ISSN 2349-7203
IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
HUMAN

Human Journals
Research Article
November 2022 Vol.:25, Issue:4

Comparison of Acuity and Crusade Scores in Predicting Bleeding During Acute Coronary Syndrome in A Tertiary Care Hospital

ISSN 2349-7203
IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
HUMAN

Deepthi C Denny, Janaranjani.L*, Shanti Priya.C, Sobitha.S, P.Kathir Nilavan

Psg College Of Pharmacy, Peelamedu, Coimbatore, Tamil Nadu, India

Submitted: 25 October 2022
Accepted: 31 October 2022
Published: 30 November 2022

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Acute Coronary Syndrome(ACS), Bleeding risk, Acute Catheterization and Urgent Intervention Triage Strategy(ACUITY), Can Rapid risk stratification of Unstable angina patients Suppress Adverse outcome with Early implementation of the ACC/AHA guidelines(CRUSADE), Bleeding Academic Research Consortium (BARC).

ABSTRACT

Background: Bleeding due to ACS drug therapy is associated with mortality, so the clinical decision should be made to balance the risk of ischemia and bleeding. The purpose of the study was to determine the bleeding risk in ACS patients using ACUITY and CRUSADE scores and to assess the association between ACUITY and CRUSADE score parameters and major bleeding. **Methods:** The prospective study included 92 consecutively admitted patients for Acute Coronary Syndrome. The patient details were collected from medical records, and the ACUITY and CRUSADE bleeding risk scores have been calculated. We have considered major bleeding events during therapy (not related to any cardiac surgery) according to the Bleeding Academic Research Consortium (BARC). Patients were followed for a period of 3 months to assess the risk of bleeding. **Result:** Major bleeding was observed in 15 patients with an incidence of 16.3%. While both scores were associated with bleeding, CRUSADE demonstrated better C-Statistics (0.567, 95% CI : 0.4107-0.7226) as compared to ACUITY (0.497, 95% CI: 0.3329-0.6611). Exploratory analysis suggested that the presence of variables "Hematocrit" and "Signs of CHF presentation" in CRUSADE was the main reason for its superiority. **Conclusion:** The CRUSADE score was a better predictor of bleeding risk when compared with the ACUITY score in patients hospitalized for ACS.

INTRODUCTION:

Patients admitted with Acute Coronary Syndrome are at increased risk of developing ischemic complications. Thus, intensive pharmacological therapies are adopted to minimise the risk of cardiovascular events. However, these interventions have been found to have an increased risk of major bleeding during hospital admission. Several risk prediction multivariate models of cardiovascular events in ACS are available. The ACUITY (Acute Catheterization and Urgent Intervention Triage strategy) and CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress Adverse outcomes with Early implementation of the ACC/AHA guidelines) scores are available for the prediction of major bleeding events in Acute Coronary Syndrome. The comparative performances of these scores are not known in tertiary care hospitals among the South Indian population. Only a few models have been evaluated for the prediction of risk in an Indian population with different characteristics and treatment patterns. Very recently, very few literatures on bleeding risk predictability in the Indian population using CRUSADE and ACUITY scores have been validated. So the main aim is to determine the bleeding risk in ACS patients using ACUITY and CRUSADE score, to assess the association between ACUITY and CRUSADE scores parameters and major bleeding and compare the accuracy of these scores at a tertiary care hospital.

The creation of an easy-to-use risk score for bleeding could help to standardise the quality of care and patient outcomes. ACUITY and CRUSADE are two predictive scores for bleeding risk in ACS patients receiving DAPT and anticoagulant therapy. It is necessary to identify patients who are at high risk for hemorrhagic complications.

The CRUSADE score consists of 8 variables, including female sex, signs of heart failure, history of vascular disease/stroke, history of diabetes mellitus, baseline hematocrit value, creatinine clearance (CG Formula), heart rate, and systolic BP.

ACUITY score consists of seven variables, including female sex, presence of anemia, use of bivalirudin, type of ACS, age, serum creatinine, and white blood cell count.

The Bleeding Academic Research Consortium (BARC) was proposed to standardise bleeding endpoint definitions and reporting in cardiovascular trials involving antithrombotic therapies. It has five types of definition for bleeding where we consider types 3a, b, and 5 as major bleeding; type 3a, overt bleeding plus haemoglobin drop of 3-5 g/dl; type 3b, overt bleeding plus haemoglobin drop of 5 g/dl; cardiac tamponade; bleeding requiring surgical intervention for control (excluding dental/ nasal/ skin/ hemorrhoid); bleeding requiring intravenous vasoactive agents; type 3c, intracranial haemorrhage (does not include micro bleeds or hemorrhagic transformation, but does include intraspinal bleeding); and type 5, fatal bleeding—type 5a, probable; type 5b, definite. A practical CRUSADE scoring system with 8 variables and an ACUITY scoring system with 7 variables can predict the rate of non-CABG-associated severe bleeding in patients with ACS and its impact on subsequent mortality within a year. Such knowledge will aid in the precise prognostication of ACS patients, allowing for proper individualized decision-making for individuals who are at high risk of bleeding and mortality.

The literature review includes Luis C. L. Correia, et al.,-Comparison of ACUITY and CRUSADE Scores in Predicting major bleeding during Acute Coronary Syndrome: This study included 519 patients consecutively admitted for unstable angina, NSTEMI or STEMI. A 6% incidence of major bleeding was observed in 31 patients (23 from femoral puncture, 5 from digestive, and 3 from other sites). While both scores were associated with bleeding, ACUITY had a higher C-statistic (0.73, 95% CI = 0.63 - 0.82) than CRUSADE. They concluded that the ACUITY Score, when compared to the CRUSADE Score, is a better predictor of major bleeding in patients hospitalised for ACS.

Albert Ariza-Sole´,et al., -Efficacy of Bleeding Risk Scores in Elderly Patients with Acute Coronary Syndromes: They prospectively included consecutive acute coronary syndromes patients. They collected baseline characteristics, laboratory findings, and hemodynamic data. Each patient's CRUSADE, Mehran, and ACTION bleeding risk scores were calculated. Binary logistic regression, receiver operating characteristic curves, and area under the curves were used to assess these scores ability to predict major bleeding. There were 2036 patients in total, with a mean age of 62.1 years; 369 patients (18.1%) were 75 years old. Patients over the age of 65 had a higher risk of bleeding (CRUSADE, 42 vs 22; Mehran, 25 vs 15; ACTION, 36 vs 28; P<.001) and major bleeding events occurred at a higher rate in the CRUSADE group (5.1% vs. 3.8%; P≤.250).The predictive ability of these 3 scores was lower in the elderly (area under the curve, CRUSADE: 0.63 in older patients, 0.81 in young patients; P ≤ .027; Mehran: 0.67 in older patients, 0.73 in younger patients; P ≤ .340; ACTION: 0.58 in older patients, 0.75 in younger patients; P ≤ .041).They concluded that

Current bleeding risk scores showed poorer predictive performance in elderly patients with acute coronary syndromes than in younger patients.

Peerawat Jinatongthai, BSc Pharm, et al.,-Use of the CRUSADE Bleeding Risk Score in the Prediction of Major Bleeding for Patients with Acute Coronary Syndrome Receiving Enoxaparin in Thailand: A retrospective cohort study was performed using patients with ACS who were hospitalised at a university hospital in Bangkok between 2006 and 2009 and had received enoxaparin. The CRUSADE risk score was calculated. The overall incidence of major bleeding was 18.3%. Median CRUSADE score for entire study population, UA, NSTEMI, and STEMI were 49, 47, 53, and 39, respectively. Across the ACS spectrum, CRUSADE risk score was able to estimate in-hospital major bleeding of Thai patients with ACS who received treatment with enoxaparin. The application of these results in Thailand may be helpful in the identification of patients at high bleeding risk and also may lead to implementation of appropriate prevention.

Mohamed M Al-Daydamony et al. Indian Heart J-CRUSADE bleeding score as a predictor of bleeding events in patients with acute coronary syndrome in Zagazig University Hospital : They investigated the utility of the CRUSADE bleeding score in predicting bleeding events in our local ACS patients at Zagazig University Hospitals. Their study included 240 patients with ACS. They underwent history and clinical examination; 12-lead electrocardiography; echocardiography; troponin I, hematocrit value; e-GFR; application of CRUSADE score; and follow-up of the hospital stay and documentations of events. The highest predictor of major bleeding was the CRUSADE bleeding score. In the overall study group, the sensitivity of CRUSADE score ≥ 33 in predicting major bleeding was 80%, specificity was 73.4%, positive predictive value was 26.9%, negative predictive value was 96.9%, and overall accuracy was 74.1%. The CRUSADE score of ≥ 38.5 predicted major bleeding in STEMI patients with a 70% sensitivity, an 84.8% specificity, a 50% positive predictive value, a 92.9% negative predictive value, and an overall accuracy of 82.1%. They came to the conclusion that the CRUSADE score is a good predictor of major bleeding in Egyptian patients with ACS.

MATERIALS AND METHODS:

Research design: A Prospective study

Subjects: A total of 92 study subjects among inpatients admitted for Acute Coronary Syndrome were studied for 6 months. The approval for the study was obtained from the

Institutional Human Ethics Committee (IHEC, PSG IMSR), Project No.21/141. The study site was PSG Hospitals, Peelamedu, Coimbatore, India-641004. This study included both male and female patients with ACS (STEMI, NSTEMI, unstable angina) and an age of ≥18 years. Patients lacking lab parameters, with irregular follow-up, and not willing to participate were excluded from the study.

Materials used: Data of the patients were collected from July 7, 2021 to September 7, 2021, and they were followed for three months. Patients who underwent coronary artery bypass graft (n=10) or those with no follow-up (n=16) data were excluded from the analysis. During the index hospitalization, data on demographic and clinical characteristics, medication, as well as laboratory parameters were collected in detail using a standardised data collection form. The baseline characteristics are listed in [TABLE 1]. CRUSADE and ACUITY scores were calculated, assessed, and categorized.

Statistical method: Statistical analysis was carried out using IBM SPSS Statistics version 26. Methods like Chi-square (categorical variable) [TABLE 2], Fisher's Method (nominal variables) [TABLE 3] were used to correlate the parameters to the bleeding outcome. The Hosmer and Lemeshow test is used to check the goodness of fit model of CRUSADE and ACUITY bleeding score. C-statistics (ROC curve) are used to compare the ACUITY and CRUSADE bleeding scores to establish the better prediction of bleeding risk.

Table: 1 Baseline Characteristics

Sample size	92
Age (years)	60 ±17
Female sex	25 (27.17%)
INDEX DIAGNOSIS:	
Unstable Angina	2 (2.17%)
Non –ST Elevated Myocardial Infraction	30 (32.60%)
ST Elevated Myocardial Infraction	60 (65.21%)
Serum Creatinine	0.8 ± 1.0
IN-HOSPITAL MEDICATION:	
Aspirin	90 (97.82%)
Clopidogrel	72 (78.6%)
Ticagrelor	19 (20.65%)
Unfractionated Heparin	7 (7.60%)
Enoxaparin	79 (85.86%)
Coronary Artery Bypass Surgery	10 (10.86%)

Table: 2 Mean and Standard Deviation of categorical parameters

Parameters	**Mean± Standard deviation**		**P value**
	Bleeding	**Non-bleeding**	
HEART RATE (beats/min)	99.466±30.619	86.818±22.764	0.157
SYSTOLIC BLOOD PRESSURE(mmHg)	130.133±23.633	124.493±25.160	0.412
HEMATOCRIT (%)	44.56±5.848	40.884±5.616	0.0369
CREATININE CLEARANCE(ml/min)	84.133±37.211	85.624±33.481	0.886
AGE(yrs)	55.333±8.989	59.194±11.044	0.157
BASELINE SERUM CREATININE(mg/dl)	1.0454±0.731	0.951±0.419	0.6365
WBC COUNT(giga/L)	12.646±4.040	11.875±4.503	0.033

Table:3 Incidence of ordinal variable among bleeding and non-bleeding patients

Parameters	Bleeding patients	Non- bleeding patients	P value
Anemia	13%	10%	0.738
History of diabetes mellitus	66.6%	46%	0.158
History of vascular disease	73.3%	55%	0.208
Signs of CHF	46%	26%	0.047
Clinical presentation :			0.598
NSTEMI -normal biomarker	6.6%	6.7%	
NSTEMI- raised biomarker	33.3%	31.1%	
STEMI	60%	62.3%	

RESULTS:

This study assessed 92 patients (mean age of 60±17 years, 27.17% female), 2.1% of whom had an index diagnosis of unstable angina, 32.6% with non-ST Elevated MI and 60% ST Elevated MI. During the hospital stay, all patients received dual antiplatelet therapy and anticoagulation therapy. No patients received Bivalirudin therapy. 10.8% of patients underwent Coronary Artery Bypass Graft.

According to CRUSADE, 40 patients were categorised as high risk, of which 9 patients had major bleeding, and as of ACUITY 48 patients were categorised as high risk, of which 6 patients had bleeding.

In predicting the bleeding incidence, ACUITY and CRUSADE were similarly calibrated, according to Hosmer and Lemeshow's chi-square of 9.9027 (p = 0.2719) and 7.1754 (p = 0.5178), respectively.

The discriminatory ability of the CRUSADE Score for bleeding events was demonstrated by a C-statistics of 0.567 (95% CI: 0.4107-0.7226) which is significantly better than ACUITY's C-statistics of 0.497 (95% CI: 0.3329-0.6611).

The optimal threshold points for ACUITY and CRUSADE were 0.163 and 0.162, respectively. Based on these points, ACUITY has sensitivity of 66.67% (95% CI = 17,46% – 80%) which is the same as with CRUSADE 66.67% (95% CI = 46.67,21% – 93.33%) but at the expense of worse specificity of ACUITY 54.5%(95%CI = 7.79% – 62.28%) in relation to CRUSADE 40.3% (95% CI = 12.99% – 70.13%).

ROC value of CRUSADE (AUC=0.626) is higher than the ACUITY bleeding score (AUC=0.597)[FIGURE 1], suggesting the CRUSADE score has more true positives. The percentage of true positive predicted by CRUSADE and ACUITY score is illustrated in [TABLE 4]. This reassures the CRUSADE score's superiority over the ACUITY score.

The C-statistics' superiority of CRUSADE over ACUITY was consistent across STEMI ACS (0.626 versus 0.597, respectively)[FIGURE 2], but was not consistent across NSTEMI ACS (0.492 versus 0.68, respectively).

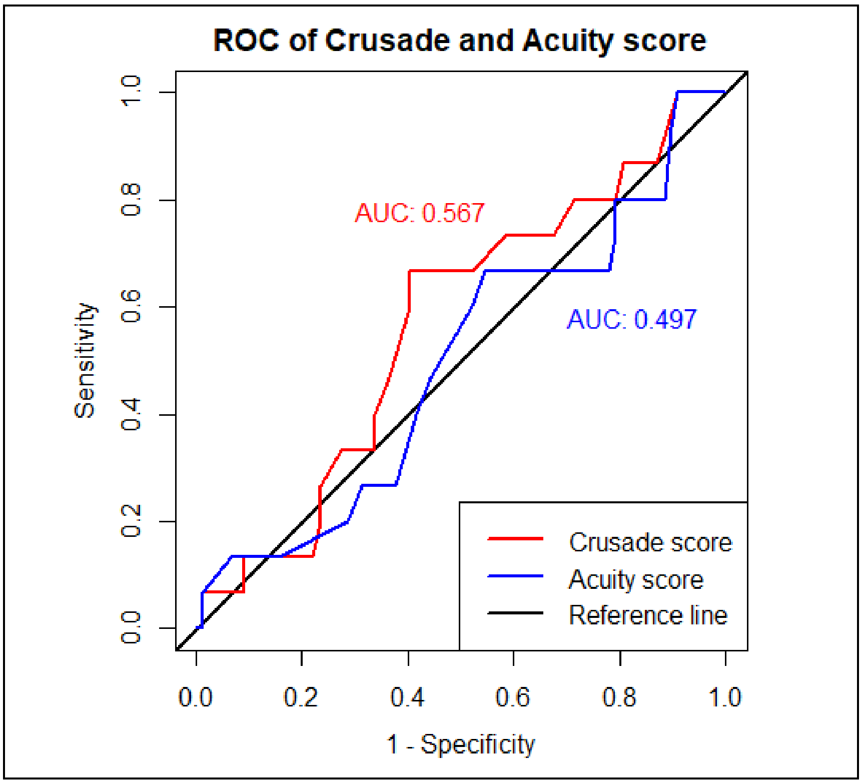

Fig.1: ROC value of CRUSADE and ACUITY score

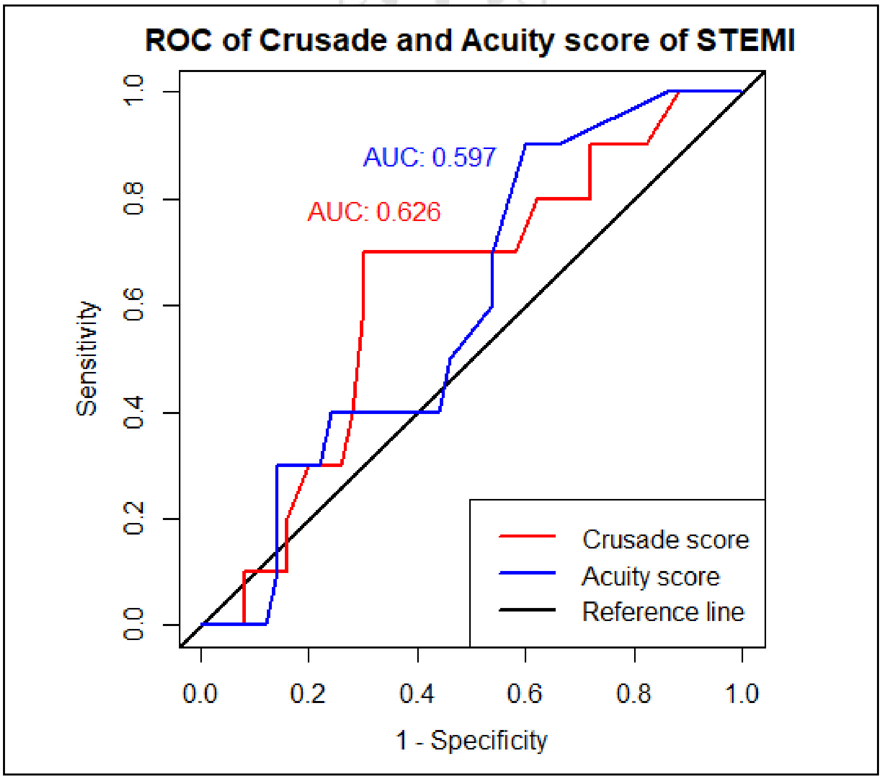

Fig.2: ROC curve of ACUITY and CRUSADE scores for STEMI

Table No.: 4 Percentage of true positive predicted by CRUSADE and ACUITY score

CRUSADE SCORE:	
PREDICTED RISK	**MAJOR BLEEDING (%)**
LOW RISK (≤30)	12% (5/42)
MODERATE RISK (31-40)	10% (1/10)
HIGH RISK (>40)	22.5% (9/40)
ACUITY SCORE:	
LOW RISK (<10)	12% (3/25)
INTERMEDIATE RISK (10-14)	25% (6/24)
HIGH RISK (>14)	14% (6/42)

DISCUSSION

This is one of the few studies to compare the two most validated techniques for predicting severe bleeding episodes in patients with ACS head-to-head. In ACS, intensive antithrombotic therapy and early coronary intervention are useful in preventing recurrent ischemic episodes. However, this efficiency comes at the cost of increased bleeding events. Because significant bleeding is linked to an elevated risk of mortality and morbidity, clinicians must weigh the ischemia danger against the hemorrhagic risk. Multivariate models for predicting ischemia episodes in the ACS exhibit strong discriminatory performance and are well calibrated.

In our sample population, the CRUSADE score performed better as compared to the ACUITY score. CRUSADE’s superiority was indicated by an absolute 0.029 difference in ROC value. CRUSADE's (AUC=0.626) is higher than the ACUITY bleeding score (AUC=0.597), suggesting the CRUSADE score has more true positives.

The data was extensively distributed based on gender, age, diagnosis, treatment, and co-morbidities. Out of 92 samples, 67 were male patients (72.8%) and 25 were female patients (27.2%). Males were more predominantly found with ACS than females.

Multivariate models for predicting ischemic events in Acute Coronary Syndrome are well calibrated and have good discriminatory performance. Previous studies have compared the two most popular models, the TIMI and GRACE scores. These studies have established the GRACE score as the best model for predicting outcomes in Acute Coronary Syndrome patients.

On the other hand, the models CRUSADE and ACUITY-HORIZONS have found no significant differences in the predictive accuracy of the two scores for overall and major bleeding when compared to each other. Their results were consistent with the study by Ariza-Sole et al., which enrolled exclusively patients with STEMI, and with the results of Costa et al., that obtained similar accuracy between CRUSADE and ACUITY-HORIZONS scores in the prediction of out-of-hospital major bleedings in an all-comer population treated with coronary stent and prolonged dual antiplatelet therapy. Abu-Assi et al. demonstrated the superiority of the CRUSADE and the ACTION risk models over the ACUITY-HORIZONS score using risk model specific bleeding definitions, while the superiority was confirmed only in NSTEACS patients using the TIMI (minor plus major) bleeding definition.

Prior to the present study, one could hypothesise that the CRUSADE score was the best predictor of bleeding. First, because it has more variables, which are disposed of in a more quantitative manner than ACUITY.

The present study does indeed show some limitations, the first of which is the relatively low number of bleeding events, which was our study's major limitation. It implies imprecision in the magnitude of CRUSADE’s superiority; the second limitation was that this was a single-institution experience, and this reduced the generalizability of our findings to other populations. On the other hand, the major problem was the small sample size. The difference in the ROC curve between the two studies reached significance. Although not definitive, the present study is the first indication that CRUSADE is a more promising tool in the risk/benefit stratification of patients with ACS in the Indian population.

Further studies and more data are needed to justify CRUSADE as a better score for predicting bleeding risk.

CONCLUSION

Our study shows reasonable predictive accuracy of the CRUSADE and the ACUITY scores regarding major bleeding events and significant differences found between their performances. As for the comparison between CRUSADE and ACUITY bleeding scores, the present study suggests that the former has better accuracy as compared with the latter. We can conclude that for individuals with ACS, there is a marked variation in the risk of non-CABG-related major bleeding.

A practical CRUSADE scoring system with 8 variables and an ACUITY scoring system with 7 variables can predict the rate of non-CABG-associated severe bleeding in patients with ACS and its impact on subsequent mortality within a year. The CRUSADE bleeding risk score is a good predictor for major bleeding among Indian patients with ACS. The risk was found to be applicable in UA, NSTEMI, and STEMI patients, in both men and women. Application of the CRUSADE bleeding risk score may be helpful in India. Such knowledge will aid in the precise prognostication of ACS patients, allowing for proper individualized decision-making for individuals who are at high risk of bleeding and mortality.

ACKNOWLEDGEMENT

This project behind it would not have been possible without the exceptional support of my guide Mrs. Deepthi C Denny, Dr. G. Rajendiran (HOD of Cardiology), Dr. Aashiq Ahamed Shukkoor (Clinical Pharmacist-Cardiology), statistician and fellow mates. Their enthusiasm, knowledge and exacting attention to detail have been an inspiration and kept our work on track from our first encounter with the topic to the final draft of this paper. The generosity and expertise of one and all have improved this study in innumerable ways and saved us from many errors; those that inevitably remain are entirely our own responsibility.

ABBREVIATIONS:

ACS	Acute Coronary Syndrome
ACUITY	Acute Catheterization and Urgent Intervention Triage Strategy
ACC/AHA	American College of Cardiology/American Heart Association
AUC	Area under the curve

ACUITY-HORIZONS Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction

BARC Bleeding Academic Research Consortium

BP	Blood Pressure
CHF	Congestive Heart Failure
CG	Cockcroft-Gault
CRUSADE	Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines
DAPT	Dual Antiplatelet Therapy
e-GFR	Estimated glomerular filtration rate
GRACE	Global Registry of Acute Coronary Events
HOD	Head of a Department
IHEC	Institutional Human Ethics Committee
PSG IMSR	PSG Institute of Medical Sciences & Research
IBM	International Business Machines
NSTEMI	Non-ST-Elevation Myocardial Infarction
NSTEACS	Non-ST-Elevated Acute Coronary Syndrome
ROC	Receiver operating characteristic curve
SPSS	Statistical Package for the Social Sciences
STEMI	ST-Elevation Myocardial Infarction
TIMI	Thrombolysis in myocardial infarction
UA	Unstable Angina

REFERENCES:

1.Correia LC, Ferreira F, Kalil F, Silva A, Pereira L, Carvalhal M, Cerqueira M, Lopes F, Sá ND, Noya-Rabelo M. Comparison of ACUITY and CRUSADE scores in predicting major bleeding during acute coronary syndrome. ArquivosBrasileiros de Cardiologia. 2015;105:20-7.

2. Rodriguez F, Harrington RA. Management of antithrombotic therapy after acute coronary syndromes.New England Journal of Medicine. 2021 Feb 4;384(5):452-60.

3. Wang WT, James SK, Wang TY. A review of sex-specific benefits and risks of antithrombotic therapy in acute coronary syndrome.European heart journal. 2017 Jan 14;38(3):165-71.

4. Moser M, Olivier CB, Bode C. Triple antithrombotic therapy in cardiac patients: more questions than answers. European heart journal. 2014 Jan 21;35(4):216-23.

5. Tersalvi G, Biasco L, Cioffi GM, Pedrazzini G. Acute coronary syndrome, antiplatelet therapy, and bleeding: a clinical perspective. Journal of clinical medicine. 2020 Jul;9(7):2064.

6. Mehran R, Pocock SJ, Nikolsky E, Clayton T, Dangas GD, Kirtane AJ, Parise H, Fahy M, Manoukian SV, Feit F, Ohman ME. A risk score to predict bleeding in patients with acute coronary syndromes. Journal of the American College of Cardiology. 2010 Jun 8;55(23):2556-66.

7. Wells GA, Elliott J, Kelly S, Bai Z, Boucher M, Skidmore B, So D, Laplante S, Lee K. Dual antiplatelet therapy following percutaneous coronary intervention: clinical and economic impact of standard versus extended duration.PMID: 31246386

8. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, Serebruany V. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. Circulation. 2011 Jun 14;123(23):2736-47.

9. Sánchez-Martínez M, Flores-Blanco PJ, López-Cuenca ÁA, Sánchez-Galián MJ, Gómez-Molina M, Cambronero-Sánchez F, Guerrero-Pérez E, Valdés M, Januzzi JL, Manzano-Fernández S. Evaluation of the CRUSADE Risk Score for Predicting Major Bleeding in Patients with Concomitant Kidney Dysfunction and Acute Coronary Syndromes. Cardiorenal medicine. 2017;7(3):179-87.

10. Al-Daydamony MM, Farag ES. CRUSADE bleeding score as a predictor of bleeding events in patients with acute coronary syndrome in Zagazig University Hospital.Indian Heart Journal. 2016 Sep 1;68(5):632-8.

11.Subherwal S, Bach RG, Chen AY, Gage BF, Rao SV, Newby LK, Wang TY, Gibler WB, Ohman EM, Roe MT, Pollack Jr CV. Baseline risk of major bleeding in non–ST-segment–elevation myocardial infarction: the CRUSADE (can rapid risk stratification of unstable angina patients suppress ADverse outcomes with early implementation of the ACC/AHA guidelines) bleeding score. Circulation. 2009 Apr 14;119(14):1873-82

12. Costa F, Tijssen JG, Ariotti S, Giatti S, Moscarella E, Guastaroba P, De Palma R, Andò G, Oreto G, Zijlstra F, Valgimigli M. Incremental value of the CRUSADE, ACUITY, and HAS-BLED risk scores for the prediction of hemorrhagic events after coronary stent implantation in patients undergoing long or short duration of dual antiplatelet therapy. Journal of the American Heart Association. 2015 Dec 7;4(12):e002524.

13. Ben-Yehuda O, Redfors B. Validation of the Bleeding Academic Research Consortium bleeding definition: towards a standardized bleeding score. Journal of the American College of Cardiology. 2016 May 10;67(18):2145-7.

14. Ndrepepa G, Schuster T, Hadamitzky M, Byrne RA, Mehilli J, Neumann FJ, Richardt G, Schulz S, Laugwitz KL, Massberg S, Schömig A. Validation of the Bleeding Academic Research Consortium definition of bleeding in patients with coronary artery disease undergoing percutaneous coronary intervention. Circulation. 2012 Mar 20;125(11):1424-31.

15. Vranckx P, White HD, Huang Z, Mahaffey KW, Armstrong PW, Van de Werf F, Moliterno DJ, Wallentin L, Held C, Aylward PE, Cornel JH. Validation of BARC bleeding criteria in patients with acute coronary syndromes: the TRACER trial. Journal of the American College of Cardiology. 2016 May 10;67(18):2135-44.

16. Bento D, Marques N, Azevedo P, Guedes J, Bispo J, Silva D, Amado J, Santos W, Mimoso J, de Jesus I. CRUSADE: Is it still a good score to predict bleeding in acute coronary syndrome?.Revista Portuguesa de Cardiologia (English Edition). 2018 Nov 1;37(11):889-97.

17. Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy: A Pathophysiologic Approach, ed. Connecticut: Appleton and Lange. 2014;4:141-2.

18. Ramrakha, Punit, and Jonathan Hill (eds), Oxford Handbook of Cardiology, 2nd edition, Oxford Medical Handbooks(Oxford, 2012 Feb 23; online edn, Oxford Academic, 1 May 2012), https://doi.org/10.1093/med/9780199643219.001.0001, accessed 1 Nov. 2022.

19. Phillip S Cuculich, Andrew M. Kates, editors. The Washington Manual Cardiology Subspecialty Consult.2nd edition.Lippincott Williams & Wilkins; 2008 Jul 1.

20. KD Tripathi. Essentials of Medical Pharmacology.7th Edition.JP Brothers Medical Publishers (P) Ltd; 2013 Sep 30.

21. Kawashima H, Gao C, Takahashi K, Tomaniak M, Ono M, Hara H, Wang R, Chichareon P, Suryapranata H, Walsh S, Cotton J. Comparative assessment of predictive performance of PRECISE-DAPT, CRUSADE, and ACUITY scores in risk stratifying 30-day bleeding events. Thrombosis and Haemostasis. 2020 Jul;120(07):1087-95.

22. Flores-Ríos X, Couto-Mallón D, Rodríguez-Garrido J, García-Guimaraes M, Gargallo-Fernández P, Piñón-Esteban P, Aldama-López G, Salgado-Fernández J, Calviño-Santos R, Vázquez-González N, Castro-Beiras A. Comparison of the performance of the CRUSADE, ACUITY-HORIZONS, and ACTION bleeding risk scores in STEMI undergoing primary PCI: insights from a cohort of 1391 patients. European Heart Journal: Acute Cardiovascular Care. 2013 Mar 1;2(1):19-26.

23. Xi S, Zhou S, Wang X, Liu J, Qin L, Liu J, Yin T, Chen Y. The performance of CRUSADE and ACUITY bleeding risk scores in ticagrelor-treated ACS patients who underwent PCI. Thrombosis and Haemostasis. 2017 Nov;117(11):2186-93.

24.Overbaugh KJ. Acute coronary syndrome. AJN. The American Journal of Nursing. 2009 May 1;109(5):42-52..

25. Shi H, Li T, Wei J. Evaluation of the gridded CRU TS precipitation dataset with the point raingauge records over the Three-River Headwaters Region. Journal of Hydrology. 2017 May 1;548:322-32.

26. Fitzmaurice DA, Blann AD, Lip GY. Bleeding risks of antithrombotic therapy.Bmj. 2002 Oct 12;325(7368):828-31.

27. Ariza-Solé A, Formiga F, Lorente V, Sánchez-Salado JC, Sánchez-Elvira G, Roura G, Sánchez-Prieto R, Vila M, Moliner P, Cequier A. Efficacy of bleeding risk scores in elderly patients with acute coronary syndromes. Revista Española de Cardiología (English Edition). 2014 Jun 1;67(6):463-70.

28. Jinatongthai P, Khaisombut N, Likittanasombat K, Chaiyakunapruk N, Watcharathanakij S, Nathisuwan S. Use of the CRUSADE bleeding risk score in the prediction of major bleeding for patients with acute coronary syndrome receiving enoxaparin in Thailand. Heart, Lung and Circulation. 2014 Nov 1;23(11):1051-8.

29. Castini D, Centola M, Ferrante G, Cazzaniga S, Persampieri S, Lucreziotti S, Salerno-Uriarte D, Sponzilli C, Carugo S. Comparison of CRUSADE and ACUITY-HORIZONS bleeding risk scores in patients with acute coronary syndromes. Heart, Lung and Circulation. 2019 Apr 1;28(4):567-74.

30. Authors/Task Force Members, Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European heart journal. 2011 Dec 1;32(23):2999-3054.

31. Ariza-Solé A, Sánchez-Elvira G, Sánchez-Salado JC, Lorente-Tordera V, Salazar-Mendiguchía J, Sánchez-Prieto R, Romaguera-Torres R, Ferreiro-Gutiérrez JL, Gómez-Hospital JA, Cequier-Fillat A. CRUSADE bleeding risk score validation for ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Thrombosis research. 2013 Dec 1;132(6):652-8.

32. Lopes RD, Alexander KP, Manoukian SV, Bertrand ME, Feit F, White HD, Pollack CV, Hoekstra J, Gersh BJ, Stone GW, Ohman EM. Advanced age, antithrombotic strategy, and bleeding in non–ST-segment elevation acute coronary syndromes: results from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. Journal of the American College of Cardiology. 2009 Mar 24;53(12):1021-30.

33. Abu-Assi E, Gracía-Acuña JM, Ferreira-González I, Peña-Gil C, Gayoso-Diz P, González-Juanatey JR. Evaluating the performance of the can rapid risk stratification of unstable angina patients suppress adverse outcomes with early implementation of the acc/aha guidelines (crusade) bleeding score in a contemporary Spanish cohort of patients with non–ST-segment elevation acute myocardial infarction. Circulation. 2010 Jun 8;121(22):2419-26.

34. Kawashima H, Gao C, Takahashi K, Tomaniak M, Ono M, Hara H, Wang R, Chichareon P, Suryapranata H, Walsh S, Cotton J. Comparative assessment of predictive performance of PRECISE-DAPT, CRUSADE, and ACUITY scores in risk stratifying 30-day bleeding events. Thrombosis and Haemostasis. 2020 Jul;120(07):1087-95.
35. Castini D, Centola M, Ferrante G, Cazzaniga S, Persampieri S, Lucreziotti S, Salerno-Uriarte D, Sponzilli C, Carugo S. Comparison of CRUSADE and ACUITY-HORIZONS bleeding risk scores in patients with acute coronary syndromes. Heart, Lung and Circulation. 2019 Apr 1;28(4):567-74.

	***JANARANJANI. L*** *PHARM.D* ***PSG COLLEGE OF PHARMACY,*** *Peelamedu,* *Coimbatore – 641 004*
	***SHANTI PRIYA. C*** *PHARM.D* *PSG COLLEGE OF PHARMACY,* *Peelamedu,* *Coimbatore – 641 004*
	***SOBITHA. S*** *PHARM.D* *PSG COLLEGE OF PHARMACY,* *Peelamedu,* *Coimbatore – 641 004*
	***KATHIR NILAVAN. P*** *PHARM.D* *PSG COLLEGE OF PHARMACY,* *Peelamedu,* *Coimbatore – 641 004*
	***DEEPTHI C DENNY*** *M.PHARM* *Assistant Professor* *PSG COLLEGE OF PHARMACY,* *Peelamedu,* *Coimbatore – 641 004*