

Ischemic Cardiomyopathy (ICM) Versus Non-Ischemic Cardiomyopathy (NICM): Findings from a Single-Centred Observational Study at Hospital Serdang, Malaysia

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ABSTRACT

Introduction: Cardiomyopathy is a serious health concern associated with heart failure (HF) and sudden cardiac death (SCD). Clinically, HF patients are categorized under ischemic and non-ischemic origin based on myocardial infarction, coronary artery disease, or evident angiographic presentation.

Objective: To determine the existence of cardiomyopathy cases and assess factors associated to ischemic versus non-ischemic outcome among Malaysian population.

Methodology: This retrospective, cross-sectional study involved a total of 170 patients from cardiology unit at Hospital Serdang in Selangor, Malaysia. All cardiomyopathy patients' data including clinical notes and lab investigations from 2006 till 2018 were reviewed and analyzed for interpretation of results.

Results: The mean age of our study population was 54.8 ± 14.8 (range 18-92 years), with males (68.8%) and females (31.2%), while ethnic distribution focused on Malay (59.4%), Chinese (25.9%) and Indian (12.9%). Ischemic cases were slightly higher ($n = 96$, 56.5%) and most frequently occurring type was dilated cardiomyopathy (88.8%). Majority of the patients had reduced LVEF ($n = 140$, 82.4%); and a chi-square test revealed significant association with ischemic group ($p < 0.016$). Men having ICM were more ($n = 69$) in comparison to NICM ($n = 48$) while women developed cardiomyopathy at a greater age. Smokers among NICM was slightly more (51.9%) than ICM (48.1%). An independent t-test showed that mean age (58.3 ± 13.3) was significantly higher (95% CI; $p < 0.0001$) among ICM patients. Diabetes and LDL were also significantly greater among ischemic group (65.5%, $p < 0.015$) and (85.2%, $p < 0.001$), respectively. There was no significant association between gender or ethnicity in relation to ICM or NICM.

Conclusion: Ischemic heart disease prevails as a leading cause of death in Malaysia. Therefore, our study highlighted some of the factors significantly associated with higher risk of developing ischemic cardiomyopathy and established better awareness.

Keywords: Ischemic, Non-ischemic, Cardiomyopathy, Heart Muscle Diseases, Malaysia.

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INTRODUCTION

Heart failure (HF) is a rapidly expanding public health concern with an estimated prevalence of >37.7 million people, globally (1). It is a chronic condition related to cardiac dysfunctionality and linked to many secondary etiologies; although the underlying cause may vary according to age, gender, ethnicity, comorbidities, and environmental factors. HF patients often develop symptoms like dyspnea, fatigue, poor exercise tolerance, fluid retention, and can also experience a severe impact on their quality of life (1). Heart failure, yet remains a highly prevalent clinical condition associated with increased morbidity and mortality despite several therapeutic advancements (2).

Clinically, patients are classified under HF due to ischemic or non-ischemic etiology based on a history of myocardial infarction (MI), coronary artery disease (CAD), or any objective evidence such as angiography and functional testing. (3). One of the most common and important etiologies of heart failure is ischemic cardiomyopathy (ICM) (4) (5). While, more than one-third of HF cases are due to

non-ischemic cardiomyopathy (NICM) (6); hence, in 30%–40% of heart failure patients, the underlying cause is found to be non-ischemic (2).

Cardiomyopathy is a chronic progressive myocardial ailment with a definite pattern of morphological, functional and electrophysiological changes (7). The expert consensus panel (2006) of the American Heart Association (AHA) proposes the following definition: “Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic. Cardiomyopathies are either confined to the heart or are part of generalized systemic disorders, often leading to cardiovascular death or progressive heart failure-related disability” (7) (8).

During in the early stages, cardiomyopathies may be asymptomatic. However, most symptoms are typically observed in any type of heart failure, whether systolic (reduced ejection fraction) or diastolic (preserved ejection

fraction). Life expectancy of cardiomyopathy patients can vary by etiology, though for most patients who develop HF- the mortality rate is 20 percent at one year and 70 to 80 percent at eight years (9).

In simple terms, cardiomyopathy is a heart muscle disease that can occur in any age group or gender, and can be acquired or inherited. It affects the shape, function, and/or electrical system of the heart. Therefore, cardiomyopathy patients are often at risk of experiencing dysrhythmias or sudden cardiac death (10).

METHODS

An observational, cross-sectional study was conducted from March to June 2019 at the cardiology unit of Hospital Serdang in Selangor, Malaysia. It is considered as one of the major cardiac referral centres in Malaysia, and currently holds the third-highest number of cardiac patients or admissions according to the NCVD Registry Annual Report 2014 – 2015.

All heart failure patients were diagnosed by the physicians and/or cardiologists based on the following clinical signs: fatigue, shortness of breath, fluid retention in the presence of abnormal cardiac contractility and reduced left ventricular ejection fraction (LVEF \leq 40%).

Ischemic cardiomyopathy (ICM) patients were identified through the following criteria: documented clinical history, presence of increased cardiac biomarkers and presence of electrocardiograph findings consistent with ST-elevation myocardial infarction (STEMI) and coronary artery disease (CAD). Those having a previous history of coronary revascularization; stenosis or obstruction on coronary angiography, reversible ischemia or myocardial infarction identified on stress nuclear perfusion imaging or stress echocardiogram were also defined under ICM. While patients with none of the above criteria or classified as hypertensive, alcohol/ drug abuse, chemotherapy-induced, viral, postpartum, familial, or unknown/idiopathic categories were considered under NICM etiology.

The ICM and NICM patients' data including clinical notes and lab investigations were collected retrospectively from the Electronic Hospital Information System (eHIS) – an online database system operated at Hospital Serdang. All existing cardiomyopathy patients were included except for the paediatric cases mainly new-borns, infants, and children

below the age of 18 years. Patients with defaulted appointments and hospital visits, missing data or insufficient information, or unwilling to participate into the study were also excluded.

The minimum required sample size was 132 at a 95% confidence interval, beta value of 0.20, by setting the power of study as 80, allowing 5% error margin, and by using the two-proportions estimation method on EpiCalc 2000. We were able to collect data from around 170 cardiomyopathy patients who reportedly visited the hospital since 2006 until 2018, and were further reviewed for statistical analysis.

Categorical data were presented as proportions or percentages while continuous data presented as mean \pm standard deviations. Independent t-test, Chi-square, Fisher's test and One-way Anova were performed depending on the variables and where appropriate. Stratified analysis was done to compare age, sex, ethnicity, diabetes, smoking status, low density lipids, left ventricular ejection fraction among ICM and NICM patients. By using the IBM Statistical Package for Social Sciences (SPSS) version 22.0, all study analysis was performed. A two-tailed probability value <0.05 was considered statistically significant.

Patient anonymity and confidentiality was strictly ensured by the researchers. We obtained ethical approval from the Medical Research and Ethics Committee (MREC) and the Ministry of Health Malaysia (MOH), and the study was registered under the National Medical Research Register - NMRR-19-2585-47819.

RESULTS

The mean age of our study population was 54.81 ± 14.82 years (range 18-92 years) with 44.1% of patients aged between 40-60 years. The proportion of male patients was higher in existence (68.8%) in comparison to females (31.2%), while ethnic distribution focused vastly on Malay population (59.4%) followed by Chinese (25.9%) and Indian (12.9%). The ischemic cases were slightly higher (56.5%) and the total number of current smokers were about 30.6%. The most commonly occurring cardiomyopathy was reported to be DCM (88.8%). Majority of the patients had poor LVEF (82.4%), diabetes (51.2%) and about 35.9% had LDL >3 . Table 1 shows the demographics and clinical characteristics of these patients.

Table 1: Demographics and Clinical Characteristics of Patients

Variable	Mean \pm SD	n (%)
Gender		
Male		117 (68.8)
Female		53 (31.2)
Age	54.81 \pm 14.815	
Less than 20 years		1 (0.59)
20-40 years		31 (18.2)
40-60 years		75 (44.1)
60-80 years		56 (32.9)
More than 80 years		7 (4.1)
Ethnicity		
Malay		101 (59.4)
Chinese		44 (25.9)
Indian		22 (12.9)
Others		3 (1.8)
Smoking Status		
Current Smoker		52 (30.6)
Non-smoker		83 (48.8)
Diabetes		
Yes		87 (51.2)
No		83 (48.8)
LVEF		
Poor EF (≤ 40)		140 (82.4)
Good EF (≥ 40)		30 (17.6)
LDL		
≤ 3		109 (64.1)
≥ 3		61 (35.9)
Cardiomyopathy Category		
Ischemic		96 (56.5)
Non-ischemic		74 (43.5)
Total		170 (100.0)

Table 2: Clinical Diagnosis of Cardiomyopathy

Cardiomyopathy	Frequency	Percent	Valid Percent	Cumulative Percent
Dilated CM	151	88.8	88.8	90.0
Hypertrophic CM	13	7.6	7.6	97.6
Takotsubo CM	1	0.6	0.6	96.9
Hypertensive CM	3	1.5	1.5	98.2
Idiopathic CM	2	1.2	1.2	100.0
Total	170	100.0	100.0	

Table 3: Comparing mean age between ICM and NICM patients

Cardiomyopathy	n	Age (years) Mean (SD)	Mean Difference (95% CI)	t statistic (df)	p-value ^a
Ischemic	96	58.3 (13.3)	7.96	3.59	0.0001
Non-ischemic	74	50.3 (15.5)	(12.33, 3.59)	(168)	

^a Independent t-test

The results showed that mean age is significantly different ($p = 0.0001$) between ischemic and non-ischemic cardiomyopathy patients. Therefore, there is a significant association between age and type of cardiomyopathy.

Table 4: Association between Gender and Cardiomyopathy

Gender (n)	Cardiomyopathy			χ^2 statistic (df)	p-value ^a
	n	Ischemic n(%)	Non-ischemic n (%)		
Male	117	69 (59.0)	48 (41.0)	0.957	0.328
Female	53	27 (50.9)	26 (49.1)	(1)	
Total	170 (100.0)	96 (56.5)	74 (43.5)		

^a Chi-square test

Results show that there is no significant association (p value = 0.328) between gender and type of cardiomyopathy.

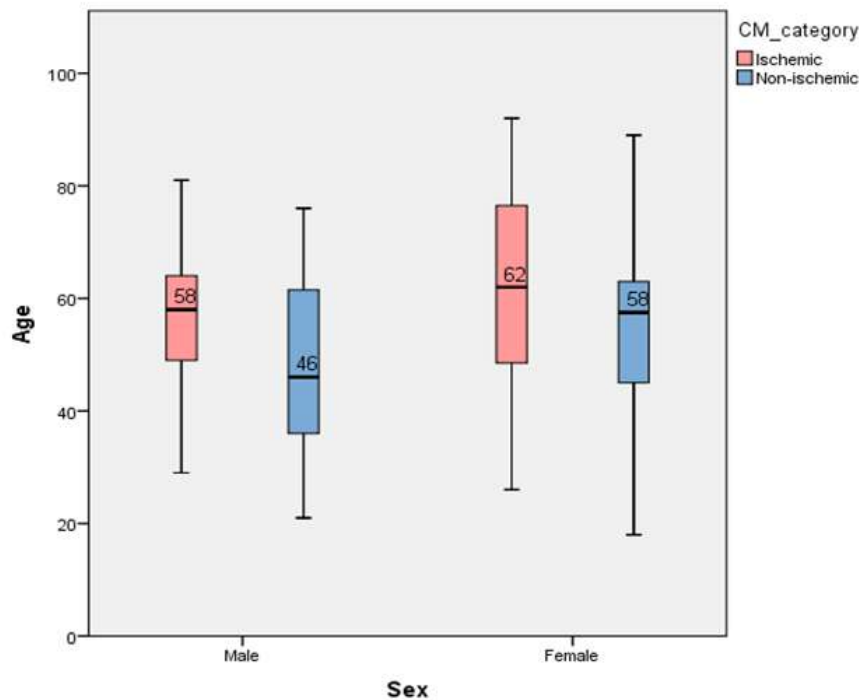


Figure 1: Clustered boxplot to compare mean age differences in regards to gender and cardiomyopathy outcome (ICM versus NICM)

Table 5: Association between Ethnicity and Cardiomyopathy

Ethnicity	n	Ischemic n (%)	Non-Ischemic n (%)	p-value ^a
Malay	101	58 (57.4)	43 (42.6)	0.732
Chinese	44	22 (50)	22 (50)	
Indian	22	14 (63.6)	18 (36.4)	
Others	3	2 (66.7)	1 (33.3)	

^a Fisher's exact test

Results indicated that there is no significant association ($p > 0.05$) between different ethnicities and types of cardiomyopathy, though the highest proportion of ischemic cases were found in Malay people (57.4%).

Table 6: Association between Smoking and Cardiomyopathy

	Total (n)	Cardiomyopathy category		χ^2 statistic (df)	p-value ^a
		ICM n (%)	NICM n (%)		
Smokers	52	25 (48.1)	27 (51.9)	2.147 (1)	0.143
Non-smokers	118	71 (60.2)	47 (39.8)		
Total	170	96 (56.5)	74 (43.5)		

^a Chi-square test

Results show that there is no significant association (p value = 0.143) between smoking and type of cardiomyopathy.

Table 7: Association between DM and Cardiomyopathy

Diabetic	n	Cardiomyopathy		χ^2 statistic (df)	p-value ^a
		ICM n (%)	NICM n (%)		
Yes	87	57 (65.5)	30 (34.5)	5.933 (1)	0.015
No	83	39 (47.0)	44 (53.0)		
Total	170	96 (56.5)	74 (43.5)		

^a Chi-square test

Results indicated that there is significant association (p value = 0.015) between diabetes and type of cardiomyopathy. It was observed that diabetes was slightly more prevalent among patients with ischemic cardiomyopathy (65.5%).

Table 8: Association between LVEF and Cardiomyopathy category

LVEF	n	Cardiomyopathy		χ^2 statistic (df)	p-value ^a
		ICM n (%)	NICM n (%)		
Poor (≤ 40)	140	85 (60.7)	55 (39.3)	5.812 (1)	0.016
Good (≥ 40)	30	11 (36.7)	19 (63.3)		
Total	170	96 (56.5)	74 (43.5)		

^a Chi-square test

Results indicated that there is significant association (p value = 0.016) between LVEF and type of cardiomyopathy. It was

observed that poor LVEF was slightly higher among ischemic patients (60.7%).

Table 9: Association between LDL and Cardiomyopathy type

LDL levels	n	ICM n (%)	NICM n (%)	χ^2 statistic (df)	p-value ^a
LDL>3	61	52 (85.2)	9 (14.8)	32.047 (1)	0.0001
LDL<3	109	44 (40.4)	65 (59.6)		
Total	170	96 (56.5)	74 (43.5)		

^a Chi-square test

Results showed that there is a statistically significant association (p value = 0.0001) between LDL and type of cardiomyopathy. It was found that LDL levels were highest among patients having ischemic cardiomyopathy (85.2%).

Table 10: Association between Gender and LVEF

LVEF	n	Male n (%)	Female n (%)	χ^2 statistic (df)	p-value ^a
Poor (≤ 40)	140	102 (72.9)	38 (27.1)	6.016 (1)	0.014
Good (≥ 40)	30	15 (50.0)	15 (50.0)		
Total	170	117 (68.8)	53 (31.2)		

^a Chi-square test

We found a statistically significant relationship ($p = 0.014$) between gender and LVEF. Women tend to present with better left ventricular ejection fraction in comparison to male patients, as 72.9% patients experiencing reduced/poor LVEF in our study were men.

Table 11: Comparing mean age with left ventricular ejection fraction (LVEF)

LVEF	n	Age (years) Mean (SD)	F statistic (df)	p-value ^a
HFrEF	139	54.3 (14.19)	0.464	0.630
HFmEF	9	57.0 (12.99)	(2, 167)	
HFpEF	22	57.2 (19.21)		

^a One-way ANOVA test

One-way ANOVA test indicated that there is no significant association between mean age and LVEF categories.

Table 12: Comparing mean LVEF among smokers and non-smokers

Cardiomyopathy	n	LVEF (%) Mean (SD)	Mean Difference (95% CI)	t statistic (df)	p-value ^a
Smoker	52	29.6 (13.68)	-4.61	-1.99	0.049
Non-smoker	118	34.2 (14.05)	(-0.31, 9.19)	(168)	

^a Independent t-test

An independent t -test indicated statistically significant relationship between LVEF and smoking as $p < 0.049$, showing reduced mean left ventricular ejection fraction among smokers.

DISCUSSION

The estimated prevalence of HF in Malaysia is around 1-2% (3-20 per 1,000) or 10% >65 years old (100 per 1,000). The overall estimated HF costs in Malaysia was USD 194 million, approximately 1.8% of the total health expenditure, with 3.6% GDP spent on health, according to the Statistics Report On Causes of Death, Malaysia, 2018 (11).

The management of HF has evolved significantly over the last 30 years (12). HF does not comprise of a single entity; it is a clinical syndrome that may present with different characteristics mostly due to factors like age, gender, ethnicity, left ventricular ejection fraction status, and HF etiology (13). Some studies have associated heart failure of ischemic etiology with poor prognosis in comparison to HF from non-ischemic cardiomyopathy (14, 15).

Ischemic and non-ischemic cardiomyopathy (ICM and NICM) both causes heart failure, but the different etiologies can result in differences in management and outcome of the disease (4). Nevertheless, limited studies have been carried out to investigate the different factors associated to ischemic and non-ischemic cardiomyopathies in a Malaysian healthcare setting. Therefore, we conducted this single-centred, observational study and identified patients' factors that were significantly associated with ischemic versus non-ischemic cardiomyopathy.

The mean age of our study population was 53.2 ± 13.3 years for males and 58.3 ± 17.4 years for females, while age range was 21–81 years for men and 18–92 years for women. The mean age of male patients with ICM was 58 years and NICM was 46 years; while in case of female patients the mean age was 62 years and 58 years respectively. Our findings suggest that the mean age of men was much lower in both ICM and NICM groups. This shows men were more prone to developing cardiomyopathy at a younger age than women, regardless of the ischemic or non-ischemic etiology. However, there was no significant relationship between gender and type of cardiomyopathy (CI: 95%; $p = 0.328$).

We also found that the mean age of our study population was significantly higher among ischemic group of patients as compared to non-ischemic cardiomyopathy patients (58.3 ± 13.3 vs. 50.3 ± 15.5 , $p < 0.0001$); with the majority of males (59.0%), high LDL levels (85.2%) and diabetics (65.5%) in the ischemic group.

Our findings were quite similar to Lourenço et al., (15) in which the ischemic group patients were older in age (62.2 ± 10.4 vs. 55.9 ± 15.2 years, $p < 0.001$), with higher proportion of males, diabetes, dyslipidemia and smokers. However, we observed higher proportion of non-smokers (60.2%) in the ischemic group. We also discovered the LVEF was significantly reduced (60.7%, $p = 0.016$) in the ICM patients but their study noted no significant differences in the left ventricular ejection fraction status.

A recent multicentre study (16) revealed their study population's mean age was 54.3 ± 12.2 years for women and 52.1 ± 12.5 years for men, with the age ranging between 18–

87 years for women, and 18–92 years for men. The mean LVEF value for women was higher ($66.6 \pm 7.7\%$) than men ($64.6 \pm 8.1\%$; $P < 0.001$). Our study also found the mean LVEF for females was higher (37.8 ± 17.4) than males ($30.5 \pm 11.6\%$; $p < 0.05$), with 72.9% men having poor ejection fraction rate. Furthermore, their study indicated a strong and positive correlation between age and LVEF in females and weaker correlation in males (females: Pearson $r = 0.2$, $P < 0.001$; males: Pearson $r = 0.1$; $P = 0.005$). But we have not deduced any significant association between age and LVEF ($p = 0.630$). It has been previously reported that data derived from smaller populations may indicate reduced or unchanged LVEF with age and gender (16).

Another study reported that patients with ICM were older (4), and more likely to have diabetes mellitus (DM), peripheral arterial disease, and a history of tobacco use ($p < 0.05$) (17). Furthermore, it's evident that LV function is strongly associated with typical risk factors such as diabetes mellitus, hypertension, smoking, and dyslipidemia (16). Although, our study did not find a significant relationship between LVEF and DM, but we noted significant differences between LVEF and smoking as the mean left ventricular ejection fraction was low (29.6 ± 13.68 ; $p < 0.049$) among smokers.

In the US., ischemic cardiomyopathy is accountable for more than 60% of the congestive heart failure cases (18) and approximately 50% patients who die suddenly in childhood or adolescence or have cardiac transplantation are mostly due to cardiomyopathies (19). Even though in-hospital mortality is greater among ischemic cardiomyopathy patients, it is not an independent predictor of mortality and may fade in the long-term (15, 20). The limited presence of population-based epidemiological studies based on ischemic cardiomyopathy as a distinct clinical entity has undermined the meticulous knowledge of its prevalence and incidence (5).

CONCLUSION

Ischemic heart diseases remain as the principal cause of death (15.6%) in Malaysia (21). Hence, we highlighted upon the burden of ischemic versus non-ischemic cardiomyopathy cases, and identified that factors including age, diabetes mellitus, low density lipoprotein levels and reduced LVEF status were significantly associated to ischemic cardiomyopathy; whereas gender, ethnicity and smoking did not relate to an ischemic presentation. Our study findings also indicated that Malaysian men were at higher risk of developing cardiomyopathies at a much younger age and majority suffered from reduced ejection fraction rate. Furthermore, the left ventricular ejection rate was significantly associated to smoking and gender, but had no evident association with age.

Cardiomyopathies are a serious public health concern and it's mostly asymptomatic in early stages. Thus, it is essential to promote better awareness among doctors and patients- to provide a perspicuous impression on the disease and its management especially, in terms of ischemic versus non-ischemic presentation.

CONFLICT OF INTEREST

The authors report no financial relationships or conflicts of interest regarding the content herein.

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