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Untangling the difficult interplay between ischemic and hemorrhagic risk: The role of risk scores

Simone Persampieri, Diego Castini, Alessandro Lupi, Marco Guazzi

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Abstract

BACKGROUND

Bleedings are an independent risk factor for subsequent mortality in patients with acute coronary syndromes (ACS) and in those undergoing percutaneous coronary intervention. This represents a hazard equivalent to or greater than that for recurrent ACS. Dual antiplatelet therapy (DAPT) represents the cornerstone in the secondary prevention of thrombotic events, but the benefit of such therapy is counteracted by the increased hemorrhagic complications. Therefore, an early and individualized patient risk stratification can help to identify high-risk patients who could benefit the most from intensive medical therapies while minimizing unnecessary treatment complications in low-risk patients.

AIM

To review existing literature and gain better understanding of the role of ischemic and hemorrhagic risk scores in patients with ischemic heart disease (IHD).

METHODS

We used a combination of terms potentially used in literature describing the most common ischemic and hemorrhagic risk scores to search in PubMed as well as references of full-length articles.

RESULTS

In this review we briefly describe the most important ischemic and bleeding scores that can be adopted in patients with IHD, focusing on GRACE, CHA2DS2-Vasc, PARIS CTE, DAPT, CRUSADE, AQUIITY, HAS-BLED, PARIS MB and

PRECISE-DAPT score. In the second part of this review, we try to define a possible approach to the IHD patient, using the most suitable scores to stratify patient risk and decide the most appropriate patient treatment.

CONCLUSION

It becomes evident that risk scores by themselves can't be the solution to balance the ischemic/bleeding risk of an IHD patient. Instead, some risk factors that are commonly associated with an elevated risk profile and that are already included in risk scores should be the focus of the clinician while he/she is taking care of a patient affected by IHD.

Key Words: Acute coronary syndrome; Ischemic heart disease; Risk score; Bleeding; Mortality; Percutaneous coronary intervention

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Core Tip: We present a review of the most relevant scores developed or adjusted for the risk stratification of patients affected by ischemic heart disease. For each score, the strengths, weaknesses, statistical pertinence and applicability are evaluated.

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INTRODUCTION

Hemorrhagic complications have emerged as an independent risk factor for subsequent mortality in patients with acute coronary syndromes (ACS) and in those undergoing percutaneous coronary intervention (PCI), representing a hazard equivalent to or greater than that for recurrent ACS[1-4]. As known, dual antiplatelet therapy (DAPT) represents the cornerstone in the secondary prevention of thrombotic events in ACS[2]. However, the benefit of such therapy is counteracted by the increased hemorrhagic complications: major bleeding also considerably prolongs the hospital stay and increases resource consumption. Minimizing bleeding complications, most of which are attributable to the use of potent antiplatelet and antithrombin medications, is therefore an important objective in the management of patients with ischemic heart disease (IHD). It must be noted that, similarly to ischemic risk, risk of bleeding is not homogeneous, and various predictive models have been developed to stratify both bleeding and ischemic risk in patients affected by IHD[5]. Clinical guidelines recommend that optimal management of patients with IHD should include early, individualized patient risk stratification by the treating physician[6,7]. In addition to informing patients about their prognosis, accurate risk assessment can help to identify high-risk patients who could benefit the most from intensive medical therapies while minimizing unnecessary treatment complications in low-risk patients. The development of simple-to-use risk scores could standardize quality of care and patient outcomes. Risk stratification could also be employed to compare outcomes across different clinical studies.

MATERIALS AND METHODS

We screened the titles and abstracts of studies against predefined terms using PubMed, EMBASE and Cochrane databases. Key words used have been "GRACE score", "CHA2DS2-Vasc score", "PARIS CTE score", "DAPT score", "CRUSADE score", "ACUITY score", "HAS-BLED score", "PARIS MB score", "PRECISE-DAPT score", "derivation" and "validation" in order to identify relevant articles published. The title and available abstracts of all returned articles were reviewed to identify relevant articles for a full-length review. Reference lists from the articles were reviewed to identify additional relevant articles. All studies that contained material applicable to the topic were considered. Data was analyzed using descriptive statistics.

RESULTS

Ischemic risk

GRACE score: The GRACE risk prediction model was developed from an earlier cohort of GRACE (Global Registry of Acute Coronary Events) patients (a total of 11389 patients enrolled in 14 countries from April 1, 1999, to March 31, 2001)[8]. It evaluates the probability of death within 6 mo of hospital discharge in patients with ACS. The components of the GRACE score are systolic blood pressure, age, Killip class, heart rate, cardiac arrest, serum creatinine, ST-segment deviation and cardiac biomarker increase. All variables refer to data at patient presentation. GRACE score was subsequently validated in a cohort of 3972 GRACE patients and 12142 GUSTO-IIb trial patients. It has been demonstrated an important predictor of in-hospital mortality across the whole spectrum of the ACS population[9]. However, the substantial geographic variation of patient cohorts used to develop the GRACE do not confirm its applicability in all the ACS patient populations and additional assessment has been performed to validate the score. Currently, GRACE score is suggested by ESC Guidelines to stratify patients according to their estimated risk of future ischemic events in order to overcome the so called "risk-treatment paradox"[10,11]. Indeed, it is well recognized that the delivery of guideline-directed care is inversely related to the estimated risk of the patient with NSTEMI and a GRACE risk score-based risk assessment has been found to be superior to the subjective physician assessment for the occurrence of death or ACS[12,13].

Moreover, benefit with an early invasive strategy is strongly associated with the patient's risk profile. In a pre-specified subgroup analysis, patients with a GRACE risk score > 140 benefited from an early invasive strategy while those with a GRACE risk score < 140 did not (TIMACS trial: HR = 0.65, 95%CI: 0.48-0.89 *vs* HR = 1.12, 95%CI: 0.81-1.56, *P* for interaction = 0.01; VERDICT trial: HR = 0.81, 95%CI: 0.67-1.00 *vs* HR = 1.21, 95%CI: 0.92-1.60; *P* for interaction = 0.02)[14,15].

C-statistics in the derivation study: 0.81 for predicting death and 0.73 for death or myocardial infarction.

CHA2DS2-VASc score: The CHA2DS2-VASc score is a well validated risk model for predicting thromboembolic events and guiding anticoagulant therapy in patients affected by atrial fibrillation (AF). It has been developed as a refinement of the older CHADS2 score by incorporating female sex and vascular disease and by assigning two points for age ≥ 75 years[16,17]. Although being developed for thromboembolic risk prediction in AF patients, both these scores contain common cardiovascular risk factors that are associated with thromboembolic events regardless of the presence of AF and are well known predictors of both coronary atherosclerosis and major cardiac adverse events (MACE) in patients with known coronary artery disease and ACS[18,19].

C-statistics in the derivation study: 0.61.

PARIS CTE score: The PARIS CTE score has been derived from The Patterns of Nonadherence to Antiplatelet Regimens in Stented Patients (PARIS) registry, an observational study of patients undergoing percutaneous coronary intervention (PCI) and stenting. From that registry, PARIS risk scores for major bleeding (MB) and for coronary thrombotic events (CTE) were created. The PARIS CTE risk score predicts the stent thrombosis and myocardial infarction risk for up to 2 years after PCI. It considers diabetes, ACS, smoker, creatinine clearance, prior PCI and prior CABG[20]. The score showed very good results both in the derivation and validation cohort. Once external validation studies had been performed, they showed limited to poor discrimination thus far. As the simplicity of the CTE score might be favorable for clinical use, its value compared to other ischemic scores is yet to be established.

C-statistics in the derivation study: 0.70.

DAPT score: The dual-antiplatelet therapy (DAPT) score is recommended by Guidelines as a tool to stratify ischemic and bleeding risk. However, the score can be used to distinguish patients suitable for standard term DAPT and long term DAPT, so it is our opinion that it can be considered mostly an ischemic risk score. The prediction rule assigns 1 point each for myocardial infarction at presentation, prior myocardial infarction or PCI, diabetes, stent diameter less than 3 mm, smoking, and paclitaxel-eluting stent; 2 points each for history of congestive heart failure/Low ejection fraction and vein graft intervention; -1 point for age 65 to younger than 75 years; and -2 points for age 75 years or older[21]. The DAPT score has been validated in several studies outside its derivation cohort; however, these studies have yielded conflicting results in which some have confirmed its predictive value and some have not[22]. Of note, most of the analyses were from registries and a substantial number of patients were treated with bare-metal stents or first-generation DES. Moreover, the present score considers among its items the use of paclitaxel-eluting stents, that are no more considered a standard in most catheterization laboratories. It is well known that using newer-generation DES mitigates the ischemic risk of patients treated with PCI. It becomes evident looking at C-statistics: in the derivation/validation study, the C-statistic for ischemic and bleeding outcomes were 0.64/0.70 and 0.68/0.64, respectively; among the validation studies, the C-statistics for composite outcomes ranged from 0.53 to 0.71 for ischemic outcomes and 0.49 to 0.71 for bleeding outcomes[23].

Bleeding risk

CRUSADE score: CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) score has been developed by investigators of the CRUSADE registry as a stratification tool for in-hospital major bleeding among NSTEMI patients[24]. Variables included are female sex, diabetes mellitus, peripheral artery disease, heart rate, systolic blood pressure, congestive heart failure, hematocrit, and creatinine clearance. Considering only the variables present at admission, the CRUSADE bleeding score is an easily applicable and useful tool in predicting patient risk that showed adequate calibration and excellent discriminatory powers in the whole population as well as in the different treatment subgroups, except in patients treated with ≥ 2 antithrombotics who did not undergo cardiac catheterization[24,25].

C-statistics in the derivation study: from 0.56 to 0.81 in different subgroups.

ACUITY: Mehran *et al*[26], using data from the ACUITY and the HORIZONS-AMI trials (17421 patients), developed a bleeding risk score. Six independent baseline predictors for major bleeding were identified: female sex, age, creatinine, white blood cell count, anemia and ST-segment-elevation. The risk score differentiated patients with a 30-d rate of non-CABG-related major bleeding ranging from 1% to over 40%. As a difference with the other bleeding risk scores, this one includes white blood cell count as a risk factor for major bleeding. It has been compared with CRUSADE score in subsequent observational study and shows an acceptable discriminative capacity[27].

C-statistics in the derivation study: 0.74.

HAS-BLED score: The HAS-BLED score, initially developed to assess the bleeding risk in patients with AF receiving chronic anticoagulant therapy[28], has shown to predict cardiovascular events and long-term outcomes in these patients. The observation by Pisters *et al*[28] that HAS-BLED predictive efficacy was particularly high in patients receiving antiplatelet therapy led to its evaluation in predicting bleeding events and major acute cardiovascular events (MACE) in patients receiving DAPT after PCI and stenting with or without AF[29]. Moreover, the HAS-BLED score predictive performance was tested in patients with ACS receiving DAPT or triple antithrombotic therapy, showing moderate accuracy[28].

C-statistics in the derivation study: 0.72 overall; 0.91 with antiplatelet only therapy.

PARIS MB score: The PARIS risk score for major bleeding was developed from the same previously mentioned PARIS registry, in which also patients on oral anticoagulation were included. This six-item risk score (age, BMI, smokers, anemia, creatinine clearance and triple therapy) showed reasonable discrimination for major bleeding up to 2 years post-PCI across different validation cohorts[20].

C-statistics in the derivation study: 0.72.

PRECISE-DAPT score: The PRECISE-DAPT (Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy) score is a simple bedside risk assessment tool, recommended from the ESC Guidelines, which can be easily implemented in everyday clinical practice, and that might be particularly useful for its applicability at the time of treatment initiation[6,7,30]. It has been developed for prediction of bleeding risk during DAPT after PCI using pooled data of 8 randomized clinical trials. It comprises 5 variables: age, creatinine clearance, hemoglobin, white blood cell count and previous spontaneous bleeding. In patients with high bleeding risk (PRECISE-DAPT score ≥ 25), the bleeding risk of 12-mo or longer DAPT could outweigh the benefit of ischemic prevention. Patients not at high bleeding risk (score < 25) might receive a standard (*i.e.* 12 mo) or prolonged (*i.e.* > 12 mo) treatment without being exposed to significant bleeding liability.

C-statistics in the derivation study: 0.71.

DISCUSSION

Risk scores or risk factors?

We now move forward looking at the multivariate analysis from which every score has been developed, focusing on repeated items among scores belonging to ischemic or bleeding category and on the real weight of these items in the score (*i.e.* the OR or HR values). We want to specify that we do not apply this analysis to the GRACE score that is composed by items of the acute phase of ACS that are not common to other scores and that has a very strong predictive value for mortality by itself. We think that the GRACE score should be applied in every ACS patient, in order to define the patient prognosis, regardless of ischemic and bleeding risk which should be analyzed separately.

Going back to the analysis in [Table 1](#) and [Table 2](#), we summarized the OR or HR derived from the multivariate analysis of the derivation cohorts and the ischemic and bleeding risk scores, respectively.

At first, looking at ischemic risk scores, it becomes evident that in the CHA2DS2-Vasc score, only the female sex was really statistically significant in the logistic regression analysis, while the other items were not. This is because, in the derivation and validation study, rather than considering the single item, patients have been grouped in 3 groups according to the score, that were low risk (0 point), intermediate risk (1 point) and high risk (≥ 2 points), and the authors demonstrated a better discrimination capacity

Table 1 Ischemic risk scores items and OR/HR

Item	OR/HR (CI)
CHA2DS2-Vasc (OR)	
Congestive HF	0.72 (0.27-1.88) NS
Hypertension	1.01 (0.38-2.66) NS
Age ≥ 65	NR
Age ≥ 75	1.46 (0.63-3.35) NS
Diabetes mellitus	1.79 (0.73-4.40) NS
Stroke	2.22 (0.78-6.35) NS
Vascular disease	2.27 (0.94-5.46) NS
Female sex	2.53 (1.08-5.92)
DAPT (OR)	
Age, per 10 yr increase	1.54 (1.34-1.78) (on bleedings)
Current smoking	1.4 (1.11-1.76)
Diabetes mellitus	1.38 (1.1-1.72)
Acute coronary syndrome	1.65 (1.31-2.07)
PCI or prior ACS	1.79 (1.43-2.23)
Stent diameter < 3 mm	1.61 (1.3-1.99)
Paclitaxel stent	1.57 (1.26-1.97)
Congestive HF	1.88 (1.35-2.62)
Saphenous vein graft stenting	1.75 (1.13-2.73)
PARIS-CTE (HR)	
Current smoking	1.69 (1.14-2.52)
CrCl < 60 mL/min	2.12 (1.46-3.05)
Diabetes mellitus	
Non-insulin dependent	1.69 (1.14-2.52)
Insulin dependent	3.42 (2.32-5.04)
Acute coronary syndrome	
Troponin negative	1.47 (1.03-2.08)
Troponin positive	2.09 (1.24-3.53)
Previous revascularization	
Previous PCI	1.91 (1.38-2.66)
Previous CABG	1.80 (1.24-2.61)

CI: Confidence interval; CrCl: Creatinine clearance; HF: Heart failure; HR: Hazard ratio; NR: Not reported; NS: Not significant; OR: Odds ratio.

of the CHA2DS2-Vasc score compared to the CHADS2 score. Therefore, they still included variables not independently associated to the outcomes but that fit the prognostic model[17]. Moving on, the other 2 scores, we found a precise statistical derivation with every single item being statistically significant.

As evident, two variables are common to all scores, these are diabetes mellitus and vascular disease (considered also as previous ACS or PCI). Some others like heart failure, age and smoking, are common to 2 out of 3 scores. Diabetes mellitus and vascular disease are also the items with the higher OR or HR in every score and that means that they have more influence on the ischemic outcome.

Diabetes is a major independent risk factor for IHD[31], particularly for myocardial infarction. The pattern of coronary artery disease in diabetic patients is often complex, with multiple lesions and widespread involvement, making it difficult to achieve complete revascularization and adversely affecting long-term prognosis[31]. Several studies have also found a greater risk of death after ACS in patients with diabetes than in those without diabetes[32,33] in every subtype of coronary syndromes

Table 2 Bleeding risk scores items and HR/OR

Item	HR/OR (CI)
PARIS-MB (HR)	
Current smoking	1.94 (1.18–3.20)
CrCl < 60 mL/min	1.81 (1.16–2.82)
Age, per year increase	1.02 (1.00–1.04)
BMI	
< 25 kg/m ²	1.68 (1.09–2.60)
≥ 35 kg/m ²	1.79 (1.04–3.08)
Anemia	2.72 (1.83–4.04)
Triple therapy on discharge	1.93 (1.08–3.43)
CRUSADE (HR)	
Heart rate per 10 bpm increase	1.08 (1.07–1.10)
Systolic blood pressure	
≤ 110 mmHg	1.26 (1.16–1.36)
≥ 180 mmHg	1.24 (1.14–1.35)
Hematocrit < 36%	2.28 (2.11–2.46)
CrCl, per 10 mL/min decrease	1.12 (1.10–1.13)
Sign of HF	1.23 (1.15–1.31)
Vascular disease	1.19 (1.12–1.27)
Diabetes	1.16 (1.10–1.23)
Female sex	1.31 (1.23–1.39)
ACUITY (OR)	
Age, per 5 yr increase	1.17 (1.13–1.21)
Acute coronary syndrome	
NSTEMI	1.26 (1.04–1.54)
STEMI	1.92 (1.52–2.44)
White blood cell count, giga/L	1.10 (1.07–1.12)
Serum creatinine, per 0.1 mg/dL increase	1.09 (1.07–1.12)
Anemia	1.98 (1.65–2.37)
Bivalirudin monotherapy	0.56 (0.47–0.67)
Female sex	2.32 (1.98–2.72)
HAS-BLED (OR)	
Age > 65 yr	2.66 (1.33–5.32) NS
Systolic blood pressure >160 mmHg	0.60 (0.21–1.72) NS
Creatinine > 2.26 mg/dL or > 200 μmol/L or cirrhosis or bilirubin > 2 x normal with AST/ALT/AP > 3 x normal	2.86 (1.33–6.18)
Prior major bleeding or anemia	7.51 (3.00–18.78)
Medication predisposing to bleeding	0.81 (0.43–1.51) NS
Stroke	0.94 (0.32–2.86) NS
Labile INR	NR
Alcohol use, ≥ 8 drinks/wk	0.00 (0.00) NS
PRECISE-DAPT (OR)	
Hemoglobin, per 1 g increase	0.67 (0.53–0.64)

White-blood-cell count, per 103 cells per μ L increase	1.06 (0.99-1.13)
Age, per 10 yr increase	1.34 (1.11-1.48)
CrCl, per 10 mL/min increase	0.9 (0.82-0.99)
Previous bleeding	4.14 (1.22-14.02)

CI: Confidence interval; CrCl: Creatinine clearance; HF: Heart failure; HR: Hazard ratio; NR: Not reported; NS: Not significant; OR: Odds ratio.

(unstable angina, STEMI and NSTEMI)[34,35].

The incidence of peripheral arterial disease (PAD) increased by 23.5% in the first 10 years of this century and 3%-12% of the earth's population is affected[36]. PAD patients share most of their atherosclerotic risk profiles with patients diagnosed with coronary artery disease. In the Global Atherothrombosis Assessment (AGATHA) study, approximately 50% of patients with PAD had IHD, and 20% of IHD patients was affected also by PAD[37]. Advanced stent technology and more potent antiplatelet agents and anticoagulant therapy have resulted in an improvement in outcomes among the overall population of patients undergoing coronary interventions. However, PAD patients demonstrated a lower benefit increase. Of note, their risk of major adverse cardiovascular events outcomes following PCI has remained unchanged across the early bare-metal stent (BMS) and drug-eluting stent (DES) eras: the only benefit has been demonstrated for a reduction in the rate of repeated PCI. Singh *et al*[38] found that patients with PAD that underwent PCI in the BMS era had an 84% relative-risk increase of an in-hospital mortality and a 48% relative-risk increase of death over a period of 3-years compared to patients without PAD. And this was evident also after adjustment for concomitant risk factors. In the Tirofiban and Reopro Give Similar Efficacy Outcome Trial (TARGET), PAD was independently associated with a 2- to 3-fold increase in mortality 12 mo after PCI. Similar to findings in the BMS era, in the DES era the study by Ramzy *et al*[39] suggests that PAD continues to be independently associated with approximately a two-fold increased risk of 12 mo mortality. Assessment of Dual AntiPlatelet Therapy with Drug Eluting Stents (ADAPT-DES) study was conducted with the aim to determine the relationship between platelet reactivity, PAD and subsequent adverse outcomes. In the study population, there was a 10.2% prevalence of PAD among the 8582 patients, all of whom received DESs. Data analysis showed PAD to be an independent predictor of MACE (adjusted HR = 1.34, $P = 0.003$)[40].

At last, we want to focus on Chronic Kidney Disease (CKD) which is only considered in the PARIS CTE score. As known, CKD is a well-known ischemic risk factor and bleeding risk factor at the same time[41]. Some studies have demonstrated that including CKD in known risk scores, increases the predictive value of the score. A modified CHA2DS2-Vasc score including CKD with a different definition showed a better discriminative capacity than the original score in mortality prediction in an ACS patient population[42].

However, the double association with ischemic and bleeding events in IHD patients is not simple to manage for the clinician and, according to this consideration, we move forward with the analysis of the bleeding risk scores, to put some lights on this risk factor.

Variables of some of the most adopted bleeding scores are summarized in Table 2. Prior bleeding/anemia and CKD are the only variables common to all scores. In particular, baseline anemia was assessed as one of the most important independent predictors of bleeding in PARIS MB and PRECISE-DAPT. As evident, HAS-BLED included some variables that were not statistically significant in the derivation cohort, like age, blood pressure, medication predisposing to bleeding and previous stroke: however, these variables were still included due to their known association with bleeding events derived from previous literature[28]. On the other hand, all scores do not consider some important variables known to be associated with increased bleeding risk because these are not common in patients with IHD or those undergoing PCI (like thrombocytopenia) or because they were rarely recorded in the derivation data. The mentioned differences in risk prediction scores are directly linked to heterogeneity in the populations studied, the variables assessed and the bleeding definitions used in the development cohorts.

Information about the subsequent bleeding risk in patients that undergo PCI with a history of prior bleeding event is scarce. Nonetheless, a prior spontaneous bleed at any time was assessed as an important predictor of bleeding in the PRECISE-DAPT score and, by itself, rises the patient bleeding risk in the highest quartile[30].

Anemia defined by World Health Organization criteria (hemoglobin < 13 g/dL in men and < 12 g/dL in women) is not uncommon in patients undergoing PCI and is directly related with the risk of future bleeding[43]. A meta-analysis of 44 studies including more than 230000 patients undergoing PCI, anemia (defined by World Health Organization criteria in the majority of studies) prevalence was 16% and was associated with a doubled risk of subsequent bleeding [as defined in individual studies; adjusted risk ratio, 2.31 (95%CI: 1.44-3.71)][44]. Furthermore, bleeding risk increased with increasing severity of anemia. In PARIS MB, anemia at baseline (defined as hemoglobin < 12 g/dL in men and < 11 g/dL in women) was assessed as an important predictor of 2-year BARC 3 or BARC 5 bleeding [9.5%

with *vs* 2.7% without anemia; adjusted HR = 2.72 (95%CI: 1.83–4.04); $P < 0.0001$][20]. In PRECISE-DAPT a reduction in the risk of TIMI major/minor bleeding at 1 year was independently associated with every 1 g/dL increase in hemoglobin between 10 and 12 g/dL [adjusted HR = 0.67 (95%CI: 0.53–0.84); $P = 0.001$][31].

Estimated glomerular filtration rate (eGFR) < 30 mL/min, which configures a severe or end-stage CKD, is considered a major ARC-HBR criterion, while eGFR between 30–59 mL/min (moderate CKD) is considered a minor ARC-HBR criterion. Unfortunately, patients with severe CKD have generally been excluded from randomized trials and only approximately 30% of patients undergoing PCI have an eGFR < 60 mL/min[45]. However, it has been demonstrated that the bleeding risk increases incrementally with worsening CKD and even mild CKD is an independent risk factor for bleeding after PCI [46–49]. In the PRECISE-DAPT score, eGFR < 30 mL/min by itself increases patients bleeding risk to the highest quartile, whereas milder CKD is associated with a slight to moderate risk. It must be noticed that in the DAPT score, CKD is not considered as a variable because the associated increased bleeding risk was balanced by an almost identical increased ischemic risk[22].

CONCLUSION

According to our analysis, it becomes clear that a single score can't be the real solution to balance the ischemic/bleeding risk of a patient. Instead, some risk factors that are commonly associated with an elevated risk profile and that are already included in risk scores should be the focus of the clinician while he/she is taking care of a patient affected by IHD. In particular, we found that diabetes mellitus and vascular disease clearly increase the risk of ischemic events, while previous bleeding, anemia and CKD bring a high risk of further bleeding events. Some scores include too many variables that can mislead the clinician choice: since a perfect score could not exist we suggest clinicians apply the most user friendly and at the same time, evaluate the cited variables separately. As suggested by Guidelines, PRECISE-DAPT could be the most suitable bleeding risk score since it is more influenced by CKD, anemia and history of bleeding, while PARIS CTE should be the ischemic risk score of choice, including diabetes mellitus and vascular disease. However, the final result of a clinical reasoning should not be the right score result but the most fitted patient therapy.

ARTICLE HIGHLIGHTS

Research background

Bleedings are an independent risk factor for subsequent mortality in patients with acute coronary syndromes (ACS) and in those undergoing percutaneous coronary intervention, representing a hazard equivalent to or greater than that for recurrent ACS. Dual antiplatelet therapy (DAPT) represents the cornerstone in the secondary prevention of thrombotic events, but the benefit of such therapy is counteracted by the increased hemorrhagic complications.

Research motivation

An early and individualized patient risk stratification can help to identify high-risk patients who could benefit the most from intensive medical therapies while minimizing unnecessary treatment complications in low-risk patients.

Research objectives

In order to review existing literature and gain better understanding of the role of ischemic and hemorrhagic risk scores in patients with ischemic heart disease (IHD).

Research methods

The authors used a combination of terms potentially used in the literature describing the most common ischemic and hemorrhagic risk scores to search in PubMed, as well as references of full-length articles. The authors briefly describe the most important ischemic and bleeding scores that can be adopted in patients with IHD, focusing on GRACE, CHA2DS2-Vasc, PARIS CTE, DAPT, CRUSADE, ACUTY (Mehran *et al.*), HAS-BLED, PARIS MB and PRECISE-DAPT score.

Research results

A single score can't be the real solution to balance the ischemic/bleeding risk of a patient. Instead, some risk factors that are commonly associated with an elevated risk profile and that are already included in risk scores should be the focus of the clinician while he/she is taking care of a patient affected by IHD. In particular, we found that diabetes mellitus and vascular disease clearly increase the risk of ischemic events, while previous bleeding, anemia and CKD bring a high risk of further bleeding events. Some

scores include too many variables that can mislead the clinician's choice: since a perfect score could not exist we suggest the clinician apply the most user friendly and at the same time evaluate the cited variables separately. As suggested by Guidelines, PRECISE-DAPT could be the most suitable bleeding risk score, since it is more influenced by CKD, anemia and history of bleeding, while PARIS CTE should be the ischemic risk score of choice with diabetes mellitus and vascular disease.

Research conclusions

Risk scores by themselves can't be the single solution to balance the ischemic/bleeding risk of an IHD patient. Instead, some risk factors that are commonly associated with an elevated risk profile and that are already included in risk scores should be the focus of the clinician while he/she is taking care of a patient affected by IHD.

Research perspectives

Future research should try to elaborate an omni-comprehensive score to be adopted in IHD and at the same time be easy to use and reliable.

FOOTNOTES

Author contributions: Persampieri S and Castini D participated in the development of the proposal to research the topic, performed literature search and review, and wrote the draft of the manuscript, reviewed, edited and approved the manuscript; Lupi A and Guazzi M participated in the supervision of the research on the topic, reviewed, wrote and revised the manuscript as senior authors.

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