

COMPARISON OF THE GRACE, HEART AND TIMI SCORE TO PREDICT ADVERSE CARDIAC EVENTS IN PATIENTS WITH CHEST PAIN PRESENTING TO EMERGENCY MEDICINE DEPARTMENT

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Abstracts: Background & Objectives: The performance of the GRACE, HEART and TIMI scores were compared to predict the probability of major adverse cardiac events (MACE) in chest pain patients. To investigate which risk score (TIMI score, GRACE or HEART score) identifies the largest population of low-risk patients at the Emergency Department (ED). To reduce the cost of diagnostic procedures and early discharge of low-risk patients by use of the scoring system in ED. To establish a standardized protocol to be used in the emergency department for patients presenting with chest pain^[4]. **Materials and Methods:** We used three well-known risk scores are the GRACE score, the HEART score and the TIMI score for risk stratification tool. All three score was calculated on arrival and during follow up on 2th & 4th week. Occurrence of any adverse coronary event like: AMI, PCI, CABG, coronary angiography revealing procedurally correctable stenosis managed conservatively, and death due to any cause were noted within 2th & 4th weeks of initial presentation. **Results:** Out of 350 patients presented with chest pain, 192 patients had acute coronary syndrome were diagnosed in emergency department. GRACE score identified 115(33%) patients with low risk out of which 14(12.2%) patients developed MACE, HEART score identified 122(35%) patients with low risk out of which 6(5%) patients developed MACE & TIMI score identified 129(36.8%) patients with low risk out of which 12(10.8%) patients developed MACE. **Conclusions:** The HEART score performed best in discriminating between those with and without MACE. The HEART score is superior to TIMI and GRACE in predicting 30-day MACE in a high acuity patient population of a tertiary ED. The HEART score identified the largest number of patients as low risk without compromising safety, compared with the TIMI score which may lead to a reduction in diagnostic procedure and hospital admission in this low risk group and thus in possible savings.

Key Words: Acute coronary syndrome and adverse cardiac events, Chest pain, GRACE score, HEART, TIMI.

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Introduction:

Chest pain is the most common presentation for which patients are admitted to the Emergency department^[5]. Any delay in diagnosis and treatment can have a negative impact on their management and prognosis. Normal values of troponin and a normal electrocardiogram still do not exclude adverse cardiac events completely. As a result, many patients presenting with chest pain are currently hospitalized and extensively evaluated with non-invasive stress testing or imaging, or with invasive coronary angiography. However, of all chest pain patients <25% will have an ACS. If patients at low risk for adverse cardiac events could be recognized early in the diagnostic process, it has the potential to reduce patient burden, length of stay at the ED, frequency of hospitalization, and costs^[3].

Material and Methods:

This study was a prospective observational study conducted over a period of 2 years on 350 adult patients who presented with chest pain to Emergency medicine department.

Inclusion criteria:-

- Any patient presented with chest pain^[4]
- Age > 18 years^[2].
- All patients providing written informed consent.

Exclusion criteria:-

- Patients presented to ED with the diagnosis of myocardial infarction^[9].
- Those with a clear sign of chest pain like trauma or surgery^[2].

- Upon the arrival of the patient, cardiac monitoring & follow by ECG will be obtained within 10 minutes of arrival [8]. Laboratory investigations including cardiac markers will be collected. The HEART score, GRACE, and TIMI score will be calculated on arrival and during follow-up on the 2nd & 4th week [9]. In case there is no follow-up, either the patient or their general practitioners will be called to inquire about their condition and check for possible hospital admission, myocardial infarction, and revascularization at other medical centres. Occurrence of any adverse coronary event like AMI, PCI, CABG, coronary angiography revealing procedurally correctable stenosis managed conservatively, and death due to any cause will be noted within 2th & 4th weeks of initial presentation [9].

According to the total HEART score calculated, patients are divided into low (0–3), intermediate (4–6), or high (7–10) risk of a MACE [5,9].

For the total GRACE score calculated, patients are divided into low (1–88), intermediate (89–118), or high (>119) risk of a MACE [7,9].

For the total, TIMI scores calculated, patients are divided into low (0–2), intermediate (3–4), or high (5–7) risk of a MACE [6,9].

Result: The study was conducted among the 350 patients presenting with chest pain to emergency department. There were 192 cases with acute coronary syndrome and 158 cases without acute coronary syndrome. Out of 192 patients diagnosed with acute coronary syndrome; 42.7% had ST segment elevation myocardial infarction, 34.3% had non ST segment elevation myocardial infarction and 23% diagnosed with unstable angina. Out of 158 patients diagnosed without acute coronary syndrome; 27% had acute anxiety, 24% had Acid peptic disease, 18% had Respiratory causes & 11% had musculoskeletal pain. 8%, 7%, 3% and 2% patients had Undetermined cause, Acute heart failure, Hypertensive urgency and Stable angina respectively.

The mean age of study population with chest pain was 55.03±16 yrs. The mean age of Patients presenting with acute coronary syndrome was 58.11±14.6 yrs. The mean age of Patients

presenting without acute coronary syndrome was 51.3±17.7 yrs. Out of 350 cases, 198 (56.6%) cases were males while 152(43.43%) cases were females. Out of 192 patients with ACS, 101 patients were male and 91 patients were female. As per sex distribution of patients presenting without acute coronary syndrome in which Male constitute 61.4% and female constitute 38.6%.

Table 1 As per GRACE score, Out of 350 cases, maximum cases of patients with chest pain were from 60–69 years age group.

From 60–69 years of the age group number of patients with ACS was 53 (51%). As per HEART score, Number of patients with ACS of age group <45 years, 45–65 yrs and >65 yrs was 42%, 59.5% and 60.6% respectively. As per TIMI score number of patients with ACS of age group <65 years, ≥65 years were 123 (53%) and 69 (57.5%) respectively. All this shows that as age progressing prevalence of ACS increases.

Age (Year)	Points	Number [n=350]	Patients With ACS[n=192]	Patients Without ACS[n=158]
<39	0	68	23	45
40–49	18	39	24	15
50–59	36	70	25	45
60–69	55	103	53	50
70–79	73	54	34	20
80–89	91	13	10	3
>89	100	3	3	0

Table 1 GRACE score; age variable

According to clinical history for HEART score; Out of 350 patients 148 were highly clinical suspicious of ACS among them 136 patients were diagnosed with ACS and 12 patients were without ACS. Total 98 patients were moderate clinical suspicious of ACS among them 48 were diagnosed with ACS and 50 patients were without ACS. Total 104 patients

were slightly clinical suspicious of ACS among them 08 were diagnosed with ACS and 96 patients were without ACS.

As per HEART score, Out of 192 cases of ACS 84 (65%) patients had more than 3 risk factor of ACS, 75(52%) patients had 1 or 2 risk factor of ACS, and 33 (42%) patients had no risk factor of ACS. Out of 158 patients without ACS 47 (36%) patients had more than 3 risk factor of ACS, 70(48%) patients had 1 or 2 risk factor of ACS and 41 (55%) patients had no risk factor of ACS. As the number of risk factor increases 0, 1-2 and >3; the patients presented with ACS were 45%, 52% and 65% increased respectively

As per TIMI score out of 350 patients; 104 patients had ≥3 Risk factor of acute coronary syndrome. Out of 104 patients, 88 (85%) patients presented with ACS and 16 (15%) patients without ACS.

Out of 350 patients, 85 patients had history of ASA use within 7 days and 265 patients had no use of ASA. Out of 192 patients, 63 patients were history of ASA use presented with ACS

As per GRACE score, figure 1 shows Number of patients with ACS according to Killip class I, II, III & IV were 119, 45, 24 & 04 respectively.

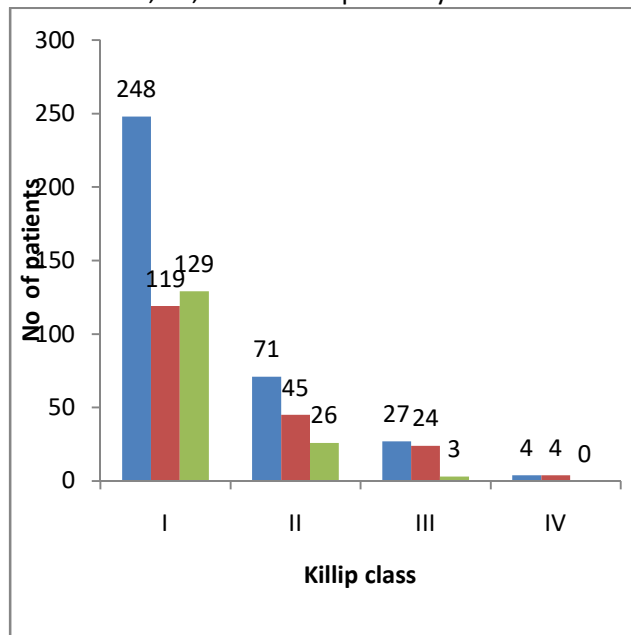


Table 2 shows ECG findings patients with chest pain having ACS

	ECG characteristic	Patients with ECG changes	Patients With ACS[n=192]
STEMI	Only	33	82
	ST E with Tall T wave	7	
	ST E With Q wave	42	
NSTEMI &	ST depression	59	66
	T wave inversion	7	
Unstable angina	ST depression	42	44
	T wave inversion	8	

Out of 42 patients with Acute Anxiety 2 patients had changes of old ischemic heart disease (Q wave); rest of 40 patients had normal ECG. Normal ECG had been seen in patients with acid peptic disease, musculoskeletal pain & few patients with undetermined causes. 5 patients diagnosed with hypertensive urgency in which 3 patients had T wave inversion and 1 patient had old changes of ischemic heart disease and 1 had ST-T changes. 4 patients diagnosed with stable angina in which 3 patients had T wave inversion, 1 patient had ST depression. 12 patients diagnosed with acute heart failure in which 2 patients had changes of old ischemic heart disease, 3 patients had T wave inversion, 2 patient had ST depression, 2 patients had atrial fibrillation, 1 patients had ECG changes of LVH, 1 patients had QRS voltage and 1 patients had RBBB. 28 patients had respiratory causes of chest pain out of them 2 patients had old Q wave and one patients had LVH, 2 patients had P pulmonale on ECG. Thus patients without ACS above ECG finding were seen. As per GRACE score Out of 350 patients 109 patients had high systolic

blood pressure and 16 patients had low systolic blood pressure. Out of 109 patients with high SBP; 71 patients with ACS and 38 patients without ACS. Out of 350 patients 179 patients had abnormal level of serum creatinine, among them 123 patients with ACS and 56 patients without ACS. As per comparison of with Troponin I. Out of 192 patients of acute coronary syndrome 82 patients of STEMI had elevated level of Troponin-I; 66 patients of NSTEMI had elevated level of Troponin-I and 44 patients of unstable angina had normal troponin I level. 60% of patients had Normal Respiratory Rate while 40% of patients had high respiratory rate. 97% of patients had normal spo₂ while 3% patients had spo₂ less than 94% patients had normal heart sound while 2% patients had abnormal heart sounds. Out of 350 patients, 192 patients were presented within 24 hours of chest pain among them 104 patients were diagnosed with ACS & 88 patients were non-ACS. After 24 hours 158 patients came, among them 88 patients with ACS & 70 patients without ACS.

TABLE 3 shows BASELINE CHARACTERISTIC

Table 4 shows Distribution of GRACE risk score variable in current study population. GRACE score identified 33 % (115) patients as low risk [GRACE Score: ≤88], 31% (109) patients as medium risk [GRACE Score: 89-118] and 36 % (126) patients as high risk [GRACE Score: ≥118].

As per table 5 showing that total 27 patients were identified major adverse cardiac events (MACE) according to this three score[low risk GRACE score-13 patients, low risk HEART score-4 patients& TIMI score-10 patients] at first cardiac marker report; at the end of second cardiac marker evaluation; total 32 patients were identified major adverse cardiac events (MACE) according to this three score[low risk GRACE score-14 patients, low risk HEART score-6 patients& TIMI score-12 patients].

In moderate & high risk patients identified by GRACE score, HEART score and TIMI score shows that major adverse cardiac events as in this population were as follow 70% & 82%; 66% & 94% and 80% & 87.5% which shows that moderate & high risk patients usually needs admission, through investigation, early therapeutic intervention and

management. These patients are never considering as early discharge patients.

It suggests that above mentioned scores are utilized exclusively for low risk patients of chest pain.

Receiver –operating –characteristic (ROC) curves and corresponding areas under curve of the GRACE, HEART & TIMI score to predict major adverse cardiac events within 4 weeks.

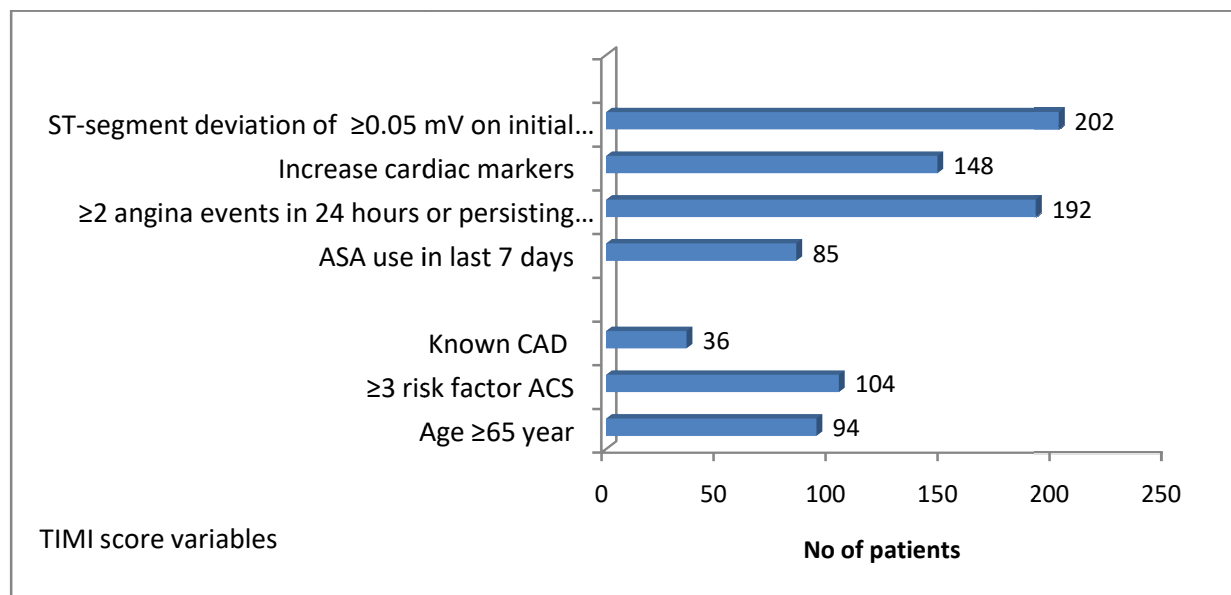
Out of 350 patients 110 patients were discharge to home, 69 patients were disposed to ICU, CCU and cath lab. 171 patients shifted to high dependency unit. In this study out of 350 patients, total 42 patients were expired. 8 patients with ACS were died within 24 hours of admission, while 1 patient without ACS was died within 24 hours of admission. Within 4 week of follow up 26 patients with ACS were expired & 7 patients without ACS were expired.

TABLE 3 shows BASELINE CHARACTERISTIC

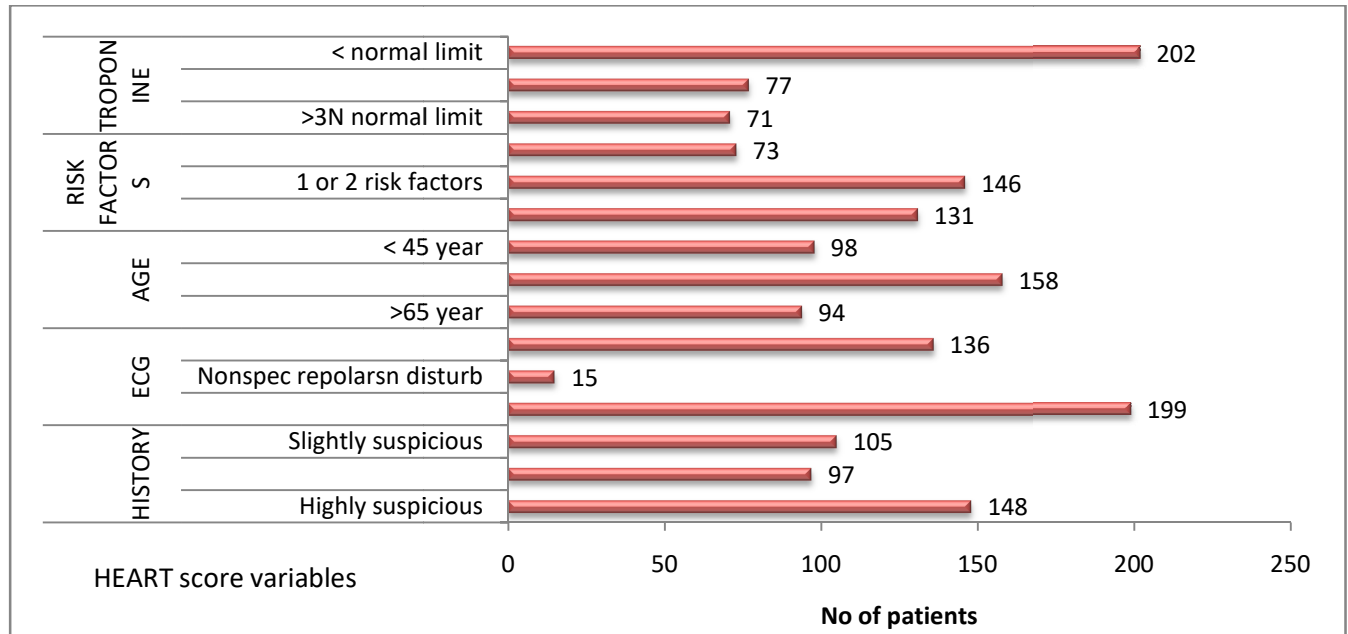
<i>Demographics</i>	All patients	Patients with MACE	Patients without MACE
Male	198	101	97
Mean age (SD)	55.03(16.6)	58(14)	51.3(18)
<i>Vital sign at presentation</i>			
Mean SBP mmhg (SD)	127.3(23)	128(23)	125.9(22)
Mean heart rate per minute (SD)	96.2(26)	90(25)	103.5(25)
Killip class I	248	119	129
<i>Cardiac risk factors</i>			
Diabetes Mellitus-II	55	36	19
Obesity (BMI >30 Kg/m ²)	68	41	27
Hypercholesterolemia	107	64	43
Hypertension	146	93	53
Positive family history	113	58	55
Current smoking	109	57	52
<i>History of CVD</i>			
History of AMI	23	17	6
History of PCI	18	17	1
History of CABG	5	5	0
History of CVA/TIA	41	23	18
History of PAD	30	16	14
<i>Laboratory result</i>			
Mean creatinin (SD)	1.4(0.98)	1.6(1.0)	1.2(0.7)
<i>Anti platelet Medication</i>	85	58	27

TABLE 4 GRACE VARIABLE

Age (yrs)	Patients [n=350]	HR (min)	Patients [n=350]	SBP (mmHg)	Patients [n=350]	S.Cr (mg/dl)	Patients [n=350]	Killip Class [n=350]	
<39	68	<70	16	<80	06	0.0-0.39	02	I	248
40-49	39	70-89	151	80-99	10	0.4-0.79	48	II	71
50-59	70	90-109	88	100-119	122	0.8-1.19	121	III	27
60-69	103	110-149	78	120-139	103	1.2-1.59	81	IV	04
70-79	54	150-199	15	140-159	80	1.6-1.99	42	Cardiac arrest [n=350]	02
80-89	13	>200	02	160-199	29	2.0-3.99	45	Elevated cardiac marker [n=350]	148
>89	03	-	-	>200	00	>4	11	St-deviation [n=350]	190



As per Figure 2 TIMI score variable; TIMI score identified 36.8 % (129) patients as low risk [TIMI score: ≤ 2], 47% (165) patients as medium risk [TIMI score: 3-4] and 16% (56) patients as high risk [TIMI score: 5-7].

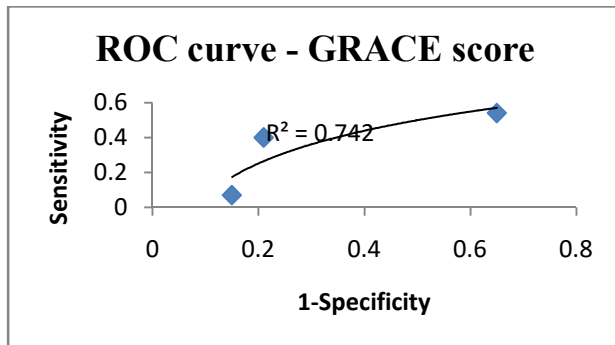


As per Figure 3 HEART score variable; HEART score identified 35 % (122) patients as low risk [HEART score: ≤3], 24 % (85) patients as medium risk [HEART score: 4-6] and 41 % (143) patients as high risk [HEART score: 7-10].

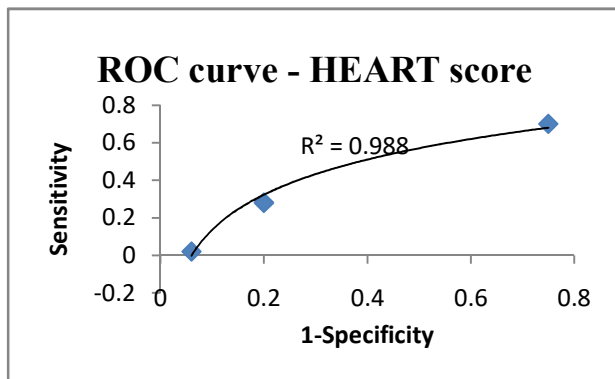
Table 5 Comparison of performance of GRACE score, HEART score and TIMI score based on first cardiac marker measurement for Low risk Patients

	GRACE score	HEART score	TIMI score
Cut-off for low risk	≤88	≤3	≤2
Number of patients with low risk / total number of patients	115/350	122/350	129/350
% MACE in low risk group	11.3%[13/115]	3.3%[4/122]	7.7%[10/129]
MACE of which ACS	13	4	10
MACE of which death	1	0	1
Positive predictive value	89%	97%	92.3%
Negative predictive value	76.2%	82.5%	82.3%

As per Figure-4 Discriminative capacity of GRACE Scores: ROC curve for GRACE score low risk patients with an area under curve of 0.74.

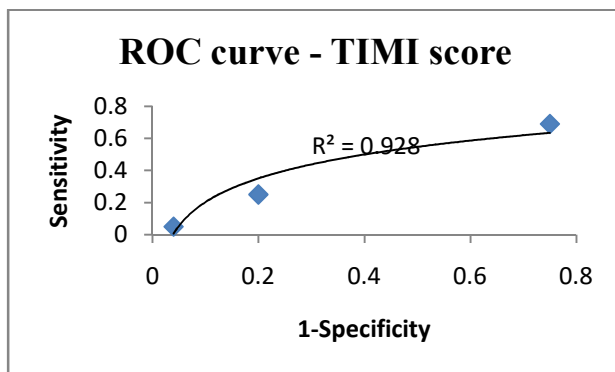


As per Figure-5 Discriminative capacity of HEART



Scores: ROC curve for HEART score low risk patients with an area under curve of 0.98.

As per Figure-6 Discriminative capacity of TIMI Scores: ROC curve for TIMI score low risk patients with an area under curve of 0.92.



Discussion: We applied three well-known and extensively validated risk scores in 350 patients presenting with chest pain at the ED, and classified them into low risk, medium risk, and high risk based on GRACE score, HEART score, and TIMI score. The prevalence of ACS was 54.8% in our study, while in a study done by Houda Baccouche et al. the prevalence of ACS was 22.3%^[9]. It may be because of the rising incidence of Coronary artery disease in our population & also because of the fact that our hospital being a tertiary level hospital, we receive a lot of referred cases of chest pain from primary care physicians for further management.

The mean age of the study population with chest pain was 55.03±16 yrs. While a previous study done by Jeff Dubin, Eric Kiechle et al. the mean age of the study population was 60±13.9 years. The mean age of patients presenting with the acute coronary syndrome was 58.11±14.6 yrs. While comparison with a study done by Jeffrey Tadashi Sakamoto^[1] & J.M. Poldervaart^[4] mean age was 60.8±13.2 & 62±14. In a previous study done by G. RAMSAY^[3] mean age was 65±0.72.

In our study, the proportions of male patients with ACS were higher compared to a female patient. While comparison with a previous study done by Jeffrey Tadashi Sakamoto^[1] et al. and J.M. Poldervaart^[4] et al. prevalence of male patients with ACS was also higher.

While comparing all patients presented with ACS as per GRACE score, HEART score and TIMI score according to age variables ≥60 years, >65 years & ≥65 yrs prevalence of ACS was 58 %, 60.6%, and 57.5 % increased respectively. Thus as the age progressing prevalence of ACS also increases. As per GRACE score according to Age variables >60 years onwards remarkable high prevalence of ACS was noted.

As per the GRACE score remarkable high prevalence (61%) of ACS was noted in the age group between 40-49 years; this may be due to the present scenario and modern lifestyle. So that no age is exempted for ACS occurrence and all patients presented with chest pain thoroughly scrutinize as per protocol. Thus, In the GRACE score age variable divided into smaller age groups with more number of different age groups shows valuable significance. As per HEART score variables, out of 192 patients with ACS; highly clinical

suspicious, moderate clinical suspicious and slightly clinical suspicious patients showing a prevalence of ACS were 136(92%), 48(49%) & 8(08%) respectively. So that clinical history is also an important tool for patients presenting with chest pain. By comparing with the study done by Alexander Kamali et al.^[10] proportion of patients with high suspicious 93.2%, moderately suspicious 38%, and slightly suspicious 38%. As per the HEART score, clearly evident that as the number of Risk Factors of coronary artery disease increases the prevalence of ACS increases. Similarly, as the number of Risk Factors of coronary artery disease decreases the prevalence of ACS is also reduced. The proportion of ACS was higher (67%) in patients with no use of ASA. Thus ASA uses are associated with a reduction in the prevalence of ACS. A previous study had done by Yuxiang Dai and Junbo Ge^[11] shows a 23% reduction of MI and a 50% reduction in reinfarction.

Respiratory foreign sounds like rales due to pulmonary edema were not very common findings in the majority of patients with ACS. Only 2 % (04) patients presented with cardiogenic shock and 36 % of patients had rales on examination. El-menyar A. et al^[12] shows that patients with higher Killip class had a worse clinical profile. Out of all patients of STEMI, approximately half of the patients had an old history of Ischemic heart disease. In patients with ACS, there was STEMI observed in 43 % of patients. While comparison with a study done by G.A.Fishbein et al.^[13] the spectrum of ECG findings was STEMI (30%), NSTEMI (25%), and unstable angina (38%). The most common presentation of Non-Cardiogenic Chest Pain was acute anxiety followed by acid peptic disease, respiratory disease, and musculoskeletal pain respectively.

As per GRACE score, we observed a high prevalence of ACS at a heart rate <70 per minute. Similarly, the highest prevalence of ACS was seen at a heart rate >200 per minute. Previous study done by Asaad N, et al.^[16] shows that high or low heart rate is a marker of high risk that needs more attention and management. Out of 192 patients with the acute coronary syndrome, 82 patients of STEMI had elevated levels of Troponin-I; 66 patients of NSTEMI had elevated levels of Troponin-I. Out of 350 patients, 202 patients had normal Troponin I level. The study was done by Benjamin M. et al.^[18] shows that testing for cardiac

troponin-I substantially improves the clinician's ability to assess the risk and guide therapeutic decision-making.

According to Peter reaney et. al.^[14] study % of MACE in low-risk patients classified in GRACE score, HEART score & TIMI score was 8.9%,0.5% &8.8 % respectively while in Jeffrey Tadashi et al.^[1] study % of MACE was 15%, 2% & 16 % respectively; in our study % of MACE in low risk patients classified in GRACE score, HEART score & TIMI score was 12.2%, 05% & 10.8 %.

The population involved in the study A.J. Six et al^[5] and B.E.Backus et al. ^[2] were 122 and 2388 respectively while our study covered a population of 350 patients. The mean age of patients involved in the study A.J. Six et al^[4] and B.E.Backus et al. ^[2] was 61 yrs and 60.6 yrs respectively while in the present study mean age of the population involved was 55.03 yrs. In A.J. Six et al^[5], B.E.Backus et al. ^[2], and the present study male predominant population was seen. As per HEART score, MACE was observed in low-risk patients in 2.5%, 0.9%, and 5% study subjects in A.J. Six et al. ^[5], B.E.Backus et al. ^[2], and present study respectively. As per HEART score, MACE was observed in moderate-risk patients in 20.3%, 12%, and 64% study subjects in A.J. Six et al. ^[5], B.E.Backus et al. ^[2], and present study respectively. As per HEART score, MACE was observed in high-risk patients in 72.3%, 66%, and 94% study subjects in A.J. Six et al. ^[5], B.E.Backus et al. ^[2], and present study respectively. As per Jeffrey Tadashi S et al^[1] Study Specificity (%), Specificity (%), PPN & NPV of GRACE score was 20.3 %, 93.5%, 39.3% &85 % respectively; while in our study it was 94%, 64%, 89.4% & 76%. As per Jeffrey Tadashi S et al^[1] study Specificity (%), Specificity (%), PPN & NPV of HEART score was 25%, 91.6%, 42.2% & 98% ; While in our study it was 98%, 75%, 97% & 82.5%. As per Jeffrey Tadashi S et al^[1] study Specificity (%), Specificity (%), PPN & NPV of TIMI score 37.5%, 93.5%, 43.5% & 83.9%; While in our study it was 95%, 75%, 92.25% & 82.35 %.

As shown in table-5; GRACE score identified 115(33%) patients with low risk out of which 14(12.2%) patients developed MACE, HEART score identified 122(35%) patients with low risk out of which 6(5%) patients developed MACE & TIMI score identified 129(36.8%) patients with low risk out of which 12(10.8%) patients developed MACE. So that, HEART score revealed fewer Major

Adverse Cardiac Events compared to TIMI & GRACE score. HEART score validated in comparing above finding. In the literature, mostly comparable results were found when comparing the HEART and TIMI scores. While comparison with A.J.Six, B.E. Backus, et al.^[19] studies, the AUC of the HEART score was 0.83 and the AUC of the TIMI score 0.75; In this study, the HEART score had a high area under a curve. We found HEART score had highest specificity 98%, sensitivity 75%, and PPV 97 %, and NPV 82.5 % accuracy 87.4 % for low risk patients. TIMI score had specificity 95%, sensitivity same as HEART score 65 %, PPV 92.25%, NPV 82.3% & accuracy 86 % for low risk patients. While GRACE score had 94% specificity, lowest sensitivity 64%, PPV 89.4%, NPV 76 % and accuracy 80.4 % for low risk patients. The HEART score may be able to convey risk quickly and efficiently, improving inter-physician communication. Using the risk categories, providers can quickly understand the evidence-based risk of a patient who presents to the ED with chest pain and triage, intervene, and admit accordingly. The GRACE score is a useful tool in risk stratification in ACS with specificity similar to the TIMI score. The HEART score specifically designs for the much broader chest pain population at the Emergency department. Interestingly, the HEART score was not developed using mathematical modelling from real-life data, but developed by a cardiologist based on clinical experience and later on validated in clinical databases. Future studies should also focus on investigating the use of the HEART score in facilitating clinical decision-making in high acuity chest pain patients.

Conclusion:

Chest pain is the most life threatening presentation in emergency department it needs systemic and complete evaluation because life threatening condition like acute coronary syndrome cannot be missed. Failure to recognize potentially serious condition can lead to major adverse cardiac events and other serious complications including death. Because in our study 54.8% of Acute coronary syndrome events with higher proportion (52.6%) of male patients. As the age increases occurrence of ACS increases. No age is exempted for occurrence of ACS. Clinical history as per physician opinion, risk factor and history of Aspirin use or no use have great significant correlation with occurrence of ACS

event. Serial ECG and two time measurement of cardiac marker has pivotal role in assigning patients presented with chest pain in emergency department specially triage low risk group. In our study HEART score is best triage instrument to classify low risk group patients presented with chest pain in ED with developing low number of Major Adverse Cardiac Event. HEART score consist of only five prognostic factors: History, ECG, Age, Risk factor and Troponin with easy scoring system. Each factor scored from 0 to 2 and classifies them in low risk, medium risk and high risk.

GRACE and TIMI score is at par with HEART score in calculating low risk group patients. Our study shows GRACE score has a low specificity and sensitivity compare to HEART score, TIMI score has equal specificity as GRACE score and same sensitivity as HEART score. In our study HEART score is more easily and practically implemental triage instrument to identify largest number of patients at low risk with minimum MACE compare to other score in emergency department.

No conflict of interest

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