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Bleeding risk in patients with acute coronary syndrome in a Turkish population: Results from the Turkish Acute Coronary Syndrome Registry (TACSER) study

Eyüp Avci[1] | **Tuncay Kiriş**[2] | **Didar Elif Akgün**[1] | **Aykan Celik**[2] | **Filiz Akyildiz Akçay**[2] | **Burak Acar**[3] | **Özge Kurmuş**[4] | **Rojuva Altındag**[5] | **Özgen Safak**[1] | **Abdullah Orhan Demirtas**[6] | **Tuncay Güzel**[7] | **Önder Öztürk**[5] | **Tarik Yildirim**[1] | **Umit Yüksek**[8] | **Asim Oktay Ergene**[9]

[1]Department of Cardiology, Medical School, Balikesir University, Balikesir, Turkey

[2]Department of Cardiology, Ataturk Training and Research Hospital, Izmir Katip Celebi University, Izmir, Turkey

[3]Department of Cardiology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey

[4]Department of Cardiolog, Faculty of Medicine, Ufuk University, Ankara, Turkey

[5]Department of Cardiology, Diyarbakır Gazi Yasargil Training and Research Hospital, Health Sciences University, Diyarbakır, Turkey

[6]Department of Cardiology, Adana Training and Research Hospital, Health Sciences University, Adana, Turkey

[7]Department of Cardiology, Faculty of Medicine, Dicle University, Diyarbakır, Turkey

[8]Department of Cardiology, Faculty of Medicine, Near East University, Lefkoşa, Turkey

[9]Department of Cardiology, Faculty of Medicine, Dokuz Eylul University, İzmir, Turkey

Correspondence
Tuncay Kiriş, Department of Cardiology, Izmir Katip Celebi University, Ataturk Training and Research Hospital, Izmir, Turkey.
Email: drtkiris@hotmail.com

Abstract

Objective: Bleeding is one of the most important causes of mortality in patients with acute coronary syndrome (ACS). This study therefore aimed to investigate bleeding risk in patients with ACS who were scheduled to receive dual antiplatelet therapy (DAPT) in Turkey.

Methods: This was a multicentre, observational, cross-sectional cohort study. The study population included 963 patients with ACS from 12 centres in Turkey. We used the Predicting Bleeding Complication in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy (PRECISE-DAPT) score to predict the bleeding risk for all the patients. The patients were divided into high (≥25) or low (˂25) bleeding risk groups based on their PRECISE-DAPT scores.

Results: The mean PRECISE-DAPT score was 21.9. Overall, 32.2% of the patients had high PRECISE-DAPT scores (≥25). Compared with the male patients, the female patients had higher PRECISE-DAPT scores (28.2 ± 15.7 vs 18.4 ± 13.6, P ˂ .001). Among the females, the rate of patients with a PRECISE-DAPT score ≥25 was 53%, while among the male patients, the score occurred at a rate of 22%. The female patients had lower haemoglobin (Hb) levels than the male patients (12.1 ± 1.7 vs 13.8 ± 1.9, P ˂ .001) and lower creatinine clearance (70.7 ± 27.5 vs 88.7 ± 26.3, P ˂ .001). The in-hospital bleeding rates were higher among the patients with high PRECISE-DAPT scores than among those who did not have high scores. Furthermore, the patients with high PRECISE-DAPT scores had a higher in-hospital mortality rate compared with those with low PRECISE-DAPT scores (1% vs 0%, P = .11).

Conclusions: The mean PRECISE-DAPT score was high among the patients with ACS in this study, indicating that the bleeding tendency was high. This study showed

The following authors are collaborators: Bihter Sentürk (Department of Cardiology, Faculty of Medicine, Dokuz Eylul University, İzmir, Turkey), Zihni Aktas (Department of Cardiology, Ministiration of Health Balıkesir Atatürk City Hospital, Balıkesir, Turkey).

that the PRECISE-DAPT score may help physicians determine the type and duration of DAPT, especially in patients with ACS in Turkey.

KEYWORDS

acute coronary syndrome, dual antiplatelet therapy, PRECISE-DAPT score

1 | INTRODUCTION

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor reduces ischaemic relapses in patients with coronary artery disease who have been treated with coronary stents [1]. However, this benefit is counterbalanced by a higher risk of bleeding, which is linearly associated with the duration of treatment.[1–3] Both ischaemic and bleeding risk have the potential to adversely affect prognosis.[4] As a result, 12 months of DAPT is recommended after stenting; however, the optimal duration of treatment is still under review.[5]

Shortening the DAPT period from 12 months to 6 or 3 months can significantly reduce the bleeding rate.[2] However, long-term treatment (ie lasting more than 12 months) reduces the occurrence of stent-related and stent-unrelated ischaemic events in selected patients who tolerate the first year of treatment without bleeding.[2,6]

International guidelines encourage the determination of bleeding risk prior to the selection of treatment duration and recommend a treatment regimen of less than 12 months in patients with a high risk of bleeding. Determining a patient's Predicting Bleeding Complication in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy (PRECISE-DAPT) score is currently recommended to reduce the risk of bleeding at the onset of DAPT.[5,7]

In this study, we aimed to evaluate bleeding risk in patients undergoing percutaneous coronary intervention (PCI) or those suffering acute coronary syndrome (ACS) who were scheduled to receive DAPT in Turkey.

2 | METHODS

This was a multicentre, observational, cross-sectional cohort study conducted in Turkey in which the mean PRECISE-DAPT score for ACS patients requiring DAPT was determined. A total of 963 consecutive ACS patients between January 2018 and January 2019 were included to the study. Patients aged 18 years or older who underwent coronary angiography for ACS and who were scheduled to receive DAPT for stent implantation were included in the study, irrespective of their treatment prior to hospital admission. The exclusion criteria were patients who could not be informed verbally of the study or did not provide approval to participate in the study, patients under the age of 18 years, pregnant women, patients with a life expectancy of less than one year, patients with contraindications to DAPT or who could not receive DAPT for any reason and patients with an intolerance to aspirin or P2Y12 inhibitors. In addition, patients who underwent coronary angiography following mechanical complications were not included in the study. The final study population consisted of 963 patients. Consent forms were obtained from all the patients who participated in the study. The study was approved by the ethics committee of the Balikesir University Faculty of Medicine (NCT03601013).

The demographic and clinical characteristics of the patients included hypertension (HT), diabetes mellitus (DM), hyperlipidemia, heart failure, peripheral arterial disease, chronic obstructive pulmonary disease, previous stroke/cerebrovascular incidents, chronic renal failure and a history of dialysis, and these were recorded on admission. The patients' body mass index (BMI) was calculated as weight [kg]/(height [cm]).[2] Medications that were in active use by patients, previous ACS and the revascularization strategy of the patients, such as PCI or coronary artery bypass graft (CABG), were also recorded. Biochemical markers and the international normalized ratio (INR) values of the patients were measured before they underwent coronary angiography. The cardiac rhythms observed during hospitalization were also recorded. The risk of bleeding was calculated using the PRECISE-DAPT score. To determine a PRECISE-DAPT score, each patient's haemoglobin (Hb) level, leucocyte level, creatinine clearance, age and bleeding risk were evaluated; in this study, the PRECISE-DAPT scores were calculated using an online calculator (http://www.precisedaptscore.com/predapt/). Creatinine clearance was calculated using the Modification of Diet in Renal Disease (MDRD) formula and presented as mL/min.[8]

The patients were grouped based on their PRECISE-DAPT scores as either high bleeding risk ($\geq$25) or low bleeding risk ($<$25). In addition, the risk of bleeding was calculated using HAS-BLED scores in all the patients. HAS-BLED scores include the presence of hypertension, impaired renal and hepatic function, stroke, bleeding history or bleeding conditions, labile INR, alcohol or drug use, and being 65 years or older, with one point given for each factor present.[9] Also, the Patterns of Nonadherence Regimens in Stented Patients (PARIS) risk score was calculated in all patients.[10] The revascularization strategy of the patients was determined in light of the European Society of Cardiology (ESC) 2018 revascularization guideline, and medical therapies were applied according to the ESC 2017 focused update on DAPT in coronary artery disease.[11]

TABLE 1 Baseline characteristics of the study population

Variables	PRECISE-DAPT < 25 (n = 655)	PRECISE-DAPT ≥ 25 (n = 308)	*P*-value
Age (y)	60.7 ± 10.3	71.3 ± 9.9	<.001
Female n (%)	148 (23)	162 (53)	<.001
Previous PAD n (%)	30 (5)	25 (8)	.027
Previous COPD n (%)	54 (8)	40 (13)	.021
Previous heart failure n (%)	96 (15)	63 (21)	.024
Previous stroke n (%)	19 (3)	18 (6)	.027
Hypertension n (%)	356 (54)	224 (73)	<.001
Diabetes mellitus n (%)	221 (34)	155 (50)	<.001
Dyslipidemia n (%)	208 (32)	109 (35)	.263
Anaemia n (%)	128 (20)	183 (59)	<.001
Previous bleeding n (%)	0 (0)	94 (31)	<.001
Current smoking n (%)	296 (45)	64 (21)	<.001
History of alcohol consumption n (%)	64 (10)	12 (4)	.002
Chronic renal failure n (%)	23 (4)	162 (54)	<.001
Under dialysis treatment n (%)	1 (1)	11 (4)	<.001
Clinical presentation			
STEMI n (%)	160 (24)	56 (18)	.030
USAP/NSTEMI n (%)	495 (76)	252 (82)	
Rhythm			
Sinus n (%)	635 (97)	282 (92)	<.001
Atrial fibrillation n (%)	25 (4)	30 (10)	<.001
Ventricular tachycardia n (%)	6 (1)	1 (0)	.314
Ventricular fibrillation n (%)	5 (1)	1 (0)	.420
In-hospital bleeding			
Major bleeding n (%)	2 (0)	21 (7)	<.001
Minor bleeding n (%)	0 (0)	29 (9)	<.001
Minimal bleeding n (%)	2 (0)	63 (21)	<.001
In-hospital mortality n (%)	11 (2)	12 (4)	.034
Medications			
Aspirin n (%)	392 (60)	211 (69)	.010
Clopidogrel n (%)	208 (32)	130 (42)	.002
Prasugrel n(%)	6 (1)	2 (1)	.671
Ticagrelor n (%)	85 (13)	26 (8)	.040
Warfarin n (%)	9 (1)	10 (3)	.051
Rivaroxaban n (%)	4 (1)	5 (2)	.128
Apixaban n (%)	1 (0)	4 (1)	.021
Dabigatran n (%)	3 (1)	5 (2)	.063
Edoxaban n (%)	3 (1)	2 (1)	.700
Beta blocker n (%)	251 (38)	131 (43)	.213
Calcium channel blockers n (%)	10 (2)	10 (3)	.081
Digoxin n(%)	4 (1)	3 (1)	.536
Antiarrhythmic drugs n (%)	9 (1)	4 (1)	.925
Statin n (%)	237 (36)	136 (44)	.018

(Continues)

TABLE 1 (Continued)

Variables	PRECISE-DAPT < 25 (n = 655)	PRECISE-DAPT ≥ 25 (n = 308)	*P*-value
Ezetimibe n (%)	1 (0)	1(0)	.584
PCSK-9 inhibitors n (%)	1 (0)	1 (0)	.584
NSAID n (%)	29 (4)	41(13)	<.001
Glycoprotein IIb/IIIa inhibitors n (%)	14 (2)	4 (1)	.546

Abbreviations: COPD, chronic obstructive pulmonary disease; NSAID, nonsteroidal anti-inflammatory drug; NSTEMI, non-STelevation myocardial infarction; PAD, peripheral arterial disease; PCSK-9, proprotein convertase subtilisin/kexin type 9; STEMI, ST-elevation myocardial infarction; USAP, unstable angina.

2.1 | Definitions

In this study, anaemia was defined based on the World Health Organization (WHO) classification: the presence of a Hb ≤ 12 g/dL for females and a Hb ≤ 13 g/dL for males. Bleeding classification was performed according to the thrombolysis in myocardial infarction (TIMI) bleeding score. A major haemorrhage was defined as a haemogram of 5 g/dL, a 15% or greater decline in haematocrit or an intracranial haemorrhage. Minor bleeding was defined as a Hb of 3-5 g/dL, a 10%-15% g/dL haematocrit decline or gastrointestinal bleeding. Minimal bleeding was defined as a Hb of <3 g/dL, a decline in haematocrit less than 10% or the presence of haematuria or nose bleeding. Two independent investigators evaluated cases of major bleeding.

2.2 | Statistical analysis

The continuous variables were presented as mean values (standard deviation [SD]) or medians with ranges, and the categorical variables were expressed as percentages. Any differences between the continuous variables were compared using the Wilcoxon rank-sum test and Student's *t* test. A chi-squared test was used for the categorical variables. We assessed calibration by using the Hosmer-Lemeshow goodness-of-fit test and plotted observed vs. predicted major bleeding. The DeLong test was used to compare the area under the curve (AUC) with each of these scores.[12] All the statistical tests were two-tailed, and a *P* value < .05 was considered significant. All the analyses were carried out using SPSS version 15 (SPSS, Inc).

3 | RESULTS

3.1 | Baseline characteristics

The mean age of the patients in the sample was 64.1 ± 11.3 years. Of the 963 patients, 653 (67.8%) were male and 310 (32.2%) were female. The baseline characteristics of the study patients are presented in Tables 1 and 2. A subgroup analysis according to gender was performed.

The patients in the high PRECISE-DAPT score group were older (71.3 ± 9.9 vs 60.7 ± 10.3 years, $P < .001$) and had a higher prevalence of bleeding history than those in the low score group (31% vs 0%, $P < .001$). Compared to the patients who had non-high PRECISE-DAPT scores, a history of heart failure, HT, DM and previous stroke were more frequent in those with high PRECISE-DAPT scores (Table 1). The in-hospital bleeding rates were higher in the patients with high PRECISE-DAPT scores than those who did not have high scores. Furthermore, the patients with high PRECISE-DAPT scores had a higher in-hospital mortality rate compared to those with low PRECISE-DAPT scores (1% vs 0%, $P = .11$). Death was observed in 3 patients with major bleeding (13%).

The female patients had higher rates of anaemia and chronic kidney disease (CKD) than their male counterparts (41.6% vs 27.9%, $P < .001$; 13% vs 6%, $P < .001$, respectively). Comparison of major bleeding in female and male population was provided in Figure 1.

3.2 | Laboratory findings

The laboratory variables of the groups are shown in Tables 3 and 4. The mean PRECISE-DAPT score of the study population was 21.9. The ratio of patients in the high score group was 32.2%. Subgroup analyses according to gender were performed. Compared with the male patients, the female patients had higher PRECISE-DAPT scores (28.2 ± 15.7 vs 18.4 ± 13.6, $P < .001$). The rate of patients with PRECISE-DAPT scores ≥25 was 53% for the female patients and 22% for the males. The high PRECISE-DAPT score group had higher leucocyte counts than the low PRECISE-DAPT score group. Those with PRECISE-DAPT scores ≥25 had lower Hb levels and lower creatinine clearance than those with scores <25. Both Hb and creatinine clearance were lower among the female patients than among the male patients (Table 4).

The differences in the clinical and laboratory characteristics between the TURCAD registry and the PRECISE-DAPT, the CardioCHUVI, the Patterns of Nonadherence Regimens in Stented Patients (PARIS) risk score, the PLATO trial and the Bern PCI registry are presented in Tables 5 and 6.

TABLE 2 Baseline characteristics of the study population

Variables	Male (n = 653)	Female (n = 310)	*P*-value
Age (y)	62.0 ± 11.1	68.5 ± 10.5	<.001
Female n (%)	148 (23)	162 (53)	<.001
Previous PAD n (%)	23 (5)	32 (7)	.116
Previous COPD n (%)	66 (10)	28 (9)	.599
Previous heart failure n (%)	100 (15)	59 (19)	.146
Previous stroke n (%)	25 (4)	12 (4)	.974
Hypertension n (%)	344 (53)	236 (76)	<.001
Diabetes mellitus n (%)	218 (33)	158 (51)	<.001
Dyslipidemia n (%)	203 (31)	114 (37)	.079
Anaemia n (%)	182 (28)	129 (42)	<.001
Previous bleeding n (%)	54 (8)	40 (13)	.024
Current smoking n (%)	303 (46)	57 (18)	<.001
History of alcohol consumption n (%)	74 (11)	2 (1)	<.001
Chronic renal failure n (%)	79 (12)	106 (34)	<.001
Under dialysis treatment n (%)	5 (1)	7 (2)	.051
Clinical presentation			
STEMI n (%)	164 (25)	52 (17)	.004
USAP/NSTEMI n (%)	258 (83)	489 (75)	
Rhythm			
Sinus n (%)	627 (96)	290 (94)	.093
Atrial fibrillation n (%)	34 (5)	21 (7)	.327
Ventricular tachycardia n (%)	5 (1)	2 (1)	.837
Ventricular fibrillation n (%)	5 (1)	1 (0)	.414
In-hospital bleeding			
Major bleeding n (%)	16 (3)	7 (2)	.855
Minor bleeding n (%)	16 (3)	13 (4)	.139
Minimal bleeding n (%)	36 (6)	29 (9)	.026
In-hospital mortality n (%)	13 (2)	10 (4)	.257
Previous medications			
Aspirin n (%)	410 (63)	193 (62)	.874
Clopidogrel n (%)	217 (33)	121 (39)	.078
Prasugrel n(%)	2 (0)	6 (1)	.009
Ticagrelor n (%)	86 (13)	25 (8)	.020
Warfarin n (%)	10 (2)	9 (3)	.153
Rivaroxaban n (%)	4 (1)	5 (2)	.132
Apixaban n (%)	2 (0)	3 (1)	.182
Dabigatran n (%)	3 (1)	5 (2)	.065
Edoxaban n (%)	4 (1)	1 (0)	.559
Beta blocker n (%)	252 (39)	130 (42)	.322
Calcium channel blockers n (%)	15 (3)	5 (2)	.487
Digoxin n (%)	4 (1)	3 (1)	.544
Antiarrhythmic drugs n (%)	7 (1)	6 (2)	.278
Statin n (%)	237 (36)	136 (44)	.024
Ezetimibe n (%)	1 (0)	1(0)	.589
PCSK-9 inhibitors n (%)	1 (0)	1 (0)	.584
NSAID n (%)	35 (5)	35 (11)	.001
Glycoprotein IIb/IIIa inhibitors n (%)	13 (2)	3 (1)	.246

Abbreviations: COPD, chronic obstructive pulmonary disease; NSAID, nonsteroidal anti-inflammatory drug; NSTEMI, non-STelevation myocardial infarction; PAD, peripheral arterial disease; PCSK-9, proprotein convertase subtilisin/kexin type 9; STEMI, ST-elevation myocardial infarction; USAP, unstable angina.

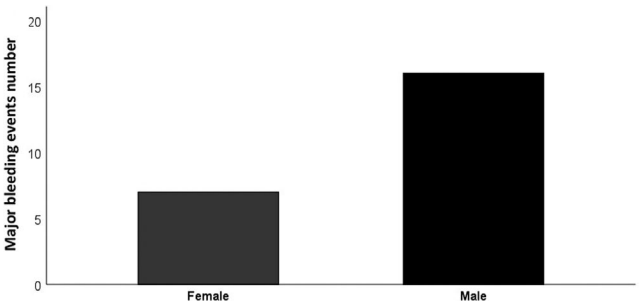

FIGURE 1 Comparison of major bleeding in female and male population

Compared with PRECISE-DAPT, patients in TACSER were younger [65.0 (56.9-73.0) vs 64.0 (56.0-72.0), $P < .001$]. Although haemoglobin levels was lower in TACSER, WBC and creatinine clearance were higher in this group compared with PRECISE-DAPT group [13.4 (12.0-14.7) vs 13.8 (12.7-14.9), $P < .001$; 83.7 (66.6-101.0) vs 79.1 (60.8-98.0), $P < .001$; 9.0 (7.1-11.2) vs 7.8 (6.3-10.2), $P < .001$, respectively]. The patients in TACSER were older compared with PLATO group [64.0 (56.0-72.0) vs 61.0 (53.0-69.0), $P < .001$]. TACSER group had low haemoglobin and creatinine clearance values than PLATO group [13.4 (12.0-14.7) vs 14.1 (13.1-15.0), $P < .001$; 83.7 (66.6-101.0) vs 84.6 (67.3-102.9), $P < .001$, respectively].

The AUC for the PRECISE-DAPT score to predict major bleeding was 0.857 (95% CI: 0.771-0.944, $P < .001$, Figure 2). Compared with the HAS-BLED and PARIS scores,

TABLE 3 The laboratory findings of study population

Variables	PRECISE-DAPT < 25 (n = 655)	PRECISE-DAPT ≥ 25 (n = 308)	*P*-value
BMI (kg/m^2)	27.9 ± 4.3	28.4 ± 5.7	.193
SCr $_{adm}$[a] (mg/dL)	0.84 (0.76-0.99)	1.10 (0.90-1.45)	<.001
Creatinine clearance (mL/min)	93.3 ± 21.3	60.6 ± 27.4	<.001
PLT (×10^3/μL)	241 ± 66	258 ± 88	.001
WBC (×10^3/μL)	9.3 ± 3.1	10.3 ± 4.4	<.001
Haemoglobin (g/dL)	14.0 ± 1.5	11.8 ± 2.1	<.001
INR	1.05 ± 0.2	1.1 ± 0.2	.148
AST[a] (U/L)	23 (18-35)	24 (18-40)	.604
ALT[a] (U/L)	20 (15-28)	18 (12-30)	.008
Total cholesterol (mg/dL)	186 ± 45	187 ± 50	.803
PRECISE-DAPT score	13.3 ± 5.7	39.1 ± 13.6	<.001
HASBLED[a] score	2 (1-2)	3 (2-3)	<.001
PARIS[a] score	4 (2-5)	7 (5-8)	<.001

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; INR, international normalized ratio; PLT, platelet; SCr, serum creatinine at admission; WBC, white blood cell.

[a]Comparison was made using Mann-Whitney *U* test at $P < .05$, and these values were described by median with inter-quartile range (25th and 75th percentile).

TABLE 4 The laboratory findings of study population

Variables	Male (n = 653)	Female (n = 310)	*P*-value
BMI (kg/m^2)	27.7 ± 4.5	28.8 ± 5.3	.002
SCr $_{adm}$[a] (mg/dL)	0.92 (0.80-1.1)	0.82 (0.70-1.10)	<.001
Creatinine clearance (mL/min)	88.7 ± 26.3	70.7 ± 27.5	<.001
PLT (×10^3/μL)	237 ± 72	267 ± 75	<.001
WBC (×10^3/μL)	9.7 ± 3.7	9.4 ± 3.4	.133
Haemoglobin (g/dL)	13.8 ± 1.9	12.1 ± 1.7	<.001
INR	1.1 ± 0.2	1.0 ± 0.1	.110
AST[a] (U/L)	23 (18-38)	22 (17-36)	.231
ALT[a] (U/L)	21 (15-31)	17 (13-24)	<.001
Total cholesterol (mg/dL)	182 ± 43	195 ± 51	<.001
PRECISE-DAPT score	18.4 ± 13.6	28.2 ± 15.7	<.001
PRECISE-DAPT score ≥ 25	146 (22)	162 (53)	<.001
HASBLED[a] score	2 (1-3)	3 (2-3)	<.001
PARIS[a] score	4 (2-6)	5 (3-7)	<.001

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; INR, international normalized ratio; PLT, platelet; SCr, serum creatinine at admission; WBC, white blood cell.

[a]Comparison was made using Mann-Whitney *U* test at $P < .05$, and these values were described by median with inter-quartile range (25th and 75th percentile).

the PRECISE-DAPT score offered good accuracy in predicting major bleeding (PRECISE-DAPT score vs HAS-BLED: AUC: 0.857 vs 0.730, $z = 2.391$, $P = .0168$; PRECISE-DAPT score vs PARIS score: AUC: 0.857 vs 0.569, $z = 3.959$, $P = .0001$). Calibration of observed against predicted major bleeding was good for PRECISE-DAPT score (Hosmer-Lemeshow goodness-of-fit test, $P = .577$, Figure 3).

Area under the curve (AUC) for PRECISE-DAPT in female was 0.921 with >100% sensitivity and 77.9% specificity with a cut-off value of 37.5 to predict major bleeding. A PRECISE-DAPT score of 24.5 in male was identified as the optimal cut-off value with sensitivity of 87.5% and specificity of 79.3% for predicting major bleeding (Figures 4 and 5). The optimal cut-off value for major

TABLE 5 Difference in clinical characteristics between TACSER, CardioCHUVI, PRECISE-DAPT score and PARIS risk scores

Variable	CardioCHUVI (n = 1.926)	TACSER (n = 963)	*P*-value	PRECISE-DAPT (n = 14.963)	TACSER (n = 963)	*P*-value	PARIS score (n = 4.190)	TACSER (n = 963)	*P*-value
Age (y)	65.1 ± 13.0	64.1 ± 11.3	.044	65.0 (56.9-73.0)	64.0 (56.0-72.0)	<.001	63.6 ± 11.0	64.1 ± 11.3	.197
Female n (%)	23.2	32.2	<.001	29.5	32.2	.075	25.4	32.2	<.001
Haemoglobin (g/dL)	14.2 ± 1.8	13.3 ± 2.0	<.001	13.8 (12.7-14.9)	13.4 (12.0-14.7)	<.001			
WBC (10^3units/μL)	9.98 ± 3.95	9.63 ± 3.58	.021	7.8 (6.3-10.2)	9. 0(7.1-11.2)	<.001			
CrCl (mL/min)	78.9 ± 37.7	82.9 ± 28.0	.004	79.1 (60.8-98.0)	83.7 (66.6-101.0)	<.001			
CrCl < 60 mL/min, (%)	21.6	19.2	<.001				17.8	19.2	<.001
Anaemia, %	16	32	<.001	-	32	-	15	32	<.001
Prior bleeding, %	1.9	9.8	<.001	1.9	9.8	<.001	-	9.8	-

Abbreviations: CrCl, creatinine clearance; WBC, white blood cell.

bleeding in all population was 29.5 with 84.2% sensitivity and 78.7% specificity.

4 | DISCUSSION

Dual antiplatelet therapy reduces the incidence of thrombotic recurrence in ACS**.** However, this benefit is counterbalanced by an increased risk of bleeding, which is itself associated with the duration of treatment. Considering the potential benefits and risk of bleeding, the most appropriate duration and treatment regimen should be determined. This is the first study to evaluate bleeding risk using the PRECISE-DAPT score in patients with ACS who were scheduled to receive DAPT in Turkey.

The duration of treatment and type of agent used in DAPT depend on patients' bleeding and thrombotic risk. Both the treatment duration and type of agent used are associated with a linear increase in the risk of bleeding.[1-3] Risk models have been established to determine the appropriate duration of treatment. For this purpose, the PARIS risk score, which considers age, BMI, smoking habits, anaemia, the use of triple therapy on discharge, DM, creatinine clearance, the presence of ACS and previous CABG, was established to determine the risk of both bleeding and ischaemia.[10]

The PRECISE-DAPT score was recently developed and validated in eight multicentre randomized trials.[13] This risk model considers age, Hb and leucocyte levels, creatinine clearance and history of bleeding. The incidence of major bleeding and fatal bleeding increased gradually with age, while there was no increase in other types of bleeding with age.[14] The PRECISE-DAPT score increases with a decrease in Hb value. It has been shown that there was a significant increase in major bleeding in patients with anaemia.[15,16]

In a PRECISE-DAPT score validation cohort, the mean Hb level was found to be 13.8 g/dL (12.7-14.9 g/dL). In the present study, the female patients were found to have lower Hb levels than the male patients compared with the aforementioned study. In a Turkish population, the prevalence of anaemia was found to be 30.0% in women and 18.2% in men, and the prevalence of anaemia in Turkey was higher than that reported in previous studies.[17] The rate of anaemia was 16% in the Cardiología del Complejo Hospitalario Universitario de VIgo (CardioCHUVI) PCI registry, while its prevalence in our study was 32.3%.[18] Moreover, anaemia was significantly more common in the female patients in our study than in the male patients. The particular presence of anaemia among the female patients may explain the high PRECISE-DAPT scores observed in these patients in the present study. In patients with low Hb, depending on the presence of anaemia, immature platelets are formed that can be less inhibited by antiplatelet agents or thrombogenesis, with bone marrow activation.[19] This may increase the risk of ischaemia in these patients.

TABLE 6 Differences in clinical characteristics between TACSER, PLATO and BernPCI registry

Variable	PLATO (n = 8.595)	TACSER (n = 963)	*P*-value	BernPCI (n = 6.172)	TACSER (n = 963)	*P* -value
Age (y)	61.0 (53.0-69.0)	64.0 (56.0-72.0)	<.001	67.2 (50.0-75.0)	64.0 (56.0-72.0)	<.001
Female n (%)	23.9	32.2	<.001	26.8	32.2	<.001
Haemoglobin (g/dL)	14.1(13.1-15.0)	13.4(12.0-14.7)	<.001	13.7 (12.1-14.9)	13.4(12.0-14.7)	<.001
WBC (10^3units/μL)	9.7 (7.8-12.1)	9.0 (7.1-11.2)	<.001	8.8 (4.2-11.3)	9.0 (7.1-11.2)	<.001
CrCl (mL/min)	84.6(67.3-102.9)	83.7(66.6-101.0)	<.001	87.6 (65.4-105.4)	83.7(66.6-101.0)	<.001
CrCl < 60 mL/min, (%)	-	19.2	<.001	-	19.2	
Anaemia, %	-	32	-	-	32	-
Prior bleeding, %	1.4	9.8	<.001	4.9	9.8	<.001

Abbreviations: CrCl, creatinine clearance; WBC, white blood cell.

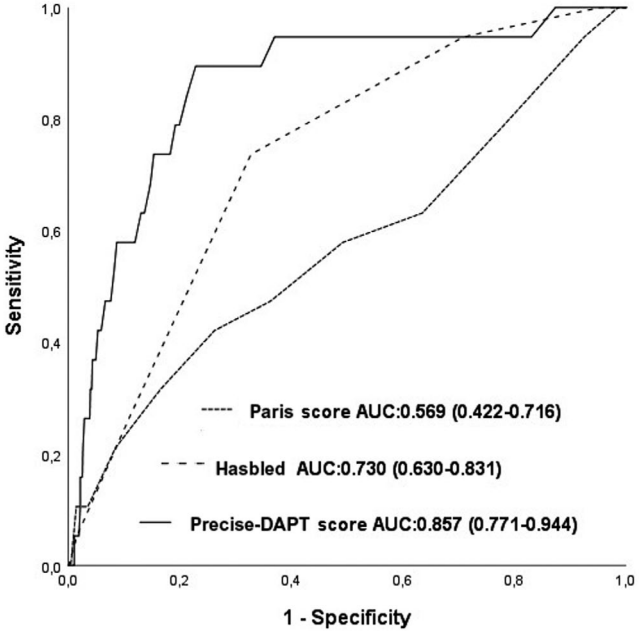

FIGURE 2 Receiver operating characteristic (ROC) curves for the PRECISE-DAPT, HAS-BLED and PARIS scores for predicting major bleeding

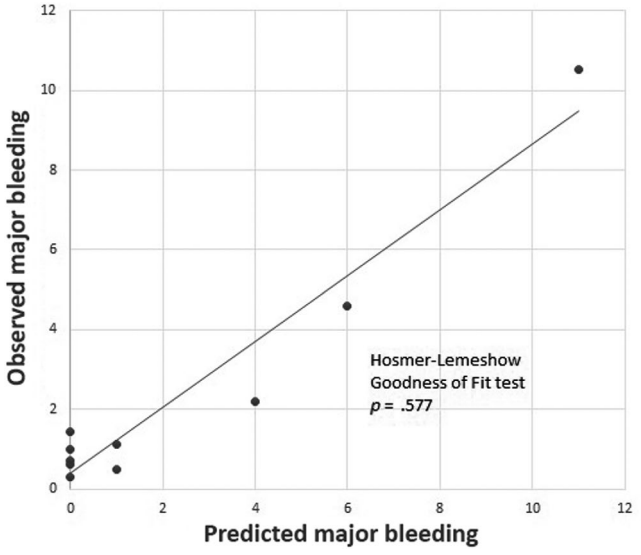

FIGURE 3 Observed and predicted rates of major bleeding by PRECISE-DAPT score

A history of bleeding is one of the most important variables in the calculation of the PRECİSE-DAPT score. The prevalence of bleeding history was found to be 1.9% in the PRECISE-DAPT score cohort, while its rate was 9.8% in our study population. Similarly, the presence of CKD (related to renal function) is included in the risk score calculation for both ischaemia and bleeding. Complications related to bleeding were significantly increased with a decrease in creatinine clearance in the EVENT study.[20] The prevalence of CKD was shown to be 15.7% in a Turkish population and was significantly more common among women than men (18.4% vs 12.8%).[21] In our study, CKD was also observed more frequently in the female patients than in the male patients.

Similarly to the studies described above, the patients with high PRECISE-DAPT scores in our study had low Hb levels and decreased creatinine clearance. Moreover, a history of bleeding was more common in the high PRECISE-DAPT score group. An increased risk of bleeding in chronic renal failure has been attributed to pathologies related to platelet dysfunction and coagulation cascade. In chronic renal failure, uraemic metabolites have been shown to contribute to the thrombotic environment by means of the von Willebrand factor, platelet-associated microparticles, coagulation enzymes and phosphatidyl serine.[22-24]

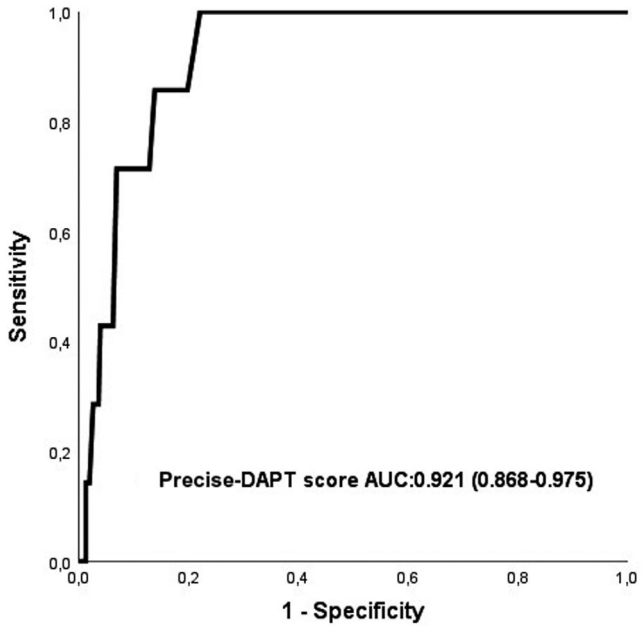

FIGURE 4 Receiver operating characteristic (ROC) curves for PRECISE-DAPT score in predicting major bleeding in female

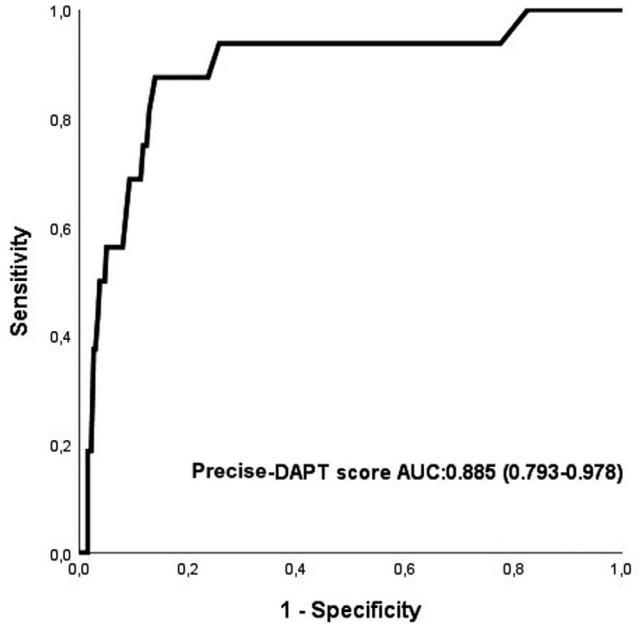

FIGURE 5 Receiver operating characteristic (ROC) curves for PRECISE-DAPT score in predicting major bleeding in male

The most controversial component of the PRECISE-DAPT score is that it takes into account the number of leucocytes. Alternative scoring systems to evaluate bleeding in these patients exclude leucocyte levels.[13] These scoring systems have been tested retrospectively in PLATO and Bern PCI study populations for TIMI major or minor bleeding. The predictive performance of the PRECISE-DAPT score without considering the white blood cell (WBC) count was found to be more compatible with the PLATO group data, whereas the predictive performance was lower for the Bern PCI registry. In our study, the WBC count was higher in the high PRECISE-DAPT group. Increased WBC levels have been shown to be associated with thrombosis, thrombus burden and newly developed heart failure and decreased epicardial blood flow and myocardial perfusion.[25]

A recent study investigated the effects of ischaemic risk (eg the complexity of the procedure) and bleeding risk (according to the PRECISE-DAPT score) on clinical outcomes and on the impact of DAPT duration after PCI.[26] Ischaemic events were found to be more common in patients who underwent complex PCI. Therefore, it may be considered that these patients would benefit from extended DAPT. However, the study also showed that those with a low bleeding risk benefitted from long-term DAPT. According to the study's analysis, bleeding risk is more important in determining DAPT duration after PCI than ischaemic risk.

In a previous study, the PRECISE-DAPT score was shown to be an independent predictor of in-hospital mortality in patients with ACS. The researchers found that the patients with high PRECISE-DAPT scores had a higher in-hospital mortality rate compared to those with low PRECISE-DAPT scores, which is consistent with the findings of our study.[27]

In our study, the mean PRECISE-DAPT score was 21.9, and approximately 33% of the patients had PRECISE-DAPT scores ≥25. The mean value of this score was 27.92 for the female patients and 19.07 for the male patients. Furthermore, the mean PRECISE-DAPT score in the patients with a PRECISE-DAPT score ≥25 was 39.28, and the mean value of the low PRECISE-DAPT score group was 13.43. Compared with the aforementioned study, both the mean PRECISE-DAPT score and the number of patients with a high bleeding risk (PRECISE-DAPT score ≥25) were higher in the current study. These results indicate the necessity of taking measures related to all the factors that increase the risk of bleeding when initiating DAPT in Turkey. Similarly to other studies conducted using the PRECISE-DAPT score, there was a significant difference in the PRECISE-DAPT score between the male and female patients in our study. The main reasons for this may be previous bleeding history, older age, low haemoglobin and creatinine clearance values whose values are different in men and women, among the variables taken into account when calculating PRECISE-DAPT score in presented study.

In a randomized controlled trial comparing prasugrel with clopidogrel in patients with ACS undergoing PCI, prasugrel significantly reduced more major adverse cardiovascular events than clopidogrel, but prasugrel resulted in higher rates of major bleeding.[28] The PLATO study, which compared ticagrelor and clopidogrel in patients with ACS, showed that there were no statistically significant differences in major bleeding between the two treatments. However, when

considering both major and minor haemorrhages, clopidogrel performed better than ticagrelor.[29]

In conclusion, we found that the PRECISE-DAPT score in our study was higher than the expected average for the Turkish population, especially among the female patients. This indicates a higher risk of bleeding in our population. In light of the research and guidelines related to DAPT, patients, particularly female patients, with anaemia and a prior history of bleeding in the Turkish population should be examined closely in terms of both their ischaemic and bleeding profiles to determine the duration and type of DAPT that should be used (ie clopidogrel, prasugrel or ticagrelor).

5 | STUDY LIMITATIONS

The TACSER study is an observational, cross-sectional cohort study. In addition, there was no follow-up in this study. We used the TIMI bleeding score to evaluate bleeding events. However, other bleeding scores, including the International Society on Thrombosis and Haemostasis (ISTH) major bleeding score and the Bleeding Academic Research Consortium (BARC) scale, were not used in the present study.

ORCID

Tuncay Kiriş https://orcid.org/0000-0001-9793-718X

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