

Smoking Status and Risk for Recurrent Coronary Events after Myocardial Infarction

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Background: Questions remain about the importance of smoking and smoking cessation after incident myocardial infarction.

Objective: To assess the association between smoking status and risk for recurrent coronary events.

Design: Retrospective, population-based, inception cohort study.

Setting: Health maintenance organization from 1986 to 1996.

Patients: 2619 persons who survived to hospital discharge after a first myocardial infarction.

Measurements: Relative risk (RR), assessed by using Cox proportional hazards regression analysis, for recurrent coronary events in nonsmokers (persons with no history of smoking), former smokers (persons who had stopped smoking before infarction), quitters (persons who stopped smoking after infarction), and active smokers (persons who continued smoking after infarction).

Results: At the time of incident infarction, 33.6% of patients were nonsmokers, 35.5% were former smokers, and 30.9% were

active smokers. Of the 808 persons who were active smokers at the time of incident infarction, 449 quit smoking during hospitalization or after discharge. With nonsmokers as the reference group, the multivariable RR for recurrent coronary events ($n = 433$) was 1.17 (95% CI, 0.93 to 1.43) for former smokers and 1.51 (CI, 1.10 to 2.07) for active smokers. Among quitters, the RR decreased as duration of cessation increased: With nonsmokers as the reference group, the RR for quitters was 1.62 (CI, 1.02 to 2.61) if the duration of cessation was 0 to less than 6 months, 1.60 (CI, 0.97 to 2.60) if the duration was 6 to less than 18 months, 1.48 (CI, 0.76 to 2.51) if the duration was 18 to less than 36 months, and 1.02 (CI, 0.54 to 1.86) if the duration was 36 months or more ($P = 0.01$ for trend).

Conclusion: After incident myocardial infarction, smoking was associated with an elevated risk for recurrent coronary events. In persons who quit smoking after infarction, the risk declined to equal that of nonsmokers by 3 years after cessation.

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Smoking is a risk factor for coronary artery disease (1). Among persons without coronary disease who quit smoking, the risk for incident coronary disease decreases and approaches that of nonsmokers within 2 to 3 years after cessation (2, 3). Some studies (4–17) show that quitting smoking after myocardial infarction also seems to reduce the risk for adverse outcomes, including death. However, these studies of persons with established disease generally focused on men 65 years of age or younger, had limited information about possible confounding factors, did not evaluate the time course of the potential benefits of smoking cessation, and did not compare results to those in nonsmokers. In contrast to these studies showing a benefit of smoking cessation after myocardial infarction, some evidence suggests that after infarction, smokers may not have an elevated risk for recurrent events compared with never-smokers, a finding termed the “smoker’s paradox” (18–24). We examined the association between smoking status and risk for recurrent coronary events and explored the time course of potential benefits of cessation in a large population-based inception cohort of persons who survived to hospital discharge after an incident myocardial infarction.

METHODS

Setting and Participants

The study setting was Group Health Cooperative (GHC), a health maintenance organization with more than 500 000 enrollees, based in western Washington State. The organization’s model of health care delivery is structured so

that most routine care for enrollees, including care after myocardial infarction, is provided by personal primary care physicians. Group Health Cooperative employs more than 300 primary care physicians and contracts with more than 500 other physicians.

Eligible patients included all GHC enrollees who survived to hospital discharge after a first myocardial infarction during the period from July 1986 (women) or July 1989 (men) through December 1996. Patients with incident myocardial infarction were identified by International Classification of Diseases, 9th revision, codes from the computerized discharge abstracts of the two GHC hospitals, bills for out-of-plan services provided by non-GHC physicians and health care facilities, and Washington State death records. A trained records abstractor, assisted by study physicians, validated the incident infarctions by reviewing available inpatient medical records. Previous work (25) has confirmed the accuracy and completeness of the methods used for ascertainment of myocardial infarction.

Persons were excluded if they were younger than 30 or older than 79 years of age at the time of the incident infarction, had previously had a myocardial infarction, had the incident infarction as a result of surgery or another procedure, died before hospital discharge, or had no information available in the medical record after the incident infarction. A total of 50 patients (1.8% of the total otherwise eligible patients) were discharged alive from the hospital but had no information in the chart after the incident infarction. Persons were also excluded if they had made

fewer than four visits to GHC or had been enrolled in GHC for less than 1 year before the incident infarction. Among persons otherwise eligible for inclusion, 9.3% were excluded because of inadequate duration of enrollment in GHC. Of the 2677 patients who were initially eligible, 58 were excluded because of indeterminate smoking status, leaving 2619 persons (97.8% of the original cohort) for analysis.

The Human Subjects Review Committees of GHC approved the study.

Smoking Status

We identified smoking status on the basis of ambulatory care and inpatient records. The GHC ambulatory medical record is an important resource because it serves as the primary method of communication among GHC physicians. It includes not only notes from ambulatory care visits but also discharge summaries of hospitalizations, results of laboratory and diagnostic tests, consultant reports, responses to annual GHC health questionnaires, and updated problem lists. Data collection included a review of the entire GHC ambulatory medical record for the period before the first infarction, the period of hospitalization associated with the incident infarction, and the period after the infarction up to a predetermined date in 1996, 1997, or 1998. Patients were classified as nonsmokers (persons with no history of smoking in the medical record), former smokers (persons who had smoked but had quit before the incident myocardial infarction), quitters (persons who were smoking at the time of the incident myocardial infarction and quit after the infarction), and active smokers (persons who were smoking at the time of the incident myocardial infarction and continued to smoke during follow-up). Only those persons who quit smoking after their incident infarction and maintained cessation for the duration of follow-up were classified as quitters. Information about the quit date, number of cigarettes smoked per day, and duration of smoking over time was also recorded. Patients were closely monitored after the incident infarction; 97.6% had a clinic visit within 3 months after hospital discharge, and the median number of visits (physician, nurse, or emergency department visits or hospitalizations) during the first year after the incident infarction was 9 (25th, 75th percentiles: 6, 14).

Clinical and Medication Covariates

Trained research assistants reviewed the ambulatory care and inpatient medical records to collect information about potential risk factors for coronary disease, such as use of health services; marital status; alcohol consumption; body weight; height; and medical conditions such as hypertension, diabetes, and congestive heart failure. Congestive heart failure was determined to have occurred on the basis of the notes of the primary care physician and consultants and the results of diagnostic tests. Hypertension was defined as pharmacologically treated hypertension; diabetes was defined as diabetes pharmacologically treated

Background

Smoking cessation decreases the risk for myocardial infarction among people without previous coronary disease, but its effect on risk reduction after a first myocardial infarction has not been well studied.

Contribution

The researchers retrospectively observed relative risk for recurrent coronary events in patients discharged from the hospital after an incident myocardial infarction. Compared to nonsmokers, active smokers were 1.5 times more likely to have reinfarction. Among persons who had stopped smoking, relative risk decreased gradually to the nonsmokers' level over 36 months.

Implications

Physicians should emphasize the proven benefits of smoking cessation to encourage patients to quit after a first myocardial infarction.

—The Editors

with oral hypoglycemic agents or insulin. In addition, laboratory values for random serum glucose, total cholesterol, and high-density lipoprotein cholesterol were recorded. Medication use was assessed at the time of hospital discharge after the incident infarction by using information from the discharge summary supplemented with information from the first outpatient visit and the GHC computerized pharmacy database. The status of the clinical and medication covariates was determined at the time of hospital discharge. Laboratory information was taken from the period before the incident infarction.

End Point

The outcome of interest was recurrent coronary events, defined as nonfatal myocardial infarction or coronary death. Information on these end points was obtained from the GHC ambulatory medical record, available inpatient records, and the results of matches between Washington State death records and GHC enrollment records. In patients with established coronary disease, if the underlying cause of death was heart disease, heart failure, or arrhythmia, the death was classified as a coronary death.

Statistical Analysis

Follow-up time began at the date of discharge from the hospital after the incident infarction, and it extended to the date of the first recurrent infarction, coronary death, or censoring. Persons were censored at the date of death from causes other than heart disease, the date of unenrollment from GHC, or the end of the assigned follow-up period. Cox proportional hazards regression analysis with a time-dependent smoking status variable was used to model the association of smoking status and recurrent coronary events after adjustment for potential confounding factors (26). A patient who quit smoking during hospitalization for the

Table 1. Characteristics of Study Patients at Time of Hospital Discharge, by Smoking Status

Characteristic	Nonsmokers (n = 880)	Former Smokers* (n = 931)	Persons Who Quit Smoking while Hospital- ized for Myocar- dial Infarction (n = 344)	Persons Who Quit Smoking after Hospital Discharge (n = 105)	Persons Who Continued To Smoke after Hos- pital Discharge (n = 359)
Median age (25th, 75th percentile), y	68.2 (58.7, 74.1)	67.6 (59.3, 73.3)	60.6 (52.4, 67.8)	60.8 (52.8, 69.0)	59.0 (49.1, 68.2)
Women, n (%)	412 (46.8)	251 (27.0)	148 (43.0)	48 (45.7)	129 (35.9)
Patients with congestive heart failure, n (%)	187 (21.3)	245 (26.3)	80 (23.2)	23 (21.9)	63 (17.5)
Patients with diabetes, n (%)	199 (22.6)	184 (19.8)	43 (12.5)	16 (15.2)	37 (10.3)
Patients with hypertension, n (%)	417 (47.4)	433 (46.5)	130 (37.8)	44 (41.9)	130 (36.2)
Patients with no alcohol consumption, n (%)	561 (63.8)	383 (41.1)	163 (47.4)	40 (38.1)	136 (37.9)
Median body mass index (25th, 75th percentile), kg/m ²	26.8 (24.4, 30.6)	27.3 (24.5, 30.7)	26.6 (23.8, 30.1)	26.2 (24.1, 29.2)	26.4 (23.6, 30.1)
Median ratio of total cholesterol to high-density lipoprotein cholesterol (25th, 75th percentile)	5.5 (4.6, 6.5)	5.6 (4.6, 6.7)	5.8 (4.7, 7.0)	5.5 (4.8, 6.5)	5.8 (4.8, 7.1)
Cigarettes/d (25th, 75th percentile), n†	Not available	20 (20, 30)	20 (13, 30)	20 (15, 30)	20 (19, 30)
Duration of smoking (25th, 75th percentile), y‡	–	28 (18, 39)	37 (30, 45)	39 (30, 44)	36 (27, 45)
Patients receiving aspirin, n (%)	807 (91.7)	855 (91.8)	326 (94.8)	99 (94.3)	328 (91.4)
Patients receiving β -blockers, n (%)	456 (51.8)	466 (50.1)	167 (48.5)	49 (46.7)	172 (47.9)

* Persons who quit smoking before the incident myocardial infarction.

† Cigarettes/d is the average number of cigarettes smoked per day for persons who quit smoking before the incident myocardial infarction and the number of cigarettes smoked per day at the time of incident myocardial infarction for persons who were actively smoking at the time of incident myocardial infarction. This information was available for 544 persons (58.4%) who quit smoking before incident myocardial infarction, 303 persons (88.1%) who quit during hospitalization for incident myocardial infarction, 96 persons who quit after discharge (91.4%), and 309 persons (86.1%) who remained active smokers after incident myocardial infarction.

‡ Information on duration of smoking was available for 457 persons (49.1%) who quit smoking before incident myocardial infarction, 237 persons (68.9%) who quit during hospitalization for incident myocardial infarction, 73 persons (69.5%) who quit after discharge, and 234 persons (65.2%) who remained active smokers after incident myocardial infarction.

incident myocardial infarction was classified as a quitter. For those who quit smoking after discharge, smoking status was modeled with person-years accrued initially as if the patient were an active smoker and then after cessation as if the patient were a quitter.

To investigate the risk for recurrent coronary events in relation to the duration of smoking cessation, we divided follow-up time into four mutually exclusive categories of duration of cessation (0 to <6 months, 6 to <18 months, 18 to <36 months, and ≥ 36 months). Because the underlying time scale used in the regression analysis was time since hospital discharge after the first myocardial infarction, the Cox model adjusts for time since infarction, enabling an assessment of the relationship of duration of cessation independent of time since infarction. In addition, because most patients who quit smoking did so very soon after the incident infarction, time since hospital discharge and time since cessation of smoking were similar for many quitters. To help discern whether the change seen among quitters in the hazard ratio over time was due to smoking cessation rather than to any other characteristic of smokers that changed over time after discharge, we also evaluated whether the coronary event hazard ratio among active smokers varied with time since infarction.

We calculated the unadjusted rates of recurrent coronary events for each category of smoking status and used Cox proportional hazards regression analysis to compute hazard ratios of recurrent coronary events associated with

smoking status after adjustment for potential confounding factors. Nonsmokers served as the reference group. Variables included in the multivariable Cox models, in addition to smoking status, were age at hospital discharge (in years); sex; body mass index (weight in kg/height in m²); alcohol consumption (none, any alcohol consumption but not physician-diagnosed alcoholism, or physician-diagnosed alcoholism); random serum glucose level; presence of congestive heart failure, hypertension, and diabetes; and use of aspirin. We examined the hazard ratio in subgroups defined by age (<65 years of age compared to ≥ 65 years of age), sex, presence of hypertension, presence of diabetes, body mass index (<30 compared to ≥ 30), thrombolytic therapy for the incident infarction, and smoking intensity at the time of the incident infarction (1 to 20 cigarettes per day compared to ≥ 20 cigarettes per day) using interaction terms in the Cox regression models. Analyses were done by using Stata 7.0 software (Stata Corp., College Station, Texas).

Role of the Funding Source

The funding source had no role in the collection, analysis, or interpretation of the data or in the decision to submit the manuscript for publication.

RESULTS

In the 2619 persons who survived to hospital discharge after a first myocardial infarction, the average age was 63.9 years; 37.7% of these persons were women. At

the time of incident myocardial infarction, 880 patients (33.6%) were nonsmokers, 931 (35.5%) were former smokers, and 808 (30.9%) were active smokers. Of the 808 active smokers, 344 (42.6%) quit smoking during hospitalization for the incident myocardial infarction and 464 (57.4%) were active smokers at the time of hospital discharge. Of the 464 persons who were active smokers at hospital discharge, 105 quit smoking after discharge and before a recurrent event or censoring. Compared to persons who were smokers at the time of the incident myocardial infarction, nonsmokers and former smokers tended to be older, to have a greater body mass index, and to have a higher prevalence of diabetes and hypertension (Table 1). Characteristics were similar across quitter subgroups defined by duration of cessation. In the three groups with a history of smoking, the average number of cigarettes smoked per day was similar, whereas smoking duration was shorter for former smokers than for persons who quit during hospitalization or who continued to smoke.

During the 8813 person-years of follow-up (median follow-up, 3.0 years), 433 recurrent coronary events occurred: 272 nonfatal myocardial infarctions, 94 fatal myocardial infarctions, and 67 other coronary deaths. A total of 229 patients were censored because they were lost to follow-up; they represented 390 years or 4.2% of total person time. The proportion of person time lost to follow-up was similar across smoking status: 4.5% among nonsmokers, 3.7% among former smokers, 5.2% among quitters, and 3.6% among active smokers. With nonsmokers as the reference group (Table 2), the hazard ratio of recurrent coronary events was elevated among those who quit smoking after incident myocardial infarction (adjusted relative risk, 1.43 [95% CI, 1.07 to 1.93]) and those who continued to smoke (adjusted relative risk, 1.51 [CI, 1.10 to 2.07]). The risk for recurrent coronary events was similar in those who quit before the incident myocardial infarction and in nonsmokers. The hazard ratio associated with smoking status and recurrent coronary events did not differ across subgroups defined by sex, age, hypertension, diabetes, body mass index, thrombolytic therapy, or smoking intensity. In sensitivity analyses, further adjustment for family history of coronary heart disease; ratio of total cholesterol to high-density lipoprotein cholesterol; pulse rate; serum creatinine level; thrombolytic therapy for the incident infarction; education; marital status; calendar year;

and use of β -blockers, angiotensin-converting enzyme inhibitors, or lipid-lowering therapy at hospital discharge changed the hazard ratio estimates associated with smoking status only slightly. Adjustment for these covariates not included in the final model typically changed the estimates by less than 5% and never by more than 10%. Confidence intervals also changed only slightly, and the statistical significance of the associations did not change. For example, adjustment for the aforementioned additional covariates resulted in a range of hazard ratios of 1.42 to 1.45 among quitters and 1.50 to 1.54 among active smokers.

Among persons who quit smoking after the incident myocardial infarction compared to nonsmokers, the hazard ratio declined as the duration of cessation increased, and it approached that of nonsmokers after 3 years (test for trend, $P = 0.01$ among persons who quit after infarction) (Table 3). By contrast, the hazard ratio among active smokers compared to nonsmokers did not decline over time since infarction. We detected no differences across subgroups defined by sex, age, hypertension, diabetes, body mass index, or smoking intensity in the association between decreasing hazard ratio and increasing duration of cessation.

DISCUSSION

In our study, persons who continued to smoke after incident myocardial infarction had a 50% increase in risk for recurrent coronary events compared to nonsmokers, an excess risk apparent across demographic, clinical, and treatment subgroups. Among those who quit smoking after incident myocardial infarction, the risk seemed to decline over time until it matched that of nonsmokers as the duration of cessation approached 3 years. Former smokers (persons who had quit smoking before the incident myocardial infarction) did not seem to have an elevated risk compared to nonsmokers.

The elevated risk for recurrent coronary events among active smokers after incident myocardial infarction is of considerable public health importance. Active smokers made up nearly 20% of our cohort, and this proportion is similar to that found in other populations with prevalent heart disease (27, 28). The magnitude of the increased risk among smokers in our study is similar to that found in other investigations of populations with prevalent disease that have found smokers to have elevated risk compared to

Table 2. Unadjusted Rate and Multivariable-Adjusted Hazard Ratio of Recurrent Coronary Heart Disease Events, by Smoking Status

Smoking Status	Coronary Heart Disease Events, <i>n</i>	Person-Years at Risk	Unadjusted Rate per 1000 Person-Years	Multivariable-Adjusted Hazard Ratio (95% CI)*
Nonsmokers	139	3084	45.1	1.00 (reference)
Persons who quit smoking before incident myocardial infarction	162	2970	54.5	1.17 (0.93–1.49)
Persons who quit smoking after incident myocardial infarction	72	1502	47.9	1.43 (1.07–1.93)
Active smokers after incident myocardial infarction	60	1257	47.7	1.51 (1.10–2.07)

* After adjustment for age, sex, presence of congestive heart failure, presence of diabetes, presence of hypertension, aspirin use, alcohol use, body mass index, random serum glucose level, and time from hospital discharge.

Table 3. Duration of Smoking Cessation and Unadjusted Rate and Multivariable-Adjusted Hazard Ratio of Recurrent Coronary Heart Disease Events

Smoking Status	Coronary Heart Disease Events, <i>n</i>	Person-Years at Risk*	Unadjusted Rate per 1000 Person-Years	Multivariable-Adjusted Hazard Ratio (95% CI)†
Nonsmokers	139	3084	45.1	1.00 (reference)
Persons who quit smoking after incident myocardial infarction				
Duration of cessation				
0 to <6 months	23	186	123.7	1.62 (1.02–2.61)
6 to <18 months	21	418	50.3	1.60 (0.97–2.60)
18 to <36 months	15	434	34.5	1.48 (0.76–2.51)
≥36 months	13	464	28.0	1.02 (0.54–1.86)
Active smokers after incident myocardial infarction	60	1257	47.7	1.51 (1.10–2.07)

* Total number of persons still under observation over time among those who quit smoking after incident myocardial infarction was 449 at 0 to <6 months, 414 at 6 to <18 months, 349 at 18 to <36 months, and 226 at ≥36 months.

† After adjustment for age, sex, presence of congestive heart failure, presence of diabetes, presence of hypertension, aspirin use, alcohol use, body mass index, random serum glucose level, and time from hospital discharge.

nonsmokers (29–31). We found no evidence to support the previously reported “smoker’s paradox” among those who continued to smoke after infarction, even among those who received thrombolytic therapy (32, 33). Given the considerably younger age of smokers at the time of the incident infarction and their elevated risk after infarction, smoking seems to have a consistently adverse effect on health.

As in other studies of postinfarction populations or populations having procedures for coronary artery disease (5, 30, 31, 34), approximately half of persons classified as smokers at the time of their coronary event or procedure permanently quit smoking; this finding underscores the strong motivating influence of myocardial infarction in achieving cessation (35). Those who quit smoking after their incident infarction had an overall risk for recurrent events that was similar to that of active smokers; however, the risk decreased over time and approached that of nonsmokers 3 years after cessation, a result consistent with the time course of benefit in the primary prevention setting (2, 3). Given this time-dependent association, the overall risk observed among quitters is in part a function of the length of follow-up. Thus, the overall risk evident among quitters in our analysis (median follow-up, 3 years) is probably an overestimate because average survival after hospital discharge substantially exceeds the length of follow-up time in our cohort (36).

Various factors may explain the time lag for decreased risk among quitters after incident infarction. Although smoking acutely potentiates thrombosis by producing oxidative stress, endothelial dysfunction, and platelet activation (37, 38), it may also promote atherosclerosis and thrombosis by longer-term means that include impaired insulin sensitivity and renal dysfunction (39, 40). Alternatively, some persons who quit smoking after myocardial infarction may have quit in part because of more (unmeasured) smoking-related symptoms and thus may have been sicker than those who continued to smoke (41). These persons would presumably have recurrent events sooner rather than later after cessation.

Our study has limitations. We defined smoking status on the basis of retrospective chart review that relied on physician assessment and documentation of smoking status. Smoking status was therefore not prospectively and systematically assessed or recorded. This limitation should be placed in the context of the postinfarction setting, where patients were followed closely and clinical attention would probably be directed toward minimizing modifiable potential risk factors, such as smoking. Smoking status was based on patient report as documented in the medical record and was not verified by biochemical assay; among those with heart disease, however, self-report seems to be reasonably accurate (4, 42). Given the relationships observed, misclassification of smoking status would probably have attenuated the true association between active smoking and risk for recurrent coronary event; thus, our findings may underestimate the risk associated with smoking. In addition, we were able to classify as quitters only those who had permanently quit smoking; those who quit and then resumed smoking were classified as active smokers.

Although the relations seen persisted in numerous sensitivity analyses, we cannot exclude the possibility of confounding (for example, confounding due to income level). In particular, persons who are able to quit smoking may be more compliant than others, and patient adherence is known to be related to improved prognosis (43). In addition, we could not adjust for the individual physician. It is possible that physicians who were better able to assist patients with cessation might also have provided other beneficial care that reduced the risk for recurrent coronary events and was not accounted for in the models. However, adjustment for other measures that might be associated with physician practice, such as use of medications (including β -blocker, lipid-lowering, and angiotensin-converting enzyme inhibitor therapies) did not alter the associations with smoking status. Moreover, unlike most treatments, smoking cessation is a complex process that is partly determined by patient characteristics (such as “readiness to quit”) rather than physician-initiated care. Finally, we could not assess for the possibility of variance inflation due

to clustering by physician. However, because there are many physicians relative to the number of patients, the variance inflation due to clustering is probably small, unless there was a high degree of variation of outcomes across physicians. This study also has many strengths: Our findings compare the various clinical groups of smokers (nonsmokers, former smokers, quitters, and active smokers) and are derived from a large, population-based cohort with information available on a broad range of important clinical, treatment, and laboratory variables.

In conclusion, smoking after incident myocardial infarction was associated with an increased risk for recurrent coronary events. However, in persons who quit smoking after the incident myocardial infarction, the risk seemed to decline to equal that of nonsmokers after 3 years of cessation. These results, taken together with the increasing array of behavioral and pharmacological therapies that help persons achieve and maintain smoking cessation (44), the safety of these interventions in those with coronary disease (45–47), and the strong motivating influence of infarction (35), support efforts to make smoking cessation an important goal for patients and physicians after myocardial infarction.

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References

1. U.S. Department of Health and Human Services. The health consequences of smoking: nicotine addiction. A report of the Surgeon General. DHHS pub. no. 88-8406, 1988. Accessed at www.cdc.gov/tobacco/sgrpage.htm.
2. Rosenberg L, Kaufman DW, Helmrich SP, Shapiro S. The risk of myocardial infarction after quitting smoking in men under 55 years of age. *N Engl J Med*. 1985;313:1511-4. [PMID: 4069159]
3. Rosenberg L, Palmer JR, Shapiro S. Decline in the risk of myocardial infarction among women who stop smoking. *N Engl J Med*. 1990;322:213-7. [PMID: 2294448]
4. Aberg A, Bergstrand R, Johansson S, Ulvenstam G, Vedin A, Wedel H, et al. Cessation of smoking after myocardial infarction. Effects on mortality after 10 years. *Br Heart J*. 1983;49:416-22. [PMID: 6838729]
5. Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. *Arch Intern Med*. 2000;160:939-44. [PMID: 10761958]
6. Mulcahy R, Hickey N, Graham IM, MacAirt J. Factors affecting the 5 year survival rate of men following acute coronary heart disease. *Am Heart J*. 1977; 93:556-9. [PMID: 851053]
7. Hedbäck B, Perk J, Wodlin P. Long-term reduction of cardiac mortality after myocardial infarction: 10-year results of a comprehensive rehabilitation programme. *Eur Heart J*. 1993;14:831-5. [PMID: 8325313]
8. Johansson S, Bergstrand R, Pennert K, Ulvenstam G, Vedin A, Wedel H, et al. Cessation of smoking after myocardial infarction in women. Effects on mortality and reinfarctions. *Am J Epidemiol*. 1985;121:823-31. [PMID: 4014175]
9. Burr ML, Holliday RM, Fehily AM, Whitehead PJ. Haematological prognostic indices after myocardial infarction: evidence from the diet and reinfarction trial (DART). *Eur Heart J*. 1992;13:166-70. [PMID: 1313369]
10. Herlitz J, Bengtson A, Hjalmarson A, Karlson BW. Smoking habits in consecutive patients with acute myocardial infarction: prognosis in relation to other risk indicators and to whether or not they quit smoking. *Cardiology*. 1995; 86:496-502. [PMID: 7585761]
11. Perkins J, Dick TB. Smoking and myocardial infarction: secondary prevention. *Postgrad Med J*. 1985;61:295-300. [PMID: 4022857]
12. Sparrow D, Dawber TR. The influence of cigarette smoking on prognosis after a first myocardial infarction. A report from the Framingham study. *J Chronic Dis*. 1978;31:425-32. [PMID: 711834]
13. Greenwood DC, Muir KR, Packham CJ, Madeley RJ. Stress, social support, and stopping smoking after myocardial infarction in England. *J Epidemiol Community Health*. 1995;49:583-7. [PMID: 8596092]
14. Toffler GH, Muller JE, Stone PH, Davies G, Davis VG, Braunwald E. Comparison of long-term outcome after acute myocardial infarction in patients never graduated from high school with that in more educated patients. Multi-center Investigation of the Limitation of Infarct Size (MILIS). *Am J Cardiol*. 1993;71:1031-5. [PMID: 8475864]
15. Salonen JT. Stopping smoking and long-term mortality after acute myocardial infarction. *Br Heart J*. 1980;43:463-9. [PMID: 7397048]
16. Wilhelmsen L. Effects of cessation of smoking after myocardial infarction. *J Cardiovasc Risk*. 1998;5:173-6. [PMID: 10201554]
17. Wilhelmsson C, Vedin JA, Elmfeldt D, Tibblin G, Wilhelmsen L. Smoking and myocardial infarction. *Lancet*. 1975;1:415-20. [PMID: 48609]
18. Kelly TL, Gilpin E, Ahnve S, Henning H, Ross J Jr. Smoking status at the time of acute myocardial infarction and subsequent prognosis. *Am Heart J*. 1985; 110:535-41. [PMID: 4036780]
19. Mølsted P. First myocardial infarction in smokers. *Eur Heart J*. 1991;12: 753-9. [PMID: 1889438]
20. Barbash GI, Reiner J, White HD, Wilcox RG, Armstrong PW, Sadowski Z, et al. Evaluation of paradoxical beneficial effects of smoking in patients receiving thrombolytic therapy for acute myocardial infarction: mechanism of the "smoker's paradox" from the GUSTO-I trial, with angiographic insights. Global Utilization of Streptokinase and Tissue-Plasminogen Activator for Occluded Coronary Arteries. *J Am Coll Cardiol*. 1995;26:1222-9. [PMID: 7594035]
21. Maggioni AP, Piantadosi F, Tognoni G, Santoro E, Franzosi MG. Smoking is not a protective factor for patients with acute myocardial infarction: the viewpoint of the GISSI-2 Study. *G Ital Cardiol*. 1998;28:970-8. [PMID: 9788035]
22. Jørgensen, Køber L, Ottesen MM, Torp-Pedersen C, Videbaek J, Kjoller E. The prognostic importance of smoking status at the time of acute myocardial infarction in 6676 patients. TRACE Study Group. *J Cardiovasc Risk*. 1999;6: 23-7. [PMID: 10197289]
23. Gottlieb S, Boyko V, Zahger D, Balkin J, Hod H, Pelled B, et al. Smoking and prognosis after acute myocardial infarction in the thrombolytic era (Israeli Thrombolytic National Survey). *J Am Coll Cardiol*. 1996;28:1506-13. [PMID: 8917265]
24. Ishihara M, Sato H, Tateishi H, Kawagoe T, Shimatani Y, Kurisu S, et al. Clinical implications of cigarette smoking in acute myocardial infarction: acute angiographic findings and long-term prognosis. *Am Heart J*. 1997;134:955-60. [PMID: 9398109]
25. Psaty BM, Heckbert SR, Atkins D, Lemaitre R, Koepsell TD, Wahl PW, et al. The risk of myocardial infarction associated with the combined use of estrogens and progestins in postmenopausal women. *Arch Intern Med*. 1994; 154:1333-9. [PMID: 8002685]
26. Hosmer DW, Lemeshow S. Applied survival analysis: Regression modeling of time to event data. New York: John Wiley & Sons; 1999.
27. EUROASPIRE. A European Society of Cardiology survey of secondary prevention of coronary heart disease: principal results. EUROASPIRE Study Group. European Action on Secondary Prevention through Intervention to Reduce Events. *Eur Heart J*. 1997;18:1569-82. [PMID: 9347267]
28. Qureshi AI, Suri MF, Guterman LR, Hopkins LN. Ineffective secondary prevention in survivors of cardiovascular events in the US population: report from the Third National Health and Nutrition Examination Survey. *Arch Intern Med*. 2001;161:1621-8. [PMID: 11434794]
29. Jafri SM, Tilley BC, Peters R, Schultz LR, Goldstein S. Effects of cigarette smoking and propranolol in survivors of acute myocardial infarction. *Am J Car-*

- diol. 1990;65:271-6. [PMID: 2405619]
30. **Hermanson B, Omenn GS, Kronmal RA, Gersh BJ.** Beneficial six-year outcome of smoking cessation in older men and women with coronary artery disease. Results from the CASS registry. *N Engl J Med.* 1988;319:1365-9. [PMID: 3185646]
31. **Hasdai D, Garratt KN, Grill DE, Lerman A, Holmes DR Jr.** Effect of smoking status on the long-term outcome after successful percutaneous coronary revascularization. *N Engl J Med.* 1997;336:755-61. [PMID: 9052653]
32. **Grines CL, Topol EJ, O'Neill WW, George BS, Kereiakes D, Phillips HR, et al.** Effect of cigarette smoking on outcome after thrombolytic therapy for myocardial infarction. *Circulation.* 1995;91:298-303. [PMID: 7805231]
33. **de Chillou C, Riff P, Sadoul N, Ethevenot G, Feldmann L, Isaaz K, et al.** Influence of cigarette smoking on rate of reopening of the infarct-related coronary artery after myocardial infarction: a multivariate analysis. *J Am Coll Cardiol.* 1996;27:1662-8. [PMID: 8636551]
34. **van Domburg RT, Meeter K, van Berkel DF, Veldkamp RF, van Herwerden LA, Bogers AJ.** Smoking cessation reduces mortality after coronary artery bypass surgery: a 20-year follow-up study. *J Am Coll Cardiol.* 2000;36:878-83. [PMID: 10987614]
35. **Siegel D, Grady D, Browner WS, Hulley SB.** Risk factor modification after myocardial infarction. *Ann Intern Med.* 1988;109:213-8. [PMID: 3291658]
36. **Jacobs DR Jr, Kroenke C, Crow R, Deshpande M, Gu DF, Gatewood L, et al.** PREDICT: A simple risk score for clinical severity and long-term prognosis after hospitalization for acute myocardial infarction or unstable angina: the Minnesota heart survey. *Circulation.* 1999;100:599-607. [PMID: 10441096]
37. **Vogel RA.** Coronary risk factors, endothelial function, and atherosclerosis: a review. *Clin Cardiol.* 1997;20:426-32. [PMID: 9134272]
38. **Zhu BQ, Parmley WW.** Hemodynamic and vascular effects of active and passive smoking. *Am Heart J.* 1995;130:1270-5. [PMID: 7484781]
39. **Manson JE, Ajani UA, Liu S, Nathan DM, Hennekens CH.** A prospective study of cigarette smoking and the incidence of diabetes mellitus among US male physicians. *Am J Med.* 2000;109:538-42. [PMID: 11063954]
40. **Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE.** Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. *Ann Intern Med.* 2000;133:585-91. [PMID: 11033585]
41. **Hermanson B, Omenn GS, Kronmal RA, Gersh BJ.** Beneficial six-year outcome of smoking cessation in older men and women with coronary artery disease. Results from the CASS registry. *N Engl J Med.* 1988;319:1365-9. [PMID: 3185646]
42. **Patrick DL, Cheadle A, Thompson DC, Diehr P, Koepsell T, Kinne S.** The validity of self-reported smoking: a review and meta-analysis. *Am J Public Health.* 1994;84:1086-93. [PMID: 8017530]
43. **Petitti DB.** Coronary heart disease and estrogen replacement therapy. Can compliance bias explain the results of observational studies? *Ann Epidemiol.* 1994;4:115-8. [PMID: 8205277]
44. **Goldstein MG, Niaura R.** Methods to enhance smoking cessation after myocardial infarction. *Med Clin North Am.* 2000;84:63-80, viii. [PMID: 10685128]
45. **Joseph AM, Norman SM, Ferry LH, Prochazka AV, Westman EC, Steele BG, et al.** The safety of transdermal nicotine as an aid to smoking cessation in patients with cardiac disease. *N Engl J Med.* 1996;335:1792-8. [PMID: 8943160]
46. **Mahmorian JJ, Moyé LA, Nasser GA, Nagueh SF, Bloom MF, Benowitz NL, et al.** Nicotine patch therapy in smoking cessation reduces the extent of exercise-induced myocardial ischemia. *J Am Coll Cardiol.* 1997;30:125-30. [PMID: 9207632]
47. **Nitenberg A, Antony I.** Effects of nicotine gum on coronary vasomotor responses during sympathetic stimulation in patients with coronary artery stenosis. *J Cardiovasc Pharmacol.* 1999;34:694-9. [PMID: 10547086]

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