Comparative Prospective Study of the Performance of Chest Pain Scores and Clinical Assessment in an Emergency Department Cohort in Singapore

Ng Mingwei (mingwei.ng@mohh.com.sg)
Singhealth https://orcid.org/0000-0003-0614-2061
Hong Jie Gabriel Tan
Singhealth
Fei Gao
Singhealth
Jack Wei Chieh Tan
Singhealth
Swee Han Lim
Singhealth
Marcus Eng Hock Ong
Singhealth
R Ponampalam
Singhealth

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Abstract

Background Chest pain scores allow emergency physicians to identify low-risk patients for whom discharge can be safely expedited. While their utility have been extensively studied and validated in Western cohorts, data in patients of Asian heritage is lacking. This study aimed to determine the accuracy of HEART, EDACS and GRACE in risk-stratifying which emergency patients with chest pain or angina-equivalent symptoms are at risk of major adverse cardiovascular events (MACE) within 30 days (composite of all-cause mortality, acute myocardial infarction, and coronary revascularization). This single-centre prospective cohort-study enrolling 1200 patients was conducted by a large urban tertiary centre in Singapore. The chest pain scores were reported prior to disposition by research assistants blinded to the physician's clinical assessment. Outcome adjudication was performed by an independent blinded cardiologist and emergency physician, while a second cardiologist adjudicated in the case of discrepancies. \

Results Of 1200 patients enrolled, 5 withdrew consent and were excluded from analyses. 135 patients (11.3%) suffered MACE within 30 days. HEART, which ruled-out acute coronary syndrome in 52.8% of patients with 88.1% sensitivity, and EDACS, which ruled-out acute coronary syndrome in 57.5% of patients with 83.7% sensitivity, proved comparable to clinical judgment which ruled-out acute coronary syndrome in 73.0% of patients with 85.5% sensitivity. GRACE was weaker – ruling-out acute coronary syndrome in 79.2% of patients but with a dismal sensitivity of 45.0%. The correlation-statistic for HEART (79.4%) was also superior to EDACS (69.9%) and GRACE (69.2%).

Conclusions HEART more accurately identified low-risk chest pain patients in an Asian emergency department who were suitable for expedited discharge and demonstrated comparable performance characteristics to clinical judgment. This has major implications on the use of chest pain scores to safely expedite disposition decisions for low-risk chest pain patients in the emergency department.

Background

Chest pain is among the leading causes for ED presentations. Emergency physicians (EPs) must determine which high-risk patients require urgent admission and further testing for acute coronary syndrome (ACS) such as angiography, and which low-risk patients can be safely discharged expediently to avoid unwarranted hospitalizations and unnecessary testing.[1]

In 2015, the landmark study by Mahler *et al* in *Circulation*[2] found that the HEART (History, ECG, Age, Risk factors, Troponins) tool significantly reduced hospitalization rates and length-of-stay while maintaining a low miss-rate for major adverse cardiovascular events (MACE)[3,4]. While the HEART pathway has gained traction for its ease of use, other EPs favour a slew of other scores such as Global Registry of Acute Coronary Events (GRACE), ED Assessment of Chest Pain Score (EDACS), Vancouver Chest Pain Rule or Troponin-only Manchester ACS Score (TMACS).

The American Heart Association (AHA) has published scientific statements to support the use of these scores to guide ACS rule-out for low-risk chest pain patients as well[5], whilst leaving the decision of which particular chest pain risk score to favour to the discretion of individual EPs and institutions. While there has been a long history of attempts to derive and validate chest pain risk scores, few studies have done head-to-head comparisons that direct pit the performance of various scores against each other or against unstructured clinical judgment – and especially not in a population of predominantly Asian heritage.

Rationale

While the literature favours chest pain scores as useful unbiased risk-stratification tools, the same results have not been reproduced consistently. This difference has been attributed to the varying demographics and disease burden of different populations, and the varying coronary catheterization rates across the Cardiology departments of various institutions. Moreover, it remains unclear if chest pain scores can be safely applied in a predominantly Asian population as most studies were derived and validated in Western populations such as in the United States, Australia, New Zealand and the Netherlands. A small single-centre study in Hong Kong (2018) found that both HEART and EDACS had 100% sensitivity, but this study was inadequately powered to find a significant difference between both scores[6].

Methods

This study aimed to address this knowledge gap by providing a validation of HEART, EDACS and GRACE in an Asian population. The accuracy with which the various scores identified ED patients at risk of MACE within 30 days was evaluated against clinical judgment. The primary outcomes are the sensitivities and percentage rule-outs of the various chest pain scores, while the secondary outcomes are their specificities and correlation statistics (C-statistic). The cut-offs used (GRACE <109[7]; EDACS <16[8]; HEART 0-3[9]) were derived from the original studies of the respective scores.

We hypothesize that a score incorporating some element of clinical gestalt (such as HEART, which requires the physician to determine if various aspects are slightly/moderately/highly suspicious) would prove superior to scores that do not incorporate clinical gestalt (such as EDACS and GRACE).

For the purposes of this study, MACE was defined as a composite of three outcomes: all-cause mortality, acute myocardial infarction (MI) or coronary revascularization. MI was defined based on the Third Universal Definition of Myocardial Infarction[10,11] and the cardiac biomarker used was the high-sensitivity troponin-T assay.

This study conformed to the principles in the Declaration of Helsinki. Data was obtained from the chest pain registry of the “Evaluation of High-Sensitivity Troponin-I in the Management of Patients with Chest Pain in the Emergency Department” study, which was registered at the United States’ National Institutes of Health National Library of Medicine ClinicalTrials.gov (NCT02789904). While the original registry was funded by Abbott Diagnostics and Beckman-Coulter to investigate the validity of high-sensitivity troponin-I versus troponin-T, the sponsors did not play any role in study construct, data collection, data analysis or paper writing.

This was a prospective single-centre cohort study, conducted from October 2015 to November 2017, that comprised 1200 ED patients with a chief complaint of chest pain or angina-equivalent symptoms. Full-time trained research assistants used non-probability sampling methods (continuous convenience sampling) for patient recruitment. The study was conducted in a large urban tertiary hospital in Singapore with an annual census of 135,000 patients that had dedicated Cardiology and Cardiothoracic specialty services. Subjects recruited had to be above 21 years old with capacity to provide written informed consent. Their physician had to order an electrocardiogram and troponin for ACS rule-out. Subjects with ST-elevation MI or poor premorbid status with a life expectancy less than a year were excluded.

The various chest pain scores were calculated for each patient prior to disposition by trained full-time research assistants. The research assistants interviewed the patients and their families directly to obtain data for the scores but were deliberately kept blinded to the clinical assessment of the attending EP. The ECGs were reviewed and classified by the attending physician and this interpretation was recorded in the patient’s electronic medical reports.

For the purpose of this study, patient history was classified based on the narrative provided by the patient: typical chest pain was defined as “substernal chest pain/discomfort” “provoked by exertion/emotional stress” and “relieved by rest/nitro-glycerine” and assigned two points under the “History” subsection of the HEART score; atypical chest pain as two of the abovementioned criteria and was assigned one point; while chest pain with none of these was deemed non-specific and given no

points. This is the same definition adopted by the Coronary Artery Disease consortium (comprising 18 different hospitals across Europe and United States) to estimate the pre-test probability of coronary artery disease[12]. The individual variables of the EDACS score (diaphoresis, pain radiating to arm/shoulder/neck/jaw, pain occurred/worsened with inspiration and pain reproducible by palpation) were also prospectively sought by the research assistants from each patient.

The patient and EP were likewise blinded to the chest pain scores obtained by the research assistants. None of the scoring tools were made available to the EP, nor was there any external influence exerted by the study investigators on the EP to utilize any score in their decision-making process. The eventual admitting diagnosis and disposition were left to the EPs' discretion. Outcome adjudication was performed by two independent clinicians blinded to the results of the chest pain scores (a cardiologist and an EP), and a second cardiologist was engaged to resolve any discrepancy.

To benchmark the accuracy of chest pain scores against clinical judgment, patients admitted to Cardiology telemetry-monitored beds with a provisional impression of acute coronary syndrome were deemed "high-risk" by clinical judgment. Patients discharged directly from ED (including those who were discharged after extended ED observation, which involves three sets of serial troponins and ECGs obtained over an eight-hour observation period and which does not offer any provocative or invasive cardiac stress tests) and patients admitted to non-Cardiology beds (e.g. Medical) or admitted under provisional non-cardiac diagnoses were deemed "low-risk". Abscondments and discharges against medical advice were excluded from analyses of the performance characteristics of clinical judgment.

On follow up, all subjects were both contacted by telephone and had their medical records reviewed after 30 days for chest pain, angina-equivalent symptoms or clinical events relevant to adjudication.

Statistical Analysis

Clinical characteristics were summarized using mean ± standard deviation for continuous data and proportion for categorical data. Receiver-operating-characteristic curves were generated, with calculation of area-under-curve and estimation of sensitivity, specificity, positive predictive value and negative predictive value for 30-day MACE performed to determine the diagnostic accuracy of each score. STATA version 15 was used in the analysis. Logistic regression was used in the determination of area-under-curve.

Results

1200 patients were enrolled, of which five withdrew consent after recruitment (**Figure 1**). An estimated 300 patients were assessed for eligibility but not enrolled due to the time-sensitive nature of the condition studied. Of the 1195 patients analysed, 42 patients (3.5%) absconded or discharged against medical advice at the index ED visit but these patients were still followed up at 30 days via telephone call and by reviewing their medical records.

Attempts were made to contact all patients by telephone follow-up 30 days after the index visit. While 456 patients (38.2%) could not be contacted via telephone follow-up, this is unlikely to have a significant impact as all patients had their medical records reviewed. Researchers would be aware of return visits to other hospitals and would be able to verify outcomes even amongst these patients due to the centralized nature of the electronic healthcare records system in Singapore.

The cohort recruited had a high burden of chronic diseases, with 73.4% (877 patients) having at least one of hypertension, hyperlipidaemia or diabetes mellitus, and 20.9% (250 patients) having all three (**Table 1**). As this hospital had a dedicated Cardiology and Cardiothoracic unit, a significant proportion of patients (17.2%) had pre-existing ischemic heart disease as well.

The eventual MACE rate at 30 days in this study was 11.3% (135 patients). HEART had the highest sensitivity of 88.1% (95% CI: 81.5%-92.6%) among the chest pain scores, comparable to clinical judgment at 85.5% sensitivity (95% CI: 78.3%-90.6%) (**Table 2**). Of the 135 patients who suffered a MACE within 30 days, HEART missed 16 patients (11.9%) while EDACS missed 22 (16.3%). The C-statistic for HEART (79.4%) (95% CI: 0.76-0.83) was also higher than EDACS (69.9%) (95% CI: 0.66-0.74) and GRACE (69.2%) (95% CI: 0.65-.74); affirming that HEART is superior to both EDACS and GRACE at discriminating which chest pain patients are at increased risk of MACE.

Abscondments and discharges against medical advice were excluded from analyses in pre-planned sensitivity analyses. The results were consistent with the main study findings and did not yield any major disparity: HEART with 87.8% sensitivity was superior to clinical judgment (85.5% sensitivity). Subgroup analyses of only hospitalized patients revealed that clinical judgment (which ruled-out 40.1% of patients with 96.6% sensitivity) outperformed HEART (which ruled-out 38.2% of patients with 91.4% sensitivity), while HEART in turn outdid EDACS and GRACE.

Discussion

The MACE rate in this study (11.3%) is similar to that found in other papers (10-12%, depending on institution). HEART was found to be the most reliable of the chest pain scores, EDACS trailed closely and GRACE fared the poorest – likely because GRACE, like TIMI, was first developed for patients with established ACS rather than undifferentiated chest pain. HEART exhibited comparable performance characteristics to clinical judgment, despite the latter often entailing a much more rigorous and lengthy evaluation (including an extended eight-hour period of observation for serial troponins and ECGs).

Head-to-head comparisons of chest pain scores are scarce and it remains contentious which is superior. While HEART remains the dominant risk stratification score in the United States[13], AHA and European Society of Cardiology (ESC) reserve judgment on which has the best performance. Chapman *et al* found that HEART has the best test characteristics with 99.4% sensitivity when pitted against TIMI and EDACS, while another multicentre study by Stopyra *et al* reported that EDACS identified 10% more patients as low-risk, with a nearly identical negative predictive value as HEART[14]. A comparison of four decision aids (EDACS, TIMI, HEART, T-MACS by Body *et al* found that EDACS ruled-out MI in 48.3% of patients, outperforming T-MACS (46.5%) and HEART (34.9%)[15]. Our postulation that a score that incorporates clinical gestalt (such as HEART) would prove superior to the others that did not (EDACS, GRACE) was affirmed by the study findings, although this remains a single-centre study and further validation is needed.

Limitations

It is difficult to evaluate for incorporation bias arising from inherent, independent use of chest pain scores by some of the physicians, as the decision-making process of the EPs were not captured in this study. Currently, few attending EPs in this institution employ chest pain scores in their daily practice. The typical approach to chest pain evaluation remains largely based on clinical gestalt as department guidelines advise admitting typical angina patients to Cardiology, offering atypical/non-specific chest pain patients with cardiovascular risk-factors an extended observation protocol, and discharging patients with atypical symptoms and no cardiovascular risk-factors with an outpatient Cardiology review.

As no provocative/invasive stress tests are available as part of either initial assessment or observation protocol in the ED of this institution, the discharge/admitting diagnoses closely represent the impression of the attending EP based solely on receipt of initial cardiac markers and clinical gestalt – and would therefore act as a good surrogate for unstructured clinical judgment. In addition, the disposition and admitting discipline would strongly reflect the likely impression of the EP from clinical judgment, because department guidelines mandate that any patient for whom the EP is concerned of having acute coronary syndrome (i.e. “high-risk” patient by clinical judgment) must be admitted to a telemetry-monitored bed in Cardiology.

However, the retrospective methods by which clinical judgment was derived meant that patients who absconded or discharged against medical advice could not be analysed in the clinical judgment arm, but were included for the chest pain risk scores (which were prospectively sought). Sensitivity analyses were performed to mitigate concerns of bias, since this subgroup are more likely to have incomplete evaluations and possibly higher rates of adverse outcomes arising from non-adherence. The data was re-analysed with these 42 patients (3.5%) excluded from all arms, with no significant resultant difference in the results.

The history component of HEART (as developed in the original 2008 Backus study[16] or the 2015 Mahler study) is inherently subjective, as it depends on the physician’s evaluation of certain qualitative clinical parameters (such as chest pain characteristics). The variability in history obtained and interpreted by research assistants invariably introduces bias and leads to concerns for whether they demonstrate similar inter-observer reliability to physicians. While research assistants may have less clinical acumen, the CAD Consortium definition of the nature of chest pain as adopted by this study is standardized, well-validated and objective. The research assistants were given prior case-based training to instruct them on how to evaluate the subjective aspects of these scores. Research by Cruz *et al* had also reaffirmed that trained research assistants tasked with prospective data collection of subjective chest pain characteristics in ED patients exhibit comparable inter-rater reliability to physicians[17].

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Conclusion

This study demonstrated that HEART more accurately identified low-risk chest pain patients in an Asian ED safe for expedited discharge, compared to EDACS and GRACE. HEART proved comparable to clinician judgment for chest pain risk stratification, EDACS trailed closely behind, while GRACE is significantly weaker as a chest pain score or accelerated diagnostic protocol.

These findings are promising and have major implications on disposition decisions, since low-risk chest pain patients may potentially be safely discharged within a shorter turnaround time in future, without resorting to extensive serial testing and observation for ACS rule-out.

Declarations

Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available due to patient confidentiality issues but are available from the corresponding author on reasonable request.

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Tables

Table 1. Demographics of Chest Pain Patients

Demographic Data	No MACE		MACE at 30 days	
	N, (%)		N, (%)	
Total no. of patients	1060	(88.7)	135	(11.3)
Mean age (y)	55.9	(SD 11.7)	59.5	(SD 9.2)
Gender				
Male	694	(65.5)	123	(91.1)
Female	366	(34.5)	12	(8.9)
Race				
Chinese	573	(54.1)	70	(51.9)
Malay	219	(20.7)	22	(16.3)
Indian	224	(21.1)	39	(28.9)
Others	44	(4.2)	4	(3.0)
Chronic diseases				
Diabetes mellitus (DM)	316	(29.8)	52	(38.5)
Hypertension (HTN)	550	(51.9)	103	(76.3)
Dyslipidaemia (HLD)	600	(56.6)	96	(71.1)
Nil chronic diseases	302	(28.5)	16	(11.9)
DM + HTN + HLD	204	(10.3)	40	(29.6)
Smoking history				
Current smoker	204	(19.3)	39	(28.9)
Ex-smoker	182	(17.2)	39	(28.9)
Never smoker	673	(63.6)	57	(42.2)
Family history of Acute MI	479	(45.2)	61	(45.2)
Past medical history of Acute MI	165	(15.6)	40	(29.6)
Disposition				
Discharged from ED (includes observation unit)	561	(52.9)	15	(11.1)
Absconded or discharged against medical advice	38	(3.6)	4	(3.0)
Admitted inpatient with non-cardiac diagnoses	185	(17.5)	4	(3.0)
Admitted inpatient to Cardiology for ACS	276	(26.0)	112	(83.0)

Table 2a. Test Characteristics of the Various Chest Pain Scores ($n = 1195$)

	HEART	EDACS	GRACE
Sensitivity (%)	88.1 (81.5-92.6)	83.7 (76.5-89.0)	45.2 (37.0-53.6)
Specificity (%)	52.8 (49.8-55.8)	57.5 (54.5-60.4)	78.9 (76.3-81.2)
NPV (%)	97.2 (95.9-98.6)	96.5 (95.1-97.9)	91.9 (90.1-93.6)
PPV (%)	19.2 (16.1-22.3)	20.0 (16.7-23.3)	21.4 (16.6-26.2)
AUC (%)	79.4 (76-83)	69.9 (66-74)	69.2 (65-74)

Table 2b. Test Characteristics of the various Chest Pain Scores and Clinical Judgment

(patients who absconded or discharged against medical advice excluded; $n = 1153$)

	Clinical Judgment	HEART	EDACS	GRACE
Sensitivity (%)	85.5 (78.3-90.6)	87.8 (80.9-92.4)	84.0 (76.6-89.3)	45.0 (36.8-53.6)
Specificity (%)	73.0 (70.2-75.6)	53.0 (50.0-56.1)	57.6 (54.6-60.6)	79.2 (76.6-81.5)
NPV (%)	97.5 (96.4-98.6)	97.1 (95.7-98.5)	96.6 (95.1-98.0)	91.8 (90.0-93.6)
PPV (%)	28.9 (24.4-33.4)	19.3 (16.2-22.5)	20.3 (16.9-23.6)	21.7 (16.8-26.6)

42 patients who discharged against medical advice or absconded were excluded from analyses of the performance characteristics of clinical judgment. Data for HEART/EDACS/GRACE were re-analysed with the 42 patients excluded as part of sensitivity analysis.

Table 2c. Test Characteristics of the various Chest Pain Scores and Clinical Judgment

(only patients admitted for further evaluation included; $n = 577$)

	Clinical Judgment	HEART	EDACS	GRACE
Sensitivity (%)	96.6 (91.1-98.9)	91.4 (84.6-95.4)	84.5 (76.7-90.0)	49.1 (40.2-58.1)
Specificity (%)	40.1 (35.8-44.7)	38.2 (33.9-42.7)	45.8 (41.3-50.3)	70.5 (66.2-74.5)
NPV (%)	97.9 (95.8-99.9)	94.6 (91.4-97.9)	92.1 (88.7-95.6)	84.6 (81.0-88.2)
PPV (%)	28.9 (24.4-33.4)	27.1 (22.7-31.5)	28.2 (23.4-32.9)	29.5 (23.1-36.0)

Figures

Figure 1. Flowchart describing Enrolment and Outcomes of Chest Pain Patients in the ED

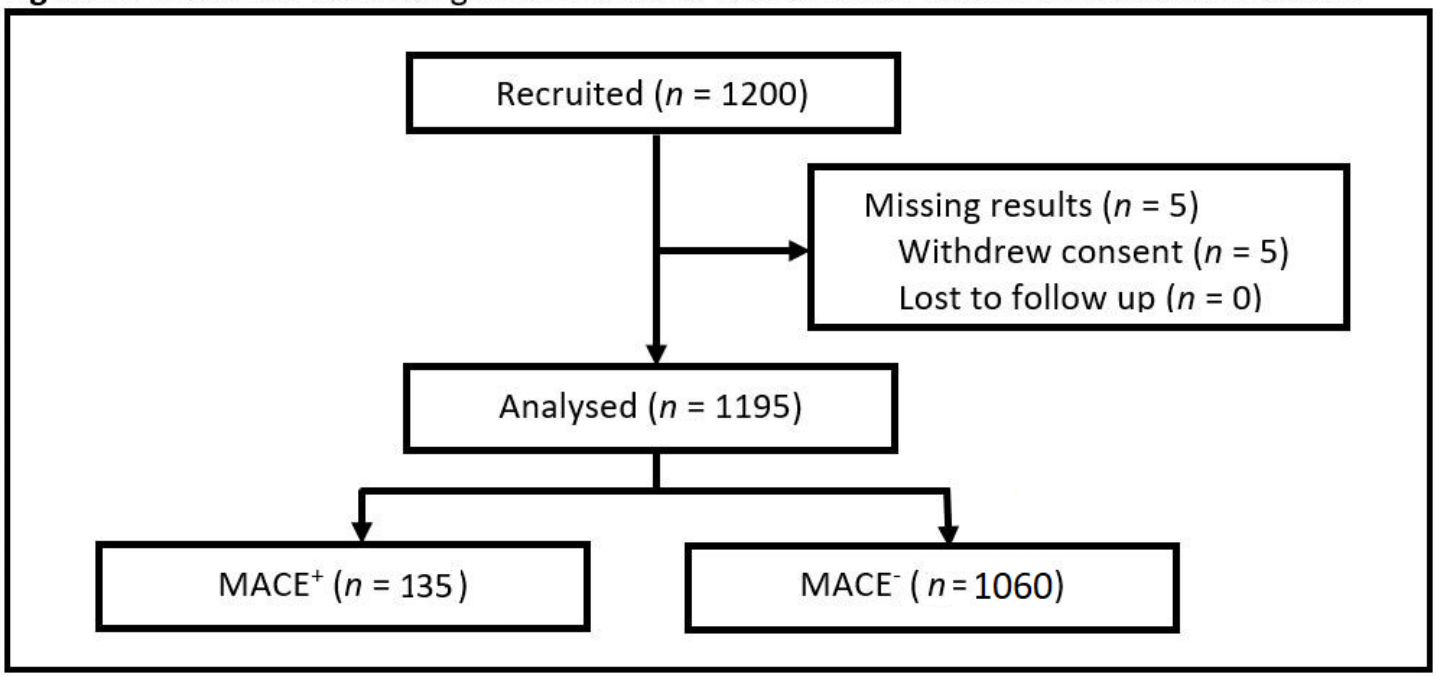

Figure 1

Flowchart describing Enrolment and Outcomes of Chest Pain Patients in the ED

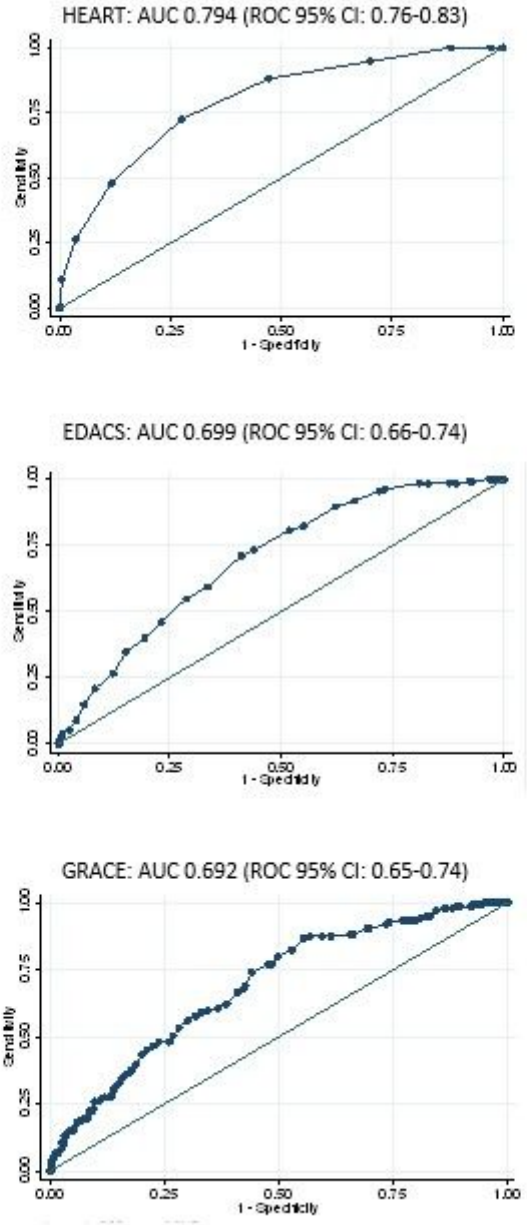

Figure 2

Area under ROC curves for the various chest pain scores