

Risk Factors of Secondary Cardiovascular Events in a Multi-ethnic Asian Population with Acute Myocardial Infarction: a Retrospective Cohort Study from Malaysia

1. Supplementary Table S1: Participating hospitals

Region	Included hospitals
Northern region	1. Hospital Sultanah Bahiyah, Kedah 2. Hospital Raja Permaisuri Bainun, Perak
East coast region	1. Hospital Raja Perempuan Zainab II, Kelantan
Central region	1. Hospital Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur 2. Hospital Serdang, Selangor 3. Hospital Shah Alam, Selangor 4. Hospital Sungai Buloh, Selangor 5. Hospital Tengku Ampuan Rahimah, Selangor
Southern region	1. Hospital Sultanah Aminah, Johor
Borneo	1. Pusat Jantung Sarawak, Sarawak

2. Supplementary Table S2: Baseline characteristics of cohort individuals by age group

Variables	Age ≤50 years		Age >50 years	
	With MACE	No MACE	With MACE	No MACE
	N=101	N=667	N=130	N=720
Demography, n (%)				
Male sex	93 (92)	635 (95)	110 (87)	638 (89)
Ethnicity				
Bumiputera	61 (60)	426 (64)	77 (59)	429 (60)
Chinese	7 (7)	95 (14)	22 (17)	118 (16)
Indian	33 (33)	146 (22)	31 (24)	173 (24)
Comorbidities, n (%)				
Self-reported hypertension	41 (42)	160 (25)	66 (53)	289 (42)
Self-reported diabetes	28 (29)	136 (21)	59 (48)	225 (33)
Self-reported dyslipidaemia	21 (22)	110 (17)	47 (38)	188 (28)
Smoking	72 (74)	450 (70)	54 (44)	366 (54)
Body mass index ≥25 kg/m ²	69 (75)	426 (72)	99 (84)	525 (84)
Blood parameters, mean (SD)				
Total cholesterol, mmol/L	5.5 (1.7)	5.8 (1.5)	5.6 (1.8)	5.6 (1.6)
LDL, mmol/L	4.2 (1.8)	4.2 (1.4)	3.9 (1.7)	3.9 (1.4)
HDL, mmol/L	1.3 (0.5)	1.3 (0.4)	1.3 (0.3)	1.3 (0.4)
Triglyceride, mmol/L	2.1 (1.0)	2.3 (1.2)	2.0 (1.1)	2.1 (1.0)
Lipoprotein (a), mmol/L	37.2 (28.2)	32.8 (28.1)	36.1 (28.1)	33.3 (27.8)
HbA1c, %	7.2 (2.4)	6.0 (2.1)	7.7 (2.3)	7.1 (2.1)
Blood parameters, n (%)				
LDL > 2.6 mmol/L	80 (89)	554 (92)	92 (81)	543 (84)
Lipoprotein (a) > 30mg/dL	44 (51)	226 (40)	50 (46)	246 (41)
HbA1c >6.5%	32 (33)	222 (35)	70 (59)	285 (42)
Cardiac characteristics, n (%)				
NSTEMI	39 (5)	217 (28)	61 (7)	259 (31)
Left bundle branch block	1 (1)	7 (1)	5 (4)	5 (1)
Any arrhythmia	8 (8)	50 (8)	17 (13)	53 (7)
Heart failure	7 (7)	34 (5)	15 (12)	48 (7)
LVEF in %, mean (SD)	43.0 (13.1)	48.9 (10.7)	44.7 (12.7)	47.6 (11.1)
LVEF ≤40%	31 (46)	110 (22)	34 (40)	141 (27)
LVEF 41–49%	14 (21)	141 (28)	22 (26)	134 (25)
LVEF ≥50%	23 (34)	249 (50)	30 (35)	254 (48)
Cardiogenic shock	16 (16)	62 (9)	16 (12)	67 (9)
Cardiac arrest	1 (1)	12 (2)	3 (2)	15 (2)

Abbreviations: HDL – high density lipoprotein; LDL – low density lipoprotein; LVEF – left ventricular ejection fraction; MACE – major adverse cardiovascular events; SBP – systolic blood pressure.

Categorical variables are presented as counts (column percentages). Continuous variables are presented as mean (standard deviation).

3. Supplementary Table S3: Baseline characteristics of cohort individuals by ethnicity

Variables	Bumiputera		Chinese		Indian	
	With MACE	No MACE	With MACE	No MACE	With MACE	No MACE
	N=138	N=855	N=29	N=213	N=64	N=319
<i>Demography</i>						
Age (years), mean (SD)	51.1 (9.2)	49.7 (9.2)	54.5 (6.5)	50.6 (9.3)	50.9 (9.3)	49.8 (10.0)
Age ≤50 years, n (%)	61 (44)	426 (50)	7 (24)	95 (44.6)	33 (52)	173 (54)
Male sex, n (%)	122 (88)	788 (92)	25 (86)	194 (91.1)	56 (88)	291 (91)
<i>Comorbidities, n (%)</i>						
Self-reported hypertension	60 (45)	263 (32)	15 (53)	83 (41.3)	32 (53)	103 (33)
Self-reported diabetes	50 (38)	209 (26)	12 (43)	50 (24.9)	25 (42)	102 (33)
Self-reported dyslipidaemia	42 (32)	184 (22)	12 (43)	45 (22.4)	14 (23)	69 (22)
Smoking	78 (59)	504 (62)	11 (39)	123 (62.8)	37 (62)	189 (61)
BMI ≥25 kg/m ²	101 (80)	585 (77)	21 (81)	133 (76)	46 (79)	233 (83)
<i>Blood parameters, mean (SD)</i>						
Total cholesterol, mmol/L	5.6 (1.9)	5.8 (1.9)	5.5 (2.0)	5.8 (1.5)	5.4 (1.4)	5.6 (1.4)
LDL, mmol/L	4.2 (1.9)	3.9 (1.9)	5.5 (2.0)	4.1 (1.5)	3.8 (1.3)	3.9 (1.2)
HDL, mmol/L	1.2 (0.3)	1.3 (0.3)	1.2 (0.3)	1.3 (0.3)	1.3 (0.6)	1.3 (0.4)
Triglyceride, mmol/L	2.1 (1.1)	2.2 (1.1)	2.0 (1.1)	2.3 (1.4)	2.0 (0.8)	2.2 (1.0)
Lipoprotein (a), mmol/L	35.3 (26.1)	33.8 (29.6)	39.6 (38.8)	30.2 (23.2)	38.0 (27.5)	33.1 (26.2)
HbA1c, %	7.4 (2.3)	7.0 (2.3)	7.7 (2.6)	7.0 (2.1)	7.5 (2.3)	7.1 (2.0)
<i>Blood parameters, n (%)</i>						
LDL > 2.6 mmol/L	105 (85)	676 (88)	18 (72)	170 (86)	49 (89)	251 (87)
Lipoprotein (a) > 30mg/dL	58 (48)	289 (41)	10 (44)	70 (38)	26 (48)	113 (42)
HbA1c >6.5%	60 (46)	298 (37)	15 (58)	82 (39)	27 (47)	127 (42)
<i>Cardiac characteristics, n (%)</i>						
NSTEMI	48 (5)	247 (27)	17 (7)	95 (39)	25 (7)	105 (27)
LBBB	4 (3)	6 (1)	1 (4)	4 (2)	1 (2)	2 (1)
Any arrhythmia	14 (10)	74 (9)	2 (7)	14 (7)	9 (14)	15 (5)
Heart failure	10 (7)	46 (5)	4 (14)	18 (9)	8 (13)	18 (6)
LVEF in %, mean (SD)	44.7 (12.2)	48.4 (12.2)	39.4 (10.5)	46.6 (11.1)	44.8 (14.9)	49.2 (10.4)
LVEF ≤40%	35 (39)	161 (25)	12 (56)	50 (31)	18 (42)	40 (18)
LVEF 41–49%	20 (23)	179 (28)	6 (27)	29 (18)	10 (23)	67 (30)
LVEF ≥50%	34 (38)	303 (47)	4 (18)	82 (51)	15 (35)	118 (52)
Cardiogenic shock	19 (14)	84 (10)	4 (14)	16 (8)	9 (14)	29 (9)
Cardiac arrest	2 (2)	20 (2)	1 (4)	2 (1)	1 (2)	5 (2)

Abbreviations: BMI – body mass index; HDL – high density lipoprotein; LBBB – left bundle branch block; LDL – low density lipoprotein; LVEF – left ventricular ejection fraction; MACE – major adverse cardiovascular events; SBP – systolic blood pressure.

Categorical variables are presented as counts (column percentages). Continuous variables are presented as mean (standard deviation).

4. Supplementary Table S4: Associations between risk factors of first MI and risk of MACE

Variables	Model 1	Model 2	Model 3	Model 4
Adjusted variables	None	Age, sex, and ethnicity	Model 2 + hypertension, diabetes, BMI, smoking, Lp (a), and HbA1c	Model 3 + mutual adjustments of cardiac characteristics
Demographics				
Age >50 years vs ≤50 years	1.17 (0.90–1.53)	1.14 (0.88–1.49)		
Female	1.51 (1.01–2.24)	1.47 (0.98–2.18)		
Chinese vs Bumiputera	0.86 (0.57–1.28)	0.84 (0.57–1.26)		
Indian vs Bumiputera	1.21 (0.90–1.63)	1.21 (0.90–1.62)		
Comorbidities				
Hypertension	1.77 (1.36–2.30)	1.60 (1.22–2.12)		
Diabetes	1.63 (1.23–2.14)	1.46 (1.09–1.97)		
Dyslipidaemia	1.50 (1.11–2.02)	1.41 (0.95–2.08)		
BMI ≥25 kg/m ² vs <25 kg/m ²	1.04 (0.74–1.45)	1.05 (0.52–2.14)		
Smoking	0.82 (0.63–1.08)	0.93 (0.66–1.30)		
Blood Parameters				
LDL >2.6mmol/L vs ≤2.6mmol/L	0.84 (0.26–2.77)	0.88 (0.27–2.83)		
Lp(a) >30mg/dL vs ≤30mg/dL	1.06 (0.60–1.87)	1.05 (0.59–1.86)		
HbA1c >6.5% vs ≤6.5%	1.36 (1.01–1.85)	1.29 (0.94–1.76)		
Cardiac Characteristics				
NSTEMI vs STEMI	1.41 (1.08–1.83)	1.37 (1.05–1.79)	1.32 (1.01–1.73)	1.57 (1.07–2.30)
Right bundle branch block	2.37 (1.16–4.81)	2.36 (1.16–4.82)	2.09 (1.02–4.29)	1.88 (0.89–3.95)
Left bundle branch block	2.85 (1.26–6.43)	2.98 (1.32–6.75)	2.86 (1.25–6.55)	1.88 (0.74–4.76)
2 nd degree heart block	2.88 (0.71–11.67)	2.70 (0.66–10.99)	2.45 (0.59–10.16)	2.09 (0.48–9.14)
Atrial fibrillation	0.71 (0.23–2.24)	0.67 (0.21–2.11)	0.67 (0.21–2.13)	0.57 (0.17–1.85)
Ventricular fibrillation	1.43 (0.73–2.80)	1.44 (0.73–2.82)	1.51 (0.76–3.00)	1.21 (0.56–2.63)
Supraventricular tachycardia	1.39 (0.69–2.83)	1.49 (0.73–3.04)	1.58 (0.77–3.23)	1.38 (0.64–2.96)
Heart failure	1.59 (1.02–2.47)	1.54 (0.99–2.41)	1.47 (0.94–2.30)	1.18 (0.69–2.01)
LVEF ≤40% vs ≥50%	2.11 (0.33–13.34)	2.19 (0.34–14.21)	2.20 (0.33–14.56)	2.24 (0.27–18.39)
LVEF 41–49% vs ≥50%	1.18 (0.41–3.43)	1.21 (0.41–3.58)	1.19 (0.40–3.53)	1.30 (0.40–4.23)
Cardiogenic shock	1.56 (1.07–2.27)	1.56 (1.07–2.26)	1.56 (1.07–2.27)	1.49 (0.99–2.26)
Cardiac arrest	0.94 (0.35–2.53)	0.93 (0.34–2.50)	0.91 (0.33–2.47)	0.82 (0.29–2.36)

Abbreviations: BMI – body mass index; LDL – low density lipoprotein; Lp(a) – lipoprotein (a); LVEF – left ventricular ejection fraction; MACE – major adverse cardiovascular events.

Values are presented as Hazard Ratio(95% Confidence Interval)

Model 1: Unadjusted Cox regression analysis

Model 2: Cox regression adjusted for age, sex, and ethnicity

Model 3: Cox regression adjusted for Model 2 + hypertension, diabetes, BMI, smoking, lipoprotein (a), and HbA1c

Model 4: Cox regression adjusted for Model 3 + mutually adjusted cardiac characteristics

Dark Background: No comparisons could be made for those coloured as it's the same variables.

5. Supplementary Table S5: Associations between risk factors of first MI and risk of MACE by age

Risk Factors	Age Group	Model 2		Model 3	
		HR (95%CI)	p-value	HR (95%CI)	p-value
Comorbidities					
Hypertension	Age ≤50 years	1.92 (1.29–2.86)	0.265		
	Age >50 years	0.90 (0.61–1.33)			
Diabetes	Age ≤50 years	1.42 (0.93–2.19)	0.756		
	Age >50 years	1.15 (0.74–1.77)			
Dyslipidaemia	Age ≤50 years	1.22 (0.76–1.96)	0.800		
	Age >50 years	1.17 (0.71–1.94)			
BMI ≥25 kg/m²	Age ≤50 years	1.03 (0.65–1.62)	0.625		
	Age >50 years	1.11 (0.83–1.49)			
Smoking	Age ≤50 years	1.12 (0.72–1.75)	0.097		
	Age >50 years	0.93 (0.66–1.32)			
Blood Parameters					
Lp(a) >30mg/dL	Age ≤50 years	1.17 (0.79–1.73)	0.778		
	Age >50 years	1.10 (0.76–1.60)			
HbA1c >6.5%	Age ≤50 years	0.81 (0.53–1.24)	0.041		
	Age >50 years	1.57 (1.03–2.38)			
Cardiac Characteristics					
NSTEMI	Age ≤50 years	1.28 (0.86–1.91)	0.605	1.23 (0.82–1.83)	0.612
	Age >50 years	1.23 (0.82–1.85)		1.10 (0.73–1.67)	
RBBB	Age ≤50 years	2.11 (0.52–0.57)	0.843	2.15 (0.53–8.81)	0.966
	Age >50 years	1.31 (0.27–6.53)		1.04 (0.21–5.22)	
LBBB	Age ≤50 years	1.00 (0.14–7.17)	0.093	1.02 (0.14–7.34)	0.127
	Age >50 years	5.53 (0.64–47.50)		4.39 (0.50–38.36)	
2 nd degree HB	Age ≤50 years	16.17 (2.24–116.73)	0.136	18.27 (2.51–133.07)	0.108
	Age >50 years	0.11 (0.01–1.81)		0.08 (0.01–1.33)	
LVEF ≤40%	Age ≤50 years	1.14 (0.74–1.74)	0.577	1.11 (0.72–1.69)	0.684
	Age >50 years	1.03 (0.71–1.50)		0.96 (0.66–1.40)	
Cardiogenic shock	Age ≤50 years	1.77 (1.04–3.02)	0.539	1.74 (1.02–2.98)	0.656
	Age >50 years	0.94 (0.47–1.87)		0.88 (0.44–1.77)	

Abbreviations: BMI – body mass index; HB – heart block; LBBB – left-bundle branch block; Lp(a) – lipoprotein (a); LVEF – left ventricular ejection fraction; MACE – major adverse cardiovascular events; RBBB – right bundle branch block.

Model 2: Cox regression adjusted for sex and ethnicity

Model 3: Cox regression adjusted for Model 2 + hypertension, diabetes, BMI, smoking, HbA1c and lipoprotein (a)

Subgroup analysis was performed using multivariable Cox regression analysis with addition of age-group as interaction term and linear combinations of model parameters

P-value was calculated using Wald test. P-value of >0.05 demonstrates no difference between age ≤50 years and age >50 years.

Dark Background: No comparisons could be made for those coloured as it's the same variables.

6. Supplementary Table S6: Associations between risk factors of first MI and risk of MACE by sex

Risk Factors	Gender	Model 2	
		HR (95%CI)	p-value*
Comorbidities			
Hypertension	Female	1.46 (0.91–2.33)	0.048
	Male	1.55 (1.17–2.06)	
Diabetes	Female	1.72 (1.07–2.77)	0.050
	Male	1.36 (1.01–1.83)	
Dyslipidaemia	Female	1.69 (0.95–3.00)	0.410
	Male	1.22 (0.89–1.66)	
Body mass index ≥25 kg/m²	Female	1.22 (0.78–1.91)	0.016
	Male	1.07 (0.75–1.54)	
Smoking	Female	1.66 (0.41–6.71)	0.764
	Male	0.85 (0.64–1.13)	
Blood Parameters			
Lipoprotein (a) >30mg/dL	Female	1.10 (0.61–2.01)	0.184
	Male	1.19 (0.91–1.57)	
HbA1c >6.5%	Female	1.45 (0.89–2.36)	0.884
	Male	1.12 (0.84–1.48)	
Cardiac Characteristics			
NSTEMI	Female	1.22 (0.71–2.09)	0.511
	Male	1.43 (1.08–1.89)	
Left bundle branch block	Female	2.32 (0.27–20.06)	0.688
	Male	2.81 (1.15–6.84)	
LVEF ≤40%	Female	1.64 (0.93–2.87)	0.207
	Male	1.09 (0.80–1.47)	
Cardiogenic shock	Female	1.75 (0.61–5.01)	0.739
	Male	1.52 (1.02–2.27)	

Abbreviations: LVEF – left ventricular ejection fraction; MACE – major adverse cardiovascular events.

Model 2: Cox regression adjusted for age, and ethnicity

Subgroup analysis was performed using multivariable Cox regression analysis with addition of gender as interaction term and linear combinations of model parameters

P-value was calculated using Wald test. P-value of >0.05 demonstrates no difference between male and female groups.

7. Supplementary Table S7: Associations between risk factors of first MI and risk of MACE by ethnicity

Risk Factors	Ethnic Group	Model 2	
		HR (95%CI)	p-value*
Comorbidities			
Hypertension	Bumiputera	1.53 (1.08–2.15)	0.697
	Chinese	0.79 (0.45–1.39)	
	Indian	1.35 (0.88–2.06)	
Diabetes	Bumiputera	1.47 (1.03–2.09)	0.916
	Chinese	0.94 (0.50–1.77)	
	Indian	1.18 (0.75–1.86)	
Dyslipidaemia	Bumiputera	1.31 (0.91–1.89)	0.282
	Chinese	1.01 (0.58–2.00)	
	Indian	0.95 (0.53–1.71)	
Body mass index ≥25 kg/m ²	Bumiputera	1.01 (0.66–1.56)	0.706
	Chinese	0.86 (0.55–1.33)	
	Indian	1.15 (0.82–1.59)	
Smoking	Bumiputera	0.89 (0.63–1.27)	0.109
	Chinese	0.57 (0.30–1.07)	
	Indian	1.30 (0.89–1.91)	
Blood Parameters			
Lipoprotein (a) >30mg/dL	Bumiputera	1.09 (0.78–1.53)	0.969
	Chinese	0.86 (0.49–1.53)	
	Indian	1.28 (0.82–2.00)	
HbA1c >6.5%	Bumiputera	1.18 (0.84–1.67)	0.457
	Chinese	0.95 (0.54–1.67)	
	Indian	1.02 (0.65–1.60)	
Cardiac Characteristics			
NSTEMI	Bumiputera	1.42 (1.01–2.00)	0.762
	Chinese	0.86 (0.50–1.48)	
	Indian	1.09 (0.68–1.74)	
Left bundle branch block	Bumiputera	3.58 (1.33–9.70)	0.849
	Chinese	0.47 (0.05–4.19)	
	Indian	0.89 (0.10–7.97)	
LVEF ≤40%	Bumiputera	0.81 (0.56–1.16)	0.052
	Chinese	0.95 (0.54–1.68)	
	Indian	1.67 (1.10–2.52)	
Cardiogenic shock	Bumiputera	1.50 (0.92–2.43)	0.917
	Chinese	1.06 (0.36–3.14)	
	Indian	1.25 (0.56–2.77)	

Abbreviations: LVEF – left ventricular ejection fraction; MACE – major adverse cardiovascular events.

Model 2: Cox regression adjusted for age and sex

Subgroup analysis was performed using multivariable Cox regression analysis with addition of ethnic group as interaction term and linear combinations of model parameters
P-value was calculated using Wald test. P-value of >0.05 demonstrates no difference between Bumiputera and other ethnic groups.