

Gender Differences in Outcome After an Acute Myocardial Infarction in Singapore

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ABSTRACT

Objectives: To characterise gender and age-related differences in presentation and outcome after an acute myocardial infarction (AMI).

Design: Data were derived retrospectively from the Singapore Myocardial Infarction Registry from 1988 through 1997. This database comprised all AMI cases for ages between 20 and 64 years (group A). For approximately three months a year, data were also collected for all AMI cases above the age of 64 years (group B). There were 13,048 and 4,425 cases in groups A and B respectively.

Results: In age – standardised AMI rates, males outnumbered females by a factor of 4.0 and 1.7 for groups A and B respectively. The median age of presentation was higher in females for both age groups being 58 years versus 54 years for group A and 75 years versus 72 years for group B. Younger females had worse survival at 28 days and were more likely to have prior ischaemic heart disease and require resuscitation. They were also more likely to have atypical symptoms. Previous myocardial infarction was not different between the sexes in both groups. Among the older age group, there was no gender difference in prior ischaemic heart disease, 28-day survival and requirement for resuscitation.

Conclusion: Women who have AMI tend to be older than men. Gender differences are age-specific. Women who are 64 years and below have more atypical symptoms, prior ischaemic heart disease and worse prognosis than men after AMI. These differences are not seen in those over the age of 64.

Keywords: myocardial infarction, females, survival, symptoms, age

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INTRODUCTION

In 1999, ischaemic heart disease (IHD) accounted for 25% of all deaths in Singapore, second only to cancer,

which accounted for 27%⁽¹⁾. In developed countries like the United States and Europe, age and gender-standardised mortality due to ischaemic heart disease has declined⁽²⁾ while in many developing countries of Asia, the rate continues to rise. In Singapore, the prevalence of risk factors such as smoking, hypertension, hypercholesterolaemia, obesity and diabetes, as assessed by nationwide health surveys in 1992 and 1998, has markedly increased and may account for the rise in IHD rates.

In recent years, much interest has been generated regarding gender differences in the diagnosis, treatment and outcome of ischaemic heart disease. The age of presentation and prevalence of risk factors differ between males and females. Studies from Western countries have shown that, on the whole, women with AMI are older than males and have poorer prognosis⁽⁶⁻¹⁹⁾. Atypical chest pain is more prevalent among women than men⁽³⁾. In the Coronary Artery Surgery Study, (CASS) a history of typical chest pain was found to predict significant artery disease (CAD) in a higher percentage of men compared to women⁽⁴⁾. This study was conducted to determine if similar differences exist in our local population and the effect of age on these differences, if any.

METHODS

The Singapore Myocardial Infarction Registry (SMIR) was established by the Ministry of Health of Singapore in 1988 to collect basic demographic and clinical data for every case of AMI, aged between 20 to 64 years, diagnosed clinically, biochemically and/or post mortem examination. Data collection for the registry was confined to the ages 20 to 64 years to conform to the WHO MONICA (World Health Organisation MONItor trends in Cardiovascular diseases) protocol for similar registries worldwide. Because the incidence of myocardial infarction is greatest in those over the age of 64 years, additional data were also gathered for this age group for mostly three months a year. However, data were available for 11, 12 and six months in 1988, 1989 and 1994, respectively.

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Table I. Age-standardised* AMI incidence rates, 1988 - 1997 per 100,000 resident population.

Year	Aged 20 - 64 years (1988 - 1997)			Aged \geq 65 years (1988 - 1996)			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
1988	164.7	43.1	104.3	838.2	516.9	664.7	243.3	98.4	169.7
1989	158.1	38.0	98.2	839.6	480.5	647.0	237.6	89.6	162.3
1990	147.9	39.3	93.7	847.2	501.3	657.9	229.5	93.2	159.5
1991	153.0	45.0	99.0	756.3	480.5	606.6	223.4	95.8	158.2
1992	160.9	42.6	101.7	1042.8	515.7	762.9	263.8	97.8	178.8
1993	151.5	41.8	96.6	1003.5	502.8	735.5	250.9	95.6	171.2
1994	142.7	35.0	88.8	916.2	556.6	720.2	232.9	95.8	162.5
1995	133.8	28.7	81.2	649.7	475.2	560.0	194.0	80.8	137.1
1996	144.4	29.8	87.0	664.4	419.6	534.1	205.0	75.3	139.1
1997	131.3	34.0	82.6	–	–	–	–	–	–
1988-96	150.0	37.8	94.1	835.7	493.7	651.8	230.2	91.0	159.2
1988-97	148.1	37.3	92.7	–	–	–	–	–	–

* Age standardised to the "Old World" Population

Three main sources of notification are discharge diagnoses from all hospitals, National Registry of Births and Deaths or post mortem reports and biochemistry laboratory listing of raised creatine phosphokinase (CPK) enzyme levels. Experienced research nurses retrieve the clinical records and evaluate these findings based on the MONICA protocol. All electrocardiograms are read using the Minnesota coding system. The diagnosis of AMI is based on three criteria: clinical symptoms, raised CPK enzymes and electrocardiographic (ECG) changes (presence of Q waves, ST segment elevation or depression and T wave inversion). Necropsy findings are analysed where available. The cases are then grouped into several diagnostic categories, namely definite AMI, possible AMI, ischaemic cardiac arrest, non-AMI, clinical AMI, cardiac death with necropsy and cardiac death without necropsy. Only cases with definite AMI, clinical AMI and cardiac death with or without necropsy are included for analysis.

Data from the SMIR were evaluated for the years 1988 through 1997 (group A). Data were also collected for those aged 65 years and above (group B) during the same period. In both groups, the following variables were compared between males and females: (i) ethnic distribution; (ii) previous history of ischaemic heart disease (IHD); (iii) previous history of AMI; (iv) site of AMI management; (v) survival at 28 days, (vi) symptoms; and (vii) resuscitation.

Characteristics of AMI patients

A positive history of chronic IHD was defined as presence of previous myocardial infarction or angina pectoris upon review of medical records. Previous AMI was defined as previous myocardial infarction occurring more than 28 days before the current event.

Site of management of AMI patients

The term "medically unattended" refers to those cases where no decision on management could be taken because the patient was already dead or in cardiac arrest when first seen by a doctor. The term "other medical consultation" refers to cases where the patient was seen in the event by a doctor, but death occurred too rapidly, or the event was not diagnosed at the time and no decision was made to admit the patient for bed rest, or the patient died in transit.

Symptoms

"Typical" symptoms refer to chest pain of \geq 20 minutes in duration. "Atypical" means pain at an unusual site (upper abdomen, arms, jaw or neck) or pain $<$ 20 minutes in duration, acute left ventricular failure without typical chest pain, and shock or syncope. "Other symptoms" refer to symptoms, which do not satisfy the criteria for "typical", or "atypical" such as nausea or vomiting without the presence of pain.

STATISTICAL ANALYSIS

Categorical variables are expressed as percentages and the chi square test was used to determine if there were any significant association between gender and characteristics of interest e.g. previous history of IHD and survival at 28 days. A p value of $<$ 0.05 was taken as significant. Age standardisation of incidence rates was done by the direct method using the "Old World" population as proposed by Segi⁽⁵⁾.

RESULTS

Age standardised AMI incidence

There were 13,048 AMI cases in group A from 1988 through 1997. Data for 46 out of a total of 108 months over the same period captured a total of 4,425 AMI cases in group B. The age standardised

Table II. Age-standardised* AMI incidence rates by gender and ethnicity, 1988 - 1997 per 100,000 resident population.

Race	Aged 20 - 64 years (1988 - 1997)			Aged ≥ 65 years (1988 - 1996)		
	Male	Female	Total	Male	Female	Total
Chinese	115.3	28.3	71.3	632.5	393.0	567.7
Malay	234.2	65.0	147.3	1009.2	569.1	927.8
Indian	331.9	102.6	229.8	1062.5	986.0	1218.4
All races	148.1	37.3	92.7	748.8	439.3	582.5

* Age standardised to the "Old World" Population

Table III. Characteristics of AMI patients.

	Patients aged 20 - 64 years (1988 - 1997)			Patient aged 65 years and above (1988 - 1996)		
	Male % (n=10,578)	Female % (n=2,470)	Total % (n=13,048)	Male % (n=2,509)	Female % (n=1,916)	Total % (n=4,425)
Previous history of IHD	18.0	21.1	18.6 p=0.001	25.9	26.1	26.0 p=0.211
Previous AMI	32.5	32.9	32.6 p=0.69	50.8	49.8	50.4 p=0.150
Alive at 28 days	75.4	69.2	74.2 p<0.001	56.3	55.3	55.9 p=0.509
Required resuscitation	11.7	17.7	12.9 p<0.001	23.4	25.7	24.4 p=0.137

Table IV. Site of AMI management.

	Patients aged 20 - 64 years (1988 - 1997)			Patient aged 65 years and above (1988 - 1996)		
	Male % (n=10,578)	Female % (n=2,470)	Total % (n=13,048)	Male % (n=2,509)	Female % (n=1,916)	Total % (n=4,425)
Hospital	89.7	91.3	90.0 p=0.017	84.7	86.0	85.3 p=0.216
Nursing home	0	0.2	0.1 p=0.13	0.2	0.3	0.2 p=0.514
At home by a doctor	1.2	2.5	1.5 p<0.001	4.3	4.7	4.5 p=0.531
Medically unattended	5.8	4.0	5.5 p<0.001	8.0	6.1	7.2 p=0.012
Other medical consultation	1.7	1.1	1.6 p=0.029	1.1	0.8	0.9 p=0.319
Insufficient	1.5	1.1	1.4 p=0.122	1.7	2.1	1.9 p=0.303

AMI incidence rates are shown in Table I. The male to female ratio was 4.0 for group A and 1.7 for group B. The median age in group A was 54 years for males and 58 years for females. Similarly, the median age in group B was lower in women (72 vs 75 years).

Age standardised AMI incidence by gender and ethnicity

Table II shows the age standardised AMI incidence rates by gender and ethnicity for groups A and B. Among the three main ethnic groups (Chinese, Malays and Indians), AMI has the highest predilection

for Indians, followed by Malays and Chinese. Indian females over the age of 64 years appear to be a particularly high risk group compared to the other two ethnic groups. For those >64 years, the male to female ratio was 1.6, 1.8 and 1.1 for Chinese, Malays and Indians respectively.

Characteristics of AMI patients

Table III summarises the percentages of patients in groups A and B respectively who had previous history of IHD or AMI, survival at 28 days, and the percentage of patients who required resuscitation. Females in group

Table V. Distribution of AMI symptoms.

	Patients aged 20 - 64 years (1988 - 1997)			Patient aged 65 years and above (1988 - 1996)		
	Male % (n=10,578)	Female % (n=2,470)	Total % (n=13,048)	Male % (n=2,509)	Female % (n=1,916)	Total % (n=4,425)
Typical	70.9	63.0	69.4 p<0.001	58.5	55.0	56.9 p=0.019
Atypical	7.2	9.6	7.7 p<0.001	8.3	8.8	8.5 p=0.572
Others	6.4	10.6	7.2 p<0.001	15.9	20.6	17.9 p<0.001
None	0.9	0.7	0.9 p=0.309	1.0	0.3	0.7 p=0.004
Inadequately described or insufficient data	14.6	16.1	14.9 p<0.001	16.4	15.5	15.9 p=0.254

A were more likely to have a previous history of IHD (21.1% vs 18.0% in males, $p=0.001$). Previous AMI occurred with similar frequencies among males and females in both groups. As expected, overall 28-day survival was much lower in group B, (55.9% versus 74.2%). However, females fared worse than males in group A at 28 days, (69.2% versus 75.4%, $p<0.001$) but not in group B. Although females in group A were more likely to require resuscitation, (17.7% versus 11.7%, $p<0.001$) this difference was not observed in group B.

Site of management of AMI patients

Table IV illustrates the site of AMI management after the onset of event for group A and B respectively. Males were more likely to be medically unattended for both groups, being already dead or in cardiac arrest by the time a doctor first saw them. "Other medical consultation" (see Methods for definition) was also more common in males but in group A only.

Symptoms

Table V illustrates the distribution of symptoms for groups A and B respectively. Irrespective of age, typical symptoms occurred more frequently among men. Atypical symptoms were slightly more common among women but only in group A. Other symptoms tended to be more frequent in women, irrespective of age. Less than 1% of patients in both groups had no presenting symptoms, and the incidence was slightly lower for the older women.

DISCUSSION

In Singapore, as with many other urban Asian cities, death rates from IHD have risen sharply to the levels seen in the industrialised nations. Conversely, these nations have evidenced a gradual decline in their age and gender-standardised IHD death rates over the same period⁽²⁾. This alarming trend is likely to be the result

of rapid urbanisation and rising affluence, leading to adoption of unhealthy lifestyles such as fat-rich diets and smoking. Table 1 shows that age standardised rates of AMI peaked in 1992, and then declined subsequently in 1993 to 1995, but has plateaued off from 1995.

There is a sharp rise in the incidence of AMI in females after the age of 64, causing a marked drop in the male to female ratio from 4.0 to 1.7. It has been estimated that the percentage of population aged 65 and greater in Singapore will rise from the present 7% to 18% by the year 2030. Since the average life expectancy in Singapore is 79.6 years for females, and 75.6 years for males⁽¹⁾, we can expect that the number of elderly female AMI patients will rise drastically in the next three decades.

At presentation, the median age was three to four years older for the women compared to men in both groups. Previous studies have suggested that the age lag in presentation could be partially due to delayed or missed diagnosis in women^(6,7). In contrast, we found that younger females were more likely to have a previous history of chronic IHD. This finding implies that the diagnosis of IHD is not being missed in females in the younger age group. Surprisingly, we observed that younger females had a higher mortality at 28 days and were more likely to require resuscitation. This gender difference was not observed among the older age group. The higher mortality observed in females in the younger age group could be due to differences in risk factors, co-morbidities, severity of infarction, therapy assignment, or response to treatment. However, as the SMIR is a population-based registry, information on disease severity and co-morbidities was not available for analysis. Data from many other studies have reported that women have higher mortality after AMI⁽⁸⁻¹⁹⁾. It is unclear whether age, co-morbidities and differences in MI severity and treatment assignments

can account for all of the observed differences. Some studies have found that correction for age and other prognostic factors can eliminate the observed gender differences in outcome⁽⁹⁻¹⁷⁾, whereas other studies have found that adjustment for these factors failed to account for higher mortality in women⁽¹⁸⁻²⁴⁾. Our observation that the higher mortality is confined to the younger age group is also supported by other studies⁽²⁵⁻³⁰⁾. In fact, Vaccarino et al found that the higher mortality in women was confined to those less than 75 years of age and that in those older than 75 years women had a lower mortality compared to men^(28,29). They went further by dividing their cohort into age groups by five-year decrements and were able to show that the younger the women, the higher was their relative risk death compared to men. These findings are also confirmed by a more recent study from the Swedish National Acute Myocardial Infarction Registry⁽³⁰⁾ which is very similar to our study in that data were derived from a population-based rather than a hospital-based registry.

Our data showed that men are more likely to be “medically unattended”, regardless of age. This finding implies that they are more likely to present in cardiac arrest or sudden death on first contact with the doctor. This trend was also evident in the RESCATE study, which was an AMI registry from four teaching hospitals in Spain⁽¹⁶⁾. The study confirmed that ventricular fibrillation and sustained ventricular tachycardia requiring immediate attention were significantly more frequent in men within 72 hours of AMI onset.

Our study also supports previous observations that atypical symptoms are more common in women^(3,27), but only in the younger age group. “Other” symptoms are more frequent in females, irrespective of age group as a whole, and irrespective of gender.

The pattern of management after AMI reflects modern practice, with the vast majority being managed in the hospital, without gender bias. In fact, more females were managed in hospital for the younger age group.

CONCLUSION

Our study shows that women, on average, present with AMI three to four years later than men. This gap is narrowed slightly with age.

Gender-specific differences in AMI are influenced by age. Women in the younger age group are more likely to require resuscitation and have a higher mortality at 28 days. There is no gender difference in survival for the older age group. A prospective study looking at baseline characteristics and therapy differences is essential to understand why younger females have a poorer prognosis.

Younger females are more likely to have a previous history of chronic IHD. Males are more likely to be dead or in cardiac arrest at first contact with the doctor, irrespective of age. The majority of both men and women present with typical symptoms of AMI. Atypical and other symptoms are common in the older age group. In the younger age group, atypical symptoms are more common among women. Other symptoms are more frequent in females in both age groups.

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2nd National Addictions Conference

Medical Conference

23 June 2002

Grand Hyatt Singapore

Sir Stamford Room, Mezzanine Floor

2pm - 5pm

PROGRAM

1400-1430	Registration	
1430-1440	Opening Address	Prof Tan Chorh Chuan, Director of Medical Services
1440-1500	The Challenges of Prescription Drug Misuse	Prof Walter Ling
1500-1520	The Local Experience	Dr Patrick Kee
1520-1550	Tea Break & Video Presentation	

Plenary Session

1550-1610	Interventions for Prescription Drug Dependence.	Dr R Munidasa Winslow
1610-1630	Law Regulating the Use of Prescription Drugs	Dr Kelvin Tan
1630-1700	Q & A	

Chairperson

Dr R Munidasa Winslow

(Head, Community Addictions Management Programme)

Lunchtime Symposium (sponsored by Schering-Plough)

New Advances in Opiate Dependence

12.45pm - 1.45pm

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