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Risk factors and incident coronary heart disease in Chinese, Malay and Asian Indian males: the Singapore Cardiovascular Cohort Study

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Objective	This prospective study in Singapore investigated the relationships of established coronary risk factors with incident coronary heart disease (CHD) for Chinese, Malay, and Asian Indian males.
Subjects	A cohort (consisting of 2879 males without diagnosed CHD) derived from three previous cross-sectional surveys.
Methods	Individual baseline data were linked to registry databases to obtain the first event of CHD. Hazard ratios (HR) or relative risks for risk factors were calculated using Cox's proportional hazards model with adjustment for age and ethnic group and adjustment for age, ethnic group and all other risk factors (overall adjusted).
Results	There were 24 986 person-years of follow-up. The overall adjusted HR with 95% CI are presented here. Asian Indians were at greatest risk of CHD, compared to Chinese (3.0; 2.0–4.8) and Malays (3.4; 1.9–3.3). Individuals with hypertension (2.4; 1.6–2.7) or diabetes (1.7; 1.1–2.7) showed a higher risk of CHD. High low density lipoprotein cholesterol (LDL-C) (1.5; 1.0–2.1), high fasting triglyceride (1.5; 0.9–2.6) and low high density lipoprotein cholesterol (HDL-C) (1.3; 0.9–2.0) showed a lesser but still increased risk. Alcohol intake was protective with non-drinkers having an increased risk of CHD (1.8; 1.0–3.3). Obesity (body mass index ⩾30) showed an increased risk (1.8; 0.6–5.4). An increased risk of CHD was found in cigarette smokers of ⩾20 pack years (1.5; 0.9–2.5) but not with lesser amounts.
Conclusions	The increased susceptibility of Asian Indian males to CHD has been confirmed in a longitudinal study. All of the examined established risk factors for CHD were found to play important but varying roles in the ethnic groups in Singapore.

Keywords	Coronary heart disease, risk factors, prospective, Chinese, Malays, Asian Indians
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Coronary heart disease (CHD) is a leading cause of morbidity and mortality in many countries world-wide and is estimated that it will be the single largest cause of disease burden globally by the year 2020.[1]

Despite the search for novel risk factors for CHD, established risk factors still play a major role.[2] These are the dyslipidaemias (high low density lipoprotein cholesterol [LDL-C], low high density lipoprotein cholesterol [HDL-C] and high fasting triglyceride [TG]), hypertension, cigarette smoking, diabetes, obesity and physical inactivity. These have been shown to be associated with an increased risk in major prospective epidemiological studies.[3–7] However, these studies were conducted predominantly on Caucasian and migrant Asian populations. Recently interest has also been focused on populations in Asia with regard to the impact and role of established risk factors of CHD in times of economic development and westernization.[8–12]

Singapore is an island nation consisting of 3.9 million people comprising 76% Chinese, 14% Malays, 7% Asian Indians and 3% other ethnic groups. Over the past few decades it

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has undergone rapid socioeconomic development and cardiovascular diseases and cancer are the major causes of morbidity and mortality. It is thus important to assess the role of the established risk factors for CHD in this population. This article describes a prospective cohort study that identifies associations of the established risk factors with incident CHD for Singapore's Asian population.

Subjects and Methods

Full details of amalgamation, standardization of baseline information, data linkage with morbidity and mortality data-bases (using an individual identity number), and outcome measures have been fully described[13] and will only be briefly described here.

Sample

The Singapore Cardiovascular Cohort Study is composed of participants from three previous cross-sectional surveys. Detailed methodologies of these three surveys have been described: the Thyroid and Heart Study 1982–1984,[14] the National Health Survey 1992,[15] and the National University of Singapore (NUS) Heart Study 1993–1995.[16]

A total of 5920 people, of which 2920 were male, comprised the cohort. After excluding 41 males who had pre-existing diagnosed CHD, 2879 males were followed-up. Females are not presented at this time because the number of events is small.

Risk factors

Risk factors studied were age, ethnicity (Chinese, Malay and Asian Indian), lipids, body mass index (BMI), diabetes, hypertension, cigarette smoking and alcohol intake.

For serum lipids, categories for high low density lipoprotein cholesterol (LDL-C) $\geqslant$4.14 mmol/l, low high density lipoprotein cholesterol (HDL-C) $<$0.90 mmol/l and high fasting triglyceride (TG) $\geqslant$2.82 mmol/l follow the NCEP ATP II guidelines.[17] Body mass index was categorized into four groups ($<$18.5, 18.5–24.9. 25.0–29.9 and $\geqslant$30.0).[18]

Diabetics were people who were previously diagnosed and on treatment or with plasma glucose $\geqslant$11.1 mmol/l, 2 hours after a 75-g oral glucose tolerance test.[19] Individuals were classified as hypertensive if they were previously diagnosed and currently on medication or had a systolic blood pressure of $\geqslant$140 mmHg or diastolic blood pressure of $\geqslant$90 mmHg.[20] Smokers were grouped into non-smokers, current smokers $<$20 pack years, current smokers $\geqslant$20 pack years and former smokers. Alcohol intake was divided into drinkers (irrespective of amount) and non-drinkers (including teetotallers and occasional drinkers).

Outcome measures

Outcomes were obtained by linking individual records (using unique national registry identity card numbers: NRIC) to three national registers. These are: (i) the Registry of Births and Deaths, (ii) the Central Claims Processing System and its predecessor the Hospital Inpatient Discharge System, which are databases that capture inpatient discharge information from all hospitals in Singapore, both government and private and (iii) the Singapore Myocardial Infarct Registry, a population-based registry with comprehensive coverage of acute myocardial infarction (AMI) occurring in people in Singapore.

All obtained outcome measures were in coded form using the Ninth Revision of the International Classification of Diseases (ICD-9). An event was based on occurrence of AMI or ischaemic heart disease (IHD) (ICD-9 410–414) recorded in the above registries. The first event of IHD (same as CHD) was used for analysis. Subjects were censored at 1 March 1999 or their date of event occurrence or death, whichever occurred first.

Data analysis

Analyses were performed using SPSS X. The person years and number of CHD events were calculated for each of the risk factor categories. Hazard ratios (HR) or relative risks with 95% CI and *P*-values for each of the risk factors were calculated using Cox's proportional hazards regression; both adjusted only for age and ethnic group, and adjusted for age, ethnic group and all other risk factors (overall adjusted). Adjustment for each factor was made using LDL-C, HDL-C, TG and BMI as continuous variables and ethnic group, diabetes, hypertension, smoking and alcohol intake as categorical variables.

Results

Table 1 gives details of the person years and number of individuals who did or did not develop CHD by risk factor category at baseline. There was a total of 24 986 person-years of follow-up, the average length of follow-up being 8.9 years. During the follow-up period 125 males subsequently developed CHD whilst 2713 did not.

Table 2 shows HR adjusted for age and ethnic group, and adjusted for age, ethnic group and all other risk factors (overall). Ethnicity was found to play a major role, with Indian males having a greater risk than both Chinese and Malay males. They were found to have three times the risk of CHD compared to Chinese (age-adjusted HR = 3.0, 95% CI : 2.0–4.5). This increased risk was not affected by further adjustment of other risk factors (overall-adjusted HR = 3.1, 95% CI : 2.0–4.8). There was no important difference between Malays and Chinese. Compared to Malay males, Indian males were found to be at increased risk with age-adjusted and overall-adjusted HR of 2.4 (95% CI : 1.4–4.1) and 3.4 (95% CI : 1.8–3.3) respectively.

Males with high LDL-C showed moderately increased risk compared to males with normal LDL-C with an age- and ethnic group adjusted HR of 1.3 (95% CI : 0.9–1.8). There was little change after overall adjustment (HR = 1.5, 95% CI : 1.0–2.1). However people with low HDL-C (HR = 1.9, 95% CI : 1.3–2.7) or high TG (HR = 2.3, 95% CI : 1.4–3.6), compared to those with normal levels showed a greater age- and ethnic group adjusted risk. Unlike LDL-C, the risk is moderately reduced for both with HR of 1.3 (95% CI : 0.9–2.0) and HR of 1.5 (95% CI : 0.9–2.0) respectively after overall adjustment.

The HR for BMI adjusted for age and ethnic group was found to increase with increasing categories of BMI. Compared to males with a BMI of $<$18.5, those with BMI of 18.5–24.9, 25.0–29.9 and $\geqslant$30 had HR of 1.7 (95% CI : 0.7–4.4), HR of 2.6 (95% CI : 1.0–6.6) and HR of 5.7 (95% CI : 2.0–16.1), indicating a linear relationship. Diabetics compared to non-diabetics had a 2.5 times greater risk of CHD (age- and ethnic group adjusted HR = 2.5, 95% CI : 1.7–3.6). Hypertensives compared to normotensive people were found to be at markedly increased risk of CHD with an age- and ethnic group adjusted

Table 1 Person-years of follow-up and number of males with and without incident coronary heart disease (CHD) for each risk factor

Factor	Person years	CHD (Total =125) No. (%)	No CHD (Total = 2713) No. (%)
Ethnic group			
Chinese	16 282.8	64 (51.2)	1718 (63.3)
Malay	4945.3	21 (16.8)	554 (20.4)
Indian	3757.7	40 (32.0)	441 (16.3)
LDL-C[a] (mmol/l)			
<4.14	15 175.5	51 (45.1)	1775 (67.1)
⩾4.14	9191.1	62 (54.9)	869 (32.9)
HDL-C[b] (mmol/l)			
⩾0.90	13 733.3	50 (42.4)	1767 (65.5)
<0.90	10 274.3	68 (57.6)	930 (34.5)
TG[c] (mmol/l)			
<2.82	22 882.9	93 (79.5)	2460 (91.1)
⩾2.82	1863.5	24 (20.5)	240 (8.9)
Body mass index			
<18.5	2561.3	6 (4.8)	263 (9.7)
18.5–24.9	15 921.0	62 (49.6)	1722 (63.5)
25.0–29.9	5222.0	43 (34.7)	610 (22.5)
⩾30	985.5	13 (10.4)	113 (4.2)
Diabetes[d]			
No	23 120.3	88 (70.4)	2493 (91.9)
Yes	1865.5	37 (29.6)	220 (8.1)
Hypertension[e]			
No	20 729.0	51 (40.8)	2232 (82.3)
Yes	4256.8	74 (59.2)	481 (17.7)
Smoking			
Non-smoker	12 972.0	52 (41.6)	1406 (51.8)
Current smoker (pack years) <20.0	6347.9	13 (10.4)	682 (25.1)
⩾20.0	3016.5	34 (27.2)	311 (11.5)
Former smoker	2649.4	26 (20.8)	314 (11.6)
Alcohol			
Drinker	3971.0	15 (12.0)	454 (16.7)
Non-drinker	21 014.8	110 (88.0)	2259 (83.3)

[a] Low density lipoprotein cholesterol.

[b] High density lipoprotein cholesterol.

[c] Triglycerides.

[d] Diabetes: previous and newly diagnosed diabetics.

[e] Hypertension: previously diagnosed hypertension or systolic blood pressure ⩾140 mmHg or diastolic blood pressure ⩾90 mmHg.

HR of 3.4 (95% CI : 2.3–5.1). However for individuals who were diabetic or had increased BMI, the high risks were markedly reduced after overall adjustment, with HR of 1.7 (95% CI : 1.1–2.7) for diabetes and HR of 1.0 (95% CI : 0.4–2.6), HR of 1.0 (95% CI : 0.4–2.8) and HR of 1.8 (95% CI : 0.6–5.4) for BMI groups of 18.5–24.6, 25.0–29.9 and ⩾30 respectively. Although this effect was also observed for hypertension, the HR still remained markedly high (overall-adjusted HR = 2.4, 95% CI : 1.6–2.7).

Current smokers ⩾20 pack years were found to be at moderately increased risk of CHD compared to non-smokers with an overall-adjusted HR of 1.5 (95% CI : 0.9–2.5). However, current smokers who smoked <20 pack years were not found to have an increased risk of CHD (HR = 0.9, 95% CI : 0.5–2.0). Former smokers were found to have a slightly increased risk of CHD although this was not statistically significant with an overall adjusted HR of 1.2 (95% CI : 0.7–2.1). Drinking alcohol was found to be protective with non-drinkers having 1.8 times increased risk of CHD compared to drinkers (overall-adjusted HR = 1.8, 95% CI : 1.0–3.3).

Discussion

This follow-up study in Singapore has examined the role of ethnicity and established risk factors for CHD in Asian men. It confirms previous mortality statistics and cross-sectional surveys in Singapore and other countries that Indians have an increased risk of CHD compared to other ethnic groups.[21–26]

Importantly, this study has shown relatively different contributions to the risk of CHD from the three major established risk factors of hypertension, high LDL-C and smoking, suggesting possible differences in the response of Asians compared to Caucasians. In Asians, hypertension seems to be the most important factor. The high HR may be attributed to healthcare factors including underdiagnosis or inadequate control of previously diagnosed hypertension. However, studies in Singapore[14,27] have shown that the proportions of previously undiagnosed hypertensive people or those currently on treatment are comparable to Western countries.[28] Hence hypertension may indeed have a greater relative effect on CHD in Asians compared to Caucasians. This is further substantiated with evidence that hypertension has been documented in Asian prospective studies to markedly increase the risk of stroke.[8] However, further comparisons between Asians and Caucasians within the same prospective studies are needed to confirm this.

High LDL-C has been found in this study to be of relatively less importance in Asians compared to hypertension as a risk factor for CHD. It also has slightly less effect on CHD when compared to studies in Caucasian populations.[4,29] Rapid economic development has changed Singapore from a developing nation to a developed one within the last three decades. Similarly, increased adoption of a Western lifestyle, in particular an increase in saturated fat in the diet is likely to have occurred during this time. However, it may not have been of sufficient duration to show the full effect of high LDL-C as a risk factor for CHD. Further follow-up of this risk factor may show LDL-C to have a greater role. Low HDL-C and high fasting TG have been found to have comparable risks of developing CHD as in other studies.[4,6,29]

Smoking was the only risk factor not found to contribute greatly to the development of CHD. An increased risk after overall adjustment was found for smokers of ⩾20 pack years with no significantly increased risk for smokers of <20 pack years or former smokers. Other prospective studies in Asians have found that smoking seems to have an increased but lesser impact on CHD than in Caucasians.[9,10,11] It may be that smoking has been of shorter duration in Asians and the full impact has not yet been felt. The findings of an ongoing Asia Pacific collaborative study assessing risk factors including smoking and CHD may help to clarify the situation.[12]

Diabetes is also an important risk factor for CHD. Of note, 29.6% of individuals in this study who developed CHD were

Table 2 Hazard ratios (HR) for coronary heart disease (CHD) by risk factors adjusted for age and ethnic group only and adjusted for age, ethnic group and other risk factors for males

Factor	HR (95% CI)[a]	*P*-value	HR (95% CI)[b]	*P*-value
Ethnic Group				
Chinese	1		1	
Malay	1.2 (0.7–2.0)	0.405	0.9 (0.5–1.5)	0.572
Indian	3.0 (2.0–4.5)	0.001	3.1 (2.0–4.8)	<0.001
LDL-C[c] (mmol/l)				
<4.14	1		1	
⩾4.14	1.3 (0.9–1.8)	0.235	1.5 (1.0–2.1)	0.057
HDL-C[d] (mmol/l)				
⩾0.90	1		1	
<0.90	1.9 (1.3–2.7)	0.001	1.3 (0.9–2.0)	0.160
TG[e] (mmol/l)				
<2.82	1		1	
⩾2.82	2.3 (1.4–3.6)	<0.001	1.5 (0.9–2.6)	0.110
Body mass index				
<18.5	1		1	
18.5–24.9	1.7 (0.7–4.4)	0.231	1.0 (0.4–2.6)	0.988
25.0–29.9	2.6 (1.0–6.6)	0.044	1.0 (0.4–2.8)	0.919
⩾30	5.7 (2.0–16.1)	<0.001	1.8 (0.6–5.4)	0.306
Diabetes[f]				
No	1		1	
Yes	2.5 (1.7–3.6)	<0.001	1.7 (1.1–2.7)	0.013
Hypertension[g]				
No	1		1	
Yes	3.4 (2.3–5.1)	<0.001	2.4 (1.6–2.7)	<0.001
Smoking				
Non-smoker	1		1	
Current smoker (pack years) <20.0	0.7 (0.4–1.3)	0.266	0.9 (0.5–2.0)	0.691
>20.0	1.3 (0.8–1.3)	0.231	1.5 (0.9–2.5)	0.091
Former smoker	1.3 (0.8–2.2)	0.259	1.2 (0.7–2.1)	0.442
Alcohol				
Drinker	1		1	
Non-drinker	1.6 (0.9–2.8)	0.092	1.8 (1.0–3.3)	0.052

[a] Adjusted for age and ethnic group (for ethnic group adjustment was only for age).

[b] Adjusted for age, ethnic group and other risk factors (LDL-C, HDL-C, TG and BMI as continuous variables and smoking, diabetes, hypertension and alcohol as categorical variables).

[c] Low density lipoprotein cholesterol.

[d] High density lipoprotein cholesterol.

[e] Triglycerides.

[f] Diabetes: previously and newly diagnosed diabetics.

[g] Hypertension: previously diagnosed hypertension or systolic blood pressure ⩾140 mmHg or diastolic blood pressure ⩾90 mmHg.

diabetic at baseline. The risk for diabetics was reduced after adjustment for all risk factors therefore indicating much of the increased risk in diabetics may be due to the hypertension or hyperlipidaemia with which it is associated.[30,31] Obesity was another important risk factor that declined greatly as a risk factor for CHD after overall adjustment**.** Again, this is likely to be due to the actions of hypertension and hyperlipidaemia that have been accounted for with adjustment.[32,33] However despite this, the moderately elevated HR, after adjustment for all factors, for diabetes and obesity still shows that they remain as important risk factors for CHD themselves, thus indicating that hypertension and hyperlipidaemia are not the only explanations for diabetics or obese individuals having an increased risk of CHD.

Interestingly, there is evidence that alcohol consumption is protective. However, the relatively small proportion of drinkers in this population allowed only a dichotomy between drinkers and non-drinkers and so the effect of drinking alcohol could not be fully investigated.

There are several limitations of this study. Despite an average follow-up of 8.9 years, the number of individuals who developed CHD did not allow for ethnic group specific analysis

at this time. This is mainly because the cohort is relatively young. However, it would be feasible in the future with further follow-up as the cohort ages allowing for more cases to accumulate. Risk factor data is also dependent on the original baseline measurements without subsequent repeated measurements. Thus the effect of changes in baseline risk factors on the development to study endpoints could not be assessed. Although guidelines were strictly followed, it has been recommended that repeated measurements be made at intervals to allow for regression dilution bias.[34] Because of this, the study may underestimate the true magnitude of the effect of the risk factors.

However, this study does have several strengths. We were able to trace 95.2% of participants by the use of three national registry databases to link baseline data with outcomes of morbidity and mortality. Being a cohort study we were able to exclude individuals with pre-existing diagnosed CHD, follow-up healthy individuals and assess outcome for each risk factor concerned. This is also the first community-based follow-up study in Singapore.

In conclusion, this study has identified and measured the magnitude of the established risk factors of CHD. All have been found to increase the risk of development of CHD in this cohort of Chinese, Malay and Asian Indian males but with varying levels of importance. Interestingly cigarette smoking was not found to be as strong a risk factor as in other populations. Public health measures such as health education and possibly screening for these established risk factors should continue in Singapore as in other countries. Also, the increased susceptibility of Asian Indians to CHD has been confirmed in a longitudinal study.

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KEY MESSAGES

- Established risk factors of coronary heart disease (CHD) play a role in Chinese, Malays and Asian Indian males.
- The increased susceptibility of Asian Indians to CHD has been confirmed in a longitudinal study.

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