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ACEF vs PARIS score in Predicting Cardiovascular Events in Patients With Acute Coronary Syndrome: Insights From the START ANTIPLATELET Registry

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Abstract

Several scores can predict clinical outcomes of patients with Acute Coronary Syndromes (ACS). The validated PARIS (Patterns of Non-Adherence to Anti-Platelet Regimen in Stented Patients) score is poorly used in clinical practice because it needs items that are not always easily available. The ACEF (Age, Creatinine, and Ejection Fraction) score is more attractive because it only includes three items. We compared these scores to risk-stratify ACS patients enrolled into the START (Survey on anti-coagulated pAtients RegisTer)-ANTIPLATELET registry. ACS patients who completed 1-year follow-up (n = 1171) were grouped in tertiles (low, medium, and high-risk) according to their ACEF/PARIS scores. Primary endpoints were: one-year MACCE (major adverse cardiac and cerebrovascular events: death, non-fatal myocardial infarction, stroke or target vessel revascularization) and NACE (net adverse cardiac and cerebrovascular events): MACCE plus major bleeding). MACCE incidence was higher in the high-risk tertile (15%) VS low/medium (3/7 %) risk tertiles ($P < .001$). NACE incidence in the high-risk tertile was 24% VS low/medium (9/15 %) risk tertiles ($P < .001$), independently of the risk score used**.** The ACEF score has similar accuracy as the validated PARIS score for the estimation of ischemic/bleeding risk. Thereby, we strongly suggest its use in clinical practice to risk-stratify ACS patients and select optimal therapeutic strategies.

Keywords

acute coronary syndromes, clinical outcome, risk scores

Introduction

Acute coronary syndromes (ACS) represent one of the most important causes of morbidity and mortality worldwide.[1] Despite impressive advances in medical therapy and invasive strategies over the last years, the risk of further cardiovascular events remains substantial.[2] Therefore, an accurate risk assessment and patient stratification is crucial to select

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those patients who would benefit the most from closer follow-up and of a tailored optimal medical therapy. It follows that many risk scores have been developed to predict short and long-term clinical outcome after the acute event.

The PARIS (Patterns of Non-Adherence to Anti-Platelet Regimen in Stented Patients) score has been validated to predict risks for out-of-hospital coronary thrombotic and bleeding events.[3] However, since several items are required to calculate these scores, they might be difficult to use in clinical practice. In contrast, the ACEF score includes only three items: Age, Creatinine, and Ejection Fraction. It was introduced in 2009 by *Ranucci et al.* for predicting in-hospital mortality in patients undergoing elective cardiac surgery.[4,5] This risk-assessment model has an impressive prognostic performance compared with other more complex scores.[6] Moreover, it has a good discriminative ability for short and long-term outcomes, not only in cardiac surgery patients, but also in patients undergoing percutaneous coronary intervention (PCI) or transcatheter aortic valve implantation (TAVI).[7,8] ACEF score is associated with a satisfactory predictive value, in terms of short and long-term mortality and major adverse cardiovascular events, such as myocardial infarction, bleeding, revascularization of the target lesion, thrombosis of the stent, and post-PCI acute renal failure. Thus, aim of the present study was to compare the PARIS score, that has several items to be calculated and the ACEF score that needs only three items, to risk-stratify ACS patients enrolled in the START (Survey on anticoagulated pAtients RegisTer) antiplatelet registry.

Methods

The START-ANTIPLATELET is a branch of START registry (Survey on anticoagulated pAtients RegisTer).[9] It is a multicenter observational prospective registry conducted between January 2014 and December 2016, including 8 Italian centers. The registry was all inclusive: no explicit exclusion criteria were applied. In this sub-study a total of 1171 consecutive patients, presenting with ACS (either non-ST-segment elevation "NSTEMI" or ST-segment elevation myocardial infarction "STEMI") and undergoing revascularization plus medical therapy or referred to medical therapy alone, who completed 1-year follow-up have been enrolled.[10,11] ACEF and PARIS score were calculated for all patients and then grouped into tertiles according to either the ACEF or the PARIS scores. ACEF score value was calculated by the following equation: Age (years)/EF (%) + 1 (if preoperative serum creatinine value >2.0 mg/dL).[4,5] The PARIS ischemic risk score was calculated as previously shown by considering the following items: diabetes mellitus (+1 point or +3 points if on treatment with insulin), acute coronary syndrome (+2 or +1 if unstable angina), current smoking (+1), creatinine clearance <60 mL/min (+2), prior PCI (+2), and prior coronary artery bypass grafting (+2).[3]

Primary endpoints were:

(1) Major adverse cardiac and cerebrovascular events (MACCE), a composite of death, myocardial infarction (MI), stroke or target vessel revascularization (TVR);
(2) Net adverse cardiac and cerebrovascular events (NACE), based on MACCE plus major bleeding.

Composite endpoints were analyzed at the time of the first event. MI, cardiovascular death and all-cause death were defined by the Academic Research Consortium criteria.[12] Stroke was defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal ischemic or hemorrhagic infarction with residual symptoms 24 h after event or leading to death.[13] Target vessel revascularization was defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel including the target lesion.[12] Major bleeding was classified according to TIMI (Thrombolysis In Myocardial Infarction) criteria, as intracranial bleeding or clinically overt bleeding associated with a decrease in hemoglobin >5 g/dl.[14] All participants signed an informed consent before participating to the study.

Statistical Analysis

All the analyses were stratified for ACEF and PARIS scores. Categorical data are presented as numbers and percentages and compared using χ^2 or Fisher's exact test. Continuous data are shown as means and standard deviations and compared by ANOVA test with appropriate *post-hoc* analysis. Cumulative event rates were estimated by the Kaplan–Meier method and compared using the log rank test. Hazard ratios and confidence intervals were generated using a multivariable Cox regression model. This analysis was then adjusted based on the Propensity Score (PS) calculated for each group according to the clinical and procedural characteristics that differentiated them. A 2-sided P value <.05 was considered as statistically significant. All analyses were performed with SPSS software, version 25.0 (IBM Corp., Armonk, NY) and Prism 10.0 (GraphPad, Software, Boston, MA 02110).

Results

A total of 1171 patients have been enrolled. ACEF and PARIS score were calculated for each patient and then grouped into tertiles (low, medium, and higher risk) of either ACEF score: Group 1 (n = 405, ACEF *score* <1.20), Group 2 (n = 384, ACEF *score* ≥1.20 and ≤1.52), and Group 3 (n = 382, ACEF *score* >1.52) or PARIS score: Group 1 (n = 451, PARIS score <6), Group 2 (n = 409, PARIS score ≥6 and <8), and Group 3 (n = 311, PARIS score ≥8). Baseline clinical characteristics and medical therapy at discharge are presented in Table 1.

At the PS adjusted Cox analysis (Table 2), the incidence of MACCE was significantly greater in patients included in ACEF score group 3 [58 patients (15%)] compared with group

Table 1. Baseline clinical characteristics and therapy at discharge.

	PARIS score				ACEF score			
	I *n* = 451	II *n* = 409	III *n* = 311	*P*	I *n* = 405	II *n* = 384	III *n* = 382	*P*
Age (years)	63 ± 12	65 ± 13	71 ± 13	<0.001	55 ± 11	69 ± 9	75 ± 9	<0.001
Age >75 years, n (%)	64 (14)	108 (26)	127 (41)	<0.001	14 (3)	89 (23)	196 (51)	<0.001
Male sex, n (%)	356 (79)	293 (72)	198 (64)	<0.001	326 (80)	267 (69)	254 (66)	<0.001
BMI (Kg/m^2)	28 ± 3	27 ± 4	24 ± 4	<0.001	27 ± 4	27 ± 4	26 ± 4	0.001
LVEF (%)	50 ± 10	49 ± 12	48 ± 15	0.24	57 ± 15	51 ± 6	40 ± 8	<0.001
LVEF <40%, n (%)	70 (15)	85 (21)	100 (32)	<0.001	11 (3)	29 (8)	215 (56)	<0.001
Previous myocardial infarction, n (%)	78 (17)	71 (17)	64 (21)	0.44	61 (15)	50 (13)	102 (27)	<0.001
Previous PCI, n (%)	82 (18)	73 (18)	76 (24)	0.05	59 (15)	74 (19)	98 (26)	<0.001
Previous stroke, n (%)	9 (2)	19 (5)	16 (5)	0.04	7 (2)	19 (5)	18 (5)	<0.001
PAD, n (%)	20 (4)	32 (8)	36 (12)	<0.001	19 (5)	26 (7)	43 (11)	0.002
Hypertension, n (%)	314 (70)	274 (67)	229 (74)	0.15	238 (59)	279 (73)	300 (78)	<0.001
Hyperlipidemia, n (%)	249 (55)	204 (50)	157 (50)	0.23	201 (50)	218 (57)	191 (50)	0.08
Chronic Kidney disease (eGFR<30 mL/min), n (%)	1 (0)	6 (2)	45 (15)	<0.001	0 (0)	5 (1)	47 (12)	<0.001
Current smoker, n (%)	139 (31)	235 (57)	185 (59)	<0.001	264 (65)	165 (43)	130 (34)	<0.001
Familiar History, n (%)	150 (33)	117 (29)	68 (22)	0.003	138 (34)	121 (31)	76 (20)	<0.001
Diabetes mellitus	107 (24)	99 (24)	103 (33)	0.007	71 (17)	102 (27)	136 (36)	<0.001
Indication to PCI, n (%)				0.005				0.25
STEMI	232 (51)	209 (51)	126 (40)		184 (45)	187 (49)	196 (51)	
NSTEMI/unstable angina	2019 (49)	200 (49)	185 (60)		221 (55)	197 (51)	186 (49)	
Treatment strategy, n (%)				0.13				0.12
CABG	14 (3)	12 (3)	9 (2)		14 (4)	12 (3)	9 (2)	
PCI	350 (86)	312 (81)	315 (82)		350 (87)	312 (81)	315 (82)	
Medical therapy, n (%)	41 (10)	60 (16)	58 (15)		40 (10)	59 (15)	58 (15)	
DES, n (%)	350 (95)	301 (96)	212 (95)	0.02	302 (95)	284 (96)	277 (96)	0.72
SAPT	26 (6)	30 (7)	21 (7)	0.64	29 (7)	20 (5)	28 (7)	0.42
DAPT	419 (93)	372 (91)	280 (90)	0.34	367 (91)	356 (93)	348 (91)	0.55

Abbreviations: BMI = Body Mass Index; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; PAD = peripheral artery disease; STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment elevation; CABG = Coronary artery bypass graft; DES = drug eluting stent; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; ASA = acetylsalicylic acid.

1 [14 patients (3%); Hazard Risk (HR): 4.03 (2.15–7.54) $P <$ .001] and group 2 [26 patients (7%), HR: 2.22 (1.40–3.54) $P <$ .001]. Similarly, the incidence of NACE was significantly greater in patients included in ACEF score group 3 [71 patients (24%)] compared with group 1 [26 patients (9%), HR: 2.45 (1.50–4.01) $P <$ .001] and group 2 [40 patients (15%), HR: 1.65 (1.11-2.45) $P <$ .001]. Similar results were observed when patients were grouped according to the PARIS score (Table 3); the incidence of MACCE was significantly greater in patients included in group 3 [51 patients (16%)] compared with group 1 [26 patients (6%) HR: 2.31 (1.41–3.80) $P <$ .001] and group 2 [21 patients (5%), HR: 3.01 (1.80–5.03) $P <$ .001]. As already observed for ACEF score, the incidence of NACE was significantly greater in patients included in PARIS score group 3 [64 patients (28%)] as compared with group 1 [37 patients (11%), HR: 2.03 (1.32–3.11) $P <$ .001] and group 2 [36 patients (12%), HR: 2.20 (1.44–3.30) $P <$ .001].

At the Kaplan–Meier analysis (Figure 1), both MACCE and NACE free survival was significantly lower in patients included in the group 3 of both PARIS (respectively, long rank: 24.04, $P <$ .001 and long rank: 25.0, $P <$ .001) and ACEF score (respectively, long rank: 36.0, $P <$ .001 and long rank: 23.35, $P <$ .001).

In addition, at the ROC analysis (Figure 2), both the ACEF and the PARIS scores showed a similar moderate accuracy in predicting NACE at 1 year follow-up (AUC ACEF score: 0.70 (0.64–0.75) vs PARIS score: 0.65 (0.60–0.71), $P <$ .001, ΔAUC: 0.05, $P =$ .27). At the same time, both the ACEF and the PARIS scores showed a similar moderate accuracy in predicting MACCE at 1 year follow-up (AUC ACEF score: 0.70 (0.65–0.80) vs PARIS score: 0.65 (0.60–0.71), $P <$ .001, ΔAUC: 0.05, $P =$ .23).

At logistic regression analysis, a significant direct association was observed between ACEF score, as a continuous variable, and the occurrence of MACCE or NACE at 12 months of follow-up [respectively, HR: 1.66 (1.44–1.91) and HR: 1.56 (1.36–1.80)]. Respectively, a 66% and 56% increase in risk of MACCE and NACE was observed for each 0.50 unit increase in ACEF score. Similarly, a significant direct association was observed between the PARIS score, as a

Table 2. One-year clinical outcomes for patients grouped according ACEF score tertiles.

	ACEF 1T *n* = 405	ACEF 2T *n* = 384	Unadjusted HR	p	PS adjusted HR	p	ACEF 3T *n* = 382	Unadjusted HR	p	PS adjusted HR	p
Death, n (%)	4 (1)	12 (4)					46 (16)				
	Reference		3.13 (1.01–9.72)	0.05				11.5 (4.14–31.94)	<0.001		
		Reference						3.72 (1.97–7.03)	<0.001		
Major Bleeding, n (%)	2 (1)	5 (2)					9 (3)				
	Reference		2.60 (0.50–13.40)	0.25				4.51 (0.97–20.90)	0.05		
		Reference						1.80 (0.60–5.30)	0.30		
TVR, n (%)	6 (2)	5 (2)					7 (2)				
	Reference		0.90 (0.30–2.83)	0.81				1.20 (0.40–3.54)	0.75		
		Reference						1.40 (0.44–4.35)	0.60		
MI, n (%)	4 (1)	9 (3)					15 (5)				
	Reference		2.40 (0.73–7.70)	0.15				3.80 (1.30–11.50)	0.02		
		Reference						1.62 (0.71–3.70)	0.25		
Stroke, n (%)	1 (0)	4 (1)					3 (1)				
	Reference		4.17 (0.50–37.32)	0.20				2.93 (0.30–28.24)	0.35		
		Reference						0.75 (0.17–3.34)	0.70		
Stroke + TVR + MI n (%)	11 (4)	18 (7)					25 (8)				
	Reference		1.71 (0.81–3.63)	0.16				2.31 (1.14–4.71)	0.02		
		Reference						1.40 (0.74–2.50)	0.32		
MACCE, n (%)	14 (3)	26 (7)					58 (15)				
	Reference		2.03 (1.06–3.90)	0.03	1.82 (0.93–3.57)	0.08		4.70 (2.61–8.40)	<0.001	4.03 (2.15–7.54)	<0.001
		Reference						2.33 (1.50–3.70)	<0.001	2.22 (1.40–3.54)	<0.001
NACE, n (%)	26 (9)	40 (15)					71 (24)				
	Reference		1.60 (1.01–2.63)	0.06	1.50 (0.90–2.50)	0.13		2.80 (1.80–4.40)	<0.001	2.45 (1.50–4.01)	<0.001
		Reference						1.74 (1.20–2.60)	<0.001	1.65 (1.11–2.45)	0.01

Table 3. One-year clinical outcomes for patients grouped according PARIS score tertiles.

	PARIS 1T *n* = 451	PARIS 2T *n* = 409	Unadjusted HR	*P*	PS adjusted HR	*P*	PARIS 3T *n* = 311	Unadjusted HR	*P*	PS adjusted HR	*P*
Death, n (%)	10 (3)	13 (4)					39 (17)				
	Reference		1.47 (0.65–3.34)	0.35				5.89 (2.94–11.80)	<0.001		
		Reference						3.95 (2.11–7.41)	<0.001		
Major Bleeding, n (%)	3 (1)	5 (2)					8 (3)				
	Reference		2.0 (0.46–8.0)	0.38				4.10 (1.10–15.47)	0.04		
		Reference						2.11 (0.70–6.46)	0.20		
TVR, n (%)	8 (2)	3 (1)					7 (2)				
	Reference		0.42 (0.11–1.60)	0.20				1.34 (0.50–3.70)	<0.001		
		Reference						3.14 (0.81–12.16)	0.09		
MI, n (%)	11 (3)	4 (1)					13 (6)				
	Reference		0.41 (0.13–1.30)	0.13				1.81 (0.81–4.05)	0.15		
		Reference						4.35 (1.42–13.35)	0.01		
Stroke, n (%)	3 (1)	1 (0)					4 (2)				
	Reference		0.40 (0.04–3.65)	0.40				2.04 (0.46–9.11)	0.35		
		Reference						5.40 (0.60–48.20)	0.13		
Stroke + TVR +MI n (%)	21 (6)	10 (3)					23 (10)				
	Reference		0.54 (0.25–1.14)	0.11				1.70 (0.92–3.02)	0.09		
		Reference						3.11 (1.48–6.53)	<0.001		
MACCE, n (%)	26 (6)						51 (16)				
	Reference	21 (5)	0.90 (0.50–1.58)	0.70	0.86 (0.47–1.53)	0.60		3.11 (1.48–6.53)	<0.001	2.31 (1.41–3.80)	<0.001
		Reference						3.40 (2.02–5.60)	<0.001	3.01 (1.80–5.03)	<0.001
NACE, n (%)	37 (11)	36 (12)					64 (28)				
	Reference		1.12 (0.70–1.77)	0.64	1.06 (0.66–1.70)	0.80		2.70 (1.80–4.02)	<0.001	2.03 (1.32–3.11)	<0.001
		Reference						2.40 (1.60–3.60)	<0.001	2.20 (1.44–3.30)	0.01

Abbreviations: HR = hazard ratio; TVR = target vessel revascularization; MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; NACE = net adverse cardiovascular events; PS: Propensity Score; T = tertile.

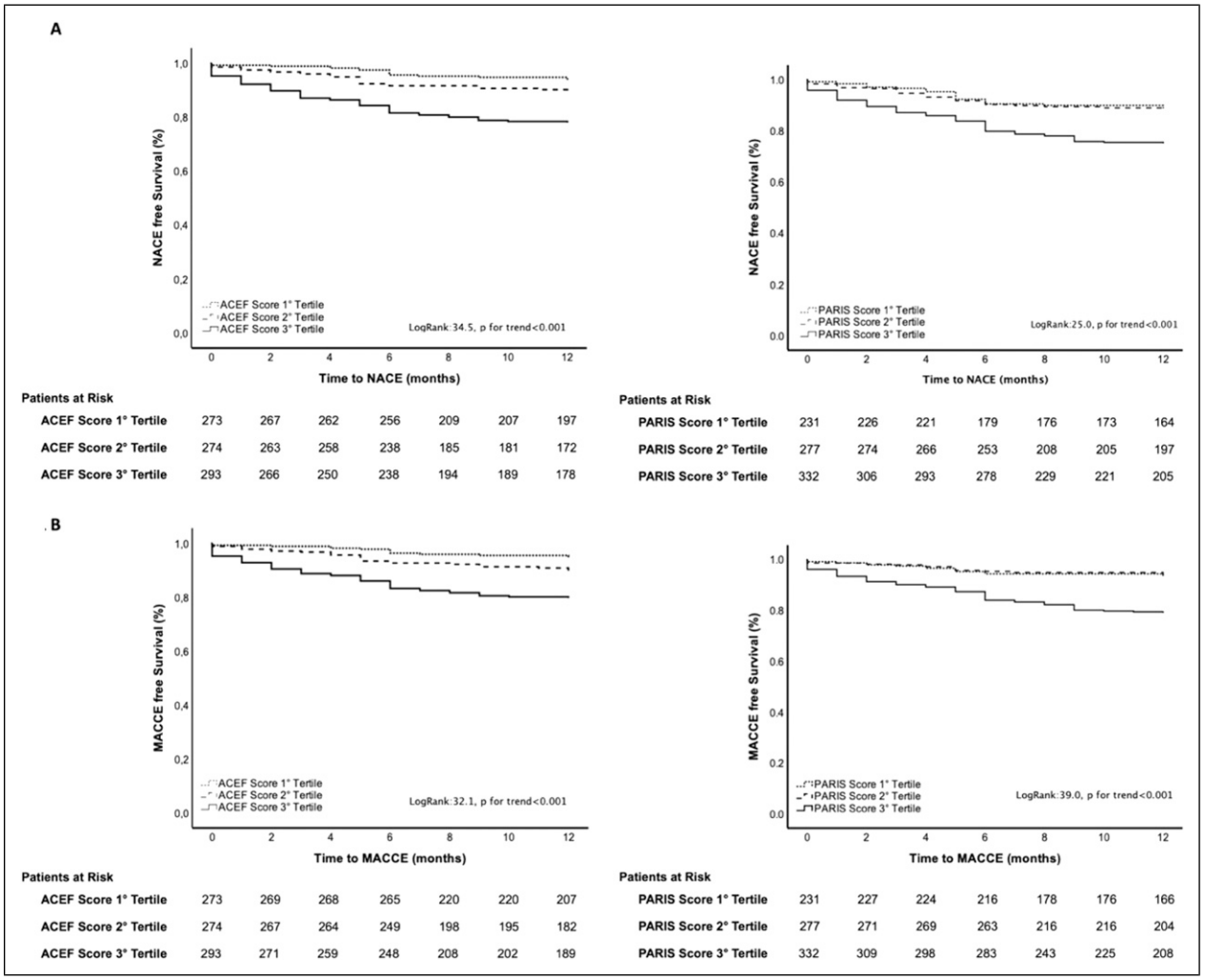

Figure 1. One-year free survival from NACE and MACE. Panel A, Kaplan–Meier curves for survival free from net adverse cardiovascular events (NACE) according to ACEF and PARIS scores (respectively, long rank: 23.35, $P < .001$ and long rank: 25.00, $P < .001$). Panel B, Kaplan–Meier curves for survival free from major adverse cardiac and cerebrovascular events according to ACEF and PARIS scores (respectively, long rank: 36.00, $P < .001$ and long rank: 24.04, $P < .001$).

continuous variable, and the occurrence of both MACCE and NACE at 12 months of follow-up [respectively, HR: 1.26 (1.16–1.37) and HR: 1.20 (1.11–1.30)], with a 26% increase in the risk of MACCE and 20% in the risk of NACE for each increase of 1 unit of PARIS score (Figure 3).

Discussion

The main result of the present study is that, in a real-world population of the START ANTIPLATELET registry, the ACEF score, a risk score very easy to calculate, was equally useful to risk-stratify ACS patients as compared with the more complex and widely validated PARIS score. In fact, patients with the highest values of both ACEF and PARIS scores showed a significantly higher rate of NACE and MACCE at one-year follow-up.

With the rapidly expanding indications for invasive assessment in patients presenting with ACS and several comorbidities, risk assessment has become a very important aspect of daily practice to guide clinical decision making. Several risk scores have been proposed to calculate risk stratification at different timepoints of patient clinical history. Some of them such as the Emergency Department Assessment of Chest pain Score (EDACS),[15] or the Troponin-only Manchester Acute Coronary Syndromes (T-MACS)[16] or the Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker (ADAPT-ADP)[17] were considered at patient initial presentation, in order to, first, identify patients at low risk for major adverse cardiac events (MACE) and second, as a decision rule to decide whether these patients needed additional invasive testing or not. Other risk scores are available to estimate the in-hospital or short-term risk of mortality and/or

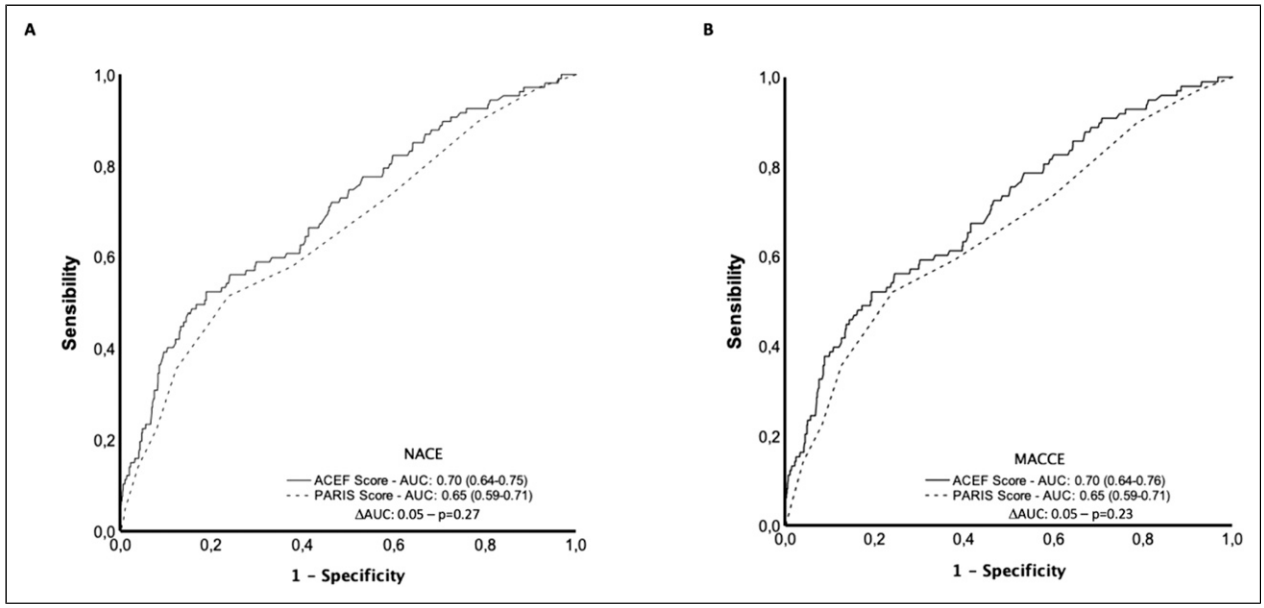

Figure 2. Receiver operating characteristic curve analysis for ACEF and PARIS scores. Panel A. Both the ACEF and the PARIS scores showed a similar moderate accuracy in predicting NACE at 1 year follow-up (AUC ACEF score: 0.70 (0.64–0.75) vs PARIS score: 0.65 (0.60–0.71), $P < .001$, ΔAUC: 0.05, $P = .27$). Panel B. Both the ACEF and the PARIS scores showed a similar moderate accuracy in predicting MACCE at 1 year follow-up (AUC ACEF score: 0.70 (0.65–0.80) vs PARIS score: 0.65 (0.60–0.71), $P < .001$, ΔAUC: 0.05, $P = .23$).

bleeding in order to guide further in-hospital management and, finally, some risk scores have been developed to calculate ischemic-bleeding trade-off risk to obtain a tailored optimal antithrombotic management by estimating long-term risk for future cardiovascular events.[18] One of these scores is the PARIS score, derived by The Patterns of Nonadherence to Antiplatelet Regimens in Stented Patients (PARIS) registry, a prospective, multicenter, observational study enrolling patients treated with coronary angioplasty and stenting placement.[19] The PARIS ischemic risk score predicts the risk of stent thrombosis and myocardial infarction for up to 2 years after coronary intervention. It includes several items: acute coronary syndrome (ACS), current smoking, diabetes mellitus, creatinine clearance <60 mL/min, prior PCI, and prior coronary artery bypass grafting (CABG). Moreover, to be more accurate, it is necessary to know whether the diabetic patients need insulin or not and the troponins values. Similarly, the PARIS score for bleeding risk has several items to know to be calculated: age, BMI, smoking, creatinine clearance, triple antithrombotic therapy, and anemia. Thus, these two scores might be considered not easy to calculate and, consequently, not routinely used in the clinical practice.

The age, creatinine, and ejection fraction (ACEF) score is a simpler cardiovascular risk score that has been demonstrated to have predictive value in patients with cardiovascular disease. Several studies clearly showed that this score has good predictive value for adverse cardiovascular events associated with an increased risk of all-cause mortality and stroke.[20–23] Moreover, the ACEF score was previously associated with satisfactory predictive value not only in terms of short- and long-term mortality, adverse cardiac and cerebrovascular events, but also other clinical events including bleeding after PCI.[21,24,25] Of note, although the ACEF score needs only three items to be calculated, previous studies have found that this score has an impressive prognostic performance compared with other more complex scores.[26–28] In line with these studies, we observed that ACEF and PARIS score were comparable in indicating the incidence of MACCE and NACE in the three groups of patients who had a different risk profile, low, medium, and high. These results might be considered of great importance from a clinical point of view because only three items, very easy to collect in clinical practice, permit to have a complete evaluation on both risk profiles, ischemic and bleeding, finally leading to better risk stratification allowing a more optimal therapeutic strategy.

In daily clinical practice, risk scores might be considered useful to evaluate patient treatment. The "ideal" risk score should be simple to calculate, accessible at the bedside, and easy to interpret. Thus, it should be the compass for the physician, helping clinical decisions and choosing optimal medical therapy. The ACEF score meets these criteria since it is user friendly and quick to apply. Originally designed to assess the risk of elective cardiac surgery,[4] this score has been evaluated in several subgroups of patients treated in the cath-lab with coronary stenting such as those with left main disease, bifurcations, calcified lesions, total occlusions, or those treated with valve implantation for severe aortic stenosis.[4,6,26,28–30] Then, as reported above, it has been investigated in the clinical setting of ACS and results of the present study involves this

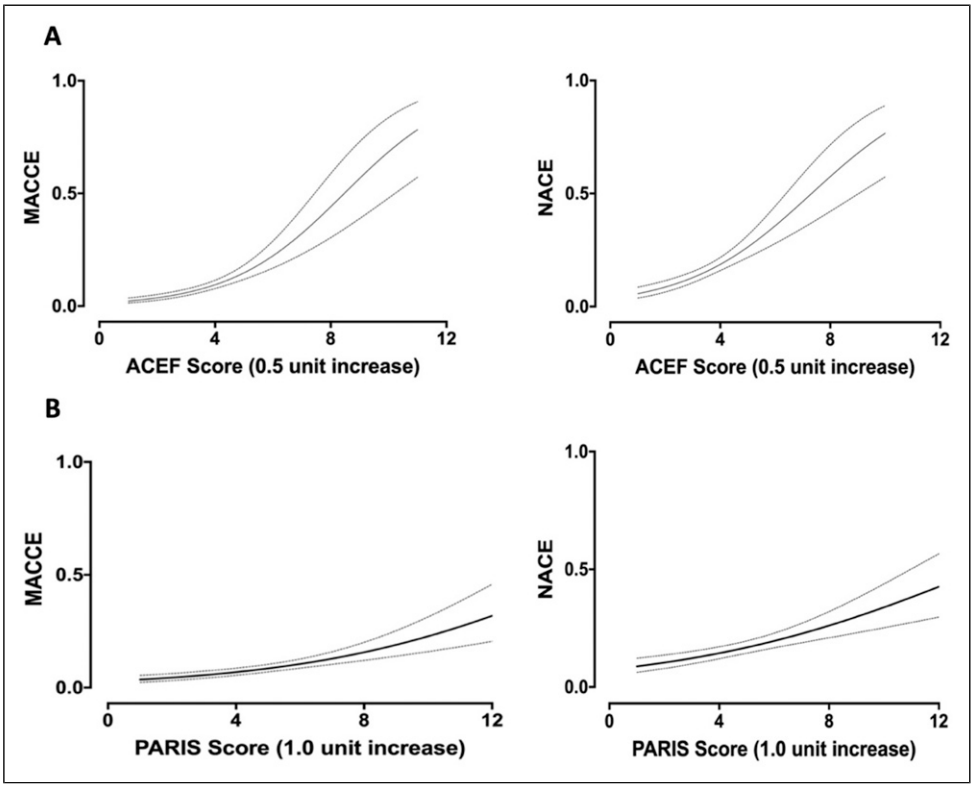

Figure 3. Risk of NACE and MACCE at 1 year follow-up for each unit increase of ACEF and PARIS scores. Panel A. A significant direct association was observed between ACEF score, as a continuous variable, and the occurrence of MACCE or NACE at 12 months of follow-up [respectively, HR: 1.66 (1.44–1.91) and HR: 1.56 (1.36–1.80)]. A 66% and 56% increase in risk of MACCE and NACE, respectively, was observed for each 0.50 unit increase in ACEF score. Panel B. A significant direct association was observed between the PARIS score, as a continuous variable, and the occurrence of both MACCE and NACE at 12 months of follow-up [HR: 1.26 (1.16–1.37) and HR: 1.20 (1.11–1.30), respectively], with a 26% increase in the risk of MACCE and 20% in the risk of NACE for each increase of 1 unit of PARIS score.

patient subset.[20,22,25] Finally, the predictive value of ACEF scores has been demonstrated for identifying the risk of cardiovascular disease or stroke also in individuals without a cardiovascular history.[30] Taken together, all these observations, suggest that this simple to use risk score might have important potential implications for clinical practice across different healthcare settings.

This study has several inherent limitations related to its retrospective nature. Of note, the scores have been calculated at baseline without assessing changes at discharge or during follow-up, thereby we cannot evaluate the impact of any therapeutic strategy on the clinical follow-up. In addition, since our hypothesis has been investigated in a small patient population, future larger and prospective studies are necessary to validate our results.

In conclusion, the results of the present study sustain the experimental hypothesis that a risk score can be developed based on a very limited number of risk factors in conflict with the general hypothesis that the higher the number of items considered, the more accurate and better calibrated the model will be. This agrees with the aphorism *"less is more"* by Ludwig Mies van der Rohe to indicate that simplicity is preferable to complexity.[31]

Declaration of Conflicting Interests

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References

1. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023;44:3720-3826.
2. Timmis A, Vardas P, Townsend N, et al. European Society of Cardiology: cardiovascular disease statistics 2021. Eur Heart J. 2022;43:716-799.

3. Baber U, Mehran R, Giustino G, et al. Coronary thrombosis and major bleeding after PCI with drug-eluting stents: risk scores from PARIS. J Am Coll Cardiol. 2016;67:2224-2234.
4. Ranucci M, Castelvecchio S, Menicanti L, Frigiola A, Pelissero G. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. Circulation. 2009;119:3053-3061.
5. Ranucci M, Castelvecchio S, Conte M, et al. The easier, the better: age, creatinine, ejection fraction score for operative mortality risk stratification in a series of 29,659 patients undergoing elective cardiac surgery. J Thorac Cardiovasc Surg. 2011;142:581-586.
6. Wykrzykowska JJ, Garg S, Onuma Y, et al. Value of age, creatinine, and ejection fraction (ACEF score) in assessing risk in patients undergoing percutaneous coronary interventions in the 'All-Comers' LEADERS trial. Circ Cardiovasc Interv. 2011;4:47-56.
7. Di Serafino L, Borgia F, Maeremans J, et al. The age, creatinine, and ejection fraction score to risk stratify patients who underwent percutaneous coronary intervention of coronary chronic total occlusion. Am J Cardiol. 2014;114:1158-1164.
8. Arai T, Lefèvre T, Hayashida K, et al. Usefulness of a simple clinical risk prediction method, modified ACEF score, for transcatheter aortic valve implantation. Circ J. 2015;79:1496-1503.
9. Antonucci E, Poli D, Tosetto A, et al. The Italian START-register on anticoagulation with focus on atrial fibrillation. PLoS One. 2015;10:e0124719.
10. Marcucci R, Patti G, Calabrò P, et al. Antiplatelet treatment in acute coronary syndrome patients: real-world data from the START-Antiplatelet Italian Registry. PLoS One. 2019;14: e0219676.
11. Cirillo P, Di Serafino L, Taglialatela V, et al. Optimal medical therapy on top of dual-antiplatelet therapy: 1-year clinical outcome in patients with acute coronary syndrome: the START antiplatelet registry. Angiology. 2020;71:235-241.
12. Garcia-Garcia HM, McFadden EP, Farb A, et al. Standardized end point definitions for coronary intervention trials: the academic research consortium-2 consensus document. Eur Heart J. 2018;39:2192-2207.
13. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44:2064-2089.
14. Rao AK, Pratt C, Berke A, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial--phase I: hemorrhagic manifestations and changes in plasma fibrinogen and the fibrinolytic system in patients treated with recombinant tissue plasminogen activator and streptokinase. J Am Coll Cardiol. 1988;11:1-11.
15. Than M, Flaws D, Sanders S, et al. Development and validation of the emergency department assessment of chest pain score and 2 h accelerated diagnostic protocol. Emerg Med Australasia (EMA). 2014;26:34-44.
16. Body R, Carlton E, Sperrin M, et al. Troponin-only manchester acute coronary syndromes (T-MACS) decision aid: single biomarker re-derivation and external validation in three cohorts. Emerg Med J. 2017;34:349-356.
17. Than M, Cullen L, Aldous S, et al. 2-Hour accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponins as the only biomarker: the ADAPT trial. J Am Coll Cardiol. 2012;59:2091-2098.
18. Chan P, Yin D, Azzahhafi J, James S. Risk assessment using risk scores in patients with acute coronary syndrome. J Clin Med. 2020;9.
19. Mehran R, Baber U, Steg PG, et al. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. Lancet. 2013;382:1714-1722.
20. Gao S, Ma W, Huang S, Lin X, Yu M. Predictive value of the age, creatinine, and ejection fraction score in patients with myocardial infarction with nonobstructive coronary arteries. Clin Cardiol. 2021;44:1011-1018.
21. Stähli BE, Wischnewsky MB, Jakob P, et al. Predictive value of the age, creatinine, and ejection fraction (ACEF) score in patients with acute coronary syndromes. Int J Cardiol. 2018;270:7-13.
22. Liu L, Yang X, Gu Y, Jiang T, Xu J, Xu M. Predictive value of the age, creatinine, and ejection fraction (ACEF) score in patients with acute fulminant myocarditis. Front Physiol. 2021;12: 596548.
23. Reindl M, Reinstadler SJ, Tiller C, et al. ACEF score adapted to ST-elevation myocardial infarction patients: the ACEF-STEMI score. Int J Cardiol. 2018;264:18-24.
24. Dziewierz A, Siudak Z, Rakowski T, Zasada W, Krzanowska K, Dudek D. The ACEF (age, creatinine, ejection fraction) score predicts ischemic and bleeding outcomes of patients with acute coronary syndromes treated conservatively. Postepy Kardiol Interwencyjnej. 2017;13:160-164.
25. Pelliccia F, Gaudio C. The ACEF score in patients undergoing percutaneous coronary intervention: "Keep it simple and focus on what matters". Int J Cardiol. 2019;286:54-55.
26. Pyxaras SA, Mangiacapra F, Wijns W, et al. ACEF and clinical SYNTAX score in the risk stratification of patients with heavily calcified coronary stenosis undergoing rotational atherectomy with stent implantation. Cathet Cardiovasc Interv. 2014;83:1067-1073.
27. Pyxaras SA, Mangiacapra F, Wijns W, et al. ACEF and clinical SYNTAX score in the risk stratification of patients with heavily calcified coronary stenosis undergoing rotational atherectomy with stent implantation. Cathet Cardiovasc Interv. 2014;83: 1067-1073.
28. Capodanno D, Caggegi A, Miano M, et al. Global risk classification and clinical SYNTAX (synergy between percutaneous coronary intervention with TAXUS and cardiac surgery) score in patients undergoing percutaneous or surgical left main revascularization. JACC Cardiovasc Interv. 2011;4:287-297.
29. D'Ascenzo F, Ballocca F, Moretti C, et al. Inaccuracy of available surgical risk scores to predict outcomes after transcatheter aortic valve replacement. J Cardiovasc Med (Hagerstown). 2013;14:894-898.
30. Xiong S, Yin S, Deng W, et al. Predictive value of the age, creatinine, and ejection fraction (ACEF) score in cardiovascular disease among middle-aged population. J Clin Med. 2022;11:6609.
31. Sennott RS. Encyclopedia of twentieth century architecture. Fitzroy Dearborn, 2005,vol 2.