Weight gain after smoking cessation does not modify its protective effect on myocardial infarction and stroke: evidence from a cohort study of men

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Aims

This study aimed to investigate the association between smoking cessation, post-cessation body mass index (BMI) change and risk of myocardial infarction (MI) and stroke in men.

Methods and results

A prospective cohort study using the National Health Insurance Service (NHIS) data set collected from 2002 to 2013 was implemented. Based on the first (2002–03) and second (2004–05) NHIS health check-up periods, 108 242 men aged over 40 years without previous diagnoses of MI or stroke were grouped into sustained smokers, quitters with BMI gain, quitters without BMI change, quitters with BMI loss, and non-smokers. Body mass index change was defined as the difference of more than 1.0 kg/m² between the two health check-up periods. The participants were followed-up from 1 January 2006 to 31 December 2013. Hazard ratios (HRs) and 95% confidence intervals (HR, 95% CI) were computed using Cox proportional hazard models adjusted for sociodemographic, health status, and family health history. Compared to the sustained smokers, the risk of MI and stroke was significantly reduced in both quitters with BMI gain (HR 0.33; 95% CI 0.16–0.70 for MI and HR 0.75; 95% CI 0.57–1.00 for stroke) and quitters without BMI change (HR 0.55; 95% CI 0.37–0.83 for MI and HR 0.75; 95% CI 0.62–0.92 for stroke), but no significant association was found in quitters with BMI loss (HR 0.91; 95% CI 0.43–1.91 for MI and HR 0.86; 95% CI 0.57–1.31 for stroke), respectively. Non-smokers had lower risk of MI (HR 0.37; 95% CI 0.32–0.43) and stroke (HR 0.68; 95% CI 0.64–0.73) compared to the sustained smokers.

Conclusion

Post-cessation BMI change did not significantly modify the protective association of smoking cessation with MI and stroke.

Keywords

Smoking cessation • BMI change • Myocardial infarction • Stroke • Men

Introduction

Smoking continues to be a major global health risk for mortality and cardiovascular diseases (CVD) in spite of the variation in the prevalence and intensity of smoking between and within different continents. Currently, smoking remains as one of the major global risk burdens for CVD potentially been multiplied by additional factors such as high saturated fat diet, high blood pressure, elevated cholesterol level, and diabetes. Therefore, prevention strategies are necessary to reduce the disease burden of CVD across the globe.
Although smoking cessation is known to significantly reduce the risk of coronary heart disease (CHD) and cerebrovascular accident in both the Asian and Western populations, subsequent weight gain has been recognized as one of the minor disadvantages and concerns among smokers who may attempt to quit smoking. According to a previous study, it is not clear whether the severity of weight gain after quitting smoking is similar between the Asians and non-Asians, and only a few studies have addressed the issue of weight gain following smoking cessation in the Asian male population.

While weight gain is widely known as a risk factor for CHD and CVD, the effect of post-cessation weight gain on the risk of CHD and CVD is not well understood, especially among the Asian population. In the High-Risk and Population Strategy for Occupation Health Promotion (HIPPO-OHP) study conducted in Japan, weight gain and 24% reduction in the risk of CHD were observed in male workers who had successfully stopped smoking compared to the sustained smokers. However, this study was only able to compute the risk of CHD based on the prediction scores, not through the actual events. In the US community-based cohort study, the results show that the risk of CVD events was significantly lower among the non-diabetic sustained non-smokers. Up to now, not enough evidence is available for clinicians in the Asian countries to evaluate whether the post-cessation weight change is associated with the risk of CHD and CVD events or not. To assess the relationship of smoking cessation and post-cessation BMI change to the risk of myocardial infarction (MI) and stroke, we used the health survey, examination, and claims database of the NHIS collected from Korean men.

### Methods

#### Data source and study population

The data set for this population-based cohort study was obtained from the NHIS National Health Screening Cohort (NHIS-HealS) to investigate the association between smoking cessation, post-cessation change in BMI, and risk of MI and stroke in men. After the Ministry of Health and Welfare implemented the National Health Insurance Act in 1989 in the Republic of Korea, enrolling health insurance provided by the NHIS became mandatory for citizens. Currently, the enrollment rate is about 97%, which makes almost the entire population covered under the compulsory health care system in the country. Enrolees of the NHIS are required to undergo biennial health checkups after they turn 40. The Ministry of Health and Welfare implemented the National Health Insurance Act in 1989 in the Republic of Korea, enrolling health insurance provided by the NHIS became mandatory for citizens. Currently, the enrollment rate is about 97%, which makes almost the entire population covered under the compulsory health care system in the country. Enrolees of the NHIS are required to undergo biennial health checkups after they turn 40. The NHIS provides research data sets consisting of sociodemographics (i.e. age, sex, insurance premium, etc.) and hospital utilization (i.e. admission and discharge dates) along with the results from the biennial health checkup (i.e. BMI, blood pressure, etc.), in accordance with the Privacy Act. The NHIS-HealS research database is constructed with simple random sampling with a sampling rate of 10% from the entire population of the Republic of Korea who underwent the biennial health checkups provided by the NHIS. Validity and representativeness of the NHIS research database have been described in detail elsewhere.

We abstracted data on 121,497 male enrolees of NHIS with complete data on their smoking status between the first (2002–03) and second (2004–05) health check-up periods. Female enrolees were not considered in this study due to a significantly low proportion of those who reported as smokers (less than 2%). Within the male enrolees, we included only those who were alive with no previous diagnosis of MI or stroke at the beginning of the follow-up. Accordingly, we excluded those who met the following criteria: (i) death of from any cause including MI and stroke and (ii) with records of MI or stroke diagnosis prior to the follow-up. Therefore, we excluded the participants who were deceased (n = 433) or diagnosed with MI or stroke (n = 12,822) before the index date (1 January 2006). As a result, 108,242 male participants were selected for the final study population. The Institutional Review Board (IRB) at the Seoul National University Bundang Hospital approved our study (IRB No: X-1701/378-902), which was in compliance with the Declaration of Helsinki. We were waived from obtaining informed consent from the participants for this study because all the data set provided by the NHIS for research purposes have been anonymized in adherence to the strict confidentiality guidelines.

### Assessment of change in smoking behaviour and body mass index

At each health check-up period, the NHIS enrolees responded to a self-reported health survey questionnaire and participated in a physical examination. The participants of the NHIS biennial health checkup were grouped into smokers, quitters, and non-smokers based on the responses of the self-reported survey between the first and second health check-up periods. Body mass index was calculated by weight in kilograms divided by height in square meters. In addition, quitters were further classified as quitters with BMI gain, without BMI change, and with BMI loss to address weight change following smoking cessation. Compared to the first health check-up period, we defined a change of more than +1.0 kg/m² in BMI in the second health check-up period as BMI gain to reflect the average post-cessation weight gain observed in the Asian men based on the previous studies. Similarly, we defined BMI change between -1.0 kg/m² and +1.0 kg/m² as no BMI change, and BMI loss of more than 1.0 kg/m² as BMI loss. Finally, participants were categorized as sustained smokers, quitters with BMI gain, quitters without BMI change, quitters with BMI loss, and sustained non-smokers.

### Ascertainment of myocardial infarction and stroke

We used the International Classification of Diseases, Tenth Revision (ICD-10) along with hospital admission records to identify Incident MI and stroke that occurred between 1 January 2006 and 31 December 2013. The following ICD-10 codes were used to identify the main outcomes of this study: MI (ICD-10 codes: I21–124) and total stroke (ICD-10 codes: I60–I69) and its subtypes: ischaemic stroke (ICD-10 code: I63) and haemorrhagic stroke (ICD-10 codes: I60–I62). We determined the cases with at least 2 days of hospital admission as true events of MI and stroke in the NHIS records to rule out the cases that did not happen to be the actual MI and cerebrovascular accidents. Using ICD-10 codes with hospital admission records in the NHIS data set to identify confirmed cases of MI and stroke have been previously described.

### Statistical analyses

Characteristics of the study participants at the baseline were assessed using numbers (percentages) for categorical variables and means [standard deviations (SD)] for continuous variables. Change in BMI between the first and second health check-up periods were described using mean [standard error (SE)] with corresponding 95% confidence intervals (95% CI), along with median [interquartile range (IQR)]. European Society of Cardiology Systematic Coronary Risk Evaluation (ESC SCORE) was calculated from the low risk chart for men based on the comparison of cardiovascular mortality rates between the Republic of Korea and European countries included in the low-risk region.

In this study, the follow-up period began on the index date (1 January 2006) and lasted until 31 December 2013. Starting on 1 January 2006, the...
Post-cessation BMI change and risk of myocardial infarction and stroke

Participants were censored at the event of MI, stroke, or death of any cause. When there was no occasion of censoring, the participants were censored at 31 December 2013. To estimate the risk of MI and stroke according to smoking behaviour and change in BMI, we used Cox proportional hazards model to compute the hazard ratios and 95% confidence intervals (HR; 95% CI). We developed a model with minimal adjustment (adjusting only for age) and Multivariable Model 1 adjusting for age, residential area, income status, body mass index (BMI), fasting serum glucose, total cholesterol, blood pressure, alcohol consumption, physical activity, and the Charlson Comorbidity Index (calculated based on the pre-existing comorbid conditions including MI, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer, mild liver disease, diabetes with and without complications, paraplegia or hemiplegia, renal disease, any or metastatic cancer, moderate or severe liver disease, and acquired immune deficiency syndrome before the beginning of the follow-up period). Multivariable Model 2 was constructed by adjusting for family history of MI or stroke in addition to the variables included in the Multivariable Model 1. We used scaled Schoenfeld residuals to test the proportionality assumptions of the Cox regression models.

Since health survey data and health care claims in the NHIS records do not refer to the possibility of individuals who quit smoking due to critical health issues, we carried out sensitivity analysis by repeating multivariable adjusted Cox regression after excluding the MI and stroke events that occurred within the first year of the follow-up period. In addition, we conducted subgroup analysis by splitting the participants into different sociodemographic and health-related categories and assessed the risk of MI and stroke based on the Multivariable Model 2 in the relevant categories.

Secondary analyses were performed to examine the association between smoking cessation, post-cessation BMI change, and risk of MI and stroke in detail. We treated BMI change as a continuous variable to test the moderating effect of post-cessation change in BMI. Without categorizing quitters based on post-cessation BMI change, we assessed the association between smoking cessation and risk of MI and stroke with Multivariable Model 2 and additionally adjusted for BMI change as a continuous variable. Also, we stratified quitters in tertiles of BMI change to examine the change in BMI in relation to the events of MI and stroke. To estimate the risk of composite outcome of cardiovascular events (MI and stroke) among quitters, we compared quitters without BMI gain and with BMI change to quitters with BMI gain. Propensity score was estimated for quitters with and without BMI gain based on the following variables: age, place of residence, income status, BMI, blood pressure, fasting serum glucose, total cholesterol, alcohol consumption, physical activity, Charlson Comorbidity Index, family history of MI, and family history of stroke. In the propensity score analysis, risk of cardiovascular events was assessed with adjustment for the estimated propensity score in quitters without BMI gain compared to quitters with BMI gain.

Statistical significance was set to two-sided $P < 0.05$. Data collection and statistical analyses in this study were performed using SAS 9.4 (SAS Institute, Cary, NC, USA) and STATA 14.0 (StataCorp LP, College Station, TX, USA), respectively. Propensity score analysis was performed in SPSS Statistics version 23.0 (IBM Software Group, Chicago, IL, USA) with R package implementation.

Results

During the follow-up period from 1 January 2006 to 31 December 2013, a total of 108 242 participants generated 836 962 person-years. There were 1420 cases of MI and 3913 cases of stroke. Compared to the first health check-up period, 46% of the participants continued to smoke ($n = 49 997$), and 48% remained as non-smokers ($n = 52 218$), and 8% of the participants ($n = 6027$) reported that they had quit smoking at the second health check-up period. None of the participants included in the final study population started smoking between the first and second health check-up period. Of those who underwent smoking cessation, BMI gain of more than $+1.0 \text{kg/m}^2$ occurred in 1633 quitters (median 1.54; IQR 1.23 to 2.06) whereas 3710 quitters had no significant BMI change (median 0.07; IQR -0.33 to 0.52) and 684 quitters had BMI loss of more than 1.0 kg/m$^2$ (median -1.43; IQR -1.92 to -1.14). Significant BMI change was not observed among sustained smokers (median 0; IQR -0.67 to 0.63) and non-smokers (median 0; IQR -0.70 to 0.62). The general characteristics of participants according to smoking status and BMI change are summarized in Table 1.

Compared to the sustained smokers, the risk of MI significantly reduced among quitters with BMI gain (HR 0.33; 95% CI 0.16–0.70) and without BMI change (HR 0.55; 95% CI 0.37–0.83) after adjusting for potential confounders (Multivariable Model 2). However, significant risk reduction of MI was not found in quitters with BMI loss (HR 0.91; 95% CI 0.43–1.91). Similarly, quitters with BMI gain and without BMI change had 25% (HR 0.75; 95% CI 0.57–1.00 and HR 0.75; 95% CI 0.62–0.92) reduction in risk of total stroke, respectively. Among quitters with BMI loss, the risk reduction for total stroke did not reach statistical significance (HR 0.86; 95% CI 0.57–1.31). The risk of ischaemic stroke was reduced in quitters regardless of the post-cessation BMI change, but statistical significance was only found among quitters with BMI loss (HR 0.56; 95% CI 0.43–0.97). Although the quitters with BMI gain (HR 0.62; 95% CI 0.34–1.12) and without BMI change (HR 0.80; 95% CI 0.52–1.23) showed reduced risk of haemorrhagic stroke, the results were not statistically significant. No association between post-cessation BMI loss and risk haemorrhagic stroke was found (HR 1.70; 95% CI 0.53–5.47). In addition, non-smokers had lower risk of MI (HR 0.37; 95% CI 0.32–0.43) and total stroke (HR 0.68; 95% CI 0.64–0.73) (Table 2).

The overall result of risk estimates for MI and stroke were consistent across the categories (age, place of residence, income status, Charlson Comorbidity Index, and ESC SCORE) for subgroup analyses, but the statistical significance was attenuated in each category except for non-smokers. Results of the subgroup analyses are presented in Figures 1 and 2. The difference in measurable CVD risk factors from the second health checkup compared to the first health checkup among sustained smokers, quitters with BMI gain, without BMI change, with BMI loss, and non-smokers are reported in Supplementary material online, Table S1. In addition, the results from sensitivity analysis showed that the association between smoking cessation, post-cessation BMI change, and risk of MI and stroke remained consistent owing to the fact that most of the events did not take place within the first year of follow-up (see Supplementary material online, Table S2).

Protective association of smoking cessation with MI and stroke was found in quitters and non-smokers when BMI change was treated and adjusted as a continuous variable (see Supplementary material online, Table S3). No significant difference in results was observed when quitters were stratified in tertiles of BMI change (see Supplementary material online, Table S4) compared to the initial categorization. Comparison of risk estimates for cardiovascular events
Table 1  Descriptive statistics of the study population at the inception of the study according to the change in smoking status based on the first (2002–03) and second (2004–05) National Health Insurance Service National Health Screening Cohort in men

| Characteristics at baseline | Sustained smokers | Smoking cessation | Quitters with BMI gain<sup>a</sup> | Quitters without BMI change<sup>b</sup> | Quitters with BMI loss<sup>c</sup> | Non-smokers |
|----------------------------|-------------------|-------------------|-----------------------------------|-----------------------------------|-----------------------------------|-------------|
| No. of subjects, n         | 49 997            | 1633              | 3710                              | 684                               | 52 218                            |             |
| Age                        | 52.1 (7.92)       | 52.0 (42)         | 52.3 (7.9)                        | 53.2 (8.5)                        | 55.1 (9.14)                       |             |
| Residence, n (%)           |                   |                   |                                   |                                   |                                   |             |
| Capital                    | 12 255 (24.5)     | 412 (25.2)        | 928 (25.0)                        | 180 (26.3)                        | 13 713 (26.3)                     |             |
| Metropolitan               | 20 192 (40.4)     | 638 (39.1)        | 1459 (39.3)                       | 240 (35.1)                        | 19 273 (36.9)                     |             |
| City/town                  | 17 550 (35.1)     | 583 (35.7)        | 1323 (35.7)                       | 264 (38.6)                        | 19 232 (36.8)                     |             |
| Income status              |                   |                   |                                   |                                   |                                   |             |
| 1st quartile               | 6384 (12.8)       | 181 (11.1)        | 315 (8.5)                         | 63 (9.2)                          | 5583 (10.7)                       |             |
| 2nd quartile               | 9639 (19.3)       | 228 (13.9)        | 548 (14.8)                        | 111 (16.2)                        | 9083 (17.4)                       |             |
| 3rd quartile               | 15 891 (31.8)     | 524 (32.1)        | 1036 (27.9)                       | 182 (26.6)                        | 15 184 (29.1)                     |             |
| 4th quartile               | 18 083 (36.1)     | 700 (42.9)        | 1811 (48.8)                       | 328 (48.0)                        | 22 368 (42.8)                     |             |
| Prevalence of obesity<sup>d</sup>, n (%) | 15 514 (31.1) | 788 (48.3) | 1288 (34.7) | 201 (29.4) | 18 542 (35.5) |             |
| Body mass index            | 23.6 (2.84)       | 25.0 (2.75)       | 24.0 (2.68)                       | 23.3 (2.74)                       | 24.1 (2.71)                       |             |
| Change in BMI<sup>e</sup> |                   |                   |                                   |                                   |                                   |             |
| Mean (SE) [95% CI]         | -0.04 (0.01)      | 1.79 (0.02)       | 0.09 (0.01)                       | -1.73 (0.04)                      | -0.06 (0.01)                      |             |
| [−0.05 to -0.03]           | [1.74 to 1.83]    | [0.076 to 0.11]   | [−1.80 to -1.66]                 | [−0.07 to -0.05]                  |                                  |             |
| Median (IQR)               | 0 (-0.67 to 0.63) | 1.54 (1.23 to 2.06) | 0.07 (-0.33 to 0.52) | -1.43 (-1.92 to -1.14) | 0 (-0.70 to 0.62) |             |
| FSG, mg/dL                 | 99.9 (32.8)       | 99.5 (27.2)       | 99.8 (28.8)                       | 105.0 (41.2)                      | 98.9 (28.8)                       |             |
| Total cholesterol, mg/dL   | 196.8 (36.7)      | 203.3 (36.5)      | 199.0 (36.0)                      | 195.0 (37.8)                      | 194.4 (35.3)                      |             |
| Blood pressure, mmHg       |                   |                   |                                   |                                   |                                   |             |
| SBP                        | 127.1 (16.5)      | 128.5 (16.3)      | 126.9 (15.9)                      | 125.6 (15.6)                      | 128.4 (16.6)                      |             |
| DBP                        | 80.4 (10.9)       | 81.3 (10.4)       | 80.3 (10.8)                       | 79.4 (10.5)                       | 81.0 (10.9)                       |             |
| Alcohol consumption, n (%) |                   |                   |                                   |                                   |                                   |             |
| 1–2 times/week             | 20 808 (41.7)     | 792 (48.7)        | 1791 (49.0)                       | 341 (50.7)                        | 35 464 (68.0)                     |             |
| 3–4 times/week             | 24 679 (49.4)     | 710 (43.7)        | 1635 (44.8)                       | 279 (41.5)                        | 14 573 (27.9)                     |             |
| ≥5 times/week              | 4456 (8.9)        | 123 (7.6)         | 226 (6.2)                         | 53 (7.8)                          | 2083 (4.1)                        |             |
| Physical activity, n (%)   |                   |                   |                                   |                                   |                                   |             |
| 1–2 times/week             | 40 160 (80.6)     | 1211 (75.1)       | 2582 (71.7)                       | 439 (66.5)                        | 38 071 (73.6)                     |             |
| 3–4 times/week             | 7000 (14.1)       | 301 (18.7)        | 783 (21.7)                        | 169 (25.6)                        | 9109 (17.6)                       |             |
| ≥5 times/week              | 2669 (5.3)        | 100 (6.2)         | 237 (6.6)                         | 52 (7.9)                          | 4542 (8.8)                        |             |
| Cigarettes smoked per day, n (%) |          |                   |                                   |                                   |                                   |             |
| <10                        | 10 141 (20.3)     | —                 | —                                 | —                                 | —                                 |             |
| 10–19                      | 28 058 (56.1)     | —                 | —                                 | —                                 | —                                 |             |
| 20–39                      | 11 093 (22.2)     | —                 | —                                 | —                                 | —                                 |             |
| ≥40                        | 705 (1.4)         | —                 | —                                 | —                                 | —                                 |             |
| Smoking history, n (%)     |                   |                   |                                   |                                   |                                   |             |
| <10 years                  | 2628 (5.3)        | 294 (18.0)        | 828 (22.3)                        | 162 (23.7)                        | —                                 |             |
| 10–19 years                | 11 033 (22.1)     | 411 (25.2)        | 977 (26.3)                        | 178 (26.0)                        | —                                 |             |
| ≥20 years                  | 36 336 (72.6)     | 928 (56.8)        | 1905 (51.4)                       | 344 (50.3)                        | —                                 |             |
| Family history of MI, n (%) |                   |                   |                                   |                                   |                                   |             |
| Yes                        | 929 (1.9)         | 35 (2.1)          | 95 (2.6)                          | 18 (2.6)                          | 841 (1.6)                         |             |
| No                         | 49 068 (98.1)     | 1598 (97.9)       | 3615 (97.4)                       | 666 (97.4)                        | 51 377 (98.4)                     |             |
| Family history of stroke, n (%) |           |                   |                                   |                                   |                                   |             |
| Yes                        | 2561 (5.1)        | 96 (5.9)          | 230 (6.2)                         | 29 (4.2)                          | 2455 (4.7)                        |             |
| No                         | 47 436 (94.9)     | 1537 (94.1)       | 3480 (93.8)                       | 655 (95.8)                        | 49 763 (95.3)                     |             |

Continued
between quitters showed null association (see Supplementary material online, Table S5). Risk estimates for cardiovascular events adjusted for the estimated propensity score in quitters without BMI gain compared to quitters with BMI gain was not significant. The result from the propensity score and multivariable analyses were not significantly different from each other (see Supplementary material online, Table S6).

**Discussion**

Based on the nationally representative database, containing health survey and examination data linked to clinical records of more than 100,000 Korean men, we found that smoking cessation is associated with a reduced risk of MI and stroke regardless of post-cessation BMI change. Secondary analyses confirmed that post-cessation BMI change had no moderating effect on the protective association of smoking cessation with MI and stroke. Although some studies suggest weight gain is a minor disadvantage from quitting smoking, our study highlights the beneficial role of smoking cessation for potentially reducing disease burden of CHD and CVD despite the subsequent weight change.

Data from the previous studies in both the Asia and the North America show that smoking cessation is attributable to subsequent weight gain. According to a study conducted in the Japan, men between 19 and 69 years of age who successfully quit smoking had about 2.0 kg of weight gain within and after 6 months of smoking cessation. Similarly, Korean men over 30 who reported that they stopped smoking within a mean interval time of 1.7 years had a median weight gain of 1.3 kg based on hospital records. Taking the average weight and height of Korean men over 40 into account, BMI gain of more than 1.0 kg/m² among quitters in our study translates into an approximate post-cessation weight gain of more than 2.0 kg. In the cohort study of US men and women, weight gain was more predominant among those who had stopped smoking within 4 years compared to those who had quit for more than 4 years. The weight gain following smoking cessation is attributable to vessel dilation after discontinuation of nicotine vessel constriction supplying the intestine, which often result in increased nutritional absorption.

The protective association of smoking cessation with MI and stroke despite post-cessation weight change are consistent with previous studies. However, our study evaluated the risk reduction of MI and stroke from smoking cessation a step further based on the degree of post-cessation BMI change. We found that BMI loss following smoking cessation was not associated with significant risk reduction of MI and stroke. We suspect that lack of protective association in quitters with loss of BMI (more than 1.0 kg/m²) is because of sarcopenic obesity (decreased muscle mass with aging resulting in elevated level of body fat mass). A cross-sectional study conducted from the fifth Korea National Health and Nutrition Examination Survey (KNHANES V) has shown that older Korean adults with muscle loss are at higher risk of CVD due to elevated body-fat percentage leading to increased insulin resistance. Unlike the KNHANES data set, body composition data was not available for this study. Therefore, further investigation accounting for change of fat mass (e.g. visceral fat) and lean mass proportion following smoking cessation is necessary to update this evidence.

Currently, only a few studies have examined the effect of subsequent weight gain after quitting smoking on CHD and CVD events. In the analysis of the HiPOP-OHP study, data comprised of 1995 Japanese workers indicates that those who had stopped smoking over a half-year period experienced weight gain and their blood
Since smoking cessation can begin to reverse negative health effects on the cardiovascular system from cigarette smoking, a few biological mechanisms associated with post-cessation change in health status and cardiovascular risk factors may explain the findings of our study. Cigarette smoking can lead to the onset of accelerated heart rate and elevated blood pressure in the short-term, and if continued over time, it can induce atherosclerosis. Additionally, smoking may initiate an increase in the levels of inflammatory markers. When individuals stop smoking, they may start to experience improvement in both health status and inflammatory markers. In the third National Health and Nutrition Examination Survey, Bakhru et al. found that smoking cessation is associated with resolved changes in C-reactive protein, white blood cells, albumin, and serum fibrinogen in temporal- and dose-dependent manners. Although quitters may not immediately benefit from smoking cessation compared to continued smokers and also suffer from the residual effects of smoking, benefits of long-term smoking cessation on the prevention of MI and stroke from improved levels of HDL-cholesterol and insulin sensitivity may

| Table 2 | Hazard ratios and 95% confidence intervals (HR, 95% CI) of myocardial infarction and stroke according to smoking behaviour in men in the National Health Insurance Service National Health Screening Cohort |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | Sustained smokers (n = 49,997) | Smoking cessation | Smoking cessation | Non-smokers (n = 52,218) |
|                  |                  | Quitters with BMI gaina | Quitters without BMI changeb | Quitters with BMI lossc |
| Myocardial infarction | No. of cases | Person-years | Age-adjusted HR (95% CI) | Multivariable Model 1st HR (95% CI) | Multivariable Model 2nd HR (95% CI) | No. of cases | Person-years | Age-adjusted HR (95% CI) | Multivariable Model 1st HR (95% CI) | Multivariable Model 2nd HR (95% CI) |
|                  | 533             | 387,145         | 1.00 (referent) | 0.38 (0.18–0.80)** | 0.64 (0.44–0.94)* | 27               | 28,996         | 0.62 (0.41–1.08) | 0.43 (0.38–0.50)** |
|                  |                 |                 |                 | 0.34 (0.16–0.71)** | 0.55 (0.37–0.83)** |                 |                 |                 | 0.37 (0.32–0.43)** |
|                  |                 |                 |                 | 0.33 (0.16–0.70)** | 0.55 (0.37–0.83)** |                 |                 |                 | 0.37 (0.32–0.43)** |
| Total stroke     | No. of cases | 1880             | 383,099         | 1.00 (referent) | 0.79 (0.60–1.05) | 0.76 (0.63–0.93)** | 111           | 12,607         | 0.62 (0.56–1.11) | 0.67 (0.63–0.72)** |
|                  |                 |                 |                 | 0.75 (0.57–1.00)* | 0.62 (0.46–0.92)** |                 |                 |                 | 0.68 (0.64–0.73)** |
|                  |                 |                 |                 | 0.75 (0.57–1.00)* | 0.62 (0.46–0.92)** |                 |                 |                 | 0.68 (0.64–0.73)** |
| Ischemic stroke  | No. of cases | 1178             | 12,607         | 1.00 (referent) | 0.90 (0.61–1.33) | 0.79 (0.57–1.27) | 27              | 7              | 0.62 (0.41–1.08) | 0.43 (0.38–0.50)** |
|                  |                 |                 |                 | 0.84 (0.56–1.25) | 0.62 (0.57–1.27) |                 |                 |                 | 0.68 (0.64–0.73)** |
|                  |                 |                 |                 | 0.85 (0.57–1.27) | 0.62 (0.57–1.27) |                 |                 |                 | 0.68 (0.64–0.73)** |
| Haemorrhagic stroke | No. of cases | 347              | 13              | 1.00 (referent) | 0.59 (0.33–0.95) | 0.32 (0.16–0.70)** | 13              | 7              | 0.32 (0.16–0.70)** | 0.67 (0.63–0.72)** |
|                  |                 |                 |                 | 0.62 (0.34–1.12) | 0.32 (0.16–0.70)** |                 |                 |                 | 0.68 (0.64–0.73)** |
|                  |                 |                 |                 | 0.62 (0.34–1.12) | 0.32 (0.16–0.70)** |                 |                 |                 | 0.68 (0.64–0.73)** |

**With change in BMI greater than +1.0 kg/m² in the second health checkup (2004–05) compared to the first health checkup (2002–03).

***With change in BMI ranging between +1.0 kg/m² and +1.0 kg/m² in the second health checkup (2004–05) compared to the first health checkup (2002–03).

With BMI loss of more than 1.0 kg/m² in the second health checkup (2004–05) compared to the first health checkup (2002–03).

Adjusted for age, residential area, income status, body mass index, fasting serum glucose, total cholesterol, blood pressure, alcohol consumption, physical activity, and Charlson Comorbidity Index.

Adjusted for age, residential area, income status, body mass index, fasting serum glucose, total cholesterol, blood pressure, alcohol consumption, physical activity, and Charlson Comorbidity Index, family history of myocardial infarction.

Adjusted for age, residential area, income status, body mass index, fasting serum glucose, total cholesterol, blood pressure, alcohol consumption, physical activity, and Charlson Comorbidity Index, family history of stroke.

P < 0.05.

***P < 0.001.
Post-cessation BMI change and risk of myocardial infarction and stroke

Strengths of the present study come from using a large population of the Asian males with reliable health examinations and claims records to assess the impact of post-cessation BMI change on the risk of MI and stroke. Body mass index in the NHIS health checkup was measured by trained health professionals, which could be more accurate records than self-reported survey on weight change. We were also able to account for various risk factors for the study outcomes including the Charlson Comorbidity Index and family history of myocardial infarction (where *P < 0.05, **P < 0.01, ***P < 0.001). Sustained smokers are the reference group for all HRs.

Figure 1 Risk of myocardial infarction by subgroups. All hazard ratio and 95% confidence intervals (HR, 95% CI) presented above are adjusted for age, residential area, income status, body mass index, fasting serum glucose, total cholesterol, blood pressure, alcohol consumption, physical activity, and the Charlson Comorbidity Index, and family history of myocardial infarction (where *P < 0.05, **P < 0.01, ***P < 0.001). Sustained smokers are the reference group for all HRs.

outweigh the minor health disadvantages of stopping smoking such as weight gain.8,24,25

Second, we were only able to include male adults over 40 years old who were eligible for the NHIS health checkup. Further studies are necessary to confirm whether the smoking cessation has protective effects on CHD and CVD outcomes despite weight gain in younger adults or females. Third, we were not able to examine the exact reason for smoking cessation among the quitters. There is a possibility that those who decided to quit smoking had already experienced worsening health conditions due to smoking, which may have affected the study outcomes to a certain degree. However, we found that the results were consistent in the sensitivity analysis that excluded events occurring within 12 months of the follow-up period to account for this possibility. Some information from the self-reported questionnaires of the health examination was not entirely clear. For example, physical activity was ambiguously defined as number of times per week without further information on intensity and duration. Also, no information on the anthropometric measurement on post-cessation weight change was available other than BMI. Waist circumference or body composition (fat mass and lean mass) need to be assessed in further examinations for more detailed analysis. In addition, we were not able to account for additional lifestyle factors such as nutrition status and stress level because they were not included in the data set. Therefore, quality of data on self-reported questionnaire need to be improved in the NHIS-HealS database in the future.
Conclusions

In this prospective cohort study of the middle-aged Korean men, post-cessation BMI change did not alter the protective association of smoking cessation with MI and stroke after fully adjusting for sociodemographic, health status, and family health history. Clinicians should recommend quitting smoking to reduce the disease burden of MI and stroke despite the concern raised about the possible post-cessation weight change among current smokers. Based on our data, we conclude that the post-cessation weight change is not a serious
health concern for MI and stroke events in the middle aged Korean men (Figure 3). Additional studies in the multi-ethnic cohorts are warranted to test the generalizability of these finding in other ethnic groups.

Supplementary material

Supplementary material is available at European Heart Journal online.

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