

**Smoking cessation reduces mortality after coronary artery bypass surgery: a
20-year follow-up study**

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J. Am. Coll. Cardiol. 2000;36;878-883

This information is current as of January 23, 2010

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JACC

JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY



Smoking Cessation Reduces Mortality After Coronary Artery Bypass Surgery: A 20-Year Follow-up Study

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OBJECTIVES	The goal of this study was to determine the influence of smoking cessation on mortality after coronary artery bypass graft surgery (CABG), which has still not been established clearly.
BACKGROUND	Cigarette smoking is one of the known major risk factors of coronary artery disease.
METHODS	One thousand and forty-one patients underwent CABG between 1971 and 1980. The preoperative and postoperative smoking habits of 985 patients (95%) could be retrieved and were analyzed in a multivariate Cox analysis.
RESULTS	The median follow-up was 20 years (range 13 to 26 years). Smoking status before surgery did not entail an increased risk of mortality: patients who had smoked before surgery and those who had not smoked in the year before surgery had a similar probability of survival. However, smoking cessation after surgery was an important independent predictor of a lower risk of death and coronary reintervention during the 20-year follow-up when compared with patients who continued smoking. In analyses adjusted for baseline characteristics, the persistent smokers had a greater relative risk (RR) of death from all causes (RR 1.68 [95% confidence interval 1.33 to 2.13]) and cardiac death (RR 1.75 [1.30 to 2.37]) as compared with patients who stopped smoking for at least one year after surgery. The estimated benefit of survival for the quitters increased from 3% at five years to 14% at 15 years. The quitters were less likely to undergo repeat CABG or a percutaneous coronary angioplasty procedure (RR 1.41 [1.02 to 1.94]).
CONCLUSIONS	Patients who continued to smoke after CABG had a greater risk of death than patients who stopped smoking. They also underwent repeat revascularization procedures more frequently. Cessation of smoking is therefore strongly recommended after CABG. Clinicians are encouraged to start or to continue smoking-cessation programs in order to help smokers to quit smoking, especially after CABG. (J Am Coll Cardiol 2000;36:878-83) © 2000 by the American College of Cardiology

It is well established that cigarette smoking is a major contributor to the risk of coronary heart disease (1,2). Previous studies have shown that smoking is strongly related to myocardial infarction (MI) (3-5) and cardiac death (6) in the general population. A recent study has shown that cessation of smoking after percutaneous coronary angioplasty (PTCA) may have an important beneficial effect on the clinical course after the procedure (7). Some studies suggested that patients who continue to smoke are at greater risk for atherosclerosis of vein grafts than nonsmokers (8,9), whereas two other studies show a beneficial effect on clinical events after coronary artery bypass surgery (CABG) (10,11). However, the effects of smoking and smoking cessation after CABG on mortality have not been clearly established. In this study we assessed the relation between smoking cessation and the mortality risk after CABG and determined whether smoking cessation after CABG affected the need for repeat revascularization procedures. To this end a group of 985 patients who were operated on between 1971 and 1980 were, therefore, followed during a 20-year period.

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Manuscript received December 8, 1999; revised manuscript received March 1, 2000, accepted April 12, 2000.

METHODS

Patient population. All 1,041 consecutive patients who underwent a first CABG surgery between February 1971 and June 1980 at the Thoraxcenter were considered for this study. The bypass grafts in all these patients were all of saphenous vein material only. The medium-term and long-term survival probabilities of this group have been published previously (12-14). The smoking habits before and after surgery could be retrieved from 985 patients. The population consisted of 866 men (88%) and 119 women (12%) with a mean age of 53 and 55 years, respectively. Multivessel disease was present in 81% of the patients, and impaired left ventricular ejection fraction (<55%) was found in 27% of the patients.

Follow-up procedure. Follow-up procedure for vital status was obtained by contacting the civil registry in writing and was complete in 98%. Median follow-up was 20 years (range 13 to 26 years). Mortality was divided into perioperative mortality (death occurring within 28 days after surgery) and late mortality. The latter was subdivided into: 1) death at re-CABG or PTCA; 2) acute cardiac death (within 1 h after beginning of complaints, believed to be of cardiac origin); 3) death caused by MI (ascertained by enzyme measurement

Abbreviations and Acronyms

- CABG = coronary artery bypass graft surgery
- CI = confidence interval
- MI = myocardial infarction
- PTCA = percutaneous transluminal coronary angioplasty
- RR = relative risk

and electrocardiogram); 4) death caused by chronic cardiac failure; 5) death from a noncardiac cause; 6) unknown cause of death. The cause of death was determined by checking our own hospital records, by contacting the referring hospitals (for autopsy reports or letters to the general practitioner) or the attending general practitioner.

Smoking behavior. In 1981 all patients were queried about their smoking status before surgery and after surgery. At that time, May 1981, 64 (6.2%) of the original group of 1,041 patients had died and another 8 had moved abroad (14). The remaining patients were sent a questionnaire to ascertain their postoperative condition and smoking habits. We were able to retrieve the preoperative and postoperative (recorded at least one year after surgery) smoking habit status of 985 patients (95%) (Fig. 1). The small number of patients (20) who started to smoke after CABG were excluded from the present analysis. In the 56 patients whose smoking status at least one year after CABG was unknown, 48 of the 56 patients had died at the time when the patients were queried about their smoking behavior (perioperative mortality: 12 patients; one-year mortality: 33 patients, of which 25% were noncardiac). The baseline characteristics of these 56 patients were similar to the group of patients in whom the smoking was known. The median duration between CABG and the assessment of smoking behavior was 2.8 years (range 11 months to 9.5 years). The study population was divided into two groups: smokers and nonsmokers (ex- and never smokers) in the year before CABG; the smokers before surgery were further subdivided

into quitters who had stopped smoking in the first year after the index CABG (most immediate after CABG) and persistent smokers, those who smoked before CABG and continued to smoke for at least one year after CABG.

Data management and statistics. Differences between the smokers and nonsmokers, as well as quitters and persistent smokers, were calculated by means of the Student *t* test for continuous data or the chi-square test for categorical data. Preselected variables were age, sex, extent of vessel disease, preoperative ejection fraction and complete or incomplete revascularization. A vessel was considered diseased when the luminal diameter narrowing of at least 50% was seen in more than one projection. Ejection fraction was angiographically calculated in 705 patients and considered impaired if less than 55%. A complete revascularization was defined as “no remaining main artery stenosis of at least 50%.” The survival data were analyzed using the Kaplan Meier method. The log-rank test was used to compare survival curves. Univariable Cox proportional-hazard model was used to estimate the unadjusted relative risks (RR) for nonsmokers as compared with smokers at the time of surgery and to compare quitters and persistent smokers after surgery. A multivariate Cox model adjusting for the preselected clinical and angiographic parameters was used to estimate the adjusted RRs.

RESULTS

The baseline clinical characteristics of the smokers and nonsmokers are shown in Table 1. Smokers at the time of surgery were four years younger and more often men compared with nonsmokers. The clinical characteristics of quitters and persistent smokers were comparable except for a larger proportion of multivessel disease among the persistent smokers.

Median follow-up was 20 years (range 13 to 26 years). Death occurred in 234 (54%) of the 429 nonsmokers at the time of surgery, of which 65% were due to cardiac causes. Of the 556 smokers before CABG, 311 (56%) died within 20 years, of which 65% were due to cardiac causes (Table 2). Of the 238 patients who stopped smoking after CABG, 109 (46%) died within 20 years, whereas 202 (64%) of the 318 persistent smokers died during the follow-up. A cardiac cause of death was found in 62% of the quitters and in 68% of the nonquitters.

Mortality. In the univariable analysis (Table 3), the persistent smokers had higher risks of death from all causes (RR 1.56 [95% confidence interval [CI], 1.24 to 1.97]) and also from cardiac death (RR 1.70 [95% CI, 1.26 to 2.29]) compared with the quitters. The smoking habit was the strongest predictor of mortality in a stepwise multivariate Cox analysis, even when all other baseline risk factors were forced into the model. The persistent smokers had a significantly greater risk of death from all causes (RR 1.68, 95% CI, 1.33 to 2.13) and of cardiac death (RR 1.75 [95%

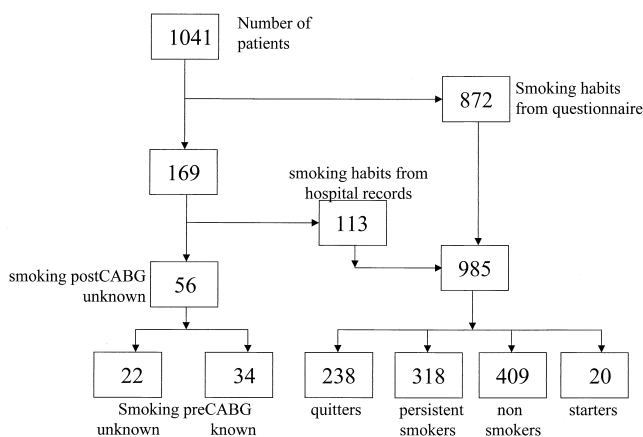


Figure 1. Flow-chart of the subdivision of the smoking habits of 1,041 consecutive patients who underwent a first CABG surgery between 1971 and 1980. CABG = coronary artery bypass graft surgery.

Table 1. Baseline Characteristics of 985 Patients Undergoing Successful Coronary Artery Bypass Surgery According to Smoking Status

Event	Nonsmokers at Time of Surgery (n = 429)	Smokers at Time of Surgery		
		All (n = 556)	Quitters (n = 238)	Persistent Smokers (n = 318)
Age (yrs)	55.1	51.2*	51.7	50.8
Men %	83	92*	90	93
Number of bypass grafts	2.8	2.6	2.6	2.7
Vessel disease %†				
1-vessel	17	20	26	16
2-vessels	32	29	25	35
3-vessels	42	42	40	43
Left main	9	7	9	6
Ejection fraction %				
Normal	58	58	58	58
Moderate (30-55%)	25	22	23	22
Poor (\leq 30%)	3	3	2	3
Unknown‡	15	17	17	17
Revascularization %				
Complete	79	79	80	79
Incomplete	21	21	20	21

Quitters were defined as patients who quit smoking for at least one year after the index procedure and persistent smokers as patients who were still smoking at least one year after the index procedure.

* $p < 0.05$ comparing smokers vs. nonsmokers; †when comparing quitters and persistent smokers (2×4 table) a $p < 0.05$ was found; ‡due to insufficient quality or absence of the ventriculogram.

CI, 1.30 to 2.37) compared with patients who quit smoking after CABG.

The estimated survival curves for the patients who quit smoking and those who continued to smoke diverged approximately four years after the index operation, and the difference between the two curves increased throughout the follow-up period (Fig. 2). The estimated benefit in survival associated with the cessation of smoking increased from 3% at 5 years (98% vs. 95%), to 10% at 10 years (88% vs. 78%) and 15% at 15 years (70% vs. 55%). After 20 years the benefit was still 8% (47% vs. 39%).

Repeat procedure. Repeat CABG was performed in 27% of the patients who quit smoking and 31% of the persistent smokers. During follow-up, repeat coronary artery revascularization (either CABG or PTCA) was performed more frequently among the persistent smokers compared with quitters (RR 1.42 [95% CI, 1.05 to 1.90]). An identical

survival rate and a repeat coronary artery revascularization rate were found between the smokers and nonsmokers at the time of surgery. Also, when adjusted for baseline characteristics, repeat CABG or PTCA was more frequently found among the persistent smokers compared with patients who quit smoking (RR 1.41 [95% CI, 1.02 to 1.94]).

The Kaplan-Meier survival curves representing freedom from repeat coronary interventions are shown in Figure 3. Due to the low intervention rates in both groups, the rates were similar up to 10 years, after which the curves for quitters and persistent smokers diverged.

DISCUSSION

This study examined the influence of patients' smoking habits before and after CABG on mortality and repeat revascularization procedures. The relatively high proportion

Table 2. Number of Events (%)

Event %	Nonsmokers at Time of Surgery (n = 429)	Smokers at Time of Surgery		
		All (n = 556)	Quitters (n = 238)	Persistent Smokers (n = 318)
Death from all causes	54	56	46	64
Sudden death	26	29	26	30
Fatal myocardial infarction	14	13	14	12
Reintervention death	8	5	5	4
Other cardiac death	17	19	18	22
Noncardiac death	26	25	26	23
Unknown death	9	10	12	9
PTCA	13	11	9	13
Repeat CABG	28	29	27	31
PTCA or repeat CABG	35	33	30	36

CABG = coronary artery bypass graft surgery; PTCA = percutaneous transluminal coronary angioplasty.

Table 3. Univariable and Adjusted Relative Risks of Total Mortality, Cardiac Death, Repeat Coronary Bypass Surgery or Coronary Angioplasty

Event		Smokers vs. Nonsmokers	Persistent Smokers vs. Quitters	
Deaths from all causes				
Unadjusted relative risks	1.04	0.88-1.22	1.56	1.24-1.97
Adjusted relative risks*	1.18	0.99-1.40	1.68	1.33-2.13
Cardiac death				
Unadjusted relative risks	1.05	0.85-1.30	1.70	1.26-2.29
Adjusted relative risks*	1.14	0.91-1.41	1.75	1.30-2.37
PTCA				
Unadjusted relative risks	0.78	0.55-1.12	1.50	0.89-2.53
Adjusted relative risks*	0.66	0.46-0.97	1.56	0.88-2.79
Repeat CABG				
Unadjusted relative risks	1.00	0.79-1.27	1.38	1.01-1.89
Adjusted relative risks*	0.82	0.64-1.04	1.42	1.01-1.97
Repeat CABG/PTCA				
Unadjusted relative risks	0.91	0.74-1.13	1.42	1.05-1.90
Adjusted relative risks*	0.76	0.61-0.95	1.41	1.02-1.94

*Adjusted for age, gender, vessel disease, ejection fraction, complete revascularization. CABG = coronary artery bypass graft surgery; PTCA = percutaneous transluminal coronary angioplasty.

of smokers at the time of surgery (56%) in our study group is due to the fact that our patients date from the 1970s. Since health care programs in the 1980s encouraged patients to stop smoking, the percentage of coronary patients who smoke has steadily decreased to around 30% in the Netherlands. However, this figure still compares unfavorably with other West-European or North American countries (15).

There has been much controversy about whether smokers should receive the same opportunities for CABG as nonsmokers (16,17). Discussion on this subject was mainly based on the consistent finding that continued smoking after CABG increased clinical complications, such as MI and repeat coronary revascularization. Voors et al. (11) demonstrated that, at one year after surgery, smokers had more than twice the risk for MI and reoperation as compared with patients who had stopped smoking since surgery. Previous short- and medium-term studies or studies on subpopulations have shown improved survival in patients who stops smoking after MI (4,18-22). A recent publication of the Mayo Clinic investigators (7) showed an increased RR of 44% of death among the persistent smokers

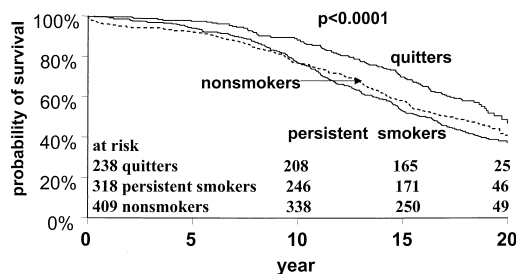


Figure 2. Twenty-year survival from all causes curves for patients who quit smoking after CABG, persistent smokers after CABG and nonsmokers. CABG = coronary artery bypass graft surgery.

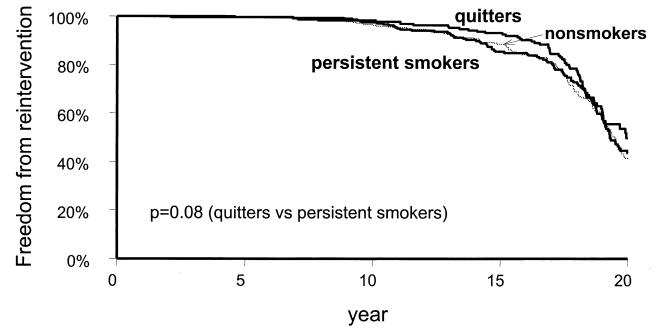


Figure 3. Twenty-year freedom from a coronary reintervention (coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty) for patients who quit smoking and persistent smokers after coronary artery bypass graft surgery.

compared with quitters after percutaneous coronary revascularization. However, to the best of our knowledge, the benefit of smoking cessation on the risk of death after CABG is still unknown.

Survival. In our study, after adjustment for clinical and angiographic characteristics, the persistent smokers had a greater risk of death from all causes as compared with patients who stopped smoking after surgery during the very long follow-up of 20 years. Improved survival rates were seen from approximately four years after CABG. During that time the risk of death from any cause was 68% greater in patients who persisted in smoking after CABG than it was in those who quit. The estimated survival curves for the two groups diverged at four to five years after surgery and continued to diverge throughout the entire follow-up period. The benefit of smoking cessation on mortality may be explained largely by the reduction in cardiac deaths since the RR of cardiac death was 75% higher for the persistent smokers than it was for the quitters. Voors et al. (11) found a similar RR of mortality of 1.7. However, probably due to the limited number of patients, this risk was statistically not significant.

Repeat procedure. In agreement with the findings of Voors et al. (11), we found that persistent smokers do need more repeat coronary revascularization procedures than quitters. In that study patients who continued to smoke after surgery had a 41% higher risk of undergoing a repeat CABG or a PTCA. In our study coronary reintervention up to 10 years was rare after CABG. Thereafter, this incidence increased, probably due to graft atherosclerosis and progression of native coronary artery disease. Nevertheless, the reintervention rates diverged starting at 10 years postoperative in favor of the quitters when compared with persistent smokers.

Smoker's paradox. Many investigations have demonstrated that smoking is associated with higher rates of heart disease. It is, therefore, surprising that smoking habits at the time of surgery did not significantly influence survival and reintervention rates during the follow-up period. In addition Hasdai et al. (7) reported that smokers had fewer adverse

events at the time of a PTCA than nonsmokers. Other studies such as the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries trial (23) have speculated on the paradoxical beneficial effects of smoking on thrombolytic therapy after MI. In these studies the better prognosis for smokers was mainly explained by the difference in clinical baseline characteristics such as an age difference. After adjustment for all clinical baseline characteristics, these studies showed no significant difference in mortality between smokers and nonsmokers. In our study the similarity in risk of death and reintervention rate between the two groups cannot completely be explained by these baseline parameters, as the smokers were only four years younger than nonsmokers. Another explanation could be selection bias since many smokers tend to die of fatal MIs before they having the chance to undergo CABG (24). Thus, those operated on are different from the entire smokers cohort with coronary artery disease. Moreover, only patients who survived the immediate postoperative period were included in our study, which could have caused further selection. Another explanation may be that CABG facilities were scarce at the time, causing long waiting lists. Only the survivors of the waiting time were operated on.

Finally, our data do not support the proposal that smokers should receive fewer opportunities for CABG than nonsmokers because the survival rates of nonsmokers and smokers were similar at the time of surgery.

The study consisted of patients who underwent CABG using vein grafts in the 1970s. To extrapolate the findings of this study to current practice, it needs to be realized that operation techniques have been changed, and present day populations are different. Total arterial revascularization is currently propagated to prevent premature death due to graft sclerosis. This study has some limitations. We did not record the number of cigarettes smoked. Second, there may have been other factors intercorrelating with smoking behavior that we did not record. For example, smoking cessation could be accompanied with other life style changes such as a diet. The Multiple Risk Factor Intervention Trial study group has investigated that, in 12,866 high-risk men, smoking cessation was the strongest predictor of lower rates of coronary disease as compared with other changes in risk factors, such as cholesterol and blood pressure lowering interventions (25). However, the effect of risk factors, such as diabetes and hypercholesterolemia, was not yet clearly established in the 1970s. Only variables already known to influence survival at that time, such as left ventricular function and extent of vessel disease, were consistently reported and therefore used for further analysis. Smoking status was assessed by asking patients about their smoking behavior and, if necessary, from the hospital records. This remains a possible cause of bias, as we were not able to check reported data against biochemical validation. However, self-reports of smoking in observational studies in an adult population such as this have a high sensitivity and specificity (26).

Conclusions. Our results strongly indicate that, after CABG, patients who do not stop smoking have a markedly elevated risk of premature death and a higher rate of repeat revascularization procedures compared with those who do stop. Cessation of smoking is therefore strongly recommended after CABG, and clinicians are encouraged to start or continue smoking cessation programs (27) in order to help patients stop smoking.

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