CLINICAL RESEARCH STUDY

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# Weight Change in Patients Attempting to Quit Smoking Post-myocardial Infarction

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## ABSTRACT

**BACKGROUND:** Current guidelines recommend smoking cessation and weight management for secondary prevention in patients post-myocardial infarction. However, little is known about the effects of smoking cessation on weight change post-myocardial infarction.

**METHODS:** We examined patterns of weight change and its effects on blood pressure and glycemic control using data from a randomized trial investigating the effect of bupropion on smoking cessation in patients post-myocardial infarction. Weight change was compared among 3 groups of patients: those who were completely abstinent (n = 92), those who smoked intermittently (n = 49), and those who smoked persistently (n = 38) during the 12-month follow-up. Analyses were restricted to patients who attended all follow-up visits.

**RESULTS:** The median weight at baseline was 77.1 kg (interquartile range [IQR], 66.0, 87.5), and 64.3% of patients were overweight/obese (body mass index $\geq$25.0 kg/m$^2$). The median weight gain at 12 months was 4.0 kg (IQR, 0-7.0), with more than one third gaining >5 kg. The proportion of patients who were overweight/obese increased by approximately 10%, and 23.2% of patients moved up a body mass index category. Abstainers gained a median of 4.8 kg (IQR, 1.0, 8.6), intermittent smokers gained a median of 2.0 kg (IQR, −2.0, 5.0), and persistent smokers gained a median of 3.0 kg (IQR, −0.8, 6.0). Weight gain was associated with an increase in blood pressure and requirements for hypoglycemic medications at 12 months.

**CONCLUSIONS:** The majority of patients attempting to quit smoking gain weight 12 months post-myocardial infarction, with abstainers gaining more weight than those who return to smoking. Weight gain was associated with an increased prevalence of hypertension and diabetes.

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**KEYWORDS:** Myocardial infarction; Randomized controlled trial; Smoking cessation; Weight change

Current treatment guidelines recommend strategies to facilitate smoking cessation and weight loss among overweight smokers who have had a myocardial infarction.[1] Despite established benefits of smoking cessation and weight loss post-myocardial infarction,[2-5] minimal attention has been afforded to the importance of weight gain in

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patients who have had a myocardial infarction and are attempting to quit smoking. Post-cessation weight gain in this patient population presents physicians with competing interests with respect to the risks and benefits of smoking cessation. Although the benefits of smoking cessation post-myocardial infarction are well established,[3,5] substantial weight gain may offset the cardiovascular benefits of smoking cessation.[6-8] Consequently, an examination of the impact of post-cessation weight change in patients post-myocardial infarction and the effect on cardiovascular risk factors is needed to help guide the implementation of optimal secondary prevention strategies post-myocardial infarction. The specific objectives are therefore to compare trends in weight change in patients who return to smoking versus those who remain abstinent post-myocardial infarction and examine the effects of weight change on blood pressure and need for anti-diabetic medications.

**CLINICAL SIGNIFICANCE**

- Among patients attempting to quit smoking post-myocardial infarction, the median weight gain at 12 months was 4.0 kg (interquartile range [IQR], 0, 7.0), with more than one third gaining more than 5 kg.
- Abstainers gained a median of 4.8 kg (IQR, 1.0, 8.6), intermittent smokers gained a median of 2.0 kg (IQR, −2.0, 5.0), and persistent smokers gained a median of 3.0 kg (IQR, −0.8, 6.0).
- Weight gain was associated with an increase in blood pressure and requirements for hypoglycemic medications at 12 months.

## METHODS

We used data from a randomized, double-blind, placebo-controlled trial investigating the efficacy of bupropion for smoking cessation in hospitalized patients immediately after a myocardial infarction. The full details of the trial have been reported by Eisenberg et al.[9] Briefly, 392 patients were randomized in-hospital to receive bupropion or placebo for 9 weeks post-myocardial infarction. Patients returned for clinic visits at 4 and 9 weeks and 6 and 12 months. Both groups received motivational support for cessation from a research nurse at baseline and all follow-up visits. Patients enrolled in the trial had to have smoked ≥10 cigarettes per day in the past year, to be ≥18 years of age, to have had an enzyme-positive myocardial infarction, and to be motivated to quit smoking.

Analyses for the current study were restricted to patients who attended all follow-up clinic visits (N = 179). Weight and height were measured, and smoking status was assessed by a research nurse at each clinic visit. Body mass index (BMI) was calculated using the standard formula (BMI = weight/[height]$^2$) and categorized as follows: underweight <18.5 kg/m$^2$, normal weight = 18.5-24.9 kg/m$^2$, overweight = 25.0-29.9 kg/m$^2$, and obese ≥30.0 kg/m$^2$. Obesity was further classified as class I obesity = 30.0-34.9 kg/m$^2$, class II obesity (severely obese) = 35.0-39.9 kg/m$^2$, and class III obesity (morbidly obese) ≥40 kg/m$^2$.[10] Self-reported smoking status was validated by expired carbon monoxide. Point prevalence abstinence was defined as zero reported cigarettes smoked in the previous 7 days with an expired carbon monoxide ≤10 ppm. Blood pressure was measured, and data regarding the use of antihypertensive and diabetic medications and the occurrence of clinical events were collected by a research nurse at each clinic visit. Antihypertensive agents were grouped by class and included angiotensin-converting enzyme inhibitor inhibitors, angiotensin II receptor blockers, beta-blockers, and calcium channel blockers. Lipid and hemoglobin A1C levels, and use of diuretics were not collected in the trial and therefore were not available for our current analyses.

Change in weight was defined as the difference in weight from baseline to 12-month follow-up. Weight change was compared among patients who were completely abstinent, smoking intermittently, and smoking persistently during the 12-month follow-up. Patients who reported being abstinent at all follow-up visits were classified as abstainers, and those who reported smoking at all follow-ups were classified as persistent smokers. Patients who reported both abstinence and smoking during the 12-month follow-up were classified as intermittent smokers.

### Data Analysis

Baseline demographic, clinical, and smoking characteristics are presented as means, standard deviations (SDs), medians, interquartile ranges (IQRs), and percentages, as applicable. Groups were compared by calculating a between-group difference in weight change (baseline to 12 months) and corresponding 95% confidence interval (CI). Comparisons in change in weight, number of cigarettes smoked per day, and blood pressure among the 3 groups are reported as mean differences and corresponding 95% CIs. The independent association between baseline characteristics and weight change at 12 months was assessed using multivariable linear regression. Initial selection of candidate variables was based on their estimates and 95% CIs and evidence of confounding in comparing the estimated coefficients between models with and without each variable. Statistical analyses were performed using SAS statistical software (Version 9.2, SAS Institute Inc, Cary, NC) and R (http://cran.r-project.org/).

## RESULTS

### Patients' Characteristics

Patients were predominantly male (84.0%), and the mean age was 53.9 years (SD, 10.0) (Table 1). The mean weight at baseline was 78.3 kg (SD, 17.7), and the mean BMI was 27.3 kg/m$^2$ (SD, 5.0). At baseline, 64.3% of patients were overweight or obese. Among obese patients, 6.2% (n = 11)

**Table 1** Baseline Patient Characteristics by 12-month Smoking Status

| Characteristics | Abstainers (N = 92) | Intermittent Smokers (N = 49) | Persistent Smokers (N = 38) |
|---|---|---|---|
| Demographics and Smoking | | | |
| Age, mean (SD) | 54.3 (9.2) | 54.6 (12.5) | 52.8 (8.3) |
| Male, % | 84.8 | 85.7 | 81.6 |
| Weight, mean (SD) | 78.9 (16.3) | 77.5 (15.5) | 78.6 (21.3) |
| BMI, mean (SD) | 27.4 (5.3) | 27.1 (4.7) | 27.3 (5.1) |
| BMI classification, % (n) | | | |
| Underweight ($<$18.5 kg/m$^2$) | 1.1 (1) | 0 | 0 |
| Normal (18.5-24.9 kg/m$^2$) | 35.9 (33) | 32.7 (16) | 36.8 (14) |
| Overweight (25.0-29.9 kg/m$^2$) | 38.0 (35) | 44.9 (22) | 31.6 (12) |
| Obese ($\geq$30.0 kg/m$^2$) | 25.0 (23) | 22.5 (11) | 31.6 (12) |
| No. years smoked, mean (SD) | 32.0 (11.0) | 35.1 (14.1) | 34.0 (11.0) |
| No. cigarettes/d (past year), mean (SD) | 22.2 (10.6) | 22.3 (10.5) | 25.1 (10.0) |
| Other smokers at home, % | 28.3 | 32.7 | 36.9 |
| Prior quit attempts, % | 71.7 | 71.4 | 68.4 |
| No. of previous serious quit attempts, % | | | |
| 0 | 28.3 | 28.6 | 31.6 |
| 1 | 23.9 | 40.8 | 10.5 |
| 2 | 19.6 | 10.2 | 23.7 |
| $\geq$3 | 28.3 | 20.4 | 34.2 |
| Prior use of abstinence aids, % | 22.8 | 44.9 | 39.5 |
| Nicotine replacement therapy* | 18.5 | 36.7 | 39.5 |
| Bupropion | 5.4 | 10.2 | 18.4 |
| Counseling | 0 | 4.1 | 2.6 |
| Clinical Characteristics | | | |
| Medical history, % | | | |
| Hyperlipidemia | 48.9 | 51.0 | 50.0 |
| Hypertension | 38.0 | 34.7 | 36.8 |
| Diabetes mellitus | 17.4 | 12.2 | 15.8 |
| Prior myocardial infarction | 17.4 | 26.5 | 26.3 |
| Prior percutaneous coronary intervention | 4.4 | 22.5 | 13.2 |
| Prior CABG | 2.2 | 0 | 2.6 |
| STEMI, % | 68.5 | 73.5 | 65.8 |
| Medications, % | | | |
| ACEI | 67.4 | 73.5 | 68.4 |
| Anti-lipid agent | 84.6 | 95.9 | 68.4 |
| ARBs | 6.6 | 4.1 | 0 |
| Beta-blockers | 82.4 | 79.6 | 84.2 |
| Insulin | 2.2 | 4.1 | 10.5 |
| Oral hypoglycemic agent | 13.2 | 12.2 | 7.9 |

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; CABG = coronary artery bypass graft surgery; SD = standard deviation; STEMI = ST-segment elevation myocardial infarction.

*Includes nicotine patch, gum, and inhaler.

were severely obese (class II) and 2.8% (n = 5) were morbidly obese (class III). Less than one fifth of patients (15.6%) had a history of diabetes mellitus, and approximately one third of patients (36.9%) had hypertension. Patients had smoked a mean of 33.7 years (SD, 12.0) and approximately 1 pack of cigarettes (ie, 25 cigarettes) per day before their myocardial infarction.

## Smoking Patterns

At 12 months, intermittent and persistent smokers reported smoking a median of 5.0 (IQR, 0.7, 6.0) and 8.0 (IQR, 3.4, 10.3) cigarettes per day, respectively. Although 45% of patients reported smoking at 12 months, intermittently or persistently, all 3 groups reported a substantial decrease in their median number of cigarettes smoked per day from baseline (abstainers: −20.0; IQR, −26.5, −15.0; intermittent smokers: −13.5, IQR, −22.9, −6.0; and persistent smokers: −12.9 IQR, −21.0, −5.0) (Online Figure 1). No clinically important differences in the number of reported cigarettes smoked per day at 12 months were noted between the intermittent and persistent smokers; however, a clinically important difference was noted between abstainers and persistent smokers (mean difference, −6.4; 95% CI, −11.0, −1.7). At the 6- and 12-month follow-ups, the median number of reported

cigarettes smoked per day increased to 1.4 (IQR, 0, 10) and 5.0 (IQR, 0.7, 11.4), respectively.

## Twelve-month Weight Change

Median weight change between baseline and 12 months in all patients was 4.0 kg (IQR, 0, 7.0), with more than one third gaining more than 5 kg and 9.0% of patients losing more than 5 kg (Figure 1). At 12 months, 50.3% of patients gained more than 5% of their baseline weight, and 22.0% gained more than 10% of their baseline weight. At the end of follow-up, 11.9% of patients lost more than 5% of their baseline weight, and 88.1% of patients did not.

Weight change varied across groups, with abstainers gaining a median of 4.8 kg (IQR, 1.0, 8.6), intermittent smokers gaining a median of 2.0 kg (IQR, −2.0, 5.0), and persistent smokers gaining a median of 3.0 kg (IQR, −0.8, 6.0). The proportion of patients who lost more than 5 kg was similar across the 3 groups (abstainers: 3.4%, intermittent smokers: 2.2%, and persistent smokers: 3.4%). A larger proportion of abstainers gained more than 5 kg versus intermittent and persistent smokers (45% vs 18% and 24%, respectively). At 12 months, patients who remained abstinent were more likely to gain weight than those who smoked persistently (mean difference, 3.4 kg; 95% CI, 1.4, 5.4). A similar trend was observed in abstainers compared with intermittent smokers; however, the 95% CI included zero (mean difference, 1.3 kg; 95% CI, −0.7, 3.3). Intermittent smokers also were more likely to have gained weight than those who smoked persistently (mean difference, 2.1 kg; 95% CI, 0.0, 4.1).

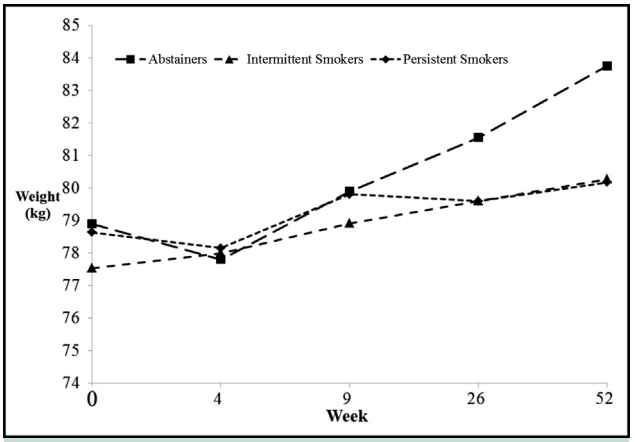


**Figure 1** Change in weight post-myocardial infarction. Analyses were restricted to patients who returned for follow-up (N = 179). Data available at 4 weeks: abstainers (n = 90), intermittent smokers (n = 48), and persistent smokers (n = 38); at 9 weeks: abstainers (n = 91), intermittent smokers (n = 48), and persistent smokers (n = 38); at 6 months: abstainers (n = 92), intermittent smokers (n = 48), and persistent smokers (n = 38); and at 12 months: abstainers (n = 90), intermittent smokers (n = 49), and persistent smokers (n = 38).

Weight fluctuated slightly during the 9-week treatment period (bupropion or placebo) in all 3 groups (Figure 1). After the treatment period, there was a substantial increase in weight gain among abstainers and intermittent smokers. However, the increase was more pronounced among abstainers and did not appear to plateau at 12 months.

## Body Mass Index

At the end of follow-up, 23.2% of patients increased a BMI category (13.0% from normal weight to overweight, 0.6% from normal weight to obese, and 9.6% from overweight to obese) (Table 2). Among patients who were overweight at baseline, 25% (n = 17) became obese at 12 months, whereas 89.1% (n = 41) of those who were obese at baseline remained obese over the 12-month follow-up. Only 7.9% of patients moved down a BMI category over the 12-month period (1.1% from normal weight to underweight, 4.0% from overweight to normal weight, and 2.8% from obese to overweight). At 12 months, abstainers were more likely to be classified as overweight and obese versus persistent and intermittent smokers (overweight: 50.7% vs 17.4% and 31.9%; obese: 50.0% vs 26.1% and 23.9%, respectively).

## Predictors of Weight Change at 12 Months

Multivariable regression analyses were performed to identify baseline predictors of weight change at 12 months. Abstinence was associated with weight gain at 12 months (difference, 3.3 kg; 95% CI, 0.77, 5.81) (Figure 2). No other important baseline predictors were identified, including age, sex, BMI, treatment (bupropion), and number of years smoked.

## Changes in Blood Pressure

In patients who gained weight at 12 months (n = 132), systolic blood pressure increased a median of 10.0 mm Hg (IQR, −2.5, 20.0), whereas diastolic blood pressure increased a median of 5.0 mm Hg (IQR, −2.5, 14.0). Among these patients, 89% were taking at least 1 hypertensive medication at the 12-month follow-up. In patients who moved up a BMI category (n = 41) at 12 months, there was a median increase in systolic blood pressure of 9.0 mm Hg (IQR, −3.0, 18.0) and a median increase in diastolic blood pressure of 6.0 mm Hg (IQR, −1.0, 10.0).

At 12 months, angiotensin-converting enzyme inhibitor use decreased (71.9% vs 56.4% at baseline and 12 months, respectively), whereas angiotensin II receptor blocker use increased (4.5% vs 12.8%, respectively) from baseline. Use of beta-blockers and calcium channel blockers remained constant across the 12-month follow-up. At 12 months, 19.7% of patients were started on or increased the number of prescribed antihypertensive agents, whereas 26.4% decreased or discontinued use of these agents.

**Table 2** Change in Body Mass Index at 12 Months

| | BMI at 12 Months, % (n) | | | | |
|---|---|---|---|---|---|
| | Underweight ($<18.5$ kg/m$^2$) | Normal Weight (18.5-24.9 kg/m$^2$) | Overweight (25.0-29.9 kg/m$^2$) | Obese ($\geq 30$ kg/m$^2$) | Total, % (n) |
| BMI at baseline, % (n) | | | | | |
| Underweight ($<18.5$ kg/m$^2$) | 100 (1) | 0† | 0† | 0† | 0.6 (1) |
| Normal weight (18.5-24.9 kg/m$^2$) | 3.2 (2)* | 58.1 (36) | 37.1 (23)† | 1.6 (1)† | 35.0 (62) |
| Overweight (25.0-29.9 kg/m$^2$) | 0* | 10.3 (7)* | 64.7 (44) | 25.0 (17)† | 38.4 (68) |
| Obese ($\geq 30$ kg/m$^2$) | 0* | 0* | 10.9 (5)* | 89.1 (41) | 26.0 (46) |
| Total, % (n) | 1.7 (3) | 24.3 (43) | 40.7 (72) | 33.3 (59) | 100 (177) |

BMI = body mass index.
*Proportion of patients who moved down a BMI category at 12 months.
†Proportion of patients who moved up a BMI category at 12 months.

## Use of Antidiabetic Medications

In patients who lost more than 5% of their baseline weight (n = 21), 1 patient reduced the use of antidiabetic medications (from 2 to 1) at 12 months (Table 3). The majority of patients (85.7%) reported no use of antidiabetic medications at baseline, which remained unchanged at the end of follow-up. In patients who gained >5% of their baseline weight (n = 89), 5.6% began using an antidiabetic medication, 3.4% reduced their use of antidiabetic medications (from 2 to 1), and 7.9% were no longer taking an antidiabetic medication at the 12-month follow-up. Among patients whose weight changed <5% from baseline (n = 66), 1.5% increased their use of antidiabetic medications (from 1 to 2), 4.5% were no longer taking an antidiabetic medication, and 3.0% reduced their use of antidiabetic medications (from 2 to 1) at the end of follow-up.

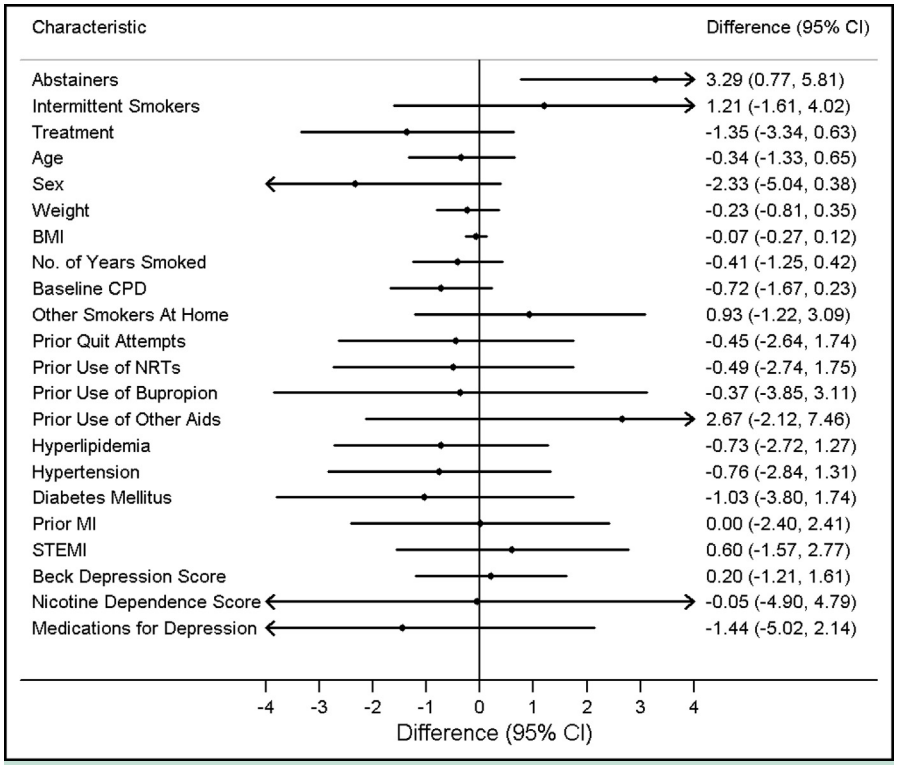


**Figure 2** Univariate predictors of weight change at 12 months. Age, weight, number of years smoked, baseline cigarettes per day, Beck depression score, and nicotine dependence score have been scaled to estimate weight change per 10-unit increase. Persistent smoking was the reference group for abstinence and intermittent smoking. BMI = body mass index; CPD = cigarettes per day; MI = myocardial infarction; NRTs = nicotine replacement therapies; STEMI = ST-segment elevation myocardial infarction.

**Table 3** Change in Diabetic Medications at 12 Months

| Use of Diabetic Medication at Baseline, % (n) | Use of Diabetic Medication at 12 Months, % (n) | | | | |
|---|---|---|---|---|---|
| | None | Hypoglycemic Agent | Insulin | Hypoglycemic Agent and Insulin | Total |
| All Patients (n = 182) | | | | | |
| None | 93.5 (144) | 5.2 (8)† | 0.6 (1)† | 0.6 (1)† | 85.2 (154) |
| Hypoglycemic agent | 5.3 (1)* | 57.9 (11) | 5.3 (1)† | 31.6 (6)† | 10.4 (19) |
| Insulin | 28.6 (2)* | 14.3 (1)* | 14.3 (1) | 42.9 (3)† | 3.8 (7) |
| Hypoglycemic agent and insulin | 0* | 0* | 50.0 (1)* | 50.0 (1) | 1.3 (2) |
| Total, % (n) | 80.8 (147) | 11.0 (20) | 2.2 (4) | 6.0 (11) | 100 (182) |
| Patients Who Lost >5% of Baseline Weight (n = 21) | | | | | |
| None | 100 (18) | 0† | 0† | 0† | 81.8 (18) |
| Hypoglycemic agent | 0* | 50.0 (1) | 50.0 (1)† | 0† | 9.1 (2) |
| Insulin | 0* | 0* | 0 | 0† | 0 |
| Hypoglycemic agent and insulin | 0* | 100 (1)* | 0* | 0 | 4.8 (1) |
| Total | 81.8 (18) | 9.1 (2) | 4.8 (1) | 0 | 100 (21) |
| Patients Who Gained >5% of Baseline Weight (n = 89) | | | | | |
| None | 93.2 (68) | 5.5 (4)† | 1.4 (1)† | 0† | 82.0 (73) |
| Hypoglycemic agent | 50.0 (5)* | 50.0 (5) | 0† | 0† | 11.2 (10) |
| Insulin | 50.0 (1)* | 50.0 (1)* | 0 | 0† | 2.2 (2) |
| Hypoglycemic agent and insulin | 25.0 (1)* | 25.0 (1)* | 50.0 (2)* | 0 | 4.5 (4) |
| Total | 87.6 (75) | 12.4 (11) | 3.4 (3) | 0 | 100 (89) |
| Patients Whose Weight Changed <5% of Baseline Weight (n = 66) | | | | | |
| None | 100 (54) | 0† | 0† | 0† | 81.8 (54) |
| Hypoglycemic agent | 42.9 (3)* | 57.1 (4) | 0† | 0† | 10.6 (7) |
| Insulin | 0* | 0* | 50.0 (1) | 50.0 (1)† | 3.0 (2) |
| Hypoglycemic agent and insulin | 0* | 33.3 (1)* | 33.3 (1)* | 33.3 (1) | 4.5 (3) |
| Total | 86.4 (57) | 7.6 (5) | 3.0 (2) | 3.0 (2) | 100 (66) |

*Proportion of patients who decreased their use of diabetic medications at 12 months.
†Proportion of patients who increased their use of diabetic medications at 12 months.

## Clinical Events

Over the 12-month follow-up, 16.8% of patients had an event. Of these patients, 2.8% (n = 5) had a recurrent myocardial infarction, 1.7% (n = 3) were revascularized (percutaneous coronary intervention or coronary artery bypass graft surgery), 5.6% had unstable angina, and 0.6% (n = 1) had a psychiatric event. By definition, none of the patients in this substudy died over the 12-month period because only patients who attended all follow-up visits were included. No important differences in serious adverse events were noted between smoking or weight change groups.

# DISCUSSION

Our study was designed to examine the effect of smoking cessation on 12-month weight change in patients post-myocardial infarction. We found that one half of patients return to smoking at 12 months and that patients who reported complete abstinence were more likely to gain weight than patients who reported intermittent or persistent smoking. We also found that a larger proportion of abstainers gained >5 kg, compared with intermittent and persistent smokers, over the 12-month period. Moreover, one quarter of patients increased in a BMI category over the 12-month period. Data suggest that weight gain may be associated with an increase in blood pressure and need for antidiabetic medications at 12 months. These results suggest that weight gain is a concern for patients attempting to quit smoking post-myocardial infarction. An aggressive weight management approach is needed to ensure that the cardiovascular benefits achieved by smoking cessation are not offset by substantial weight gain in this population.

## Previous Studies

To our knowledge, no previous studies have directly investigated the effect of smoking cessation on weight change in smokers attempting to quit post-myocardial infarction. Three studies examined patterns in weight change post-myocardial infarction, and a recent study examined the effect of weight gain after smoking cessation on the occurrence of cardiovascular events. The Prospective Registry Evaluating Myocardial Infarction: Event and Recovery study examined patterns of weight change and

factors associated with weight change in a population of patients post-myocardial infarction.[11] The authors found that weight gain varied by level of obesity (average weight gain: 0.3 kg, 0.5 kg, and 4.6 kg, for overweight, obese, and morbidly obese individuals, respectively) and that smoking abstinence was associated with greater weight gain (odds ratio, 2.67; 95% CI, 1.08, 4.27) at 12 months post-myocardial infarction. The Enhancing Recovery In Coronary Heart Disease trial also investigated weight change post-myocardial infarction.[4] The authors found that 18.0% of had gained >5% of their original weight at approximately 2 years post-myocardial infarction. Finally, a study by Fan et al[12] investigated the impact of weight gain after smoking cessation on clinical outcomes in 845 patients in Shanghai who underwent percutaneous coronary intervention after a myocardial infarction. The authors found that quitters gained an average of 1.5 kg (SD, 0.1) and that 50.6% of quitters gained >1.5 kg. Although patients in all 3 studies gained less weight than in our study, this could be explained, in part, by the inclusion of patients with different smoking status (ie, nonsmokers, past smokers, current smokers) and ethnic differences. Finally, the study by Clair et al[13] examined the effect of weight gain after smoking cessation on the occurrence of cardiovascular events in patients free of cardiovascular disease at cohort entry. The authors found that the incidence of cardiovascular events was lower in recent quitters (in ≤4 years) than in smokers (hazard ratio, 0.47; 95% CI, 0.34, 0.63) and that this relationship was minimally changed after adjusting for weight change. The authors concluded that the positive benefits of smoking cessation on the occurrence of cardiovascular events are not attenuated by the competing risk of weight gain after cessation.

## Physiologic Mechanism of Weight Gain

Two physiologic mechanisms have been proposed to explain the weight gain associated with smoking cessation. These include a decrease in basal metabolic rate and an associated decrease in energy expenditure[14,15] and an increase in appetite.[15-17] Energy metabolism and energy intake have been found to be partially regulated by the autonomic nervous system and the hypothalamus. Three key hormones—insulin, leptin, and gherlin—are implicated in energy homeostasis. Insulin acts to inhibit food intake by decreasing the expression of the neurotransmitter neuropeptide Y.[18] Aside from its effect on the nervous system, neuropeptide Y also is involved in the storage of glucose and fat. Leptin exerts its action on the hypothalamus in response to adipose storage.[19] When sufficient stores of adipose are detected, leptin levels increase and travel to the hypothalamus, where a cascade of events is initiated to send satiety signals to the brain. Gherlin, a hormone excreted by the stomach and duodenum, is involved in energy metabolism[20] and fat catabolism.[21] Gherlin has been found to be associated with weight gain by its ability to increase energy intake and decrease energy expenditure. Nicotine also has been found to play a role in food regulation at the site of the hypothalamus, and smoking has been linked to increases in metabolic rate.[22] Therefore, the weight gain seen in our study could be explained by the synergistic effects of smoking cessation and these complex signaling systems.

## Impact of Bupropion on Weight Gain

The effect of bupropion on weight change has been examined. A recent meta-analysis by Aubin et al[23] found that patients using bupropion therapy for smoking cessation gained an average of 2.7 kg (95% CI, 0.84, 4.59) at 6 months and 4.1 kg (95% CI, 3.4, 4.7) at 12 months. The results of this meta-analysis are similar to the findings of our current study, despite the inclusion of only 2 studies involving patients with cardiovascular disease[24,25] and only 1 study including administration of cessation therapy in-hospital.[24] This study also found that 34% of patients gained 5 to 10 kg at 12 months, which is similar to what was observed in our study. These trends were consistent across all follow-up periods, even while patients were on therapy. In contrast, a meta-analysis by Farley et al[26] found that bupropion helped to manage post-cessation weight gain during the treatment period (mean difference, −1.12 kg; 95% CI, −1.47, 0.77), but this effect did not persist at 6 or 12 months (−0.58 kg, 95% CI, −2.16, 1.00 and −0.38 kg, 95% CI, −2.00, 1.24, respectively). These results are similar to our study in which the trend across all 3 groups was a decrease in weight over the treatment period followed by a steady weight gain in abstainers and less pronounced increase among intermittent and persistent smokers. Although the period after a myocardial infarction is a unique opportunity for behavior modification, the results of previous studies and the current study support the need for long-term weight management in patients attempting to quit smoking post-myocardial infarction.

## Competing Risk

Although smoking cessation and weight management are important for secondary prevention in patients post-myocardial infarction,[1] post-cessation weight gain may decrease the cardiovascular benefits associated with smoking cessation in this patient population. Obesity has been found to be associated with the development or aggravation of type 2 diabetes mellitus.[27] This finding is supported in our study in the subset of patients who had clinically important increases in weight gain and were newly diagnosed with diabetes mellitus at 12 months or were switched from an oral hypoglycemic agent to insulin at 12 months. Previous studies also have found that weight gain may negatively affect blood pressure.[6,7] A similar trend was observed in our study, with clinically important increases noted for both systolic and diastolic blood pressures in patients who gained weight over the 12-month period. These results highlight the need for interventions targeted at weight gain among smokers attempting to quit post-myocardial infarction to minimize the negative effects of post-cessation weight gain on

cardiovascular risk factors. Although the study by Clair et al[13] found that weight gain did not attenuate the benefits of smoking cessation, the cohort did not include patients with a history of cardiovascular disease. Therefore, these findings may not apply to our current study population of patients post-myocardial infarction.

## Study Limitations

First, lipid and hemoglobin A1c levels were not collected in the original trial and were therefore not included in our current analyses. However, with close monitoring of patients after their myocardial infarction, abnormal fluctuations in lipid and hemoglobin A1c levels should be reflected in changes to prescribed medical therapy. Second, because data regarding doses of prescribed antihypertensive medications and use of diuretics were not available, we were not able to draw strong inferences regarding the impact of weight change on blood pressure. Finally, our study included only patients who returned for all follow-ups over the 12-month period. Patients who return for follow-up in smoking cessation trials are more likely to have quit smoking or to have substantially reduced their cigarette consumption.[28] Although the proportion of patients lost to follow-up in the original trial was lower than in previous smoking cessation trials,[24,25] the potential presence of selection bias cannot be ruled out.

## CONCLUSIONS

Our study was designed to examine the effect of smoking cessation on weight at 12 months post-myocardial infarction. We found that the majority of patients attempting to quit smoking post-myocardial infarction gain weight at 12 months, with abstainers gaining more weight than those who return to smoking. We also found that one quarter of patients moved up a BMI category and that weight gain may be associated with an increase in blood pressure and use of antidiabetic medications. An aggressive weight management approach is needed to ensure that the cardiovascular benefits achieved by smoking cessation are not offset by substantial weight gain in this population.

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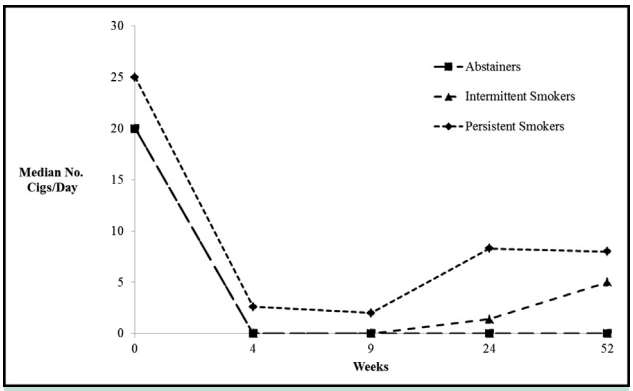


**Online Figure 1** Change in median number of cigarettes per day smoked by smoking status. Analyses were restricted to patients who returned for follow-up (N = 179). Data available at 4 weeks: abstainers (n = 92), intermittent smokers (n = 49), and persistent smokers (n = 38); at 9 weeks: abstainers (n = 92), intermittent smokers (n = 49), and persistent smokers (n = 38); at 6 months: abstainers (n = 92), intermittent smokers (n = 48), and persistent smokers (n = 38); and at 12 months: abstainers (n = 92), intermittent smokers (n = 49), and persistent smokers (n = 38).