a history of smoking at least 100 cigarettes in their entire life and had completely stopped smoking for at least 6 months prior to CD diagnosis. The factors associated with changes in smoking status at diagnosis as a result of re-evaluation were analyzed.

The Ethics Committee of Asan Medical Center approved the study protocol, and written informed consent was obtained from all patients.

3. Statistical analysis

Continuous variables were expressed as the median and interquartile range (IQR), and categorical variables were expressed as a number and percentage (%). The Mann-Whitney U test was used to compare continuous variables between groups, and the chi-square or Fisher exact test was used to compare categorical

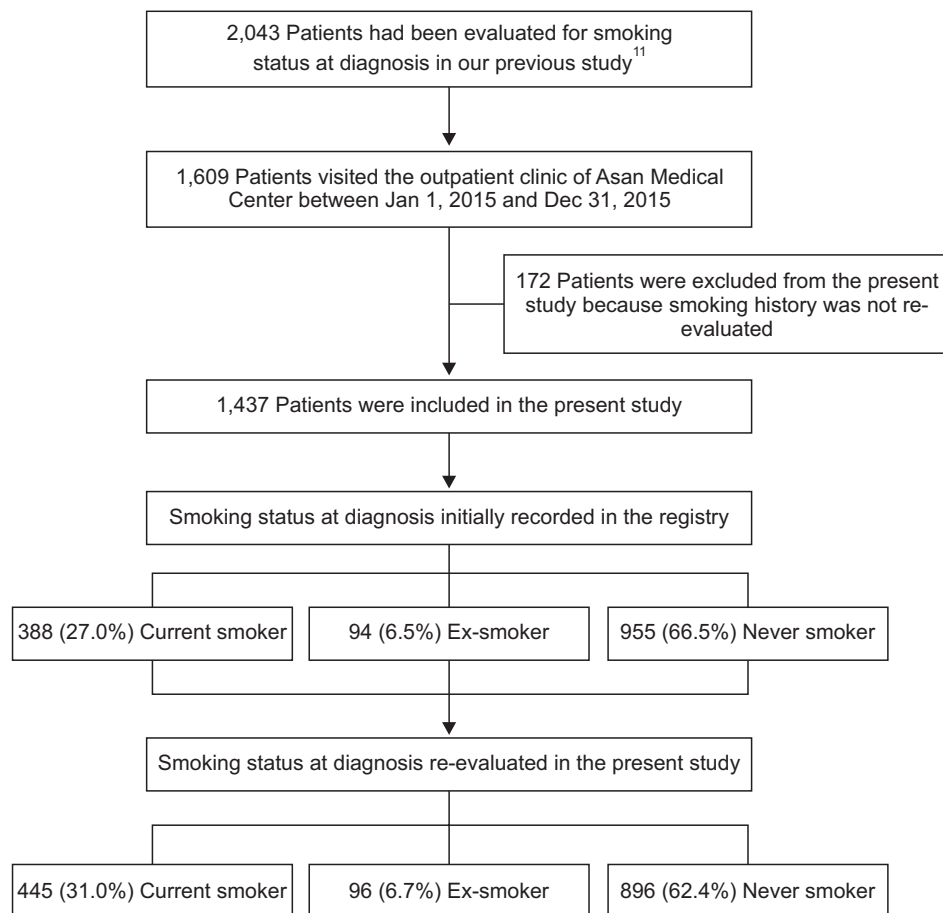


Fig. 1. Flow chart of the recruitment of patients with Crohn’s disease and the re-evaluation of smoking status at diagnosis.

variables. These analyses were performed using the IBM SPSS version 21.0 for Windows (IBM Corp., Armonk, NY, USA). A $p < 0.05$ was considered as the level of significance.

RESULTS

Of the 1,437 patients included in our study, 1,021 patients (71.1%) were male and 416 patients (28.9%) were female, yielding a male-to-female ratio of 2.45:1. The median age at CD diagnosis was 23 years (range, 9 to 75 years). Smoking status at diagnosis initially recorded in the registry for the 1,437 study patients was as follows: current smoker in 388 patients (27.0%), ex-smoker in 94 patients (6.5%), and never smoker in 955 patients (66.5%) (Fig. 1). These rates were not different from those among all 2,043 patients reported in our previous study.¹¹

Smoking status at diagnosis was re-evaluated after at least 2 years had passed from the initial evaluation, and the median interval between evaluations was 6.0 years (IQR, 3.0 to 10.0 years). After re-evaluation, smoking status at diagnosis changed from never smoker to current smoker in 41 patients and to ex-smoker in 18 patients. Also, smoking status changed from ex-smoker to current smoker in 16 patients. Consequently, the number of current smokers at diagnosis increased to 445 patients (31.0%), and the number of ex-smokers increased to 96 patients (6.7%), whereas the number of never smokers decreased to 896 patients (62.4%) (Fig. 1). This indicates that 12.8% (57 of 445 patients) of current smokers at diagnosis did not disclose their smoking status at their initial evaluation.

When analyzed by sex, the proportion of current smokers who had initially concealed their smoking status was higher in female patients (29.7%, 11 of 37 patients) than male patients (11.3%, 46 of 408 patients) ($p < 0.005$). When analyzed by age, the proportion of current smokers who had initially concealed their smoking status was higher in patients 18 years or younger at diagnosis (56.4%, 22 of 39 patients) than in patients older than 18 years at diagnosis (8.6%, 35 of 406 patients) ($p < 0.001$) (Table 1). Among patients older than 18 years at diagnosis, the proportion of current smokers who had initially hidden their smoking status was 11.1% (30 of 271 patients) in patients 30 years or younger at diagnosis in comparison to 3.7% (five

of 135 patients) of patients older than 30 years at diagnosis ($p < 0.05$).

DISCUSSION

To the best of our knowledge, our present study is the first to re-evaluate smoking status at CD diagnosis in the same group of patients. In Korea, due to the influence of Confucius on cultural practices, it is considered taboo for young people to smoke in front of their elders and for women to smoke in public. In addition, considering the fact that obeying parents and elders is one of the important values of the Confucian culture, it is highly possible that the patients do not disclose their smoking status in East Asian countries. The smoking rate of women is much lower than that of men in Korea (41.4% in adult men vs 5.7% in adult women),¹³ and the smoking rate of adolescence in Korea is 9.7% according to the Korean Centers for Disease Control (CDC) database.¹⁴ Therefore, we hypothesized that some Korean patients, especially young patients and female patients, would be reluctant to honestly reveal their smoking history to their doctors. We also hypothesized that patients would disclose the correct information regarding their smoking status at diagnosis if (1) they were older and more familiar with their attending physicians, (2) they were asked about their smoking history in the absence of family members, and (3) they realized the importance of this information to their medical treatment. Our present study demonstrated that the rate of current smoking at diagnosis was underestimated in our previous cohort of Korean CD patients, especially in young patients and female patients, thereby confirming our hypothesis.

Even after re-evaluation, however, the proportion of current smokers at diagnosis increased by only 4.0% and is apparently still low in comparison with Western CD patients.¹⁵⁻¹⁹ Western population-based studies reported the smoking status at CD diagnosis as follows: 30% to 40% current smokers, 7% to 24% ex-smokers, and 38% to 52% never smokers. The apparently lower rate of smoking in our Korean CD patients has several possible explanations. First, the median age at diagnosis in our study (23 years) was lower than that in Western studies (30 to 34 years).¹⁵⁻²⁰ More than 25% of our patients were diagnosed at

Table 1. Changes in Smoking Status at the Time of Diagnosis of Crohn's Disease as a Result of the Re-Evaluation of Smoking Status according to Sex and Age at Diagnosis

Sex	Age at diagnosis, yr	No. of patients	Current smoker at diagnosis		Proportion of initial misclassifications in current smokers at diagnosis, % (n/N)
			Before re-evaluation, n (%)	After re-evaluation, n (%)	
Female	≤18	109	1 (0.9)	3 (2.8)	66.7 (2/3)
	>18	307	25 (8.1)	34 (11.1)	26.5 (9/34)
Male	≤18	262	16 (6.1)	36 (13.7)	55.6 (20/36)
	>18	759	346 (45.6)	372 (49.0)	7.0 (26/372)

the age of 18 years or younger, thus lowering the smoking rate in our series. Second, as mentioned above, the smoking rate of women is much lower than that of men in Korea, which lowers the overall smoking rate.¹³ In fact, the rate of current smoking in Korean male CD patients older than 18 years at diagnosis was 49.0% (372 of 759 patients), which was higher than the current smoking rate of 41.4% in the Korean adult male population. Similarly, the rate of current smoking in Korean female CD patients older than 18 years of age at diagnosis is 11.1% (34 of 307 patients), which is higher than the current smoking rate of 5.7% in the Korean adult female population. Although this comparison is crude, it suggests that smoking may also play a role in the development of CD in Koreans. In contrast, the rate of current smoking at diagnosis in our male and female patients 18 years or younger at diagnosis (13.7% and 2.8%, respectively) in the present study was not higher than the current smoking rate in the Korean males and females 18 years or younger (14.4% and 4.6% according to the Korean CDC, respectively).¹⁴ This raises the possibility that some young patients may still have been withholding their true smoking status at CD diagnosis despite our re-evaluation.

Previous East Asian studies have suggested that the role of smoking in the development of CD may differ between different ethnic groups due to genetic heterogeneities and that, given the low rate of current smoking at diagnosis in East Asians, smoking is not a significant risk factor for CD in this population.^{3,8,21,22} According to the findings of previous Israeli studies, there is no association between smoking and CD in the Jewish population.²³⁻²⁶ This unusual lack of association is likely caused by the masking of smoking effects by the strong genetic predisposition for CD in this ethnic group. However, this is not the case in East Asians. Moreover, previous studies have demonstrated an association between smoking and intestinal resection in East Asian patients with CD.^{4,5,10} Considering that two recent studies from China and Japan reported relatively high rates (47% and 38.5%, respectively) of current smoking at CD diagnosis,^{9,10} and that our study demonstrated a high rate of current smoking at diagnosis in Korean adult male patients, the smoking status at diagnosis should be cautiously evaluated and interpreted in East Asian patients.

Besides deliberate false replies from patients, various factors may cause the underestimation of smoking status at diagnosis. First, some patients who quit smoking after symptom onset but before CD diagnosis may just reply that they do not smoke if the question at the time of CD diagnosis is "Do you smoke?" instead of "Have you ever smoked?" These patients may be falsely classified as never smokers at CD diagnosis, but they should be classified as ex-smokers or current smokers at CD diagnosis depending on the interval between the cessation of smoking and CD diagnosis. In our current study, 80 patients quit smoking after the onset of symptoms and before the diagnosis of CD. Of these 80 cases, 50 patients ceased smoking within 6 months

before CD diagnosis (data not shown). If these 50 patients had been falsely classified as never smokers due to inadequate history taking, the proportion of current smokers at diagnosis would have falsely appeared as 27.5% rather than 31.0%. Second, many patients quit smoking during the disease course, especially just after CD diagnosis. These patients may be falsely classified as never smokers or ex-smokers at CD diagnosis if smoking history is inappropriately taken after the cessation of smoking. In our study, 68 current smokers at diagnosis had already quit smoking when they were referred to our hospital (data not shown). If these patients had been falsely classified as never smokers or ex-smokers at diagnosis due to inadequate history-taking at their first visit, the proportion of current smokers at diagnosis would have falsely appeared as 26.2% rather than 31.0%. Third, information on smoking status may be unavailable for some patients, even in prospective studies.^{3,27} If these patients are mistakenly classified as never smokers, the smoking rate may inaccurately decrease. Taken together, smoking status at diagnosis should be cautiously evaluated before concluding that smoking is not a risk factor for the development of CD in East Asians.

Our study had some limitations. First, although we tried to be as accurate as possible when re-evaluating the smoking status at diagnosis, there was still a possibility that the result was underestimated because our assessment only relied on patient responses. Nicotine testing at the time of CD diagnosis may be necessary for the accurate evaluation of smoking status at diagnosis.²⁸ Second, the patient's memory of smoking status at diagnosis may be unclear in some cases because of the time interval between CD diagnosis and re-evaluation of smoking status. However, we believe this was unlikely because most patients were educated at the time, or in the early days following CD diagnosis, about the deleterious effects of smoking on this disease. Third, although our results suggest that smoking may play a role in the development of CD in Koreans, like in Westerners, it is still premature to conclude from our current findings that smoking is a definite risk factor for the development of CD in East Asians.

In conclusion, some Korean CD patients, especially young patients and female patients, are reluctant to disclose their smoking history. Therefore, we should be careful to obtain correct information about smoking history, and the suggestion that smoking is not a risk factor for the development of CD in East Asians who have a similar cultural background as Koreans should be made with caution.

CONFLICTS OF INTEREST

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