Worse Prognosis for Women Who Underwent Primary Percutaneous Coronary Intervention for Acute St-Elvation Myocardial Infarction

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Background : *Many reports have shown that female gender carries a worse prognosis when developing acute myocardial infarction (MI), whether or not reperfusion therapy is used. The primary percutaneous coronary intervention (1-PCI) is currently a preferable treatment for acute ST-elevation MI. However, the data concerning the difference between the outcomes in the treatment of the disease in men and women in Thailand is still insufficient.*

Material and Method : *A prospective registry of acute ST-elevation MI patients who underwent 1-PCI at King Chulalongkorn Memorial Hospital from June 1999 to December 2002 were analyzed. Kaplan Meier survival analysis is used to determine the in-hospital mortality.*

Results : *The consecutive 184 (F-52, M-131) patients who underwent 1-PCI were recruited. Female subjects were older (66.6 $\pm$ 12 y versus 59.0 $\pm$ 11.6 y, p < 0.01); they also had higher percentage of diabetes (45.1 versus 27.1, p < 0.01), but a fewer number of smoker (17.7 versus 66.2, p < 0.001). The percentage of patients who had cardiogenic shock tended to be higher in women (34.6 versus 19.9, p = 0.08); however, the number of anterior wall MI and ejection fraction were not different. The mean door to balloon time (109 $\pm$ 95 versus 99 $\pm$ 68 minutes) and pain to balloon time (454 $\pm$ 271 versus 372 $\pm$ 298 minutes) were not different in both groups. The angiographic success with TIMI 3 flow was achieved in 92.3% for females and 86.9% for the males. The in-hospital mortality was significantly higher in females (23.1 versus 6.1, p = 0.002). Univariate analyses demonstrated that the feminine gender, cardiogenic shock, smoking, ejection fraction less than 40, cardiac arrest prior PCI and angiographic were the predictors for in-hospital mortality. When using multivariate analyses by Cox proportional model, only cardiogenic shock, history of hypertension and angiographic success were the significant predictors. Women had 2.15 times of in-hospital mortality higher than males; however, the confidence interval cross-over 1 (0.74-6.42) and p value was 0.16.*

Conclusion : *Females tend to have a poor prognosis when they develop acute ST-elevation MI which requires treatment with 1-PCI.*

Keywords : *Primary percutaneous coronary intervention, Acute myocardial infarction, Female*

Male gender is one of the independent risk factors for coronary heart disease. However, when patients develop acute myocardial infarction (MI), women seem to have poorer outcomes than men[1-7], through the advancement of age, more co-morbid diseases such as diabetes; women tend to receive less aggressive treatment than men[8-13]. After age-adjusted analyses, the hazard ratio for death seems to be less than 1.2[6,14-18]. As for the primary percutaneous coronary intervention (1ry PCI), the data seems to be the same as those of patients who received conventional treatment[6,19-20].

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In Thailand, the data concerning the difference of the outcomes of treatments between patients with MI of the two genders, particularly those who underwent 1ry PCI is insufficient. This is the first data of 1ry PCI demonstrating the outcome of short-term treatments between the two genders.

Material and Method

Patients who received 1ry PCI treatment from May 1999 to December 2002 at King Chulalongkorn Memorial Hospital, were recruited. The data were prospectively collected. Diabetes was defined when the patients had already been documented, or received oral hypoglycemic agent /insulin for diabetic control or fasting plasma glucose was over 126 mg/dl. Hypertension was defined when the patients had already been documented according to the WHO criteria i.e. 140/90 mmHg. Dyslipidemia is defined when patients have already received lipid lowering agent or total cholesterol over 200 mg/dl, LDL is over 130 mg/dl or HDL is less than 40 mg/dl. The infarct-related vessel means the culpid vessel which underwent angioplasty and related to the EKG location. Angiographic success was determined when the residual stenosis of infarct related artery was less than 50% with TIMI 2 or TIMI 3 flow.

Statistical analysis

The Intercooled STATA version 6.0 was used for data analysis. The baseline characteristics for nominal variables were expressed in number and percentage and continuous variables were expressed as mean $\pm$ SD. Chi-square and student t-test were used to compare the data between the two groups. Kaplan-Meier survival analysis was used to compare in-hospital mortality. In order to determine the factors for in-hospital mortality, Log-rank test was used for univariate analysis and Cox proportional hazard with backward elimination was used for multivariate analysis. The results were reported as hazard ratio with 95% confidence interval. P-value less than 0.05 was considered statistically significant.

Results

From June 1999 to December 2002, 53 females (28.8%) and 131 males (71.21%) who received 1ry PCI at King Chulalongkorn Memorial Hospital were enrolled. The females were relatively older than the males (66.6 ± 12.0 y versus 59.0 ± 11.6; $p < 0.001$); they also had a higher prevalence of diabetes (42.2% versus 27.1%; $p = 0.026$); but there were fewer female smokers (17.3% versus 66.2%; $p < 0.001$) than males. The female patients tended to have more cardiogenic

Table 1. Baseline characteristics of the patients

	Female(N = 53)	Male(N = 131)	P-value
Age (y)	66.6 12.7	59.0 11.6	< 0.001
Diabetes (%)	44.2	27.1	0.03
Hypertension (%)	54.7	42.6	0.14
Smoking (%)	17.3	66.2	< 0.001
Dyslipidemia (%)	52.2	57.6	0.52
: Total cholesterol (mg/dl)	205 52	207 48	0.92
: Triglyceride (mg/dl)	143 75	140 82	0.87
: HDL (mg/dl)	47 12	44 10	0.08
: LDL (mg/dl)	129 45	133 43	0.60
Anterior wall infarction (%)	45.3	52.7	0.46
Left ventricular ejection fraction (%)	46.6 16.3	47.4 14.0	0.64
Cardiogenic shock (%)	34.0	19.9	0.12
Prior CPR (%)	17.0	15.3	0.77
Refer (%)	32.1	30.5	0.28
Diseased vessel			0.48
: 1-VD	41.2	40.5	
: 2-VD	25.5	33.6	
: 3-VD	33.3	25.9	
Pain duration before admission (min)	334 276	259 256	0.09
Door to balloon time (min)	111 95	99 68	0.39
Decision to balloon time (min)	85 45	77 44	0.29
Total time delay (min)	449 271	372 299	0.12

Table 2. Results of treatment in both groups

	Female(N = 53)	Male(N = 131)	P-value
TIMI-flow pre-angioplasty (%)			0.67
: 0	75.5	71.8	
: 1	15.1	12.2	
: 2	3.8	7.6	
: 3	5.7	8.4	
TIMI-flow post-angioplasty (%)			0.67
: 0	1.9	2.3	
: 1	0	1.5	
: 2	5.7	9.2	
: 3	92.5	86.9	
Angiographic success (%)	98.2	96.2	0.50
Glycoprotein IIb/IIIa blocker used (%)	42.3	48.9	0.42
Stent implantation (%)	60.0	72.8	0.11
Intra-aotic balloon pump insertion (%)	28.9	13.2	0.01
Temporally pacing (%)	19.2	7.0	0.01
Re-occlusion (%)	1.9	1.5	0.86
In-hospital mortality (%)	22.6	6.1	0.001
CCU admission duration (d)	5.3 7.0	4.1 4.6	0.16
Hospital admission duration (d)	8.2 10.2	7.7 7.7	0.70

shock than males (34.0% versus 19.9%; p = 0.12); however, this difference did not reach statistical significance. Other baseline characteristics such as hypertension, dyslipidemia, location of MI, infarct related artery, blood pressure, level of cardiac enzyme, left ventricular ejection fraction (LVEF) and diseased vessel were similar in both groups (Table 1). The female patients tended to come to hospital later than the males (334 ± 276 m versus 254 ± 256 m; p = 0.088). Hence, the total time delay from chest pain to first balloon dilatation appeared to be longer (449 ± 271 m versus 372 ± 299 m; p = 0.11). However, this difference did not have statistical significance. The intra-aortic balloon pump (IABP) and temporally pacing were used more often in the females, according to the severity of the patients' presentation (Table 2). The angiographic success (post PCI with TIMI 2 or 3 flow) rate were similar in both groups (92.5% versus 86.9%;

p = 0.50) as well as the re-occlusion rate (1.9% versus 1.5%; p = 0.86). The length of stay was also similar (8.2 ± 10.2 d versus 7.7 ± 7.7 d; p = 0.697). Twelve in the female group (22.6%) and 8 in the male group (6.1%) died. Their causes of death are demonstrated in Table 3. The univariate analyses for in-hospital mortality showed that gender, cardiogenic shock, smoking, LVEF less than 40%, cardiopulmonary resuscitation prior PCI and angiographic success were the significant predictors (Table 4). When using multivariate analyses by Cox proportional hazard, cardiogenic shock, hypertension and angiographic success were the only predictors for in-hospital mortality (Table 5). Thus feminine gender tends to be a predictor; however, it did not reach statistical significance (hazard ratio = 2.15, CI = 0.74 - 6.24; p = 0.16) Fig. 1 shows the Kaplan Meier survival curve comparing the effect of gender difference.

Table 3. Cause of death

Cause of death	Female (N = 12)	Male (N = 8)
Cardiac	10	7
: Pump failure	5	4
: Tamponade	3	1
: Electrical	1	2
: Sub-acute stent thrombosis	1	0
Non-cardiac	2	1

Discussion

This study shows that females with acute MI treated with 1[ry] PCI have increased risk of in-hospital mortality. With the advancement of age, more women developed diabetes and they were more likely to suffer from cardiogenic shock. The mortality is much higher than men. After adjusted baseline clinical characteristics, women still have a slightly higher in-hospital mortality but the power of the difference did not reach the level of statistical significance.

Table 4. Univariate analysis of factors that effect survival time

Variable	Crude hazard ratio (95% CI)	P-value
Sex		
: Male	1	
: Female	3.43(1.39-8.43)	0.007
Cardiogenic shock		
: No	1	
: Yes	13.70(3.90-48.08)	< 0.0001
Hypertension		
: No	1	
: Yes	2.35(0.88-6.31)	0.09
Smoking		
: No	1	
: Yes	0.32	0.03
Dyslipidemia		
: No	1	
: Yes	0.36	0.09
Ejection fraction		
: > 40%	1	
: < 40%	2.85	0.03
CPR prior PCI		
: No	1	
: Yes	2.62	0.04
Angiographic success		
: No	1	
: Yes	0.24	0.03

CI-confidence interval, CPR-cardiopulmonary resuscitation, 1ʳʸ PCI-primary percutaneous coronary intervention

Table 5. Multivariate analysis of factors that effect survival time

Variable	Adjusted hazard ratio (95% CI)	P-value
Sex		
: Male	1	
: Female	2.15 (0.74-6.24)	0.16
Cardiogenic shock		
: No	1	
: Yes	11.55 (2.47-53.99)	< 0.002
Hypertension		
: No	1	
: Yes	4.51 (1.22-16.72)	0.02
Dyslipidemia		
: No	1	
: Yes	0.43 (0.13-1.47)	0.19
Angiographic success		
: No	1	
: Yes	0.12 (0.03-0.54)	0.006

CI-confidence interval, CPR-cardiopulmonary resuscitation, 1ʳʸ PCI-primary percutaneous coronary intervention
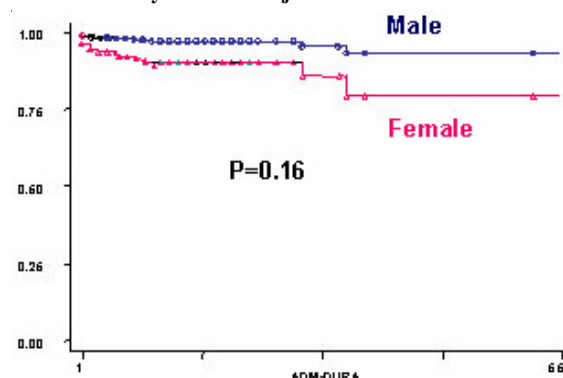
Survival analysis after adjusted

Fig. 1 Kaplan-Meier survival analysis for in-hospital mortality after adjusted baseline.

The data were similar to previous reports[6,19-20]. The mortality rate in the present study seems to be higher than that reported by European countries[21-24]. This can be explained by the fact that they have a higher number of patients with cardiogenic shock, because our center is a tertiary care center; most of the referred cases were severely ill and have cardiogenic shock. Secondly, our patients came to the hospital relatively late. The data also demonstrated a longer duration from the onset of chest pain to hospitalization (334 ± 267 minutes versus 259 ± 256 minutes; $p = 0.09$) for females. Hence, the total time delay (449 ± 271 minutes versus 372 ± 299 minutes; $p = 0.12$) was much longer than the male. However, this difference did not reach the level of statistical significance. It may also be that their symptoms are not typical (some patients come to hospital with dyspnea without chest pain) or they could tolerate the symptom more than their male counter parts which brings them to hospital much later than males. When the treatment was delayed, the outcomes could be worse[25]. How can we improve their outcome? We have to educate the patients to take care of themselves and to go to hospital as soon as possible when the symptom develops. The aggressive treatment of diabetes for prevention of coronary artery disease and acute MI seems to be a better way, as well as the control of many risk factors of coronary artery. The physicians in the emergency room should pay more attention to atypical presenting symptoms of women.

This study has some limitations as the number of patients is small and the result is only short-term.

Conclusion

Women tend to have a poorer prognosis than men when developing acute ST-elevation MI that requires treatment with 1-PCI. With the advancement of age, women have more diabetes and cardiogenic shock. Their mortality rate is also higher than their male counter parts. Risk factors modification, particularly diabetes control, better education and awareness of symptoms to present to the hospital earlier and physicians should be more alert to the atypical presentation of their symptoms which is necessary to improve their survival.

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การพยากรณ์โรคที่ไม่ดีในผู้หญิงเมื่อเกิดภาวะกล้ามเนื้อหัวใจตายเฉียบพลัน และได้รับการรักษาด้วยการทำบอลลูนขยายหลอดเลือด

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ภูมิหลัง : จากการศึกษาในอดีตพบว่าผู้หญิงเมื่อเป็นโรคกล้ามเนื้อหัวใจตายเฉียบพลันจะมีการพยากรณ์โรคที่ไม่ดีไม่ว่าจะได้รับการรักษาด้วย reperfusion หรือไม่ ปัจจุบันการรักษาด้วยการทำบอลลูนขยายหลอดเลือดถือว่าการรักษาที่มาตรฐานในผู้ป่วยกล้ามเนื้อหัวใจตายเฉียบพลัน แต่อย่างไรก็ตาม ข้อมูลเหล่านี้ในประเทศไทยยังมีน้อย และโดยเฉพาะอย่างยิ่งในผู้หญิง

วิธีการ : เป็นการเก็บรวบรวมลงทะเบียนผู้ป่วยแบบไปข้างหน้าของผู้ป่วยกล้ามเนื้อหัวใจตายเฉียบพลันที่เป็น ST elevation ในรพ.จุฬาลงกรณ์ตั้งแต่เดือนมิถุนายน 2542 ถึง ธันวาคม 2545 เพื่อเปรียบเทียบอัตราตายในโรงพยาบาล

ผลการศึกษา : ผู้ป่วยที่ถูกลงทะเบียนต่อเนื่องจำนวน 184 คน (หญิง - 52, ชาย - 131) และได้รับการทำบอลลูนขยายหลอดเลือด ผู้หญิงมีอายุมากกว่า (66.6 ± 12 ปี เทียบกับ 59.0 ± 11.6 ปี, p < 0.01) มีเบาหวานร่วมด้วยมากกว่า (ร้อยละ 45.1เทียบกับ 27.1, p < 0.01) แต่จำนวนที่สูบบุหรี่น้อยกว่า (ร้อยละ 17.7 เทียบกับ 66.2, p < 0.001) ผู้หญิงมีแนวโน้มที่จะเกิดภาวะช็อคจากหัวใจมากกว่า (ร้อยละ 34.6 เทียบกับ 19.9, p = 0.08) อย่างไรก็ตามร้อยละของการเกิด anterior infarction และ ejection fraction (EF) ไม่แตกต่างกัน ค่าเฉลี่ยระยะเวลา door to balloon (454 ± 271 นาที เทียบกับ 372 ± 298 นาที) ไม่แตกต่างกัน ร้อยละ 92.3 ในผู้หญิง และร้อยละ 86.9 ในผู้ใหญ่สามารถทำให้เลือดกลับมาไหลได้ตามปกติ (TIMI 3 flow) อัตราตายในโรงพยาบาลของผู้หญิงมากกว่าผู้ชาย (ร้อยละ 23.1 เทียบกับ 6.1, p = 0.002) เมื่อใช้วิธี univariate analyses พบว่า ผู้หญิง, ภาวะช็อค, การสูบบุหรี่, EF < 40, หัวใจหยุดเต้นก่อนทำบอลลูน และความสำเร็จของการทำบอลลูน เป็นปัจจัยที่มีผลต่ออัตราตาย แต่เมื่อใช้ multivariate analyses พบว่ามีเพียง ภาวะช็อค, ประวัติความดันโลหิตสูง และความสำเร็จของการทำบอลลูน เป็นปัจจัยที่มีผลต่ออัตราตาย ส่วนผู้หญิงมีแนวโน้มว่าจะเป็นตัวพยากรณ์โรคที่ไม่ดีโดยมีอัตราตายมากกว่าชาย 2.15 เท่า แต่อย่างไรก็ตามค่า confidence interval คลุม 1 (0.74-6.42) และค่า p = 0.16

บทสรุป : ผู้หญิงมีแนวโน้มว่าจะมีการพยากรณ์โรคที่ไม่ดีเมื่อเกิดภาวะกล้ามเนื้อหัวใจตายเฉียบพลัน และได้รับการรักษาด้วยการทำบอลลูนขยายหลอดเลือด