Risk of myocardial infarction in young female smokers

N R Dunn, B Faragher, M Thorogood, L de Caestecker, T M MacDonald, C McCollum, S Thomas, R Mann

Drug Safety Research Unit, Bursledon Hall, Southampton SO31 1AA, UK
N R Dunn
R Mann

Department of Organisational Health Psychology, Manchester School of Management, UMIST, PO Box 88, Manchester M60 1QD, UK
B Faragher

London School of Hygiene and Tropical Medicine, Keppel Street, London WC1 6FH, UK
M Thorogood

Department of Public Health, Greater Glasgow Health Board, Dalian House, 350 St Vincent Street, Glasgow G3 8YU, UK
L de Caestecker

Medicines Monitoring Unit, Department of Clinical Pharmacology and Therapeutics, Ninewells Hospital Medical School, Dundee DD1 9SY, UK
T M MacDonald

Department of Surgery, South Manchester University Hospital, Nell Lane, West Didsbury, Manchester M20 8LR, UK
C McCollum

Wolfson Unit of Clinical Pharmacology, University of Newcastle, Newcastle upon Tyne NE2 4HH, UK
S Thomas

Correspondence to:
Dr Dunn.
email: ndunn@dsru.u-net.com

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Abstract

***Objectives*—To determine the extent of risk of myocardial infarction from cigarette smoking in young women, and to examine the relation of smoking with other putative risk factors.**

***Design*—Community based case control study.**

***Setting*—England, Scotland, and Wales.**

***Patients*—Women (n = 448) between 16 and 44 years old with a diagnosis of incident myocardial infarction between 1 October 1993 and 16 October 1995. Controls (n = 1728) were age and general practice matched women without a diagnosis of myocardial infarction.**

***Outcomes measures*—Odds ratios for risk of myocardial infarction associated with smoking and other risk factors.**

***Results*—Odds ratios for myocardial infarction in smokers versus non-smokers showed a strong dose response, from 2.47 (95% confidence interval (CI) 1.12 to 5.45) in smokers of 1–5 cigarettes per day to 74.6 (95% CI 33.0 to 169) in smokers of ⩾ 40 cigarettes per day. There was no interaction of smoking with use of oral contraceptives, but there were additive risks with other clinical risk factors such as hypertension and diabetes. It is estimated that if all women aged 16–44 years were able to stop smoking, 400 cases of myocardial infarction per annum (of whom 112 would die) would be prevented.**

***Conclusions*—In young women the risk of myocardial infarction from smoking was considerable, and heavy smokers with other risk factors were especially at risk.**

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Keywords: myocardial infarction; smoking; risk factors

Coronary heart disease is the leading cause of death in men in the UK, and is also very important in women as a cause of death and disability.[1] Most coronary heart disease is found in the older age groups, but it also occurs in younger people, with a lower prevalence in women than men. The majority of epidemiological studies on coronary heart disease have concentrated on middle aged or older men, but it is possible that the importance of risk factors may vary between the sexes, especially among the young, in whom there are metabolic differences related to hormonal factors. Some studies have suggested that there is an interaction between the use of oral contraceptives and smoking.[2 3] In this paper, we present detailed data on smoking as a risk factor, and examine the relation between smoking and other potential risk factors in determining the overall risk for myocardial infarction in younger women.

Methods

The data were taken from the MICA (myocardial infarction causality) study, which was a community based case control study within England, Scotland, and Wales that examined the association between myocardial infarction and use of oral contraception.[4] Its main results have been published elsewhere.[5] Cases were women aged 16–44 years, who had a myocardial infarction between 1 October 1993 and 16 October 1995. Potential cases were identified from hospital inpatient statistics, or death certificates, using the World Health Organisation's International Classification of Diseases diagnostic codes 410 (version 9) or I21 (version 10). Each case diagnosis was validated by three cardiologists, blinded to exposure status, based on WHO criteria.[6] Controls were age, and general practice, matched women with no myocardial infarction. There were exclusion criteria for cases and controls based on factors that would make it unlikely that the woman would be taking an oral contraceptive—for example, past history of hysterectomy, cancer of the ovary or breast, or pregnancy at the time of the myocardial infarction. Data on exposure and risk factors were obtained by interview with the subject (or her proxy, when deceased), conducted by trained research nurses. These nurses were subjected to quality assessment by tape recording and accompanied interviews, and selected data were validated by checking against the subject's general practitioner (or family planning) records, although we have only used interview data in the analysis in this paper.

Statistical analysis was carried out on Stata 5 (Statacorp, Texas, USA), using unconditional logistic regression to compute odds ratios within the whole dataset, and unconditional logistic regression where subgroups were created.

Results

We identified 1224 potential cases from source data, of whom 882 (72%) were alive. There were 448 validated and interviewed cases of myocardial infarction, and 1728 controls included in the analysis. Table 1 shows the distribution of important variables between cases and controls. All the variables were associated with an increased risk of myocardial infarction, with the exception of use of oral contraceptives.

Table 1 Distribution and univariate odds ratios of selected variables between cases and controls

Variable	Positive recording (n (%) except where indicated)		Univariate odds ratio (95% CI)
	Cases	Controls	
Age (years) (median)	40.6	40.7	
(interquartile range)	(37.4–42.9)	(37.4–42.9)	
Past medical history			
Hypertension	81 (18.1)	88 (5.1)	4.23 (3.03 to 5.89)
Angina	22 (4.9)	10 (0.6)	9.27 (4.26 to 20.2)
Hyperlipidaemia	34 (7.6)	51 (3.0)	2.68 (1.70 to 4.23)
Diabetes mellitus	52 (11.6)	17 (1.0)	14.1 (7.82 to 25.5)
Smoking history			
Smoked in last year	360 (80.4)	520 (30.1)	9.99 (7.58 to 13.2)
Ever smoked cigarettes	394 (87.9)	899 (52.0)	6.88 (5.05 to 9.36)
Contraception			
Combined oral contraceptive*	40 (9.2)	180 (10.7)	0.79 (0.54 to 1.17)

*Use within three months before myocardial infarction.

Table 2 Conditional odds ratios for myocardial infarction by different levels of reported cigarette consumption, and for smoking overall

Cigarettes per day (n)	Cases n (%)	Controls n (%)	Odds ratio (95% CI)
0	88 (19.6)	1208 (70.0)	1
1–5	10 (2.2)	42 (2.4)	2.49 (1.13 to 5.52)
6–10	32 (7.1)	113 (6.5)	4.07 (2.54 to 6.52)
11–19	65 (14.5)	117 (6.8)	7.94 (5.26 to 11.99)
20–39	209 (46.7)	238 (13.8)	14.03 (10.12 to 19.47)
⩾ 40	44 (9.8)	9 (0.5)	74.64 (32.97 to 168.9)
All smokers	360 (80.4)	519 (30.1)	9.99 (7.59 to 13.2)

Table 3 Conditional odds ratios (95% confidence intervals) for myocardial infarction by combinations of reported cigarette consumption and number of clinical risk factors present

Clinical risk factors (n)*	Non-smokers	Cigarettes per day	
		1–19	⩾ 20
0	1	2.51 (1.07 to 5.91)	14.5 (7.22 to 29.3)
1	1.22 (0.62 to 2.4)	9.11 (4.66 to 17.8)	26.1 (14.0 to 48.7)
2	3.04 (1.53 to 6.06)	12.5 (5.68 to 27.4)	36.2 (18.9 to 69.5)
⩾ 3	6.74 (3.46 to 13.1)	35.8 (17.9 to 71.8)	66.8 (34.7 to 129)

*Hypertension, hyperlipidaemia, angina, or diabetes mellitus.

Table 4 Unconditional odds ratios for myocardial infarction in users of combined oral contraceptives, stratified by smoking habit, in those without clinical risk factors

Oral contraceptive	Non-smokers	Smokers	
		1–19 cigarettes/day	20+ cigarettes/day
Non-users	44/931 (4.5)	57/217 (20.8)	151/192 (44.0)
OR (95% CI)	1	1	1
Combined*	6/131 (4.4)	11/23 (32.4)	15/19 (44.1)
OR (95% CI)	0.97 (0.41 to 2.32)	1.82 (0.84 to 3.95)	1.0 (0.49 to 1.94)

Values are number of cases/controls (% cases/total).
*Containing ⩽ 35 μg ethinyloestradiol and progestogen.

Age was not considered as a risk factor because of the study design, in which we achieved very close age matching.

Table 2 shows the odds ratios for smoking stratified by the reported daily consumption of cigarettes. There was a significant increase in risk even at very low levels of smoking and a steady increase in risk with increasing cigarette consumption.

Table 3 shows the risk of myocardial infarction in women with combinations of clinical risk factors (angina, diabetes, hyperlipidaemia, or hypertension) and smoking. In each stratum of smoking, there was an additional risk with increasing risk factors. The interaction term between smoking and clinical risk factors was not significant. The effect of smoking was more pronounced than that of the clinical risk factors.

Table 4 shows the relation between smoking and use of combined oral contraceptives. Although the odds ratios for smokers of 1–19 cigarettes per day were higher than for smokers of ⩾ 20 cigarettes, the confidence intervals (CIs) were wide, and overlapped both the non-smokers and the heavy smokers. There were no significant interactions, although the numbers of women on these pills were small, and thus the results were, to an extent, inconclusive.

Discussion

These data showed the extent of the risk of myocardial infarction associated with smoking in this age group of women. This increased considerably with increasing numbers of cigarettes smoked per day. Also, there was a further increase in risk when smoking was combined with other cardiovascular risk factors, although there was no evidence of interaction with use of the contraceptive pill.

Although myocardial infarction is comparatively rare in this group of women, we have estimated the age standardised incidence of myocardial infarction among women aged 16–44 years as 4.78 cases per 100 000 woman years, with a maximum of 17.0 in the 40–44 year age group (MICA study, unpublished data, 1998). The case fatality rate was 28% in the MICA study.[5] We have also shown that the population attributable risk fraction for smoking in women aged 16–44 years was 73%.[5] If all smokers among women aged 16–44 years were able to stop, this would potentially prevent 3.5 cases per 100 000 women in a year, or 401 cases per annum (of which 112 cases would have been fatal), in England, Scotland, and Wales. Targeting advice on smoking to women with multiple risk factors would clearly have the greatest potential reward.

A potential weakness with this study is that we only interviewed 60% of the eligible cases (73% of live, 20% of proxy for deceased). This may have introduced a selection bias, if, for example, cases (or their proxy) who were heavy smokers were less likely to be interviewed. It is also possible that those controls who agreed to be interviewed were not typical of the general population, although table 2 shows that 30.1% of the controls were smokers, and this compares with national figures of 30% in the age group 35–49 years.[7] Another possible weakness is that we used interview data to assess smoking. It is probable that women underestimated their consumption of cigarettes, and this might be different between cases and controls, which would lead to misclassification bias.

Detailed risk estimates for women of this age were not easy to find in the published literature. Most studies had data for women of all age groups, in whom the relative risks for smokers versus non-smokers varied from twofold to fourfold. Prescott and colleagues found a relative risk of 2.82 (95% CI 1.45 to 5.46) for all women smokers, with the highest relative risk (6.8) found in women under age 55 years.[8] They found no interaction between smoking and other risk factors. Three recent studies found adjusted odds ratios for myocardial infarction in young female smokers versus

non-smokers compatible with the present study: 11.1 (95% CI 5.68 to 21.8),[2] 9.72 (95% CI 5.58 to 16.93),[9] and 8.31 (95% CI 4.74 to 14.57),[10] respectively. The WHO study found an interaction between oral contraceptive use and smoking: odds ratio of 87.0 (95% CI 29.8 to 254) for women with both variables.[2] Rosenberg and colleagues used data from a large case control study in the US, and found relative risks for heavy smokers (> 35 cigarettes per day) of 7.0 and 1.5 for light smokers (< 15 cigarettes per day).[3] The relative risks were considerably less than those found in the present study, but similar in magnitude to those reported by Mann and colleagues in young women.[11] This US study also found evidence of an interaction between oral contraceptive use and smoking. This interaction was also reported in the data from the study by the Royal College of General Practitioners (RCGP).[12] Comparisons between the present study and those of the RCGP[12] and Rosenberg and colleagues[3] are complicated by the fact that the predominant type of oral contraceptive used has changed over time, with oestrogen dose per pill falling and the introduction of products containing the progestogens desogestrel and gestodene, which had gained about 34% of the market in the UK by 1995.[13] The more recent WHO study[2] had few subjects taking oral contraceptives with desogestrel or gestodene (three cases and five controls, as compared to 20 cases and 61 controls in the present study), and 31 cases and 43 controls in Europe taking pills with > 50 μg of oestrogen, as opposed to only one case and two controls in the present study. Thus it is possible that the absence of an interaction between smoking and oral contraceptive use in the present study, as compared to the others, reflects the changes in formulation of the pill. Also, smoking habits (such as inhalation) and cigarette strengths have probably changed in recent years.

Finally, in view of the suggestion that women might be more sensitive to the harmful effects of smoking compared to men, possibly because of a relative oestrogen deficiency in smokers,[14] it is of interest to compare these results with odds ratios for smoking risk in men of a similar age group. However, comparable data on morbidity in the correct age group was not readily available, although Doll and Peto showed a relative risk of mortality from ischaemic heart disease of 14.8 in British male doctors aged < 45 years who smoked ⩾ 25 cigarettes per day compared to non-smokers.[15] This relative risk is comparable to the results in this paper. Morbidity data from the British regional heart study showed a relative risk of 3 (95% CI 1.8 to 4.8) for major coronary events in male smokers of 20 cigarettes per day compared with non-smokers,[16] but this cohort consisted of subjects aged 40–59 years, and age has a strong influence on the relative risk.

CONCLUSIONS

The odds ratio of myocardial infarction associated with smoking cigarettes in young women was large, and increased progressively with consumption. Although myocardial infarction was rare in this age group of women, in the UK about 400 cases per year could be prevented and about 112 lives saved (assuming a case fatality rate of 28%) if smoking ceased. Heavy smokers with other risk factors—for example, hypertension or diabetes mellitus—were particularly at risk of myocardial infarction.

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