GENDER VARIATION OF IN-HOSPITAL OUTCOME IN PATIENTS WITH UNSTABLE ANGINA BY TIMI RISK SCORE

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Abstract

Background: The TIMI (Thrombolysis in Myocardial Infarction) risk score is a seven item risk stratification tool derived from trials of patients with Unstable Angina (UA) that has been validated in Emergency Department (ED) patients with potential Acute Coronary Syndromes (ACS). To evaluate frequency, outcome and correlation of the gender variation of in-hospital outcome in patients of unstable angina by TIMI risk score. **Materials and methods:** This was an observational study of Cardiac Care Unit (CCU) patients with unstable angina. Data included demographics, medical and cardiac history, and components of the TIMI risk score. Investigators followed the hospital course daily. The outcomes were death, Acute Myocardial Infarction (AMI) heart failure and arrhythmia during hospital stay as stratified by TIMI risk score and compared between genders using 2 tests. Data were analyzed by SPSS version-19. **Results:** In this study 62% patients were male and 38% patients were female. 55.20% female had low TIMI score whereas 16.10% male and 18.40% female had very high TIMI scores. The mortality rate was 0% in low TIMI score but the rate was increased in high TIMI score e.g. 3.30% in male patients and 2.60% in female patients with unstable angina. The rate of occuring MI, Cardiogenic shock, Heart failure is increased respectively from low to high TIMI score. In case of Arrhythmia, 17.70% male and 15.70% female had low TIMI score whereas 25.80% male and 26.30% female had high TIMI score. **Conclusion:** The TIMI risk score successfully stratifies risk in both males and females with UA at the time of CCU presentation; however, males have worse outcome at low TIMI scores than female.

Key words
TIMI; Unstable angina; Myocardial infarction.

Introduction

Bangladesh has been experiencing epidemiological transition from communicable disease to Non Communicable Disease (NCD). The overall mortality rate has decreased significantly over the last couple of decades but deaths due to chronic diseases, specially the "fatal four" ie. Cardiovascular Disease (CVD) cancer, chronic respiratory disease and diabetes are increasing in an alarming rate. CAD is an important contributor to one of the four ie. CVD of all South Asian countries, Bangladesh probably has the highest rate of CVD and yet is the least studied, in the global combat against CVD, Bangladesh is a country 'missing in action'[1]. Coronary Artery Disease (CAD) is also an important medical and public health issue because it is common and a leading cause of death throughout the world. Outcome based on gender and assessed by TIMI risk score is important because it helps in different clinical decisions.

Unstable angina is a clinical syndrome that is characterized by:-

i) Rest angina or angina with minimal exertion usually lasting at least 20 minutes

ii) New onset severe angina (At least 1 CCS class increase or to at least CCS class III severity) usually defined as occurring within the last month

iii) Crescendo angina, defined as previously diagnosed angina that has become distinctly more frequent, longer in duration or more severe in nature.

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The condition shares common patho-physiological mechanisms with acute myocardial infarction & the term acute coronary syndrome is used to describe these disorders collectively[2]. UA may occur unpredictably at rest which may be a serious indicator of an impending heart attack. What differentiates stable angina from unstable angina (Other than symptoms) is the pathophysiology of the atherosclerosis. Unstable angina results from the disruption of an atherosclerotic plaque with a subsequent platelet rich thrombus that obstructs coronary blood flow[3].

The TIMI risk score has shown its relevance in predicting adverse cardiac events within 14 days of the initial presentation in patients already identified as having ACS[4,5]. This score may be especially useful in female patients, who often present with atypical symptoms and non diagnostic ECGs, making diagnosis more difficult. It relies on objective assessment of elderly patients (>65 years), prior CAD (>50% stenosis in CAG) high risk individuals for developing CAD (Presence of three or more traditional cardiac risk factors) prescribed aspirin (Indicating vascular disease) and objective evidence of ischemia (elevated cardiac markers, ST segment changes)[6]. Only "severe angina", which is most commonly interpreted as two or more symptomatic episodes, has a subjective component. The fact that it is comprised of items that are objective and may explain its ability to be an accurate risk stratification tool, even in the setting of atypical presentations, which are more common in women[7,8].

There have been a number of studies which indicate that there are distinct differences in presentation of ACS in men and women. There are also differences in the impact of individual risk factors in men and women with ACS, as well as differences in the predictive value of standard diagnostic testing between the genders. Since the TIMI risk score does not rely on presentation specific characteristics, it is plausible that it is relatively gender blind and can function equally well in men and women despite the fact that women have more atypical presentations[9,10]. Maitland et al demonstrated that without the use of risk stratification tools, a significant number of patients are admitted to inappropriate units within the hospital: high risk patients were mistriaged to floor beds and low risk patients mistriaged to intensive care units. The use of risk stratification tools allows us to optimize patient care and improves cost effectiveness[11].

Materials and methods

The study was designed as a cross sectional study to evaluate the gender variation of in-hospital outcome in patients of unstable angina by TIMI risks score. The study was conducted in Cardiology Department of Chattogram Medical College Hospital (CMCH) from April, 2013 to March, 2014 (One Year). After admission in the coronary care unit with chest pain patients were selected for the study. Initial evaluation was done with history, clinical examination and ECG findings. Patients other then unstable angina were excluded. Ethical permission was obtained from the committee.

Written consent was taken from the all patients after explanation of the study procedure. Patients were thoroughly informed about the aims, objectives and detail procedure of the study before examination. Participants were encouraged for voluntary participation and allowed freedom to withdraw from the study whenever he/she likes even after participation.

All the seven parameters of the TIMI risk score were calculated. Patients were followed up for seven (07) days to find out the in-hospital outcome. All data were checked and re-checked to avoid error. The blood was collected by a trained lab technologist. All investigations were done in the Department of Cardiology, Department of Biochemistry and Radiology Department of Chattogram Medical College Hospital and in the standard laboratories of Chattogram. All relevant information for each individual study subject was recorded on a pre tested, pre designed data collection form after getting written consent. Data was processed and analyzed by using computer based software SPSS- 19 (Statistical Package for Social Science).

Inclusion criteria

i) Patients with unstable angina characterized by
- Rest angina or angina with minimal exertion usually lasting at least 20 minutes.
- New-onset severe angina occurring within the last month.
- Crescendo angina, defined as previously diagnosed angina that has become distinctly more frequent, longer in duration, or more severe in nature.

ii) Voluntarily given consent to participate in the study.

Exclusion criteria

i) Patients with post CABG, PCI
ii) Patients with NSTEMI
iii) Patients with STEMI.

Results

This study included 100 patients, male constituted 62% and female 38% with female male ratio being 1: 1.63 (Fig 1). Table I shows that smoking (41) was the most common risk factor in male and in female most frequent risk factor was diabetes mellitus (24). Table II revealed that the distribution of TIMI risk scores in patients suggesting that the highest number of males were from TIMI 3 (13) and the highest number of females were from TIMI 4 (10).

Table III illustrated that 34 males and 21 females had low TIMI score whereas 10 male and 6 female had high TIMI scores. Table IV shows in-hospital outcome of the patients included death, myocardial infarction, cardiogenic shock, heart failure and arrhythmia with different TIMI score grades. In patients with TIMI risk score medium to high, one death occurred in male but it was 0% in female at medium TIMI grading. At a higher TIMI grading, 2 death occurred in male but it was only one in female (p=0.041).

The incidence of myocardial infarction was increased as the TIMI risk score raised in case of male but distribution of MI was statistically insignificant with female (p>0.05). In case of male, incidence of cardiogenic shock was 1.6% at low TIMI which was 0 in case of female. At medium to high grade of TIMI the incidence of cardiogenic shock was distributed insignificantly (p>0.05). In this study 10 (10%) patients developed heart failure during the study period and 66 (66%) patients developed arrhythmia during the study period.

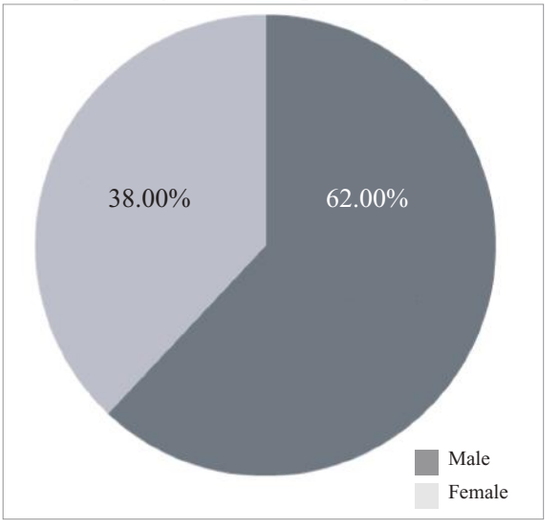

Fig 1: Gender distribution of study patients (n=100)

Table I: Distribution of the study subjects by risk factors of CAD (n = 100)

Risk factors	Male (n=62)		Female (n=38)		Total		p value
	n	Percentage (%)	n	Percentage (%)	n	Percentage (%)	
Smoking	41	66.10	5	13.10	46	46.00	0.03*
Hypertension	21	38.80	14	36.80	35	35.00	0.82
Diabetes mellitus	28	45.10	24	63.10	52	52.00	0.12
Dyslipidemia	19	30.60	16	42.10	35	35.00	0.23
Family history of CAD	17	27.40	14	36.80	31	31.00	0.56

p values calculated by Chi-square test.

Table II: TIMI risk scores of the participants (n = 100)

TIMI score	Male (n=62)		Female (n=38)		Total		p value
	n	Percentage (%)	n	Percentage (%)	n	Percentage (%)	
TIMI 1	6	66.67	3	33.33	9	9.00	0.23
TIMI 2	5	50.00	5	50.00	10	10.00	0.32
TIMI 3	13	65.00	7	35.00	20	20.00	0.01*
TIMI 4	11	52.38	10	47.62	21	21.00	0.33
TIMI 5	9	60.00	6	40.00	15	15.00	0.36
TIMI 6	10	83.33	2	16.67	12	12.00	0.23
TIMI 7	8	61.54	5	84.20	13	13.00	0.67

p values calculated by Chi-square test.

Table III: TIMI grades of the patients (n = 100)

TIMI grade	Male (n=62)		Female (n=38)		Total		p value
	n	Percentage (%)	n	Percentage (%)	n	Percentage (%)	
Low TIMI	34	54.80	21	55.20	55	55.00	0.04*
Medium TIMI	18	29.00	11	28.90	29	29.00	0.22
High TIMI	10	16.10	6	18.40	17	17.00	0.12

p values calculated by Chi-square test.

Table IV: In-hospital outcome of the patients at different TIMI grades (n= 100)

Outcome	TIMI grade	Male (n=62)		Female (n=38)		Total		p value
		N	Percentage (%)	N	Percentage (%)	N	Percentage (%)	
Death	Low	0	0	0	0	0	0	NA
	Medium	1	1.60	0	0	1	1	0.04*
	High	2	3.30	1	2.60	3	3.00	0.65
MI	Low	1	1.60	0	0	1	1.00	0.04*
	Medium	2	3.30	1	2.63	3	3.00	0.76
	High	3	4.80	2	5.60	5	5.00	0.06
Cardiogenic shck	Low	1	1.60	0	0	1	1.00	0.04*
	Medium	2	3.20	1	2.63	3	3.00	0.07
	High	3	4.80	2	5.66	5	5.00	0.6
Heart Failure	Low	1	1.60	0	0	1	1.00	0.04*
	Medium	2	3.20	1	2.53	3	3.00	0.60
	High	4	6.40	2	5.66	6	6.00	0.41
Arrhythmia	Low	11	17.70	6	15.70	17	17.00	0.01*
	Medium	14	22.50	9	23.60	23	23.00	0.27
	High	16	25.80	10	26.30	26	26.00	0.06

p values calculated by Chi-square and Fisher's exact test.

Discussion

Total 100 patients with unstable angina who were admitted in CCU in CMCH were selected for the study after considering inclusion and exclusion criteria. Among total 100 patients male was 62% and female was 38%. Minimum age was 35 and maximum age was 73, mean 58.57 ± 11.04, which was similar to the study carried out by Pollack et al. 2006 and Mukherjee et al 2005[7,10].

TIMI risk score includes seven prognostic variables age >65 years, >3 coronary risk factors, known coronary stenosis of >50%, ST-segment deviation >1 mm at presentation, ≥2 anginal events within the previous 24h, use of aspirin within the previous 7 days and elevated cardiac markers[11,12,13]. Patients scored 1 for each risk factor present. Others had various TIMI risk scores. In this study 9.00% patients have TIMI risk score 1, 10.00% patients have TIMI risk score 2, 20.00% patients have TIMI risk score 3, 21.00% patients have TIMI risk score 4, 15.00% patients have TIMI risk score 5, 12.00% patients have TIMI risk score 6 and 13.00% patients had TIMI risk score 7. Risk stratification of patients with chest pain is an integral part in the management of potential ACS.

Among the CAD risk factors highest percentage of patients was diabetic. One third patients had history of smoking; others had hypertension dyslipidemia and had family history of CAD. In the present study incidence of myocardial infraction and its relation with TIMI risk score was evaluated. The incidence of myocardial infarction was 1.61% in case of male which was 0 in female at low TIMI risk score. The incidence of myocardial infarction was increased as the TIMI risk score raised in case of male but distribution of MI was statistically insignificant with female ($p>0.05$).

The TIMI risk score was shown to predict adverse cardiac events within 14 days of the initial presentation in patients already identified as having ACS[4,6]. It also has been shown to both diagnose AMI at presentation and predict 30 day or longer outcomes in a broad based ED patient population with potential ACS[14].

In the present study, we examined the ability of the TIMI risk score to risk stratify both men and women, and found that although it worked for both genders, men were at higher risk of developing adverse outcome at lower TIMI scores. The TIMI risk score can effectively categorize patients who most benefit from hospital admission and early aggressive treatment[15,16]. This may be especially useful with female patients, who often present with atypical symptoms and non-diagnostic ECGs, making diagnosis more difficult. This may be because the TIMI risk score is not as reliant on presentation characteristics as other risk stratification tools[17]. It relies on objective assessment of age >65 years, prior diagnosed (Known coronary disease; the presence of three or more traditional cardiac risk factors, prescribed aspirin (Indicating vascular disease) and objective measures of ischaemia (Elevated markers, ST segment changes) for six of the seven items. Only "severe angina", which is most commonly interpreted as two or more symptomatic episodes, has a subjective component. The fact that it is comprised of items that are objective may explain its ability to be an accurate risk stratification tool, even in the setting of atypical presentations, which are more common in women[7].

In case of male incidence of cardiogenic shock was 1.6% at low TIMI which was 0 in case of female. At medium to high grade of TIMI the incidence of cardiogenic shock was distributed insignificantly ($p>0.05$). In this study 10(10%) patients developed heart failure during the study period. In male incidence of heart failure was 1.6%, 3.2% and 6.4% at low, medium and high TIMI respectively but in case of female it was 2.53% and 5.66% at medium and high TIMI score. Study revealed 66(66%) patients developed arrhythmia during the study period. At low TIMI, in male incidence of arrhythmia was found higher than female but at medium and high TIMI it was more or less same in percentages.

In-hospital outcome in patients with unstable angina with low TIMI score where MI, cardiogenic shock and heart failure was found high in male which was 0 in female. Arrhythmia was found in both male and female. In light of continuously emerging information pointing to the gender differences of individual risk factors, presentation, and outcomes in ACS, risk stratification for women has been reevaluated. However, the only risk stratification model specifically designed for women was proposed by Douglas and Ginsburg in 1996. Since then studies have shown that even though women and men presenting with ACS differ, their outcomes are still ultimately dependent on the severity of the illness and not gender[12,18].

While our study has shown that the TIMI risk score is a good predictive tool in both men and women, we did see a difference with low to intermediate risk patients. Men tended to have worse outcomes than women in the low to intermediate risk groups[13,15].

A study demonstrated that men were much more likely to receive revascularization procedures than women during hospitalization for AMI. Our data are similar, as they suggest that men were more likely to receive revascularization[19]. To eliminate the possibility that the relationship between gender and TIMI risk score could be impacted by workup bias (with men receiving more tests and therefore more revascularization procedures), we performed a secondary analysis that evaluated the composite outcome of death and AMI alone. The result was consistent with our primary analysis—men still had more adverse events in low to intermediate risk groups.

Limitations

Due to lack of funding and time constraint the authors could not include large number of participants and participation from different hospital of the country could not be ensured. Long term follow up of the participants could also not been attempted.

Conclusion

In terms of multivariate analyses, the TIMI risk score has proven to be an effective risk assessment tool for predicting the risk of death and ischemic events among patients with ACS. The TIMI risk score successfully risk stratifies both males and females with UA at the time of CCU presentation, however, males have worse outcome at low TIMI risk scores than females.

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Contribution of author

MSUS-Conception, desing, acquisition of data, drafting and final approval.

SD-Analysis, interpretation of data, drafting and final approval.

MKU-Acquisition of data, critical revision and final approval.

AYMNJ-Interpretation of data, critical revision and final approval.

MAH-Data Analysis, interpretation of data and final approval.

MAK-Acquisition of data, drafting and final approval.

Disclosure

All authors declared no competing interest.

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