Cigarette smoking and the risk of myocardial infarction, and acute non-infarct coronary events among Malaysian women

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Summary

In a prospective case-control study over a two-year period involving 1006 women, 264 women with acute myocardial infarction (AMI), 305 with non-infarct acute coronary syndromes (CAD) were compared with 437 women with no coronary heart disease (Controls), to determine the relationship between cigarette smoking and other risks factors with coronary heart disease.

A history of current cigarette smoking was strongly associated with the risk of coronary events for both AMI And CAD ($p < 0.001$). 23.9% of patients with acute coronary syndromes were current smokers, compared with only 12.8% among controls. Overall, women smokers had about a two-fold increase in risk for all coronary events. Younger women smokers (< 40 years) and those between 61–70 years had particularly higher risks (10.3 and 2.7 times respectively ($p < 0.01$, $p < 0.02$). A dose-response pattern of increased AMI risks (from 2.0 to 2.9 times) among women smokers was also found, corresponding to the number of cigarettes smoked per day ($p < 0.05$). Other significant coronary risk factors established were: postmenopausal status (OR 6.5), diabetes mellitus (OR 5.1), hypertension (OR 1.6), family history of premature coronary heart disease < 50 years (OR 1.3) and use of oral contraceptive pills (OR 1.4).

Our results thus emphasize that cigarette smoking is an important determinant of acute coronary events even among Malaysian women.

Key words: Smoking, coronary risk factors, coronary artery disease, acute myocardial infarction, women.

Introduction

Ever since Doll and Hill first published their report linking cigarette smoking to cardiovascular mortality in 1964,[1] it has become more and more irrefutably established that this unsavoury habit (and addiction) is causally related to coronary heart disease, particularly among men. Certainly it has been established beyond reasonable doubt that current male smokers carry

proportionately higher risks of coronary events (such as, fatal and nonfatal myocardial infarction and sudden cardiac death) depending on the degree of their addiction in a dose-response manner.[2-4]

Our earlier study had shown that cigarette smoking was the single most prevalent and independent risk factor in acute coronary events and acute myocardial infarction among Malaysian patients admitted to the coronary care unit in the General Hospital Kuala Lumpur.[5] This risk factor was most significant among men but not so in women. We suggested then, that our event rate was too small for statistical analysis to be meaningful. This low incidence of ischaemic heart disease among women was also cited as a major predicament for analysing most prospective studies of coronary heart disease.[6] The earlier reports from the Framingham study in fact found no significant correlation between cigarette smoking and coronary artery disease among women.[7] However, larger prospective studies by Rosenberg et al[8] and Willert et al[9] have established the considerably increased risks associated with this habit whether other risk factors were present or not. Both in terms of absolute and relative risks, cigarette smoking was positively associated with fatal or nonfatal coronary heart disease in a dose-response manner.[6,8-14]

Since our earlier report was inconclusive with regards the role played by cigarette smoking among female infarct patients in our study, we extended our preliminary study to two years so as to involve a study population of 1006 women admitted to the coronary care unit of General Hospital Kuala Lumpur. This report will show the significance of cigarette smoking among women in Malaysia with regards coronary heart disease. In particular we will establish that cigarette smoking among women carries a significant increased risk, even in the Malaysian population.

Methodology

From August 1986 to July 1988 inclusive, all female patients admitted to the coronary care unit of the General Hospital Kuala Lumpur, were interviewed for their smoking habits as well as for other known risk factors i.e. concomitant hypertension, diabetes mellitus, hyperlipidaemia, family history of premature ishaemic heart disease <50 years, menopausal status, and use of oral contraceptive pills. One important risk factor that was excluded from analysis was that for hyperlipidaemia. This was because most of the patients interviewed were ignorant of their preceding serum lipid status. Since our study was essentially based in the coronary care unit and coronary rehabilitation ward, where patients spend not more than a week (in general), fasting levels of lipids were not obtained at these periods of hospital stay. Besides, as discussed previously,[5] the reliability of performing such lipid estimates within the first two to three months post-infarction, remains controversial. This important statistic was thus excluded from this study and analysis. All these patients were then prospectively analysed to confirm their coronary status and risk factors using standardised protocol criteria and questionnaire as previously described.[5] A total of 1006 female patients were admitted for various complaints into the coronary care unit of General Hospital Kuala Lumpur during this two-year period.

Diagnostic criteria

Acute myocardial infarction was diagnosed when at least two of the following criteria were obtained:–[15] 1) Typical central ischaemic chest pain lasting more than 30 minutes; 2) Typical serial electrocardiographic changes of either pathological Q or non-Q evolution and ST-T changes (elevation of at least 0.1 mV) in two or more leads in a standard 12-lead ECG; 3) Serial cardiac

enzymes elevation (to more than twice the upper limit of normal) and subsequent return to normal, in at least two of the following i.e. creatine kinase, lactic dehydrogenase and aspartate transaminase. Two-hundred and sixty-four (264) had acute myocardial infarction by the above criteria.

Other acute coronary syndromes were included under 'coronary artery diseases' (CAD). These included unstable angina, acute coronary insufficiency, crescendo angina, prinzmetal angina, acute pulmonary oedema secondary to previous ischaemic heart disease. Unstable angina was defined as ischaemic chest pain of recent onset, of increasing progression in frequency and/or duration, angina at rest or unrelieved with sublingual nitroglycerin, where no diagnostic ECG changes or serial cardiac enzyme changes were found. Acute coronary insufficiency or crescendo or pre-infarction angina were variously defined by physicians admitting their patients into the coronary care unit. In general, the various terms were synonymous with unstable angina i.e. ischaemic chest pain of progressive duration, intensity and frequency not relieved by sublingual nitroglycerin, where minor ST-T changes were noted without pathological Q wave evolution or cardiac enzyme elevation. This group comprised 305 patients who qualified for inclusion in this category.

For controls, all other patients who were admitted to the coronary care unit during that period for other diseases than those described above, were included under the group Controls, which served as our reference category. These included various other diagnoses previously described.[5] The controls were thus chosen because they would be the most easily accessible and agreeable to participate fully with the interview regarding the various probable risk factors. In this control group, 437 patients were interviewed.

Patient characteristics: Of 1006 respondents surveyed, 264 had acute myocardial infarction, 305 had acute coronary syndromes, and 437 served as controls with no coronary heart disease. Malays formed 36.8% (370), Indians 22.9% (230), Chinese 35.9% (361) and Others 4.5% (45) of the total surveyed. (Others included Sikhs, Eurasians, Kadazans, Ibans, Orang Asli and few Caucasians). For those women who had coronary events, the ethnic distribution were as follows: Malays 31.8%, Indians 26.9%, Chinese 36.7% and Others 4.6%. For the controls, the distribution were as follows: Malays 43.2%, Indians 17.6%, Chinese 34.8% and Others 4.3% (see Figure 1). It should be noted here that this distribution pattern differed from the Malaysian population as a whole, in that the Indians and Others were somewhat overrepresented in this survey. However bearing in mind, the distribution among those who had coronary events, the higher prevalence rates among the Indians and Others appear to justify the acceptance of this control group. However there was a significant underrepresentation in the control group for Indians ($p < 0.05$) when compared with matched distribution characteristics of the test categories, AMI and CAD. This may be important when computing for odds ratios and their significance levels by ethnic group.

Statistical analyses: Prevalence rates for smokers versus non-smokers were computed for each test category, as well as their significance levels using the 'fourfold' contingency table and the X^2-square test for differences, with Yates' continuity correction.[16]

Odds ratios (as estimates of relative risks 'OR') of acute myocardial infarction (AMI) and acute coronary syndromes (CAD), together with their 95% confidence intervals (CI), were computed by using an unmatched approach as described by Cornfield[17] and Miettinen,[18] respectively. This was carried out for risk factors of cigarette smoking, hypertension, diabetes, menopausal

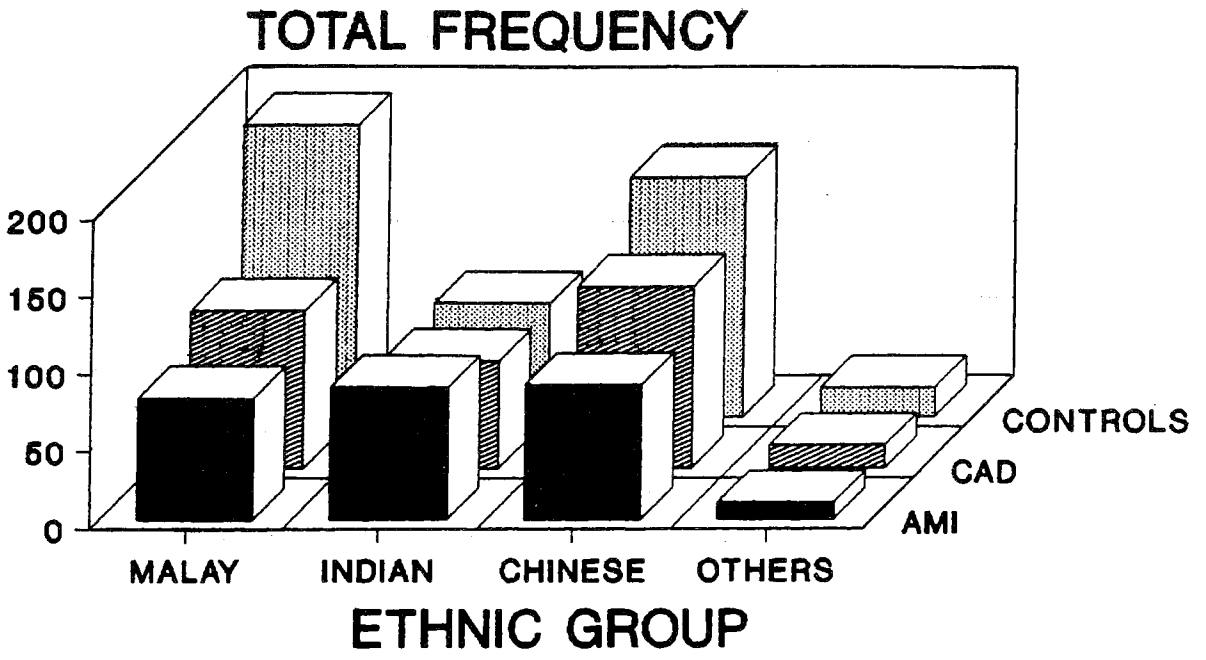

Fig. 1 Ethnic group characteristics among 1006 women admitted to the coronary care unit, General Hospital Kuala Lumpur. AMI: Acute Myocardial Infarction; CAD: acute non-infarct coronary syndromes; Controls: women patients admitted for other non-coronary diagnoses.

status, use of oral contraceptive pills. Age-group adjustments were also estimated to determine if cigarette smoking was a significant factor in the various age groups.

Results

Overall the prevalence rate for women smokers who did develop acute coronary syndromes was 23.9% which was statistically higher than the control group of only 12.8% ($p < 0.0001$; Table 1). For acute myocardial infarction (AMI) and non-infarct acute coronary events (CAD), the increased prevalence rate was also significant when compared to controls, ($p < 0.001$ for both).

Ethnic characteristics: Table II shows the relative risk estimates or odds ratios of smokers compared with nonsmokers in women with acute coronary events. In general, for acute myocardial infarction, the relative risk estimates (OR) ranged from 1.8 to 3.4 times for the various ethnic groups, with the strongest association being seen among the Chinese women where the OR was 3.4 (confidence interval 1.8–6.5, $p < 0.001$). Because the event rates for each group was small, for Malays, Indians and Others, the odds ratios did not reach significant levels. Myocardial infarction as a whole, however, was more common among women smokers by 2.4 times (confidence interval 1.6–3.6, $p < 0.001$). For acute coronary events, both Malay and Chinese women who were smokers were shown to have 2.6 and 2.3 times the risk compared to nonsmokers ($p < 0.005$, $p < 0.02$ respectively). Overall as a group women smokers had a 1.9-fold risk compared with nonsmokers ($p < 0.001$). For women of Indian and Others, the risks were not significantly greater, largely due to the smaller number of smokers in these groups.

Table I

Cigarette smoking among women patients with Acute Myocardial Infarction (AMI), Acute Non-Infarct Coronary Syndromes (CAD) and controls admitted to the Coronary Care Unit, General Hospital Kuala Lumpur from August 1986 to July 1988

	Patient Group				
Factor	**AMI**	**CAD**	**AMI+CAD**	**Controls**	**ALL**
Current smoker	69	67	136	56	192
(%)	(26.1)	(22.0)	(23.9)	(12.8)	(19.1)
Heavy smoker (>20 cigarettes/day)	12	14	26	8	34
(%)	(4.6)	(4.6)	(4.6)	(1.8)	(3.4)
Non-smoker	195	238	433	381	814
(%)	(73.9)	(78.0)	(76.1)	(87.2)	(80.9)
P value*	<0.001	<0.001	<0.0001	–*	–
Total	264	305	569	437	1006

*Degree of significance of cigarette smoking as a factor associated with acute myocardial infarction and/or acute coronary events when compared with the control group as a reference category (using the 'four-fold' table and the X^2 with Yates' correction).

Age and smoking characteristics: The average age for all women who had AMI and acute coronary events was 62 years (range 28 to 89 years). with the mode age group being the sixth decade, although those above 70 years were also sizeable (see Figure 2). Some 73.5% of women who had myocardial infarction, and 77% who had acute non-infarct coronary events, were above 55 years old. Conversely, only 26.5 and 23% of women patients with infarction and non-infarct events, respectively, were below the age of 55 years old. Furthermore, if women above 65 years were considered elderly, some 47.0% of all our infarction cases were elderly. For acute coronary syndromes, the elderly group was a similar 47.2%.

Table III shows the relative risk estimates for smoking versus nonsmoking women with coronary events, by age group and smoking category. For myocardial infarction, women smokers under 40 years and those between 61 to 70 years, had significantly elevated risks of 10.3 ($p < 0.01$) and 2.7 ($p < 0.02$) when compared with nonsmokers, respectively. However this increased risk was noted only in the (61 to 70 year) age group among those who developed non-infarct acute coronary events ($p < 0.01$).

Smoking category and acute myocardial infarction: Even when adjusted for age, the degree of cigarette use was found to significantly affect the risk for myocardial infarction in women

Table II

Relative risk estimate (OR) of smokers vs. nonsmokers by ethnic group, of women with acute coronary events admitted to the CCU, GHKL

	Malay	Chinese	Indian	Others	All
Controls (Non-Coronary Disease)					
Odds Ratio*	1.0	1.0	1.0	1.0	1.0
Acute Myocardial Infarction (AMI)					
Odds Ratio	1.8	3.4	2.5	–+	2.4
95% CI	[0.8–3.8]	[1.8–6.5]	[1.0–6.2]	–	[1.6–3.6]
P Value	ns	<0.001	0.07 ns	–	<0.001
Acute Non-Infarct Coronary Syndromes (CAD)					
Odds Ratio	2.6	2.3	0.6	1.3	1.9
95% CI	[1.4–4.9]	[1.2–4.3]	[0.2–4.0]	[0.5–3.1]	[1.3–2.9]
P Value	<0.005	<0.02	ns	ns	<0.001
All Acute Coronary Events (AMI + CAD)					
Odds Ratio	2.2	2.6	1.6	0.7	2.2
95% CI	[1.3–3.9]	[1.5–4.6]	[0.6–4.2]	[0.2–2.6]	[1.5–3.0]
P Value	<0.005	<0.001	ns	ns	<0.0001

*Odds Ratio as relative risk estimates, where controls = 1.0
+value not computed, as the case frequency was nil
95% CI: 95% confidence interval
ns: not significant where p value exceeds 5%

smokers, particularly in the younger age group (see Table III). Taking all age groups together, a dose-response relationship was dramatically demonstrated i.e. women who smoked (1–10), (11–20) and (>20) cigarettes daily had relative risk estimates of 2.0, 2.7 and 2.9 times that of nonsmokers (all $P < 0.05$). This dose-response relationship was especially notable among the younger women below 60 years. For example, although there were no smokers in the light category of (1–10 cigarettes/day) among the (<40) and (41–50) year age groups, heavier smokers (>20 cigarettes/day) had much higher risks when compared with moderate smokers (11–20 cigarettes/day) i.e. 16.0 versus 12.0 and 8.1 versus 2.7 times respectively. The corresponding risks for light (1–10 cigarettes/day), moderate (11–20 cigarettes/day) and heavy (>20 cigarettes/day) smokers for women in the (51 to 60) year age group, were 0.5, 1.3 and 2.8 times respectively. For those above 60 years of age, no consistent pattern was shown although the relative risk estimates or odds ratios were all significantly higher than controls ranging from 1.2 to 3.0 times. In fact among those between (61–70) years old, the relative risks appeared to decrease in a reverse manner from 3.0 to 2.5 to 2.1 times for light, moderate and heavy smokers respectively. This may imply that women in this age group may be influenced by other confounding factors which were more powerfully associated with acute myocardial infarction;

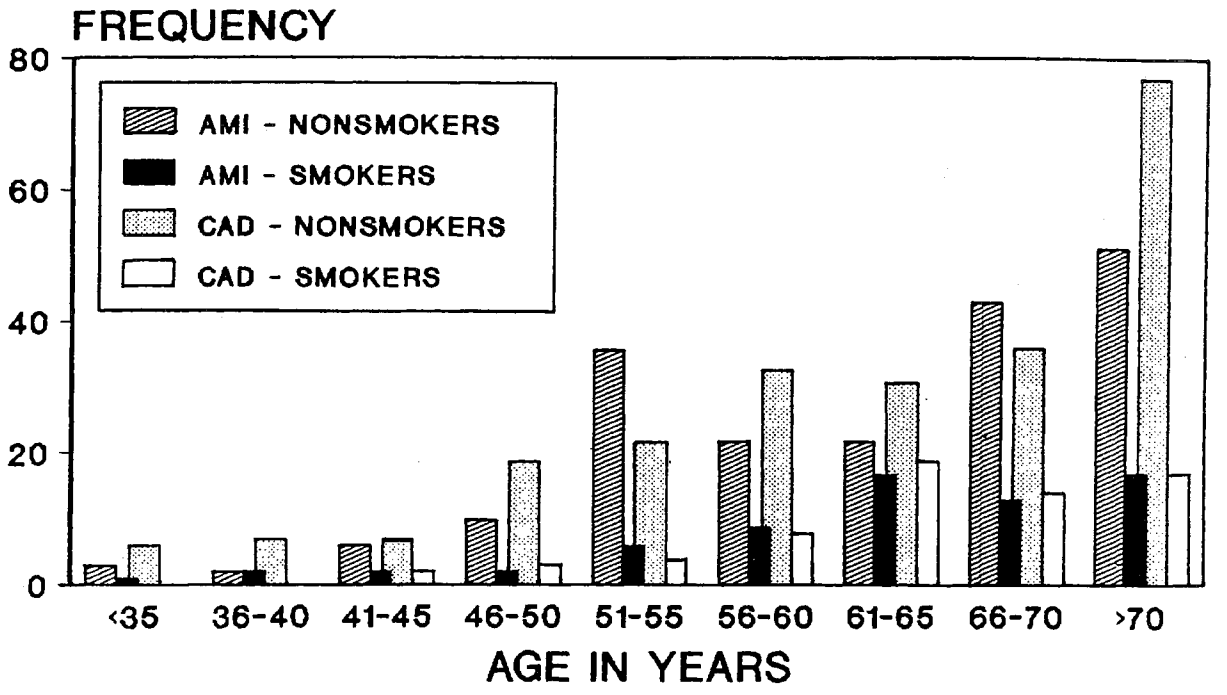

Fig. 2 Smoking and Age Characteristics among Women with acute coronary syndromes. (AMI: acute myocardial infarction and CAD: acute non-infarct coronary syndromes.)

Table III

Relative risk estimates of cigarette smoking in 264 women with Acute Myocardial Infarction and 437 controls, by age & smoking category

AGE (years)	Smoking Category (cigarettes/day)				
	Nonsmoker	1–10	11–20	21+	All
<40	1.0*	–+	12.0	16.0	10.3
41–50	1.0*	–+	2.7	8.1	2.0
51–60	1.0*	0.5	1.3	2.8	1.1
61–70	1.0*	3.0	2.5	2.1	2.7
>71	1.0*	1.4	1.6	1.2	1.5
All age groups	1.0*	2.0	2.7	2.9	2.4
95% CI	–	(1.1–3.6)	(1.6–4.8)	(1.1–7.7)	(1.6–3.6)
P value	–	<0.05	<0.001	<0.05	<0.0001

*Reference Category
95% CI: Confidence Interval at 95% significance
+Value not computed because case frequency was nil

although as a whole, this age group of women was at substantially higher risks of 2.7 times when compared with controls.

Other risk factors: Table IV shows that other known risk factors were also important in predisposing to myocardial infarction. For the group as a whole, women who sustained myocardial infarction had relative risk estimates of 1.28 for a positive family history of premature ischaemic heart disease < 50 years; 1.61 for a positive history of hypertension; 5.08 for diabetes mellitus; 6.49 for postmenopausal status and 1.42 for a past or current history of use of oral contraceptive pills. However, only those risk factors of hypertension, diabetes mellitus and postmenopausal status reached statistical significance ($p < 0.05$). Partly because our sample size was small especially with regards women smokers, when such risk factors were present, smoking appeared to attenuate the respective odds ratios. This had been reported before[8] and could be explained by the fact that relative risk estimates for smoking tend to be higher in subjects with low underlying predisposition to an infarction.[19,20]

Table IV

Relative risk estimates of some predisposing factors among 264 women with Acute Myocardial Infarction (smokers vs. nonsmokers) compared with 437 controls

Factor	Nonsmokers	Smokers	All
Family Hx IHD	#1.59 [0.30–3.57]	0.51 [0.07–3.55]	1.28 [0.59–2.77]
Hypertension	1.60 [1.11–2.32]*	1.55 [0.54–4.48]	1.61 [1.10–2.35]*
Diabetes	5.89 [3.33–10.40]+	4.30 [0.25–74.93]	5.08 [2.93–8.78]+
Postmenopause	7.87 [5.09–12.18]+	1.97 [0.68–5.66]	6.49 [4.43–9.51]+
OCP Use	1.85 [0.91–3.77]	0.39 [0.03–5.81]	1.42 [0.71–2.84]

FHx IHD: Family history of premature ischaemic heart disease <50 yr
#: Relative Risk Estimate [95% Confidence Interval]
OCP use: past or current use of oral contraceptive pills
*: $p < 0.02$; +: $p < 0.0001$

As Table V quite clearly shows, where there were no underlying predisposing factor, women smokers had significantly higher relative risk estimates when compared with nonsmokers. For example, where no family history was present, women smokers had odds ratio of 2.6 times that of nonsmokers. Similarly negative histories for hypertension, diabetes, previous use of oral contraception, and premenopause yielded higher risks of between 2.2 to 6.0 times for smokers compared with nonsmokers. Thus, although smoking was an important contributory factor to developing myocardial infarction, other risk factors were shown to be important as well as independent predisposing factors.

Discussion

In this study, we have established that even though fewer women smoked as a habit (when compared with men), those who do smoke carry a substantial risk of getting either an acute

Table V

Relative risk estimates of Acute Myocardial Infarction among women smokers compared with nonsmokers in the presence or absence of predisposing factors

Predisposing factor		Relative risk estimate [95% CI]
Family Hx IHD	Yes	0.8 (0.5 – 1.9) NS
	No	2.6 (1.8 – 3.9)*
Hypertension	Yes	2.3 (1.1 – 5.8)+
	No	2.4 (1.5 – 3.8)#
Diabetes Mellitus	Yes	2.0 (0.2 – 17.8) NS
	No	2.6 (1.7 – 3.9)*
Hypertension & Diabetes	Yes	0.8 (0.7 – 1.2) NS
	No	4.1 (2.4–6.9)*
Postmenopause	Yes	1.5 (1.1 – 2.4) NS
	No	6.0 (2.4 – 14.7) #
OCP Use @	Yes	0.6 (0.6 – 3.3) NS
	No	2.2 (1.6 – 3.1)*

95% CI: 95% confidence interval;
FHx IHD: Family history of premature ischaemic heart disease < 50 years;
@ OCP use: Use of oral contraceptive pills;
* $p < 0.00001$ + $p < 0.05$ # $p < 0.0001$
NS: not significant at the 95% confidence level

myocardial infarction or a non-infarct coronary event – a relative risk some 2.0 to 2.9 times that of nonsmoking women.

This conservative estimate of risk is comparable with those earlier reported by western researchers. Even when adjusted for age and other risk factors, cigarette smoking was an important and independent factor in predisposing to acute coronary events especially acute myocardial infarction. Willert et al,[9] in an exhaustive survey of some 119,000 female nurses, showed a most convincing dose-response relationship relating the degree of cigarette smoking to the age-adjusted risks of fatal coronary heart disease and nonfatal myocardial infarction. For those who smoked more than 15 cigarettes per day, the relative risk was 4.2 and higher; the highest risk estimate being 10.8 times for those women who smoked more than 45 cigarettes a day! (Table VI). Earlier, Rosenberg and others[8] had shown that the case-control method was able to show this trend of relative risk profiling for various predisposing factors including cigarette smoking. They too established that the odds ratios for women smokers ranged from 1.4 to 7.0 times that for nonsmokers, depending on the degree of smoking habit, the highest for those women who smoked more than 35 cigarettes a day (Table VI). In 1987, Italian workers reported very similar results detailing the relative risk estimates of women smokers (from northern Italy) compared with nonsmokers and their risk for myocardial infarction using a similar case-control

study.[6] Their results suggested that cigarette smoking among women below 55 years increased the likelihood of myocardial infarction some three to 12 times when compared with nonsmoking women!

Our data regarding younger women < 50 years old, showed significant and substantial increased relative risk estimates (some eight to 16 times greater for women smoking >20 cigarettes daily; Table III) similar to those previously described.[6,8,9]

Older women, particularly those in the postmenopausal age group are well-known to have an increased incidence of coronary events. Here the effect of cigarette smoking is somewhat attenuated but nonetheless still significant. A relative risk estimate of between 1.5 to 2.7 times for women above 61 years was found in our study. Our results approximated those estimated by the four-year follow-up study of the American Cancer Society where current smokers had relative risks for coronary heart disease mortality of 1.78, 3.00 and 1.60 for the age groups (>35 years), (35–64 years) and (>65 years) respectively.[21] Several other studies on women[13,14,20] had also reported lower risk estimates in later middle-aged or older subjects.

Why such a discrepancy occurs is unknown; but chance coincidences appear unlikely. The most plausible explanation might be related to the higher baseline incidence and mortality from coronary heart disease in these older age groups, where other stronger predisposing factors play a more definitive role in the causation of myocardial infarction. Certainly advanced age, and chronic disorders which accelerate the atherosclerotic process would be expected to manifest themselves sooner or later, as the sequelae of coronary heart disease. This would certainly be true for hypertension and diabetes mellitus, where years of persistent or intermittent suboptimal control would register their mark. In our study, hypertensive women had a relative risk estimate of 1.6 times for developing myocardial infarction compared with normotensive subjects. Smoking did not appreciably affect this result. Similarly, for diabetics, the risk estimate was even more obvious, i.e. five-fold increase when compared with nondiabetics. Cigarette smoking among diabetic women who had myocardial infarction was uncommon, thus the risk estimate was lower, 4.3 times (see Table IV). This lower rate for smokers might be due to physician discouragement of the habit during clinic visits among patients with chronic illness such as hypertension and diabetes.

What about the effect of menopause and hormones? In our study, this was the most significant factor common among women who developed myocardial infarction; 87.1% of our subjects were postmenopausal. The computed relative risk estimate was 6.5 that of premenopausal women. Among nonsmoking women, this risk approached eight times (7.87). Smoking appeared to be a less important determinant for myocardial infarction in this group although it still increased the risk by almost twice (1.97). However, cigarette smoking was clearly contributory to younger premenopausal women getting myocardial infarction, an estimated relative risk of 6.0! Certainly where the underlying predisposition to myocardial infarction is low, cigarette smoking assumes the role of a major causative factor, as suggested previously.[19,20]

This very strong association between postmenopause and coronary heart disease is somewhat at variance with some reports.[22-24] For example, Colditz et al[22] found no appreciable increase in the risk of coronary heart disease for women who had natural menopause and never taken replacement oestrogen, after adjusting for age and cigarette smoking.

However, the earlier Framingham study[25] showed that menopause elevated the coronary risk two-fold when compared with premenopausal women. This elevated risk has been challenged

Table VI

Relative risk estimates of women with Myocardial Infarction by smoking habits and age from various studies

Study (year)	Size of population	Relative Risk Estimates (Cigarettes per day)				
	1–14	1–14	15–24	25+	35+	45+
Rosenberg et al[8] (1985)	555 cases* 1864 controls	1.4	2.4	5.0	7.0	–
	< 40 years	1.0	2.9	10	13	–
	40–50 years	1.5	2.4	4.3	6.6	
Willert et al[9] (1987)	307 cases+ 119097 controls	2.1	4.2	5.4	7.1	10.8
	< 40 years	–	4.3	3.5	–	–
	40–49 years	1.6	3.6	7.0	–	–
	50–59 years	2.4	4.1	5.3	–	–
La Vecchia et al[6] (1987)	168 cases# 251 controls	3.5	8.9	12.4	–	–
Quek et al (1989)	264 cases @ 437 controls	2.0	2.7	2.9	–	–
	< 40 years	–	12.0	16.0	–	–
	41–50 years	–	2.7	8.1	–	–
	51–60 years	0.5	1.3	2.8	–	–

*Fatal and nonfatal myocardial infarctions in women < 50 years old
+Fatal and nonfatal myocardial infarctions in women between 30–55 years
#Fatal and nonfatal myocardial infarctions in women < 55 years old
@Fatal and nonfatal infarctions in women of all age groups (present study); number of cigarettes smoked daily (1–10), (11–20) and (>20) respectively

by the Nurses' Health Study group[22] for its ambiguous definitions of coronary heart disease. This issue remains controversial;[10] although it is noteworthy that this same Framingham study failed to show any association between smoking and coronary heart disease in women.[25]

Nevertheless, women in the premenopausal years appear to be protected from coronary events. Demographic and behavioural risk factor analyses could not adequately account for the sex difference in coronary artery disease incidence.[26] Possibly, female hormonal influences exert some protective mechanism by elevating blood levels of HDL-cholesterol, despite higher absolute levels of LDL- and total cholesterol.[27] Thus during the menopause, coronary protection may begin to be lost. This issue is further complicated by the various changes of risk factors occurring around the menopause, such as haemoglobin and cholesterol levels. Furthermore, cigarette

smoking is also associated with a tendency to earlier menopause.[28,29] In our study, however, most (74.4%) of our postmenopausal women were nonsmokers, thus this could not have contributed to the elevated risk in this group of nonsmoking women.

Age itself is a confounding factor. In our study population, some three-fourths of all coronary patients were above 55 years of age. Adjusting for age, greatly reduced the power of the postmenopause as a crucial factor in increasing coronary risk. One statistically acceptable method to demonstrate correlation of coronary heart disease with age, is to invoke the power-law function of age i.e. a double logarithmic plot.[30] Our study showed a straight-line relationship, which means that the ageing process increases coronary risk exponentially.

Hyperlipidaemia as a causative factor of coronary heart disease was not examined in this study because of logistic reasons, earlier described. We are thus unable to comment on this renowned hazard.

The ethnic group distribution of coronary heart disease, once again, demonstrate an overrepresentation among the Indian and Others communities. Although the proportion of Peninsular Malaysian Indians is only about 10%, Indian women accounted for some 26.9% of the women who had coronary events. In our earlier study Indians accounted for some 30.1% of infarction cases.[5] In this study however, cigarette smoking did not appear to be an important or significant factor in predisposing Indian women to getting coronary heart disease, although among Indian men, this was so.[5] Other risk factors have to be analysed separately to determine if they were different from the other races in predisposing to coronary heart disease. Other minority races e.g. Sikhs and Eurasians need further scrutiny also as they were overrepresented here as well. Their small numbers, however, make meaningful analysis difficult.

In concluding, we believe we have established the pre-eminent role of cigarette smoking as an important and independent coronary risk factor, particularly in the younger women. For myocardial infarction, cigarette smoking increased the risk some 2.0 to 2.9 times in a dose-response manner. We have also confirmed that other well-known risk factors such as hypertension, diabetes mellitus, age, use of the contraceptive pill and the postmenopausal status are important determinants of coronary heart disease in women. Where there is a low coronary predisposition, cigarette smoking assumed the major role as a contributory or even a causative factor – increasing the risks estimates some 2.2 to 6.0 times. The role of hypercholesterolaemia was not examined in this study.

Although our study sample may not be wholly representative of the general population of Malaysia, the results of our study should reflect sufficiently accurately, the coronary status of a hospital-based and urban population. For women, because of their low tendency for developing such events, previous studies have somewhat neglected and underestimated them as a group. We have now shown that at a lower level, their risk factor profiles resemble those for men. Whilst factors such as age, menopause, strong family history of premature ischaemic heart disease or ethnic origin are largely immutable, others such as hypertension, diabetes, hypercholesterolaemia and cigarette smoking are modifiable. Better control and awareness of these factors can and has been shown to decrease morbidity and mortality from coronary heart disease and its sequelae.

Cigarette smoking, in particular should be strongly discouraged, as it has been shown that even in Malaysian women, this habituation does increase coronary events by a factor of at least two-fold. Malaysian women who smoke remains a sizeable minority, our control group suggests

that this is about 13%. We should make greater efforts to prevent this public health scourge from making further inroads into the female realm. In Western populations, the proportion of women who are smokers are rising and in some even overtaking that of men. This unhealthy trend should not be allowed to succeed in Malaysia. For those who have already sustained a coronary event, quitting the habit has been shown to dramatically reduce the chance for a second event – their risk approaches that for a nonsmoker. Hence, physicians should always encourage and persuade their patients to quit smoking, NOW!

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References

1. Doll R, Hill AB: Mortality in relation to smoking: Ten years' observations on male British doctors. Br Med J 1964; 1: 1399–1410; 1460–7.
2. U.S. Department of Health and Human Services: The health consequences of smoking: cardiovascular disease. A report of the Surgeon General. U.S. Department of Healt and Human Services, Public Health Service, Office on Smoking and Health. Rockville, Md., 1983. DHHS Publication No. (PHS) 84–50204.
3. The Pooling Project Research Group. Relationship of blood pressure, serum cholesterol, smoking habit, relative weight and ECG abnormalities to incidence of major coronary events: final report of the Pooling Project. J Chronic Dis 1978; 31: 201–306.
4. Kannel WB, Castelli WP: Significance of nicotine, carbon monoxide and other smoke components in the development of cardiovascular disease. In Wynder EL, Hoffman D, Gori GB (eds.): Proceedings of the Third World Conference on Smoking and Health, 1975; DHEW Pub. No. (NIH 76–1221) 1976: 369–81.
5. Quek DKL, Lim LY, Yeo AM, Ong SBL. Smoking profile and coronary risk among patients admitted to the coronary care unit, General Hospital Kuala Lumpur. Med J Malaysia 1987; 42 (3): 156–65.
6. La Vecchia C, Franceschi S, Decarli A, Pampallona S, Tognoni G. Risk Factors for myocardial infarction in young women. Am J Epidemiol 1987; 125: 832–43.
7. Dawber TR. The Framingham Study: the epidemiology of atherosclerotic disease. Cambridge, Mass.: Harvard University Press, 1980.
8. Rosenberg L, Kaufman DW, Helmrich SP, Miller DR, Stolley PD, Shapiro S. Myocardial infarction and cigarette smoking in women younger than 50 years of age. JAMA 1985; 253: 2965–9.
9. Willert WC, Green A, Stampfer MJ et al. Relative and absolute risks of coronary heart disease among women who smoke cigarettes. N Engl J Med 1987; 317: 1303–9.
10. Johansson S, Vedin A, Wilhelmsson C. Myocardial infarction in women. Epidemiol Rev 1983: 5: 67–95.
11. Mann JI, Doll R, Thorogood M, Vessey MP, Waters WE. Risk factors for myocardial infarction in young women. Br J Prev Soc Med 1976; 30: 94–100.
12. Spain DM, Siegel H, Bradess VA. Women smokers and sudden death: the relationship of cigarette smoking to coronary disease. JAMA 1973; 224: 1005–7.
13. Doll R, Gray R, Hafner B, Peto R. Mortality in relation to smoking: 22 years' observations on female British doctors. Br Med J 1980; 280: 967–71.
14. Bush TL, Comstock GW. Smoking and cardiovascular mortality in women. Am J Epidemiol 1983; 118: 480–8.

15. Rose GA, Blackburn H. Cardiovascular survey methods. 2nd Ed. Geneva: World Health Organisation, 1982.

16. Yates F. Contigency Tables involving small numbers and the X^2 test. (Suppl.) J R Stat Soc 1934; 1: 217–35.

17. Cornfield J. A Method of estimating comparative rates from clinical data. Applications to cancer of the lung, breast and cervix. J Natl Cancer Inst 1951; 11: 1269–75.

18. Miettinen O. Estimability and estimation in case-referent studies. Am J Epidemiol 1976; 103: 226–35.

19. Slone D, Shapiro S, Rosenberg L, ét al. Relation of cigarette smoking to myocardial infarction in young women. N Engl J Med 1978; 298 : 1273–6.

20. Rosenburg L, Shapiro S, Kaufmann DW, et al. Cigarette smoking in relation to the risk of myocardial infarction in young women: Modifying influence of age and predisposing factors. Int J Epidemiol 1980; 9: 57–63.

21. U.S. Department of Health and Human Services: Reducing thesHealth Consequences of Smoking: 25 years of progress. A report of the Surgeon General. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health. Rockville, Md., 1989. DHHS Publication No. (CDC) 89–8411; p151.

22. Colditz GA, Willert WC, Stampfer MJ, Rosner B, Speizer FE, Hennekens CH. Menopause and the risk of coronary heart disease in women. N Engl J Med 1987; 316: 1105–10.

23. Wilhelmsen L, Bengtsson C, Elmfeldt D, et al. Multiple risk prediction of myocardial infarction in women as compared with men. Br Heart J 1977; 39: 1179–85.

24. Blanc J-J, Boschat J, Morin J-F, Clavier J, Penther P. Menopause and myocardial infarction. Am J Obstet Gynecol 1977; 127: 353–5.

25. Gordon T, Kannel WB, Hjortland MC, McNamara PM. Menopause and coronary heart disease: The Framingham Study. Ann Intern Med 1978; 89: 157–61.

26. Wingard DL, Suarez L, Barrett-Connor E. The sex differential in mortality from all causes and ischemic heart disease. Am J Epidemiol 1983; 117 : 165–72.

27. Gotto AM Jr, Farmer JA. Risk factors for coronary artery disease. In: Braunwald E (ed.) Heart Disease – A Textbook of Cardiovascular Medicine. 3rd Edition. WB Saunders Co. Philadelphia. 1988; Chapter 36: 1153–90.

28. Jick H, Porter J, Morrison AS. Relation between smoking and age of natural menopause. Lancet 1977; (i): 1354–5.

29. Lindquist O, Bengtsson C. Menopausal age in relation to smking. Acta Med Scand 1979; 205: 73–7.

30. Evans JG. Epidemiology. In: Martin A, Camm AJ (eds) Heart Disease in the Elderly. John Wiley & Sons Ltd. Pitman Press, Bath, Avon. Great Britain. 1984; chapter 2: 9–36.