Performance of HAS-BLED and CRUSADE risk scores for the prediction of haemorrhagic events in patients with stable coronary artery disease

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Abstract

We aimed to compare the power of the HAS-BLED and CRUSADE risk scores in predicting in-hospital bleeding events in patients with stable coronary artery disease undergoing elective coronary angiography. A total of 405 consecutive patients were included in the study. The mean HAS-BLED score was significantly higher \((p < 0.001)\) in the in-hospital bleeding group. In patients with a HAS-BLED score \(\geq 3\), the in-hospital bleeding rate was significantly higher than in those with a HAS-BLED score \(< 3\) \((p < 0.001)\). Receiver operating characteristic curve analysis revealed that the HAS-BLED score was superior in predicting in-hospital bleeding events compared to the CRUSADE score \(\text{[area under the curve (AUC) = 0.684 vs 0.569, respectively, } p = 0.002\text{]}\). Also in the percutaneous coronary intervention subgroup, the HAS-BLED score was superior to the CRUSADE score \(\text{[AUC = 0.722 vs 0.520, respectively, } p = 0.002\text{]}\). We showed that the HAS-BLED and CRUDASE scores are helpful in stable patients undergoing elective coronary angiography. Our results suggest that as a practical, easy-to-implement and more predictive scoring system, the HAS-BLED score was more useful for predicting in-hospital bleeding in patients who did not present with acute coronary syndrome.

Keywords: coronary artery disease, angiography, haemorrhage

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Bleeding is one of the most common problems in the clinic post coronary angiography. Many patients undergoing coronary angiography need antithrombotic treatment and simultaneously have other co-morbid diseases, leading to more frequent bleeding problems.\(^1\)\(^2\) For this reason, a number of risk scores have been developed in order to predict bleeding events. One of the most important ones is the CRUSADE risk score, which has been proven effective for predicting the bleeding risk in patients presenting with non-ST segment elevation myocardial infarction (NSTEMI).\(^3\) However, a reliable scoring system that can predict bleeding risk has not been identified yet for patients with stable coronary artery disease, which constitutes a large part of our daily practice.

Bleeding is an important cause of co-morbidity, not only in patients with coronary artery disease, but also for diseases requiring anticoagulation therapy, such as atrial fibrillation (AF). In patients with AF, the HAS-BLED bleeding risk score is one of the most useful scoring systems used to predict the risk of bleeding.\(^4\) Several studies have previously demonstrated that the HAS-BLED risk score is an important predictor of bleeding in patients without AF.\(^5\)\(^6\) However, a valid bleeding risk score has not been established in patients undergoing elective coronary angiography, except for those presenting with acute coronary syndrome (ACS). In this study, we aimed to determine whether significant risk scores, such as the HAS-BLED and CRUSADE, are useful in predicting the risk of in-hospital bleeding in patients undergoing elective coronary angiography.

Methods

Following ethical committee approval, 405 elective coronary angiography patients, who were treated in our coronary angiography unit, were included in the study. Patients with ST-segment elevation myocardial infarction (STEMI), NSTEMI patients, those undergoing coronary angiography after sudden cardiac events, patients with a dynamic ECG or cardiac enzyme changes, and those with unstable angina were excluded from the study. Patients with known or suspected stable coronary artery disease only were included in the study.

Data on the clinical and demographic characteristics of the patients, history of diabetes mellitus, hypertension, smoking, stroke or neurological disease, coronary artery disease, cardiac failure and medications were recorded from the patients and the patient files. Patients were divided into two groups according to whether or not bleeding occurred during in-hospital follow ups. These groups were compared in terms of demographic characteristics and risk factors.
The groups with and without bleeding were compared using the HAS-BLED and CRUSADE risk scores. When the HAS-BLED score was calculated, each of the following parameters was calculated as one point: hypertension (systolic blood pressure > 160 mmHg), abnormal renal function (defined as the presence of chronic dialysis or renal transplantation), hypertension (systolic blood pressure > 160 mmHg), abnormal renal function (defined as the presence of chronic dialysis or renal transplantation), serum creatinine > 2.3 mg/dl (203.32 mmol/l), abnormal liver function (defined as chronic hepatic disease or biochemical evidence of significant hepatic derangement, e.g. bilirubin more than twice the upper limit of normal), in association with AST/ALT/ALP more than three times the upper limit of normal), stroke (previous history of stroke), bleeding (major bleeding history or predisposition to bleeding), labile INRs (refers to unstable/high INRs or poor time in therapeutic range < 60%), elderly (age ≥ 65 years), drug therapy (concomitant therapy such as antiplatelet agents, NSAIDs) and alcohol intake (consuming eight or more alcoholic drinks per week).

The CRUSADE score was calculated using baseline haematocrit, glomerular filtration rate, heart rate on admission, systolic blood pressure on admission, prior vascular disease, diabetes mellitus, signs of congestive heart failure on admission and gender. The Cockcroft–Gault formula was used to calculate creatinine clearance rate.

In addition to comparing the mean of HAS-BLED and CRUSADE scores, patients were divided into groups according to HAS-BLED score ≥ 3 (high risk) or 0–2 (low risk), and CRUSADE score > 40 (high risk), ≥ 30 (medium-high risk) and ≤ 30 (low risk).

The risk groups were then assessed in terms of the incidence of bleeding. In addition, 130 patients (femoral artery haemorrhage in the others. Minor bleeding was observed in the remaining 61 patients (femoral artery bleeding in 57, bleeding from the nose in two, and bleeding in the gingiva in two). Erythrocyte suspension replacement was needed in only four patients with major haemorrhage. In one patient with major haemorrhage, a haematoma in the groin was evacuated and the femoral artery was sutured.

PCIs were performed via the femoral and radial route by an experienced interventional cardiologist (Siemens Axiom Artis cine Angiography System, Germany). Non-ionic low osmolality contrast medium (Omnipaque 350 MG/ml; GE Healthcare, Cork, Ireland) was used for the procedures. All stented patients were given 300 mg aspirin and a 600-mg clopidogrel loading dose during the procedure. After having visualised the arterial anatomy, 100 U/kg heparin was administered. Glycoprotein Ilb/IIIa use was left to the discretion of the physician. No vascular closure device was used in any patient. After the sheath was removed, haemostasis was obtained with direct manual pressure of the fingertips over the pulse. The pressure was held for approximately 20 minutes (about three minutes for each French size) until there was no bleeding.

All patients were transferred to the intensive care unit or cardiology service after the procedure. Bed rest is generally required for six hours after a sheath is removed. Stented patients were continued on 100 mg aspirin and 75 mg clopidogrel. In patients without stenting, treatment was continued on 100 mg aspirin, but in patients with gastrointestinal intolerance to aspirin, we used 75 mg clopidogrel instead of aspirin. The decision for concurrent use of statins, angiotensin converting enzyme inhibitors, calcium channel blocker and beta-blockers was made according to the recommendations of the American College of Cardiology/American Heart Association. No patients used new oral anticoagulants. The use of non-steroidal anti-inflammatory drugs was avoided. Patients were followed up with blood samples and the femoral artery area was checked.

### Statistical analysis

Statistical analysis was performed using the SPSS 15.0 for Windows evaluation version statistical package. Continuous variables are presented as mean ± standard deviation. Categorical variables are summarised as frequencies. Differences between the two groups according to continuous variables were determined by the independent samples t-test. Categorical variables were compared with the chi-squared or Fisher’s exact test. C-statistics and receiver operating characteristic (ROC) curve analysis were used to assess the performance of the HAS-BLED and CRUSADE bleeding scores. Comparison of ROC curves was done using the de Long test. A p-value of < 0.05 was considered statistically significant.

### Results

The mean age was higher in the group with in-hospital bleeding than in the group without bleeding (65.32 ± 11.40 vs 60.01 ± 13.57 years, respectively, p = 0.003). Diabetes mellitus was more frequent among patients in the non-bleeding group compared with the in-hospital bleeding group (33.8 vs 8%, respectively, p = 0.001). Potassium and haematocrit values were statistically significantly lower in the in-hospital bleeding group.

The results of the groups according to bleeding status are shown in Table 1. Bleeding was observed in 65 patients. Major bleeding (BARC type 3) was observed in four patients, in the form of gastrointestinal bleeding in one patient and from femoral artery haemorrhage in the others. Minor bleeding was observed in the remaining 61 patients (femoral artery bleeding in 57, bleeding from the nose in two, and bleeding in the gingiva in two). Erythrocyte suspension replacement was needed in only four patients with major haemorrhage. In one patient with major haemorrhage, a haematoma in the groin was evacuated and the femoral artery was sutured.

The mean HAS-BLED score of the patients with in-hospital bleeding was significantly higher than that of the group without bleeding (2.21 ± 1.15 vs 1.49 ± 0.95, p < 0.001). There was no significant difference between the mean CRUSADE scores of the two groups (23.69 ± 11.37 vs 21.28 ± 10.82, p = 0.105).

In the in-hospital bleeding rate in patients with a HAS-BLED score ≥ 3 was significantly higher than in patients with a HAS-BLED score < 3 (49.2 vs 14.1%, p < 0.001). Similarly, the rate of in-hospital bleeding in patients with a CRUSADE score > 30 was significantly higher than in patients with a CRUSADE score ≤ 30 (36.9 vs 18%, p = 0.001). There was no significant difference in haemorrhage rate between patients with CRUSADE scores > 40 and ≤ 40.

In the ROC curve analysis, the HAS-BLED score was found to be superior to the CRUSADE score in predicting in-hospital bleeding risk among the whole study population who underwent elective coronary angiography (AUC = 0.684 vs 0.569, respectively, p = 0.002) (Fig. 1). According to the Youden index J-statistics, the HAS-BLED score predicted in-hospital bleeding in patients undergoing coronary angiography without ACS with a sensitivity of 59.09% and a specificity of 89.81%. In this patient group, the sensitivity of the CRUSADE score was 36.36% and the specificity was 82.69%.

When patients who underwent PCI only were examined, there was no significant difference between the groups in terms of mean CRUSADE scores, although there was a significant
difference with regard to the mean HAS-BLED scores of the groups (Table 2). In the ROC curve analysis of the patient subgroup that underwent stent implantation, the HAS-BLED score was superior in predicting in-hospital bleeding events compared to the CRUSADE score (AUC = 0.722 vs 0.520, respectively, \( p = 0.002 \)) (Fig. 2). According to the Youden index, sensitivity of the HAS-BLED score was 59.09% and specificity was 89.81% in the subgroup with stenting.

According to the ROC curve analysis, the HAS-BLED score was found to be statistically significantly predictive of in-hospital bleeding in patients who underwent stenting due to stable coronary artery disease (\( p = 0.0012 \)). In the same patient group, the sensitivity of the CRUSADE score was 36.36% and...
the specificity was 82.69%, but it was not statistically significant ($p = 0.789$).

**Discussion**

The main finding of this study was that patients with stable coronary artery disease undergoing elective coronary angiography with a CRUSADE score of $> 30$ were under a significantly increased risk of in-hospital bleeding compared to those with a CRUSADE score $\leq 30$; however the HAS-BLED score was more valuable for predicting in-hospital bleeding in these patients compared to the CRUSADE score. To the best of our knowledge, this is the first study to compare bleeding risk scores in this patient group.

One of the most important causes of co-morbidity in patients with stable coronary artery disease undergoing elective coronary angiography is haemorrhage. For this reason, avoiding bleeding is as important as treating ischaemia in the patient. Since bleeding is a significant cause of morbidity and mortality in these patients, a precision risk-analysis method is needed to identify patients who are at high risk of bleeding after the invasive coronary angiography procedure.

Many risk models have been used to predict this important co-morbid situation. Rao et al. found that bleeding complications in patients presenting with ACS increased long- and short-term mortality rates, and suggested that the GUSTO bleeding risk classification was successful in identifying short- and long-term adverse cardiac event risk among this patient population. Hence, they suggested that identifying patients with ACS with high bleeding risk and using appropriate management techniques could improve outcomes. Although this study provides valuable information, it provides information only on patients presenting with ACS.

In another study, the SYNTAX score was shown to be associated with major bleeding events in patients presenting with NSTEMI who underwent PCI. It is also well known that the CRUSADE score is valuable in predicting bleeding risk in NSTEMI patients. However, all of these studies were performed on ACS patients. Bleeding complications are however an important problem in patients with stable coronary artery disease undergoing elective coronary angiography, as well as in ACS patients.

In this regard, Ndrepepa et al. included only patients with stable coronary artery disease who underwent elective PCI, and they showed that bleeding within 30 days of the procedure was associated with an increased risk of one-year mortality after PCI. These findings suggest that prevention of procedural bleeding may contribute to PCI outcomes in terms of reducing mortality rate in patients with stable coronary artery disease. However, in this study, a scoring system that could predict bleeding was not used. Our study revealed the predictive value of the HAS-BLED and CRUSADE scores on the risk of in-hospital bleeding in patients with stable coronary artery disease.

Although HAS-BLED is mainly used to predict bleeding risk in AF patients, some previous studies have demonstrated that it may also predict bleeding risk in patients with coronary artery disease. In a study conducted on NSTEMI patients, the HAS-BLED bleeding score was shown to be as effective as GRACE and CRUSADE, and even better than the TIMI scoring system with regard to future bleeding risk prediction.

In another study, the HAS-BLED score was also found to be useful in predicting in-hospital major bleeding risk in NSTEMI patients, together with the CRUSADE and ACUITY-HORIZONS scores. All these studies have emphasised that the HAS-BLED score, which is as useful as other scoring systems, is more practical and easy to apply. The ease of calculating the HAS-BLED score and its ease of implementation in clinical practice further increases the importance of this bleeding risk scoring system.

The CRUSADE score has been studied several times to predict bleeding risk in patients with coronary artery disease, especially in NSTEMI patients. In other studies, the CRUSADE score has been shown to be effective in predicting major bleeding in patients undergoing PCI, and was shown to be even more valuable than the platelet reactivity test in PCI patients. It can be used to predict mortality risk, similar to the GRACE risk score in ACS patients, and to predict bleeding risk in STEMI patients. The prognostic accuracy of the CRUSADE score can be used to predict major or moderate bleeding events even in non-invasively treated ACS patients. It is interesting that such an impressive scoring system did not give as good predictive results as the HAS-BLED scoring system in our patient group.

Costa et al. showed that the CRUSADE risk score predicted major bleeding events better than the HAS-BLED score in their study. However their study differed from ours in that it involved only patients receiving dual antiplatelet therapy after stenting and included only major bleeding events. Similar negative results for the CRUSADE risk score have also been found in some previous studies. In a study conducted in octogenarians, it was reported that the CRUSADE score was insufficient to predict the risk of bleeding in NSTEMI patients and that new scoring systems were needed. In a study by Correia et al., it was reported that the ACUITY scoring system was a better predictor of major bleeding in patients admitted to hospital with ACS compared to the CRUSADE score.

These conflicting results suggest that we do not have an ideal scoring system to use on all patients and that new developments are needed in this regard. For this reason, in our study we examined patients with stable coronary artery disease who underwent elective coronary angiography, since there is little data on them and they were often overlooked in previous studies. We included all patients with stable coronary artery disease with or without stent implantation, and examined the HAS-BLED and CRUSADE scores, which were not previously studied in this group.

We have shown that the HAS-BLED score was more predictive in these patients, even though the results of the CRUSADE score were reasonable, and that HAS-BLED may help us to predict bleeding events and reduce co-morbidity in these patients. The ease of calculating the HAS-BLED score and its ease of implementation in clinical practice further increases the importance of this bleeding risk-scoring system. The present study provides valuable data because this group of patients is frequently encountered in the angiography laboratory in daily cardiology practice and there is no scoring system as yet to predict bleeding risk among these patients.

This study has some limitations, such as it was a single-centre study with a small sample size and did not include long-term results. Another limitation is that the femoral artery was preferred to the radial artery for coronary angiography.
Conclusion
Various scoring systems are used in the prediction of bleeding risk in patients undergoing angiography due to ACS. However, in stable angina patients without ACS, there is not enough data on this subject. This study showed that the HAS-BLED and CRUSADE scores were useful in stable coronary artery disease patients who underwent elective coronary angiography. However, in these patients without ACS, we found that it would be more appropriate to use the HAS-BLED scoring, which is more practical, easy to calculate, easy to implement in clinical practice and more predictive for in-hospital bleeding. Although this study introduces a new approach, there is a need for larger studies to make a definite decision in this regard.

References