Gender Differences in Coronary Artery Disease - the Malaysian National Cardiovascular Disease Database-Percutaneous Coronary Intervention (NCVD-PCI) Registry.

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Gender Differences in Coronary Artery Disease (CAD)- Malaysian NCVD-PCI registry

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Introduction

- Cardiovascular disease (CVD) is the leading cause of mortality in both men and women.
- The risk of heart disease in women is often underestimated due to misperception that females are 'protected' against CVD.
- There are **well described differences between women and men** in epidemiology, pathophysiology, clinical manifestations, effects of therapy and outcomes.
- These differences are due to:
- A) **sex differences**:- Biological differences among women and men due to gene expression from the sex chromosomes and subsequent differences in sexual hormones. Eg. vascular function and NO signaling, myocardial remodeling under stress or metabolism of drugs by sex specific cytochrome expression.
- B) **gender differences**:- Unique to human. Arise from sociocultural processes eg. different behaviors of women and men; exposure to specific influences of the environment; different forms of nutrition, lifestyle or stress; or attitudes towards treatments and prevention.
- Both sex and gender influence human development and it is almost impossible to distinguish their effects properly.

Malaysian NCVD-PCI registry Methods

- An on-going observational prospective registry of patients who underwent PCI.
- It was started in 2007 and designed to evaluate the clinical presentation, angiographic severity, management and clinical outcomes of patients, 18 years and above with coronary artery disease who underwent PCI.
- This report is based on data collected from:
- **1)1st January 2007 through 31st December 2009** from **eleven** participating **centres**.
- **N= 10,554 patients** of which **1,961 (18.6%) were women** and 8,593 (81.4%) were men.

- **2)1st January 2014 through 31st December 2016** from **eighteen** participating **centres**.
- **N=26,710 patients** of which **4,450 (16.7%) were women** and 22260 (83.3%) were men.

- Both periods represent **3-year pooled data**.
- The NCVD-PCI is registered in the National Medical Research Register of Malaysia (ID: NMRR-07-20-250)

- Data were collected regarding:
- A) **Demographic** characteristics,
- B) **coronary risk factors** (smoking, family history of premature cardiovascular disease, dyslipidemia, hypertension, diabetes mellitus) and **other co-morbidities** (Body Mass Index [BMI], history of myocardial infarct, new onset angina less than 2-weeks prior to admission, congestive heart failure more than 2-weeks prior to admission and chronic renal failure.
- C) **Cardiac status at presentation,**
- D) **in-patient clinical care** (time to treatment),
- E) **types of adjunctive treatment** used and **angiographic severity**.
- (Normal/mild disease was defined as <50% stenosis and significant stenosis was defined as ≥70% stenosis in at least one of the epicardial vessels).
- **Outcomes** of interest were **in-hospital, 30-day and 6-month mortality** post-PCI.

Patient characteristics

- **2007-2009 cohort**: Women were *5 years older* than men but there were no significant difference in rate of premature CAD.
- CAD is more often in men below age 60, but after 60 years, more often in women
- *Women* had significantly higher rates of *diabetes mellitus, hypertension, chronic renal failure, new onset angina and prior history of heart failure*.
- Significantly more men were smokers and had past history of myocardial infarction.
- No significant difference in rates of BMI>26, dyslipidemia or documented coronary artery disease between gender (Table 1).
- **2014-2016 cohort**: All significantly different variables remained the same except *dyslipideamia* has become significantly more in *women* and new onset angina is no longer significant (Table 2).

Clinical presentations

- **2007-2009 cohort -** *women* had significantly more *rapid heart rate and a higher systolic blood pressure.*
- In the *STEMI cohort*, *more women were in Killip class III & IV* (7.9% vs 5.3%, p=0.047) (Table 1).
- **2014-2016 cohort-** All the significant variables remained the same.
- However, there is a *marked increase* in percentage of patients with *Killip class III & IV (16.7% Vs 13.6%)* for both sexes. Indicating that centers were performing more high risk cases (Table 2).

Table 1: Patients' baseline characteristics and clinical presentation on admission by gender, 2007- 2009

Variables	2007-2009			
	Female (n=1965)	Male (n=8637)	All (n=10602)	*p*-value
Demographic				
Age, mean (SD)	61.2 (9.7)	56.0 (10.0)	57.0 (10.2)	< 0.001
Smoking status, n (%)				
Former	52 (2.7)	2969 (34.4)	3021 (28.5)	< 0.001
Current	44 (2.2)	1930 (22.4)	2974 (18.6)	
BMI, n (%)				
Overweight and obese	1369 (69.7)	5963 (69.0)	7332 (69.2)	0.245
Premature heart disease, n (%)	350 (17.8)	1670 (19.3)	2020 (19.1)	0.350
Clinical history, n (%)				
Diabetes	1238 (63.0)	3656 (42.3)	4894 (46.2)	< 0.001
Hypertension	1685 (85.8)	6116 (70.8)	7801 (73.6)	< 0.001
Chronic renal failure	183 (9.3)	517 (6.0)	700 (6.6)	< 0.001
New onset angina (< 2 weeks)	519 (26.4)	2082 (24.1)	2601 (24.5)	0.007
Congestive Heart failure (> 2 weeks)	90 (4.6)	333 (3.9)	423 (4.0)	0.011

Variables	2007-2009			
	Female (n=1965)	Male (n=8637)	All (n=10602)	*p*-value
Clinical history, n (%)				
Myocardial Infarction history	606 (30.8)	3791 (43.9)	4397 (41.5)	< 0.001
Dyslipidaemia	1462 (74.4)	6318 (73.2)	7780 (73.4)	0.487
Documented coronary artery disease	1081 (55.0)	4910 (56.9)	5991 (56.5)	0.352
Clinical presentations				
Heart rate, mean (SD), beats/ minutes	73.8 (16.1)	71.1 (15.4)	71.6 (15.6)	< 0.001
Systolic BP, mean (SD), mmHg	149.0 (28.8)	135.7 (24.8)	138.2 (26.1)	< 0.001
Diastolic BP, mean (SD), mmHg	75.6 (13.2)	77.1 (13.0)	76.8 (13.0)	< 0.001
Killip class (STEMI only), n (%)				
I & II	198 (58.4)	1386 (60.5)	1584 (60.3)	0.047
III & IV	27 (7.9)	121 (5.3)	148 (5.6)	

p-values are calculated for gender, comparing all sub-categories except the unknown category for all variables.
All p-values are calculated using the Chi-square test unless stated.

Table 2: Patients' baseline characteristics and clinical presentation on admission by gender, 2014-2016

Variables	2014-2016			
	Female (n=4450)	Male (n=22260)	All (n=26710)	*p*-value
Demographic				
Age, mean (SD)	61.9 (10.0)	56.9 (10.5)	57.7 (10.6)	< 0.001
Smoking status, n (%)				
Former	125 (2.8)	5868 (26.4)	5993 (22.4)	< 0.001
Current	111 (2.5)	7069 (31.8)	7180 (26.9)	
BMI, n (%)				
Overweight and obese	2061 (62.1)	10568 (62.3)	12629 (62.3)	0.791
Premature heart disease, n (%)	560 (12.6)	2951 (13.3)	3511 (13.1)	0.442
Clinical history, n (%)				
Diabetes	2727 (61.3)	9214 (41.4)	11941 (44.7)	< 0.001
Hypertension	3564 (80.1)	14486 (65.1)	18050 (67.6)	< 0.001
Chronic renal failure	329 (7.4)	948 (4.3)	1277 (4.8)	< 0.001
New onset angina (< 2 weeks)	1616 (36.3)	8398 (37.7)	10014 (37.5)	0.185
Congestive Heart failure (> 2 weeks)	251 (5.6)	911 (4.1)	1162 (4.4)	< 0.001

Variables	2014-2016			
	Female (n=4450)	Male (n=22260)	All (n=26710)	*p*-value
Clinical history, n (%)				
Myocardial Infarction history	1423 (32.2)	8807 (39.6)	10239 (38.3)	< 0.001
Dyslipidaemia	2788 (62.7)	12118 (54.4)	14906 (55.8)	< 0.001
Documented coronary artery disease	1738 (39.1)	8517 (38.3)	10255 (38.4)	0.581
Clinical presentations				
Heart rate, mean (SD), beats/ minutes	77.4 (17.4)	74.8 (17.2)	75.2 (17.3)	< 0.001
Systolic BP, mean (SD), mmHg	147.6 (27.6)	136.2 (25.4)	138.1 (26.2)	< 0.001
Diastolic BP, mean (SD), mmHg	75.7 (14.3)	77.8 (13.8)	77.4 (13.9)	< 0.001
Killip class (STEMI only), n (%)				
I & II	560 (83.3)	4609 (86.4)	5169 (86.0)	0.033
III & IV	112 (16.7)	728 (13.6)	840 (14.0)	

p-values are calculated for gender, comparing all sub-categories except the unknown category for all variables.
All p-values are calculated using the Chi-square test unless stated.

Table 3: Comparison of patients' baseline characteristics and clinical presentation on admission by gender

Variables	2007-2009				2014-2016			
	Female (n=1965)	Male (n=8637)	All (n=10602)	*p*-value	Female (n=4450)	Male (n=22260)	All (n=26710)	*p*-value
Diabetes	1238 (63.0)	3656 (42.3)	4894 (46.2)	< 0.001	2727 (61.3)	9214 (41.4)	11941 (44.7)	< 0.001
Hypertension	1685 (85.8)	6116 (70.8)	7801 (73.6)	< 0.001	3564 (80.1)	14486 (65.1)	18050 (67.6)	< 0.001
Chronic renal failure	183 (9.3)	517 (6.0)	700 (6.6)	< 0.001	329 (7.4)	948 (4.3)	1277 (4.8)	< 0.001
Dyslipidaemia	1462 (74.4)	6318 (73.2)	7780 (73.4)	0.487	2788 (62.7)	12118 (54.4)	14906 (55.8)	< 0.001
Smoking status, n (%)								
Former	52 (2.7)	2969 (34.4)	3021 (28.5)	< 0.001	125 (2.8)	5868 (26.4)	5993 (22.4)	< 0.001
Current	44 (2.2)	1930 (22.4)	2974 (18.6)		111 (2.5)	7069 (31.8)	7180 (26.9)	
Clinical history, n (%)								
New onset angina (< 2 weeks)	519 (26.4)	2082 (24.1)	2601 (24.5)	0.007	1616 (36.3)	8398 (37.7)	10014 (37.5)	0.185
Congestive Heart failure (> 2 weeks)	90 (4.6)	333 (3.9)	423 (4.0)	0.011	251 (5.6)	911 (4.1)	1162 (4.4)	< 0.001
Killip class (STEMI only), n (%)								
III & IV	27 (7.9)	121 (5.3)	148 (5.6)		112 (16.7)	728 (13.6)	840 (14.0)	

p-values are calculated for gender, comparing all sub-categories except the unknown category for all variables.
All p-values are calculated using the Chi-square test unless stated.

Treatment

- **Time to treatment**, when available, for **STEMI** patients presenting within 24 hours of symptom onset were analysed.
- **2007-2009 cohort-** *Women* had *longer door-to-balloon time [DTB]* (mean **169.5** min. vs 127.3 min, p<0.052) and *significantly longer transfer time* (mean *300.4* min vs 166.3 min, p< 0.039) although they had similar symptom-to-door time.
- Overall, women and men has similar rates of emergent (primary & rescue) STEMI PCI, but *women* receive *less rescue PCI* compared to men (36.8% vs 47.3%, p<0.035)
- However, on further analysis of the STEMI PCI (primary, rescue and delayed) cohort alone (women n=307, men n=2,050), *women* in fact *received less primary PCI* (19.5% vs 23.6%, p=0.0047) and the difference in the rescue PCI is no longer significant.
- **2014-2016 cohort -** Although women still has *longer DTB time* (**145.25** min. vs 126.91min., p=0.048) and *Transfer time* (*144.93* min. vs 120.65 min., p=0.141) these *has improved markedly*.
- Overall, *women* now has *lower rates of emergent (primary & rescue) STEMI PCI (13.7% vs 20.9%, p<0.001*, but rates of *rescue PCI* (62.18% vs 61.2%, p<0.551) *are no longer significant* (Table 4).

Table 4: Comparing In- patient clinical care by gender

Types of treatment	2007-2009				2014-2016			
	Female (n=1965)	Male (n=8637)	All (n=10602)	*p*-value	Female (n=4450)	Male (n=22260)	All (n=26710)	*p*-value
PCI status, n (%)								
Elective	1911 (90.3)	8452 (90.1)	10363 (90.1)	0.444	3247 (73.0)	15409 (69.2)	18656 (69.9)	< 0.001
NSTEMI/UA	106 (5.0)	420 (4.5)	526 (4.6)	0.390	595 (13.4)	2192 (9.9)	2787 (10.4)	< 0.001
*STEMI	95 (4.5)	484 (5.2)	579 (5.0)	0.082	608 (13.7)	4656 (20.9)	5264 (19.7)	< 0.001
(Rescue PCI)	35 (36.8)	229 (47.3)	264 (45.6)	0.035	376 (62.1)†	2827 (61.2)†	3203 (12.0)†	0.551
Thrombolytics given prior to PCI procedure in STEMI, n (%)								
< 12 hrs	42 (28.9)	95 (20.9)	112 (21.8)	< 0.001	105 (49.3)	941 (49.5)	1046 (49.5)	0.004

*patients who underwent PCI as emergent procedure (primary and rescue) during same index admission.

†As a percentage of total emergent PCI.

p-values are calculated for gender, comparing all sub-categories except the unknown category for all variables.

All p-values are calculated using the Chi-square test unless stated.

Use of PCI adjunct and angiographic disease severity

- **2007-2009 cohort** - Use of adjunctive pharmacotherapy viz. Glycoprotein IIb/IIIa inhibitor, heparin, aspirin and clopidogrel were similar for both gender.
- Overall, women and men had similar rate of single and multi-vessel disease, lesion type (A & B1, B2 & C) and lesion length (≤ 20mm, > 20mm) but
- *Women* had *significantly more left main stem disease* (**1.3%** vs 0.6%, p<0.003), *smaller diameter vessel* (<3.0mm: **45.5%** vs 34.8%, p<0.001) and *received less drug eluting stent (DES*) (39.8% vs 54.5%, p<0.001) (Table 5).
- **2014-2016 cohort** – *Men* received *significantly more Glycoprotein IIb/IIIa and less clopidogrel* (likely receive more ticargrelor)
- *women* still had significantly *more left main stem disease* (**3.3%** vs 2.7%, p<0.015), *smaller diameter vessel* (<3.0mm: **51.8%** vs 39.8%, p<0.001) but received *more drug eluting stent (DES*) (77.0% vs 75.8%, p<0.022) (Table 5).

Table 5: Comparing the use of PCI adjunct and angiographic disease severity by gender.

Variables	2007 - 2009				2014 - 2016			
	Female (n=1965)	Male (n=8637)	All (n=10602)	*p*-value	Female (n=4450)	Male (n=22260)	All (n=26710)	*p*-value
Coronary disease, n (%)								
Graft	17 (0.8)	113 (1.2)	130 (1.1)	0.036	34 (0.8)	253 (1.1)	287 (1.1)	0.028
Left main stem	27 (1.3)	55 (0.6)	82 (0.7)	0.003	145 (3.3)	600 (2.7)	745 (2.8)	0.037
Lesion diameter, n (%), mm								
< 3.0	1337 (45.5)	4503 (34.8)	5840 (36.8)	< 0.001	2307 (51.8)	8869 (39.8)	11176 (41.84)	< 0.001
Types of stent used, n (%)								
Drug Eluting stent	339 (39.8)	2289 (54.5)	2628 (52.0)	< 0.001	3161 (77.0)	15427 (75.8)	18588 (76.0)	0.022

p-values are calculated for gender, comparing all sub-categories except the unknown category for all variables.

All p-values are calculated using the Chi-square test unless stated.

Mortality

- **2007-2009 cohort** - **In hospital mortality:** *women had significantly higher unadjusted in-hospital mortality* for all PCI, STEMI and NSTEMI.
- *After multivariable adjustment* for all significant clinical characteristics, there was still a trend towards higher mortality for all PCI and NSTEMI in women although these differences were *no longer statistically significant.*
- **30 D mortality**: *trend towards higher unadjusted mortality rates* for all PCI, STEMI and NSTEMI in *women* although not significant.
- *After multivariable adjustment* these differences were *much attenuated except for NSTEMI* where the rate was increased, but all these differences were *not significant.*
- **6 Month mortality**: *Women* had *significantly higher unadjusted mortality rates for all PCI, STEMI and NSTEMI.*
- After *multivariable adjustment*, there was still a *trend towards higher mortality* rates but these differences were *no longer significant.*

- **2014-2016 cohort** – Although the *Crude odds ratio* were *still higher in women* across all stratum these has improved markedly and *after multivariate adjustment these were no longer significant*

Table 6: In hospital mortality for women compared to men

	2007 – 2009				2014 - 2016				
	Event rates		odds Ratio (95 % CI)		Event rates		odds Ratio (95 % CI)		*p*-value
	women	men	Crude	Adjusted	women	men	Crude	Adjusted	
All PCI	39/1961 (1.99)	84/8593 (0.98)	2.06 (1.40, 3.01)	1.71 (0.96, 3.06)*	101/ 4432 (2.28)	445/22180 (2.01)	1.14 (0.92, 1.42)	0.78 (0.55, 1.11)*	0.781
STEMI	19/307 (6.19)	59/2050 (2.88)	2.23 (1.31, 3.79)	1.06 (0.37, 3.03)†	61/694 (8.79)	336/5538 (6.07)	1.49 (1.12, 1.98)	0.89 (0.59, 1.36)†	0.599
NSTEMI	10/345 (2.90)	11/1393 (0.79)	3.75 (1.58, 8.90)	2.70 (0.68, 10.73)*	16/510 (3.14)	45/2203 (2.04)	1.56 (0.87, 2.78)	1.14 (0.63, 2.05)*	0.675
Unstable angina	2/112 (1.79)	1/341 (0.29)	6.18 (0.56, 68.83)	4.25 (0.21, 84.29)*	3/335 (0.90)	9/1218 (0.74)	1.21 (0.34, 4.51)	0.85 (0.22, 3.27)*	0.810

Abbreviations: PCI = percutaneous coronary intervention; STEMI = ST- elevation myocardial infarction; NSTEMI = non-STEMI.

*Odds ratio of female vs male and 95% CI obtained through logistic regression including the following covariates: Age, smoking, diabetes, hypertension, new onset of angina, prior history of heart failure, renal failure.

†Odds ratio of female vs male and 95% CI obtained through logistic regression including the following covariates: Age, Smoking, diabetes, hypertension, new onset angina, prior history of heart failure and Killip class

Table 7: Prognostic factors for in-hospital mortality by gender

Variables	2007 - 2009							
	Male				Female			
	n	Hazard ratio	95 % CI	*p*-value	n	Hazard ratio	95% CI	*p*-value
Age group								
20 - < 60	1854	1.00						
≥ 60	962	2.92	(1.53, 5.58)	0.002				
PCI status								
Elective	2337	1.00			464	1.00		
NSTEMI/ UA	169	6.83	(2.18, 21.45)	0.001	38	8.30	(1.76, 39.06)	0.007
STEMI	310	25.04	(10.83, 57.90)	< 0.001	64	15.09	(4.30, 52.93)	< 0.001
Diabetes mellitus								
No	1625	1.00						
Yes	1191	2.02	(1.06, 3.85)	0.033				
Killip class								
I	1803	1.00			360	1.00		
II	868	2.49	(1.08, 5.71)	0.031	165	1.38	(0.38, 4.96)	0.626
III	79	6.73	(2.11, 21.52)	0.001	24	1.40	(0.15, 12.86)	0.765
IV	66	21.20	(8.98, 50.03)	< 0.001	17	10.52	(2.79, 39.62)	0.001

Abbreviations: PCI = percutaneous coronary intervention; STEMI = ST- elevation myocardial infarction; NSTEMI = non-STEMI.

Table 8: Prognostic factors for in-hospital mortality by gender

Variables	2014 - 2016							
	Male				Female			
	n	Hazard ratio	95 % CI	*p*-value	n	Hazard ratio	95% CI	*p*-value
Age group								
20 - < 60	7779	1.00			927	1.00		
≥ 60	4198	1.94	(1.59, 2.37)	< 0.001	1277	1.86	(1.08, 3.21)	0.026
PCI status								
Elective	6125	1.00			1214	1.00		
NSTEMI/ UA	1666	3.18	(1.98, 5.10)	< 0.001	446	4.29	(1.77, 10.43)	0.001
STEMI	4186	5.33	(3.54, 8.03)	< 0.001	544	7.44	(3.24, 17.08)	< 0.001
Diabetes mellitus								
No	6500	1.00			nil			
Yes	4497	1.35	(1.09, 1.68)	0.006	nil	nil	nil	
Killip class								
I	10395	1.00			1919	1.00		
II	776	3.08	(2.16, 4.39)	< 0.001	144	0.91	(0.32, 2.58)	0.858
III	135	6.1	(3.83, 9.71)	< 0.001	25	2.45	(0.74, 8.12)	0.144
IV	671	12.02	(9.41, 15.33)	< 0.001	116	5.81	(3.48, 9.71)	< 0.001

Abbreviations: PCI = percutaneous coronary intervention; STEMI = ST- elevation myocardial infarction; NSTEMI = non-STEMI.

Table 9: Risk of mortality at 30 days for women compared to men

	2007 – 2009				2014 – 2016				
	Event rates		odds Ratio (95 % CI)		Event rates		odds Ratio (95 % CI)		*p*-value
	women	men	Crude	Adjusted	women	men	Crude	Adjusted	
All PCI	9/1330 (0.68)	24/6175 (0.39)	1.75 (0.81, 3.77)	1.08 (0.40, 2.90)*	143/3412 (4.19)	573/17081 (3.35)	1.26 (1.05, 1.52)	0.90 (0.66, 1.23)*	0.510
STEMI	3/222 (1.35)	6/1558 (0.39)	3.54 (0.88, 14.27)	1.70 (0.30, 9.51)†	73/580 (12.59)	386/4465 (8.65)	1.52 (1.17, 2.00)	1.03 (0.75, 1.42)†	0.854
NSTEMI	4/260 (1.54)	5/1106 (0.45)	3.44 (0.92, 12.90)	7.51 (0.94, 60.21)*	25/401 (6.23)	59/1766 (3.34)	1.92 (1.19, 3.11)	1.18 (0.62, 2.24)*	0.624
Unstable angina	0/82 (0.00)	1/250 (0.40)	-	-	6/261 (2.30)	15/964 (1.56)	1.49 (0.57, 3.88)	0.98 (0.36, 2.67)*	0.974

*Odds ratio of female vs male and 95% CI obtained through logistic regression including the following covariates: Age, smoking, diabetes, hypertension, new onset of angina, prior history of heart failure, renal failure.

†Odds ratio of female vs male and 95% CI obtained through logistic regression including the following covariates: Age, smoking, diabetes, hypertension, new onset of angina, prior history of heart failure, renal failure and Killip class.

Table 12: Risk of mortality at 6 months for women compared to men

	2007 – 2009				2014 – 2016				
	Event rates		odds Ratio (95 % CI)		Event rates		odds Ratio (95 % CI)		*p*-value
	women	men	Crude	Adjusted	women	men	Crude	Adjusted	
All PCI	19/987 (1.93)	19/4508 (0.42)	4.64 (2.54, 8.79)	2.18 (0.97, 4.90)*	247/3337 (7.40)	838/16649 (5.03)	1.51 (1.30, 1.75)	1.04 (0.81, 1.33)*	0.773
STEMI	3/169 (1.78)	5/1169 (0.43)	4.21 (1.00, 17.77)	2.68 (0.37, 19.61)†	97/565 (17.17)	455/4344 (10.47)	1.77 (1.40, 2.25)	1.15 (0.81, 1.64)†	0.435
NSTEMI	5/202 (2.48)	5/842 (0.59)	4.25 (1.22, 14.82)	2.66 (0.73, 9.69)*	48/395 (12.15)	105/1724 (6.09)	2.13 (1.49, 3.06)	1.18 (0.73, 1.91)*	0.499
Unstable angina	1/59 (1.69)	0/188 (0.00)	-	-	14/254 (5.51)	29/939 (3.09)	1.83 (0.95, 3.52)	1.14 (0.57, 2.27)*	0.713

*Odds ratio of female vs male and 95% CI obtained through logistic regression including the following covariates: Age, smoking, diabetes, hypertension, new onset of angina, prior history of heart failure, renal failure.

†Odds ratio of female vs male and 95% CI obtained through logistic regression including the following covariates: Age, smoking, diabetes, hypertension, new onset of prior history of heart failure, renal failure and Killip class.

Discussion

- The **2007-2009 cohort** comprised of 10,554 patients, 1961 (18.6%) were women and 8,593 (81.4%) were men with *a female to male ratio of 0.23*.
- While in the Malaysian National Cardiovascular Disease Database-Acute Coronary Syndrome ***(NCVD-ACS) Registry***, *the female to male ratio* for patients admitted for acute coronary syndrome (ACS) for the period *2007-2009* was *0.32* .
- **2014-2016 cohort** comprised of 26,710 patients, 4450 (16.67%) were women and 22,260 (83.34%) were men with a *female to male ratio of 0.20*.
- This is in cont*rast to the* **general Malaysian population** *which has a female to male ratio of 0.95* (13,771,497:14,562,638) according to the year 2010 population census)
- This *lower incidence of PCI in women* could partly be *due to refusal* to undergo invasive procedure and *general lack of awareness* of women about coronary artery disease, thus failure to sought treatment.
- *Women present* with coronary artery disease *5 years later* than men. This is due to the *protective effect of oestrogen*. Upon reaching menopause the incidence of coronary artery disease catches up with that of men. This 5 years delay could partly explain why women has higher incidence of co-morbidities.

- Some of the results were similar to the **GRACE registry:** women had higher rates of *diabetes, hypertension, prior angina and heart failure*, but were less likely to smoke tobacco or have a history of myocardial infarction
- **EUGenMed,** Cardiovascular Clinical Study group:
- Ischeamic heart disease develops on average *7-10 years later in women* compared to men. However , over the past decade manifestations in younger women are increasing.
- ACS, ST-elevation infarction (*STEMI*) *or NSTEMI* (Non-STEMI) occurs *3-4 times more often in men* than women *below age 60*, but *after 75 years*, *women represent the majority* of patients.
- Premenopausal women have less often hypertension and lower lipid levels then similarly aged men but this reverses at older age
- *Women* had significantly higher rates of *diabetes mellitus*.

GRACE: Global Registry of Acute Coronary Events.

- **STEMI cohort, 2007-2009 cohort -** women had *longer door-to-balloon time* and transfer time. This could partly be due to *cultural influence* whereby Asian men are usually head of the household and also the decision maker in the family.
- Usually women patient would wait for their spouse to agree before any consent for PCI was given.
- *Inertia of physician* to refer from non-PCI centers may also be responsible.
- **STEMI cohort, 2014-2016 cohort** – The DTB time has improve for women from 169.5 to 145.5 min although still significantly longer.
- (Our center's mean is 116min in 2016 and 66.8 min in 2018).
- *Transfer time* has *decrease* markedly from 300.4 to 144.9 min for women. This could be due to:
- 1) *STEMI referral summits* that was carried out in multiple states to increase awareness of other healthcare providers and
- 2) *STEMI network* that was started in Klang valley (Central region)
- 3) *Roadshow* regarding CAD by the WH2O done in multiple states.

- *Use of PCI adjunct*, findings of the **2007-2009 cohort** *differ* from the *GRACE registry* whereby women received similar rates of adjunctive pharmacotherapy whereas the **2014-2016 cohort** it *is similar* **to GRACE registry** whereby *women* with ACS received *less glycoprotein IIb/IIIa inhibitors*.
- **Both study periods** *women* had comparable rates of single and multi-vessel disease but *higher rates of left main stem disease and smaller vessel diameter*. However, in the **Grace registry** *women were twice as likely to have normal/mild disease and were less likely to have three-vessel or left main stem disease*
- **2007-2009 cohort** - *women* received *less drug-eluting stent*. In Malaysia patients had to *pay for the drug-eluting stents* whilst use of bare-metal stents were fully subsided by the government in the public hospitals. This difference could again partly be due to *cultural influence* whereby men being the head of the household and usually the bread winner for the family occupies a more important position in the family whereas women are usually housewives and thus being deemed as less important. Thus, the family may be less willing to part with their money.
- **2014-2016 cohort** – *women* now significantly received *more DES*. This could be due to *reduction in stent price* (and subsidy by MoH), inclusion of more *private hospitals* and increased awareness of effectiveness of DES in reducing ISR among Cardiologist,

Conclusion

- Gender and sex differences do exist in coronary artery disease.
- N=37,312, women present 5 years later with more co-morbities (Diabetes, hypertension, chronic renal failure) whereas smokers and past history of myocardial infarction were higher in men.
- STEMI cohort: women has longer DTB and Transfer time.
- Women has more LMS disease and smaller diameter vessels.
- Although women has higher Crude Odds Ratio for In-hospital, 30D and 6 M mortality but these were no longer significant after adjustment for all confounding factors (age, smoking, diabetes, hypertension, new onset angina, prior history of heart failure and renal failure (including Killip class in STEMI cohort).
- More needs to be done:
- 1) integrating these knowledge into guidelines and creating awareness among healthcare professionals via forums, conferences, ect;
- 2) improving primary care in diagnosing and treating DM, hypertension, chronic renal failure
- 3) education to raise awareness among the population-public education campaign, tailored social media messages-improve health literacy, adherence to lifestyle-based primary prevention .
- 4) research –Cardiovascular outcome trials must be designed with adequate statistical power to produce meaningful results for women and men.

Thank you for your attention.