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Smoking and myocardial infarction in women: a case-control study from northern Italy

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ABSTRACT

Study objective: To examine the relationship between smoking and myocardial infarction in women.
Design: Case-control study over 5 years.
Setting: Cases were women admitted to 30 coronary care units in northern Italy. Controls were admitted to the same hospitals with other acute disorders.
Participants: These were 262 young and middle aged women with acute myocardial infarction (median age 49 years, range 24–69) and 519 controls with other acute disorders unrelated to ischaemic heart disease (median age 47 years, range 22–69).
Measurements and main results: Stratification and the Mantel-Haenszel procedure, and unconditional multiple logistic regression were used to obtain relative risks according to levels of cigarette smoking. The regression equations included terms for age, education, coffee and alcohol consumption, diabetes, hypertension, hyperlipidaemia, body mass index and oral contraceptive use. Compared to life long non-smokers, relative risk was not significantly above unity for ex-smokers but among current smokers showed a significant trend to increasing risk with larger numbers of cigarettes smoked, with risk estimates of 2·3, 5·9 and 11·0 for < 15, 15–24 and $\geqslant 25$ cigarettes per day respectively. Smoking related risks were consistently raised across strata of hyperlipidaemia, hypertension and increased alcohol and coffee intake.
Conclusions: In terms of population attributable risk, about 48% of all myocardial infarctions in young and middle aged Italian women were attributable to cigarette smoking, which is therefore by far the most important preventable determinant of the disease.

Although cigarette smoking is a recognised risk factor for myocardial infarction,[1–5] there is still some uncertainty about the strength of the association in the two sexes and in various age groups and populations. For instance, in males the relative risk (although not the absolute excess risk) is greater in younger middle age than in older age,[3–5] but the interaction between smoking and age on the risk of acute myocardial infarction is less clear in women. The American Nurses Health Study[6] showed no material differences in the relative risk of cardiovascular events between younger women (30–39 years) and earlier (40–49 years) and later (50–59 years) middle age.

Several retrospective and prospective studies[2 6–10] have reported that relative risk estimates for women are higher than for men. Part of the difference could be explained in terms of different age distribution of male and female cases, since various studies considered only younger and middle aged women and, in any case, the limited prevalence of smoking by older women reduced the influence of these age groups even in studies not restricted to younger ages. Nonetheless, even within each age group, there is a tendency for a particularly high relative risk in women.

To document further the relation between smoking and myocardial infarction in women, we report the results from a case-control study conducted in Northern Italy, ie, on a population with smoking prevalence and infarction rates still considerably lower than in several countries of Northern Europe and America.[11]

Methods

Since January 1983, data have been collected on women with acute myocardial infarction ("cases",

defined according to the standard World Health Organisation criteria) admitted to the coronary care units of 30 hospitals in Northern Italy, and on comparison subjects ("controls") admitted to the same hospitals in which the cases had been identified, because of acute conditions unrelated to known or potential risk factors for ischaemic heart disease. The methods have been described in detail previously.[11] The only modification introduced in the original protocol was the upper age limit, which was raised from 54 to 69 years in June 1987. The present analysis is based on data collected before January 1988, for a total of 262 cases (aged 24–69, median age 49 years) and 519 controls (aged 22–69, median age 47 years; see table 1 for the age distribution of cases and controls).

Table 1 *Distribution of 262 cases of acute myocardial infarction and 519 controls according to age. Northern Italy, 1983–88*

	Myocardial infarction		*Controls*	
	Number	*%*	*Number*	*%*
Age group (years)				
<40	35	13·4	138	26·6
40–49	102	38·9	173	33·3
50–59	108	41·2	167	32·2
60–69	17	6·5	41	7·9

In the comparison group, 25% of patients were admitted for traumatic conditions, 32% had non-traumatic orthopaedic disorders (mostly low back pain and disc disorders), 19% were admitted for surgical conditions (including plastic surgery), and 24% had other illnesses, such as acute infections, skin, ear, nose and throat or teeth disorders. Overall participation rate was over 97%.

Standard statistical methods for the analysis of case-control studies (ie, stratification and the Mantel-Haenszel procedure, and unconditional multiple logistic regression)[12 13] were used to obtain relative risks according to various levels of cigarette smoking. Included in the regression equations were terms for age, education, coffee and alcohol consumption, diabetes, hypertension, hyperlipidaemia, body mass index and oral contraceptive use.

Results

The distribution of myocardial infarction cases and the comparison group according to smoking habits is given in table 2. Compared to life long non-smokers, the relative risk (RR) for ex-smokers was above unity, although not significantly, and in current smokers there was a significant trend toward increasing risk with higher number of cigarettes smoked. The age adjusted estimates were 2·6, 6·7 and 12·8 respectively for < 15, 15–24 and ⩾25 cigarettes per day. Allowance for major identified potential distorting factors changed these estimates only marginally (multivariate RR for heavy smokers = 11·0).

Table 3 gives the smoking related risks in separate strata of age and selected covariates. In this study, there was little evidence that the smoking related risks decreased with increasing age, the point estimates being not materially different below and above the age of 50 years. Likewise, the relative risks were consistently and substantially above unity in various strata of hypertension, hyperlipidaemia, alcohol and coffee consumption, although the small absolute numbers in some strata made some of the risk estimates uninterpretable.

Discussion

This Northern Italian case-control study found a strong association between cigarette smoking and acute myocardial infarction in young and middle aged women: the point estimates of about 5 for average and 10 for heavy smokers are among the highest reported. These estimates may have been inflated by the simple play of chance, but even their lower confidence limits, around 3 and 5 respectively, are still higher than commonly observed in several previous studies.[4 5 14–16]

Relative risks of the order of 5 to 7 among heavy smokers have already been reported in young and middle aged women from one case-control and one prospective American study.[6 10] Thus possibly, in relative terms, the association between smoking and ischaemic heart disease is stronger in low risk groups, ie, young and middle aged women. This line of reasoning could further explain the potentially elevated relative risk in this Italian population, since mortality from coronary heart disease in Italy is considerably lower than in North America and most Northern European countries.[17]

These estimates may also have been inflated by the study design, particularly by the use of a hospital control series, which is open to debate, mostly in relation to the analysis of lifestyle habits. We carefully excluded, however, all the diagnoses related or potentially related to smoking and checked the consistency of smoking prevalence across various diagnostic categories (trauma, other orthopaedic problems, surgery and other miscellaneous). Cases and controls came from comparable catchment areas, and the participation rate was practically complete. Likewise, adjustment for a large number of potential distorting factors did not modify the strength of the smoking related risks materially.

Table 2 *Distribution of 262 women with myocardial infarction and 519 controls according to smoking habits. Northern Italy, 1983–1988*

Cigarette smoking	Myocardial infarction		Controls		Relative risk (95% CI)	
	Number	%	Number	%	M–H*	MLR†
Never smokers	90	34·4	346	66·7	1‡	1‡
Ex-smokers	10	3·8	16	3·1	1·91 (0·85– 4·29)	1·48 (0·60– 3·64)
Current smokers, cigarettes/day						
1–14	57	21·8	91	17·5	2·61 (1·72– 3·98)	2·28 (1·41– 3·68)
15–24	65	24·8	48	9·3	6·70 (4·16–10·77)	5·93 (3·16– 9·27)
⩾25	40	15·3	18	3·5	12·77 (6·43–25·11)	11·01 (5·13–23·66)
χ^2_1 trend §					110·2‖	60·7‖

CI = confidence interval
* Mantel-Haenszel estimates adjusted for age.
† Estimates from multiple logistic regression; allowance was made for age, education, diabetes, hypertension, hyperlipidaemia, alcohol and coffee consumption, body mass index and oral contraceptive use.
‡ Reference category.
§ Ex-smokers excluded.
‖ $p < 0{\cdot}001$

Table 3 *Relative risk of acute myocardial infarction according to smoking habits in separate strata of selected covariates. Northern Italy, 1983–88*

Covariates	Relative risk estimates* for smoking habits				
	Never smokers	Ex-smokers	Current smokers (cigarettes/d)		
			<15	15–24	⩾25
Age (years)					
<50	1†	2·18	2·14	4·57	7·67
⩾50	1†	0·95	2·66	7·28	NE
Hypertension					
No	1†	1·82	2·43	4·28	10·25
Yes	1†	0·94	1·99	17·16	NE
Hyperlipidaemia					
No	1†	1·22	2·56	5·03	9·99
Yes	1†	1·49	1·13	13·61	NE
Alcohol consumption (drinks per day)					
0	1†	1·33	2·53	4·35	6·94
<3	1†	3·14	2·33	5·37	11·75
⩾3	1†	1·15	1·51	28·57	NE
Coffee consumption (cups per day)					
0–1	1†	1·76	1·82	8·96	NE
2–3	1†	1·10	2·02	9·04	6·52
⩾4	1†	2·34	5·06	4·93	16·53

* Estimates from multiple logistic regression; allowance was made for age, education, alcohol and coffee consumption, diabetes, hypertension, hyperlipidaemia, body mass index and oral contraceptive use.
† Reference category.
NE = not estimable.

Information bias might have distorted the risk estimates somewhat; for example there may be systematic underreporting of smoking among controls as noted in various population based analyses. As previously suggested,[6] information bias could explain at least part of the association with ex-smoking,

assuming even a limited fraction of recidivism.

It is clear, nonetheless, that cigarette smoking is by far the major (and, in principle, preventable) risk factor for myocardial infarction among this population of young and middle aged Northern Italian women, and that, in terms of individual relative risks, the association is likely to be particularly strong, becoming grossly increased in the presence of other risk factors.

In terms of population attributable risk,[18] it can be estimated that 48% of all myocardial infarctions in this data set are attributable to smoking, again confirming the importance of action on this risk factor even in populations at low baseline risk of cardiovascular events.

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