Premature Coronary Artery Disease among Angiographically Proven Atherosclerotic Coronary Artery Disease in North East of Peninsular Malaysia

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Abstract

Introduction: Coronary artery disease features among the top three causes of premature deaths in both men and women in Malaysia.

Aim and Objectives: The objectives of the study are to determine the proportion of premature coronary artery disease (CAD), its angiographic findings and risk factors among patients with angiographically proven CAD in a tertiary center in Malaysia.

Methods / Study Designs: This was a retrospective study involving three hundred and thirty five medical records of patients undergoing coronary angiogram from 2002 until 2004 were reviewed. The socio-demographic, associated risk factors and angiographic findings were recorded.

Findings: The result of the study showed a total of 165 cases were diagnosed to have CAD based on coronary angiogram. The proportion of premature CAD was 55% (n=92). The risk factors associated with premature CAD were family history of heart disease ($p<0.05$) and low High Density Lipoprotein level (HDL) ($p<0.05$). There was a high prevalence of Premature CAD among angiographically proven CAD in this study. Family history of heart disease and low HDL level were associated with premature coronary artery disease.

Conclusion: Early cardiovascular screening in family member of patient with heart disease is important for prevention of coronary artery disease in young adult.

Key words: coronary artery disease, premature CAD, coronary angiogram, premature heart disease

Introduction

In 2005, World Health Organization (WHO) estimates 17.5 million people died of coronary artery disease. This is 30 percent of all deaths globally. WHO predicts 11.1 million deaths from CAD in 2020.[1] In Malaysia there are alarming statistic regarding cardiovascular disease scenario. The number of cardiovascular death of ischemic heart disease cases in Malaysia as reported by Ministry of Health (MOH), has increased from 2556 in 2000 to 2948 in 2005.[2] Coronary artery disease and cerebrovascular disease featured among the top three causes of premature deaths in both men and women in Malaysia. For men, these two diseases contributed 21.5 percent of total years lost to premature deaths; while for women, they contributed 25.2 percent.[3]

The study by Pineda *et al.,* shows that the prevalence of premature CAD age more than 45 years was 9.0 %. However, it is lower in Japan. The incidence in Japan was 1.26 events per 1000 patients' age < 50 years.[4] The prevalence of premature CAD in India, which was angiographically proven was 10% .[5]

There are few differences observed in the clinical presentation, risk factors profile and angiographic study of young patients who developed CAD compared with those developing it at an older age. Young patients who developed CAD tend to be from the male gender,[6] have past history of smoking,[7,8,9] more marked hyperlipidaemia and positive family history of premature coronary artery disease .[10,11] In term of angiographic findings, younger patients tend to have more normal coronary arteries and single vessel disease compared to older patient who tend to have more complex and multiple vessels involvement. [6,12,13,14] This study is done to define and describe the prevalence of premature coronary artery disease (PCAD) among angiographically proven CAD and to compare clinical characteristics as well as angiographic and biochemical features of young versus old patient with documented coronary artery disease.

Subject and Methods

This is a retrospective study that constitutes 165 men and women who had undergone angiogram at Hospital University Sains Malaysia and shown to have angiographically proven CAD in a two year period (October 2002 until December 2004). Patients included were those age more than 18 years and had their first angiogram done with a positive findings of coronary artery disease. Patients excluded were those with repeated coronary angiogram or having concomitant valvular heart disease, cardiomyopathy or non obstructive coronary disease.

Hospital Universiti Sains Malaysia is one of two tertiary hospitals in the state of Kelantan. It is also a teaching hospital for both undergraduate and postgraduate students. Its' Invasive Cardiac Laboratory (ICL) has managed to be both a service and clinical research centre. The service started in October 2002 with three cases for angiogram. Since October 2002 until 2004, HUSM cardiologist in Invasive Cardiac Laboratory (ICL) unit enrolled about 500 patients per year. From the number, about 80% were confirmed to have angiographically proven CAD

Medical records of all eligible patients who had undergone coronary angiogram from October 2002 until 2004 in HUSM were done. The demographic data, angiogram results, laboratory investigations were recorded. The demographic and clinical characteristics required were age, race, sex, marital status, occupation, history of smoking, past medical history, family history of chronic diseases and BMI. The biochemical results required were total cholesterol, LDL, HDL and triglyceride level. The angiogram results required were number and type of coronary vessels involved.

Patients were classified as having coronary artery disease when they have cardiac events or symptoms related to myocardial ischemia and / or injury. Such events include unstable angina, myocardial infarction and sudden death due to ischemic heart disease. Premature Coronary Artery Disease or young CAD is defined as cardiac events occurred in men aged 55 years or more and women age 65 years or more. Coronary angiograpy was considered abnormal when there is presence of diameter stenosis (occlusion) that occurs to one or more of the three major coronary arteries during the angiogram procedure. Significant occlusion defined as equal or more than 50% narrowing in left main branch equal or more than 70 % of other epicardial artery. One vessel disease is defined as narrowing in an each major artery coronary artery such as left anterior descending (LAD) artery, the left circumflex artery (LCx), or the right coronary artery (RCA). Tandem lesions of epicardial artery also consider as one vessels disease.

Two vessel disease is defined as narrowing of two major coronary artery. Three vessel disease is defined as narrowing of three major coronary artery. Family history of heart disease is defined as presence of family history of heart disease in first degree relatives (male siblings or parent).Hypertension is defined as systolic blood pressure equal or more than 140 mmHg or diastolic blood pressure equal or more than 90 mmHg measured before the angiogram procedure or current used of antihypertensive medication. Cigarette smoking is defined as patients who smoke up to the day of angioplasty or already stopped smoking less than one year. Non smoker were defined as patients who never smoked.

Diabetes mellitus is present if individual was receiving therapy with either insulin or oral hypoglycemic agent or on diet control documented in medical record. The diagnostic criteria for diagnosing T2DM were as follows: FPG is equal or more than 7.0mmol/L or 2HPP or RBS is equal or more than 11.1 mmol/L. Hyperlipidemia is defined as having total cholesterol of more than 5.2 mol/l, LDL of more than 3.4   mmol/l, HDL of less than 1.0 mmol/l, TG of more than 1.7 mmol /l measured before the angiogram procedure or if the patient was on lipid lowering therapy. The result was based on blood investigation before the angiogram procedure.

Statistical Analysis
All data was entered and analyzed using Statistical Program for Social Sciences (SPSS) version 12.0 (SPSS Inc.2003). Simple logistic regression was used as a screening in selection of variables for further analysis. All variables with P value less than 0.25 and clinically relevant variables were included in the multiple logistic regression analysis. The method that was used for variable selection was backward and forward stepwise procedure. All possible 2 way interactions were checked and those significant variables were included in the model. The independent variables were fitted into multiple logistic regression and multicollinearity was checked. Fitness

of model was tested by Hosmer Lemeshow Goodness of Fit test, the classification table and receiver operator characteristic curve.

Approval by research and ethics committee
The protocol was approved by the Research Ethics Committee (Human), School of Medical Sciences, Universiti Sains Malaysia on 30th October 2007 (USMKK/PPP/JEPeM [196.3(10)

Result

Socio-demographic characteristics of study subjects
The result of socio-demographic characteristics is shown in table 1. A total of 91 (55%) were in the younger age group (premature CAD). Mean (SD) age for premature CAD was 50 (6.91). In the younger age group, the age range for female was 39 to 65 year old with the mean (SD) of 51(9.24) year old. As for male, the age range is from 27 to 55 years old with mean (SD) of 50 (6.24). (See Table 1)

Medical and biochemical characteristic of study subjects
Table 2 showed the medical and biochemical characteristic the subjects. Younger CAD had higher family history of heart disease compare to older age group (38% vs. 20%). (See Table 2)

The biochemical characteristics of the study subjects were showed in Table 3. The mean (SD) of total cholesterol 5.4 (1.1) and LDL 3.4 (1.2) were high in the older age group. However, younger age group had higher TG level. (See Table 3)

Angiographic analysis of study subjects
Table 4 shows the angiographic features of coronary stenosis in younger and older age group. The older age group had higher percentage of triple vessel disease (58%). The left anterior descending artery was the vessel that commonly involved in both groups (79% vs. 82%).
The younger patients had higher percentage of revascularization procedure (PTCA) (48%) compared to the older patients. In the older age group, CABG was more predominant therapeutic procedure done (36%).

Multiple logistic regressions of associated factors for premature CAD
Multiple logistic regression analysis presented in table 5 showed that the family history of heart disease and HDL level were significant factors for premature CAD. (See Table 5)

Discussion

The incidence of CAD in young adult was reported to be 12% - 16 % in Indian by using clinical assessment.[8] In Japan the incidence of CAD among Japanese men were 1.26 events per 1,000 patients.[15] The prevalence of premature coronary disease from the epidemiological data for angiographically proven was 9.0%.[6]

The proportion of premature CAD in present study revealed 55% (n=91) compared to 45% (n= 74) in older age group. This was because most of the patients in the younger age group had CAD symptom, strong family history of heart disease and stable physical and financial support to undergo angiogram.   There was a clear male preponderance in both age groups, where 80% of the male patients had CAD. This preponderance is similar to previous studies that suggested CAD as men disease.[6,8,16]

According to INTERHEART study, the median age for the first presentation of CAD in South Asian population was 53 year old whereas, in Western Europe, China and Hong Kong it was 63 year old, with also more men than women affected.[16] Our study showed the youngest age of CAD in male is 27 years old and 39 years old in female. The median age was higher in women than in men (51 vs. 49 years).

This study shows similar findings in other study studies suggest that risk factors may differ in early onset and late onset of CAD. In this study, the percentage of smoker and family history of heart disease in young CAD group is higher compare to older CAD group. A positive family history of heart disease and low HDL have been found associated with early onset of CAD in young patients similar to the reports from other studies.[8,17]

Smoking and hypercholesterolemia were the most common risk factors encountered in patients younger than 45 years and numerous studies have supported these observations.[6,16,18,19] However, smoking and hypercholesterolemia had showed insignificant correlation with Premature CAD in this study. These could be due to small sample size and in both age group the percentage of smoking and total cholesterol level not much difference to give a significant value.

Family history of heart disease showed significant risk factor for PCAD in this study. The results of significant family history of heart disease as an associated risk for premature CAD support by other previous studies. Tewari *et al* (2005) showed family history of heart disease as a significant associated risk factors in premature CAD.[10] It was also important independent risk factor for CAD in younger patient in India.[8] In Malaysia, data from ACS registry 2006 noted 19.7% of patients CAD diagnosed based on clinical assessment, had positive family history of premature CAD.[20]

There were predominantly single vessel disease in young patients and multivessel disease in older patients accordance with previous studies.[6,16,18,19] This study also showed significant difference between younger and older age group in term of number of diseased vessel and it slightly difference to previous studies where the younger age group had more double vessels disease (33%) compare to older age group.   The less extensive coronary artery disease in the younger patients might suggest that premature coronary artery disease is associated with rapid disease progression (plaque rupture ,plaque complication, or both) rather than with gradually evolving process. This is in line with the finding that younger patients with coronary artery disease commonly present with an acute coronary syndrome compare to older patient who usually present with chronic angina.

The anatomical distribution of coronary sclerosis was also consistent with that observed in other studies.[15,21] Our study revealed that the incidence of significant sclerotic narrowing was the highest in left descending artery (72%), followed by 59% in the right coronary artery and 52% in

the left circumflex artery. However, there was no significant difference in these vessels involved in both age groups.

Conclusion

There is a high proportion of patients with premature coronary artery disease in our population with angiographically proven disease. A large number of these patients have multiple risk factors namely positive family history and low HDL level. Those with positive family history need to be screened for the other modifiable risk factors such as smoking and hyperlipidaemia and managed aggressively to prevent the onset of premature coronary artery disease.

Acknowledgement

Conflict of Interest Statement

We declare there is no financial and personal relationship with other people or organizations that could inappropriately influence the research

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Table 1: Socio-demographic characteristic of younger and older CAD patients angiographically proven atherosclerotic CAD in HUSM

	Younger CAD (n = 91)	Older CAD (n = 74)
Variable	n (%)	n (%)
Age		
Female	51.4 (9.24)[a]	66.5(3.75)[a]
Male	49.7 (6.24)[a]	60.0(7.25)[a]
Race		
Non Malay	4 (4.4)	9 (12.2)
Malay	87 (95.0)	65 (87.8)
Occupation		
Non government	40 (44.0)	34 (45.9)
Government	51 (56.0)	40 (54.1)
Smoking status		
Non smoker	31 (34.0)	23 (31.1)
Smoker	60 (66.0)	51 (68.9)
Marital status		
Not married	5 (5.5)	0
Married	86 (94.5)	74 (100)

[a]Mean (SD)

Table 2: Medical characteristics of younger and older age groups.

CAD Variable	Younger (n = 91) n (%)	Older CAD (n = 74) n (%)
Hypertension		
No	32 (35.2)	17 (23.0)
Yes	59 (64.8)	57 (77.0)
Diabetes mellitus		
No	64 (70.3)	46 (62.2)
yes	27 (29.7)	28 (37.8)
Hyperlipidemia		
No	46 (50.5)	37 (50.0)
Yes	45 (49.5)	37 (50.0)
Family history of hypertension		
No	73 (80.2)	64 (86.5)
Yes	18 (19.8)	10 (13.5)
Family history of heart disease		
No	56 (61.5)	59 (79.7)
Yes	35 (38.5)	15 (20.3)
Family history of HPL		
No	85 (93.4)	65 (87.8)
Yes	6 (6.6)	9 (12.2)
First cardiac event		
Non ACS	26 (28.6)	24 (32.4)
ACS	71 (65.0)	50 (67.6)
BMI	30 (5.8)[b]	30 (5.3)[a]

[a] Mean (SD)
[b] Median (interquartile range)

Table 3: Biochemical characteristic of younger and older age groups.

Variables	Younger CAD (n = 91) Mean (SD)	Older CAD n = 74 Mean (SD)
Total cholesterol	5.3 (1.8)[a]	5.4 (1.1)
TG	1.5 (1.1)[a]	1.3 (0.7)[a]
LDL-C	3.3 (1.3)	3.4 (1.2)
HDL-C	1.2 (0.3)[a]	1.4 (0.6)

[a] Median (Interquartile range)

Table 4: Associated risk factors for Premature Coronary Artery disease by multiple logistic regressions

Variable	Adjusted OR[a]	95% CI[b]	Wald stat[c]	df	P value
h/o HPT					
No	1.00				
Yes	0.50	0.24, 1.06	3.29	1	0.070
Family h/o heart disease					
No	1.00				
yes	3.58	1.59, 8.05	9.49	1	**0.002**
Total Cholesterol	2.17	0.96, 2.90	3.48	1	0.062
LDL	0.50	0.22, 1.14	2.74	1	0.098
HDL	0.25	0.89, 0.69	7.10	1	**0.008**
BMI	1.07	0.98, 1.16	3.53	1	0.060

[a]Odds Ratio
[b]Confidence Interval
[c]Wald statistic