

## Prevalence of Coronary Artery Disease in Young Sudden Death Cases and Correlation with Post-Mortem Computed Tomography Calcium Score

Omar E.<sup>1,3</sup>, Faizuddin R.<sup>1</sup>, Mansharan.K.<sup>1,2,3</sup>, Razuin R.<sup>1</sup>, Mahmood M.S.<sup>2</sup>, Nurliza.A.<sup>2</sup>, Zaleha A.M.<sup>2</sup>, Nawawi H.<sup>1</sup>

<sup>1</sup>Centre for Pathology Diagnostic and Research Laboratories (CPDRL), Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia

<sup>2</sup>National Institute of Forensic Medicine (IPFN), Hospital Kuala Lumpur, Kuala Lumpur, Malaysia

<sup>3</sup>Institute of Pathology, Laboratory and Forensic Medicine (I-PPerForM), Faculty of Medicine, Universiti Teknologi MARA, Malaysia

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### Corresponding author:

**Prof. Dr. Hapizah Mohd Nawawi**,  
Institute of Pathology, Laboratory and  
Forensic Medicine (I-PPerForM),  
Faculty of Medicine,  
Universiti Teknologi MARA (UiTM),  
Sungai Buloh Campus,  
47000 Sungai Buloh, Selangor,  
Malaysia.  
Email: hapizah.nawawi@gmail.com

### ABSTRACT

**Introduction:** Data on prevalence of coronary atherosclerosis and coronary artery disease (CAD) in young sudden death autopsy cases in Malaysia are still scarce. Calcium scoring (CS) on Computed Tomography (CT) was suggested to be predictive for CAD; however the reports have been conflicting. Objectives: to investigate (i) the prevalence of young CAD in sudden death cases in a Malaysian population; (ii) the association between CT CS and CAD in such cases and correlation with age. **Methods:** Sudden death cases received at the National Institute of Forensic Medicine, Kuala Lumpur between September 2012 and December 2013 were recruited. The cases were divided into young [ $\leq 40$ ] and old [ $> 40$  years old] age groups. Presence of CAD was recorded during autopsy. **Results:** A total of 155 cases was included; 64.5% of the subjects were below 40 years old. CAD was the cause of death of 34 [21.9%] cases; of these, young individuals comprise 47.1% of cases [ $n=16$ ; 10.3% of total cases, 16% of young sudden death cases]. Both young and old subjects with CAD had lower CS compared to those without CAD [ $p<0.000$ ;  $p=0.003$  respectively]. Multivariable regression analysis showed CS to be significantly correlated with CAD in both young and old subjects. In contrast, other factors such as gender, ethnicity, body-mass index and waist-hip ratio did not show any correlation with CAD in both groups. **Conclusion:** The prevalence of CAD in young sudden death cases is relatively high. CS is useful in discriminating CAD in both young and old SD subjects.

**KEYWORDS:** Coronary artery disease, sudden death, computed tomography, calcium score

### INTRODUCTION

Cardiovascular disease is the leading cause of death in Malaysia [1-3] and other middle and low income countries worldwide [4-9]. Coronary artery disease (CAD) is an important contributor to this condition, along with cerebral and peripheral vascular disease. Identification of asymptomatic persons at risk for the disease is done by risk stratification based on established risk factors such as concurrent diabetes mellitus, hypertension, cigarette smoking, family history, dyslipidaemia, age and sex [10]. Recently, coronary artery calcium scoring has been identified as a tool in stratification of asymptomatic individual for cardiovascular risk [10]. National Cholesterol Education Program (NCEP) III guideline recommends risk stratification for cardiovascular disease based on coronary artery calcium score (CS) of above 75<sup>th</sup> percentile adjusted to age and sex [10, 11]. However, other reports suggested that coronary artery

CS has an absolute relationship with cardiovascular disease regardless of age and sex factors [12].

The average age of onset of acute coronary syndrome in Malaysia is 57 years; 5 years younger than in Thailand and 10 years younger than in Canada [13]. Data on the prevalence of CAD and young coronary artery disease in sudden death autopsy cases in Malaysia is still lacking. This data would contribute to the prevalence of CAD in the population, in addition to the data obtained from live patients.

Coronary artery calcification is the process of calcium deposition in the coronary artery wall; it is highly associated with presence of an established atherosclerotic plaque [14]. Measurement of calcium within the coronary vessels of patients with sudden death using post-mortem computed tomography is a simple, rapid and non-invasive technique as compared to its gold standard, the open autopsy procedure. Calcium scoring on Computed Tomography (CT) has been suggested to be a predictive tool for

cardiovascular disease evaluation; however data on this is still lacking, especially from Asian Nations [15]. In addition, most reports of the use of calcium in atherosclerotic plaque estimations technique are in the clinical settings, using live subjects. Data on CT calcium score in post-mortem cases are scarce. The availability of data obtained from this would allow postulation on the presence of atherosclerosis without having to perform an autopsy. It could potentially benefit in situations where autopsy could not be performed, especially in a conservative society such as Malaysia, where open autopsy is frequently shunned by relatives due to desire to evade of body mutilation and religious reasons.

The objectives of this study are: (i) to investigate the prevalence of coronary artery disease in sudden death autopsy cases as well as the prevalence of younger cases with CAD in this population and (ii) to investigate the association between CT CS and presence of CAD in sudden death autopsy cases and correlation with age group of coronary artery disease cases.

## METHODS

This study had been approved by the Institutional Ethics Committee [NMRR-11-1135-10262 and 600-RMI (5/1/6/01)]. Sudden death cases received by the National Institute of Forensic Medicine (NIFM), Hospital Kuala Lumpur between September 2012 and December 2013 were recruited. Skeletonised, decomposed and charred bodies or those with severe trauma to the heart were excluded from this study. Demographic data collected included age, nationality, body mass index, and waist/hip circumference ratio. The latter two parameters were included because they are potential confounding factors contributing to the end result.

The CT images of the heart were acquired using a multislice CT machine (Toshiba Aquilion 64 TSX-101A, Japan), using 3 mm slice thickness with 3 mm interval axial sections of the heart from above the carina and proceeded caudad till below the heart. The amount of calcification on CT can be measures using calcium volume, calcium mass and Agatston score. Among these, Agatston score is the most accepted method of determining CS [16, 17]. It is a product of

the density factor and area of calcification in a coronary artery, taking into account the total burden and severity of atherosclerosis [16-18].

The presence or absence of CAD was based on autopsy findings, where the coronary vessels were sliced at 2 to 3 mm interval and observed for presence of atherosclerotic plaque. Cardiovascular disease was identified as the most likely cause of death in cases with coronary artery stenosis of more than 70% , in accordance with the Stary classification [19], in the absence of any other reason for the loss of life.

“Younger” CAD were defined as those aged 40 years and below; while “older” CAD were ages from 41 years old and above. This division was made in accordance to the Malaysian Youth Policy, whereby the cut off age for youth was 40 years old [20]. This was thought to be appropriate since the data would be useful in the local context, where this policy would be applicable.

## Statistical Analysis

The calcium scoring of the groups were compared and analysed for statistical difference using SPSS version 18. Chi-square method was used to compare the groups, non-parametric test was used for skewed data and for normally distributed data, student's t-test was performed; statistical significance was taken when p value was less than 0.05. Multivariate analysis was done using binary and linear regression methods.

## RESULTS

A total of 155 cases were included in the study, 100 (64.5%) subjects were below 40 years old and 55 subjects were above this age; 95 (61.3%) of the subjects were Malaysian, among whom 31 (32.6%) were Malay, 32 (33.7%) Chinese, 29 (30.5%) Indian and 3 (3.2%) were of Borneo ethnic groups. The rest of the demographic data, presence of CAD and CT calcium score are presented in Table 1. Coronary artery disease was the cause of death in 16 % of the young subjects and 32.7% of the older subjects ( $p=0.016$ ) (Table 1). Young CAD comprise of 10.3% of total cases in this study. Total CS was significantly higher in older compared to younger subjects [ $214.13\pm 53.9$  vs.  $28.7\pm 15.4$ ,  $p<0.000$ ] and in CAD compared to non-CAD [ $435.5\pm 131.5$  vs  $249.1\pm 40.4$ ,  $p=0.025$ ] (Table 1).

**Table 1** Demographic Data, Body Mass Index, Waist-Hip Ratio and Calcium Score of the Subjects in the Study

Parameter	≤ 40 years old		> 40 years old		P value
<b>Gender</b>					
Male	88 (66.2%)		45 (33.8%)		0.291
Female	12 (54.5%)		10 (45.5%)		
<b>Ethnic group</b>					
Malay*	24 (68.6%)		11 (31.4%)		0.024
Chinese	15 (42.9%)		20 (57.1%)		
Indian	22 (73.3%)		8 (26.7%)		
<b>Body mass index**</b>	24.6±4.6		25.7±4.9		0.548
<b>Waist-hip ratio**</b>	0.93±0.05		0.94±0.07		0.034
<b>CAD</b>	16 (10.3%)		18 (11.6%)		0.016
<b>Total calcium score***</b>	28.4±15.25		214.13±54.71		0.000
<b>Total calcium score***</b>	<b>CAD</b>	<b>Non-CAD</b>	<b>CAD</b>	<b>Non-CAD</b>	
	138.47±90.99	7.43±3.48	435.48±131.55	106.45±41.41	
	p < 0.000		p = 0.003		

\*Including Bumiputera from Sabah and Sarawak; \*\*data represented as mean±standard deviation; \*\*\* data represented as mean±standard error of mean.

There was a significant difference in the ethnic group and waist-hip ratio between the groups. Malays and Indians had a higher number of young subjects compared to Chinese ( $p=0.024$ ). Waist-hip ratio in older were higher compared to younger subjects ( $p=0.034$ ). There were no difference between the gender and body mass index (BMI) between groups ( $p>0.05$ ). CS in young CAD was lower than that of old CAD subjects ( $p<0.000$ ). In both groups, CS was higher in those with CAD than those without [ $p<0.005$ ] (Table 1).

CAD-adjusted multivariate analysis showed only CS to be significantly associated with CAD in both young and older subjects (Table 2). All the other variables did not show significant correlation. Based on the adjusted odds ratio (Table 2), younger subjects with high calcium score have 1.015 higher odds of having CAD. On the other hand, older subjects with higher CS have 1.002 higher odds of having the disease.

**Table 2** Factor associated with CAD in young and older sudden death cases. The other factors (age, ethnic group, BMI and waist-hip ratio) did not reach statistical significance ( $p>0.05$ )

Variables	< 40 years old			> 40 years old		
	Adjusted <sup>a</sup> OR	Wald statistics <sup>a</sup>	p value <sup>a</sup>	Adjusted <sup>a</sup> OR	Wald statistics <sup>a</sup>	p value <sup>a</sup>
<b>Total calcium score</b>	1.015	6.535	0.011	1.002	5.718	0.017

<sup>a</sup>Multiple logistic regression

The model reasonably fits well. Model assumptions are met. There are no interaction and multicollinearity problems.

## DISCUSSION

This study reports data on coronary atherosclerosis in young and old Malaysian post mortem subjects with associated CS assessed on CT. Most autopsy series report circulatory disease as the main cause of sudden natural deaths [3, 9, 21-23]. Large studies performed in western countries have reported high prevalence of atherosclerosis in coronary arteries young subjects, especially in the form of fatty streaks [22, 24, 25]. Complicated atherosclerosis was reported in up to 2.4% of autopsy subjects aged 25 to 34 years [25], and in 2 to 6% of young patients (less than 40 years old) with symptomatic coronary artery disease [7, 15]. Asian data had reported a prevalence of 5 to 10% CAD in young subjects [15]. In this study, we found the prevalence of young CAD subjects is 16%. Interestingly, the analysis of risk factors such as gender, BMI and waist-hip ratio in this group did not yield significant correlation with CAD. Other researchers have suggested genetic factors and coronary vessels abnormalities play a more important role in younger CAD, rather than the traditional risk factors [15]. This may also be the true in our case. We found that calcium score (CS) was significantly correlated with CAD in both young and old subjects. The CS data was analysed as an absolute number, rather than as cut off points or percentiles in relations to patients age and gender, as has been used in other studies [10, 16]. It has been suggested that the use of percentiles is advantageous to young subjects as they tend to have lower CS overall. Our results support the findings of other studies on the usefulness of CS in predicting risk of CAD in asymptomatic individuals [10, 12, 16, 17]. It needs to be emphasised that current data of coronary artery CS were reported almost exclusively from populations of western countries [26]. Malaysian recommendation for use of CT CS in cardiovascular assessment is based on such data [27]. The generation of local data on coronary artery CS is essential so as to validate the use of such data in formulating national policies and guidelines. In addition, the post-mortem setting of this study enables postulation to be made in relation to post-mortem diagnosis of cardiovascular disease without performing an autopsy.

## Limitation of the study

The main limitation of this study is the lack of information on other risk factors associated with CAD such as family history, history of hypertension, diabetes and hyperlipidaemia.

## CONCLUSION

In conclusion, CAD was highly prevalent in young sudden death cases in Malaysia. CS is greater in CAD compared to non-CAD post-mortem subjects. CS is more useful in discriminating CAD in both older and younger subjects.

## Conflict of Interest

Authors declare none.

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