Correlations of DAPT score and PRECISE-DAPT score with the extent of coronary stenosis in acute coronary syndrome

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Abstract
Dual antiplatelet therapy (DAPT) score and PRECISE-DAPT score were recommended for decision making of optimal DAPT in discriminating the risk of thrombosis and bleeding. But the relationships between 2 scoring tools with the extent of coronary stenosis have not been established.

We retrospectively enrolled 359 patients of acute coronary syndrome (ACS) who received percutaneous coronary intervention. Both DAPT score and PRECISE-DAPT score were calculated, and patients were divided by their recommended cut-offs. Gensini score and triple-vessel disease (3-VD) were chosen to evaluate the severity of coronary stenosis.

Overall, 54.9% and 10.0% of the patients had higher DAPT score (≥2) or PRECISE-DAPT score (≥25). Patients with higher DAPT score had increased stent counts, total length of stents, Gensini score, and proportion of 3-VD, but decreased minimum diameter of stent. But these differences were not found in PRECISE-DAPT subgroups. When divided into quartiles of both scoring systems, the highest Gensini score and proportions of 3-VD were found in the fourth quartile of both DAPT score and PRECISE-DAPT score. Moreover, both DAPT score and PRECISE-DAPT score were independent risk factors of Gensini score after adjustment (P < .001 and P = .047). Furthermore, an increase of 1 point of DAPT score and 5 points of PRECISE-DAPT score resulted by 51% (odds ratios [OR]: 1.51, 95% confidence interval [CI]: 1.19–1.91, P = .001) and 34% (OR: 1.34, 95% CI: 1.11–1.62, P = .003) increase in risk of 3-VD after adjustment.

Both DAPT score and PRECISE-DAPT score were independently associated with the degree of coronary stenosis in patients with ACS.

Abbreviations: 3-VD = triple-vessel disease, ACS = acute coronary syndrome, ApoA1 = apolipoprotein A1, ApoB = apolipoprotein B, CAGB = coronary artery bypass grafting, CAD = coronary artery disease, CHF = chronic heart failure, CI = confidence interval, CrCl = creatinine clearance, DAPT = dual antiplatelet therapy, DM = diabetes mellitus, ESC = European Society of Cardiology, HDL-C = high-density lipoprotein-cholesterol, LAD = left anterior descending artery, LCX = left circumflex coronary artery, LDL-C = low-density lipoprotein-cholesterol, LVEDD = left ventricular end-diastolic dimension, LVEF = left ventricular ejection fraction, MI = myocardial infarction, OR = odds ratio, PCI = percutaneous coronary intervention, RCA = right coronary artery, TC = total cholesterol, TG = triglycerides, WBC = white blood cell count.

Keywords: acute coronary syndrome, DAPT score, Gensini score, PRECISE-DAPT score, triple-vessel disease

1. Introduction
Because of the inevitable conflict between ischemia and bleeding, the duration of dual antiplatelet therapy (DAPT) especially after percutaneous coronary intervention (PCI) is a tough hotspot, which has not been resolved perfectly. According to the current guideline, the duration of DAPT after new generation of drug eluting stents is at least 6 months and is recommended to accomplish 12 months then maintain mono-antiplatelet therapy. For some patients with higher risks of thromboembolism, prolongation of DAPT to at least 18 months or even longer is suggested.\(^1\) However, all patients received DAPT regimens have to face 1 common complication, bleeding, resulting in discontinuation of DAPT, harmful impact on quality of life and subsequent adverse cardiovascular outcomes.\(^2\) Therefore, it is rather crucial to achieve an ideal balance between ischemia and bleeding. Unfortunately, DAPT duration was decided according to doctors’ personal experience and preference for most times in the last years, and the main reason for this situation was that there was not an acknowledged guideline or consensus which could assist the decision making of optimal DAPT strategies.

In 2017, European Society of Cardiology (ESC) published a guideline especially concerning about DAPT in coronary artery disease (CAD). And in this guideline, 2 scoring tools which could discriminate patients who were suitable for intensive DAPT or on the contrary were proposed and recommended for clinical practice for the first time.\(^3\) One scoring system is DAPT score, which consists of 9 items including both clinical and procedural characteristics,\(^6\) and the other one is PRECISE-DAPT (PREdicting bleeding Complications In patients undergoing Stent
implantation and subsQuent Dual Anti Platelet Therapy) score, which is made up of 5 clinical items.[7] The predominant features of the 2 prediction rules were that they were able to discriminate patients with higher risk of thromboembolism and lower risk of bleeding simultaneously and their accuracy and validity had been examined in various cohorts.[6–9]

As the new tools were recently proposed and recommended in the guideline, abundant related investigations need to be accomplished to further verify their clinical value. We noticed that patients with severe coronary atherosclerosis were associated with adverse prognosis and might obtain benefits from extensive DAPT[10–12]; however, it was also reported that these patients also combined with higher risk of both short-term and long-term major bleeding.[13,14] Besides, their poor prognosis was independent of whether they received PCI or coronary artery bypass grafting (CABG).[15,16] so the administration and management of these patients appear to be especially important and difficult. The main purpose of the present study was to illuminate if there existed an association in DAPT score and PRECISE-DAPT score with the extent of coronary stenosis in patients with acute coronary syndrome (ACS), which had not been reported in previous studies.

2. Methods

2.1. Study population

The current study was designed retrospectively, and we examined the medical information through electronic medical records system of the patients who received elective, urgent, or emergency PCI and subsequently diagnosed with ACS in the Department of Cardiology, Xiangya Hospital, Central South University between January 2012 and December 2013. ACS includes ST-elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina, and the diagnosis was made according to the current guidelines. Patients were excluded if they had atrial fibrillation, severe hepatic or renal dysfunction, current infections, previous inflammatory disorders, or existing malignant tumor. We also removed patients with incomplete items of DAPT score or PRECISE-DAPT score. After exclusion, 359 patients were enrolled in our final analysis. Our study protocol was approved by the Ethics Committee of Xiangya Hospital, Central South University.

Comorbidities and past medical information were obtained from all patients, including smoking status, hypertension, diabetes mellitus (DM), chronic heart failure (CHF), prior bleeding histories, old myocardial infarction, and PCI histories. DAPT score (ranges from –2 to 10 points) is the summation of 9 items. In details, –2 points for age ≥75 years; –1 point for age between 65 and 75 years; 0 point for age <65 years; 1 point each for cigarette smoking, DM, myocardial infarction (MI) at presentation, prior PCI or prior MI, paclitaxel-eluting stent, and stent diameter <3.5mm; 2 points each for CHF or left ventricular ejection fraction (LVEF) <30%, and vein graft stent.[6] To be mentioned, no paclitaxel-eluting stents or vein graft stents were implanted in our study population. While PRECISE-DAPT scoring system (ranges from 0 to 100 points) consists of 5 items including hemoglobin, white blood cell count (WBC), creatinine clearance (CrCl), and prior bleeding history, each item was assigned a value according to their levels and the detailed score calculation could be obtained on www.precisedapt score.com.[7]

2.2. Accessory examinations

Blood samples were taken from all patients on the next morning of admission after overnight fasting. WBC, hemoglobin, creatinine, and lipid profiles including total cholesterol (TC), triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), apolipoprotein A1 (ApoA1), and apolipoprotein B (ApoB) were measured automatically in the Central Laboratory of Xiangya Hospital using biochemical analyzer (Roche Diagnostics GmbH, Mannheim, Germany). CrCl was calculated with Cocks 0.85 × C2 formula, CrCl (mL/min)=(140–age) × weight (kg) × 0.85 (if female)/(72 × creatinine [mg/dL]). Transthoracic echocardiography was performed and 2-dimensional echocardiograms were recorded using a Hewlett-Packard Sonos 1000 ultrasound system (Hewlett-Packard, Palo Alto, CA) during hospitalization. Left ventricular end-diastolic dimension (LVEDD) was measured at end-diastole according to the recommendations of the American Society of Echocardiography, and LVEF was evaluated by modified Simpson method in the apical 4-chamber view.[11]

2.3. Assessment of coronary stenosis

 Coronary angiography and PCI were performed in the Cardiac Catheterization Room of our hospital and interventional cardiologist was blind to our study. Radial artery approach was the priority during puncturing, following femoral artery approach. Two interventional cardiologists independently evaluated the angiographic findings and the results were further cross-checked. The extent of ACS was assessed by Gensini scoring system,[16] which were calculated by 2 interventional cardiologists and the detailed computing method could be seen elsewhere in our previous study.[17] Significant coronary stenosis was defined if stenosis ≥50% of the lumen diameter was found in any of the major epicardial coronary arteries including left main coronary artery, left anterior descending artery (LAD), left circumflex coronary artery (LCX), and right coronary artery (RCA). And stenosis in left main trunk was regarded as LAD and LCX diseases concurrently and stenosis in 3 vessels (LAD, LCX, and RCA) was defined as triple-vessel disease (3-VD). The number of the stents implanted, total length, and the minimum diameter of the stents were also recorded.

2.4. Statistical analysis

Continuous variables were examined for normality by Kolmogorov–Smirnov test and were shown as means and standard deviation or medians and interquartile range, where appropriate. Categorical variables were presented as frequencies and percentages. The differences of normally distributed continuous variables were tested by t test, whereas Kruskal–Wallis test was applied for comparison of non-normally distributed continuous variables between subgroups of 2 scoring systems. The differences between categorical variables were examined by the chi-squared test or Fisher exact test, if appropriate. All patients were also divided into quartiles by DAPT score and PRECISE-DAPT score for analyzing their associations with Gensini score and distributions of stenosed vessels by 1-way analysis of variance and the chi-squared test, respectively. Multivariate stepwise linear regressions were conducted for the correlations between Gensini score and baseline characteristics, which were not components of 2 scoring systems, and DAPT score and PRECISE-DAPT score were included in separate regression model.
Multivariate logistic regressions were also performed for exploring the relationships between DAPT score (per 1 point increment) and PRECISE-DAPT score (per 1 point increment and per 5 points increment) with risk of 3-VD. All statistical analyses were conducted by the SPSS 19.0 software package (SPSS Inc, Chicago, IL) for windows. A 2-sided $P < .05$ was considered statistically significant.

### 3. Results

#### 3.1. Patient characteristics

Our study population consisted 359 patients with ACS in the final analysis, divided into subgroups by published cut-off values of 2 scoring tools (2 for DAPT score and 25 for PRECISE-DAPT score). Baseline characteristics of all patients classified as high and low DAPT score and PRECISE-DAPT score were presented in Table 1; 54.9% of the patients had a DAPT score $\geq 2$ and 10.0% had a PRECISE-DAPT score $\geq 25$, accordingly. Patients with a higher DAPT score tended to be male, younger, smokers, and combined with DM, CHF, prior or index MI, and had higher levels of WBC, hemoglobin, CrCl, LDL-C, ApoB, LVEDD, and proportions of LVEF $<$30%, besides, they had lower concentrations of HDL-C, ApoA1, LVEF, and PRECISE-DAPT score. While for those PRECISE-DAPT score $\geq 25$, they were more commonly to be female and older, had bleeding history and lower levels of hemoglobin and CrCl, which were in the contrary to those with higher DAPT score.

The procedural characteristics of the patients according to DAPT score and PRECISE-DAPT score were presented in Table 2. Patients with higher DAPT score were implanted with more stents, resulting with an increased total length of stents. In addition, minimum diameters of stents were significantly decreased in patients with DAPT score $\geq 2$, thus, resulting in an increased proportion of diameter $<$3mm. Higher percentage of stenosis in LAD and RCA, and remarkably elevated Gensini score and proportions of 3-VD were found in patients with DAPT score $\geq 2$. However, in patients whose PRECISE-DAPT score $\geq 25$, only a higher percentage of stenosis in RCA reached statistical significance.

#### 3.2. Coronary severity in quartiles of DAPT and PRECISE-DAPT scores

We also divided patients into quartiles of DAPT score and PRECISE-DAPT score accordingly. In details, the quartiles of DAPT score were classified as follows, Q1: $\leq$ 1 point (n = 72), Q2: 1 point (n = 90), Q3: 2 points (n = 99), and Q4: $\geq$ 3 points (n = 98). And the quartiles of PRECISE-DAPT score were defined as follows, Q1: 0 to 5 points (n = 75), Q2: 6 to 10 points (n = 101), Q3: 11 to 16 points (n = 84), and Q4: $\geq$ 17 points (n = 99). Means of Gensini score classified by quartiles of DAPT score and PRECISE-DAPT score were shown in Fig. 1. It was shown that with increase in quartiles of DAPT score, the Gensini score showed an increasing trend (Q1: 93.7 $\pm$ 56.7, Q2: 107.2 $\pm$ 45.2, Q3: 115.4 $\pm$ 48.3, Q4: 133.8 $\pm$ 48.7, $P < .001$). Besides, the highest Gensini scores were also found in the fourth quartile of PRECISE-DAPT score (Q4: 127.7 $\pm$ 58.9 vs. Q1: 101.9 $\pm$ 39.3, $P = .001$). Then we analyzed the distributions of stenosed vessels in quartiles of DAPT score and PRECISE-DAPT score in Fig. 2. Increasing 3-VD proportions were shown with elevating quartiles of both DAPT score (Q1: 54.2%, Q2: 72.2%, Q3: 71.7%, Q4: 86.7%, $P < .001$) and PRECISE-DAPT score (Q1: 58.7%, Q2: 70.3%, Q3: 72.6%, Q4: 84.8%, $P = .012$).
**Table 2**
Procedural characteristics of the subjects in subgroups according to DAPT score and PRECISE-DAPT score.

| Variables (n=359) | DAPT score < 2 (n=162) | DAPT score ≥ 2 (n=197) | P    | PRECISE-DAPT score < 25 (n=323) | PRECISE-DAPT score ≥ 25 (n=36) | P |
|-------------------|-------------------------|-------------------------|------|---------------------------------|---------------------------------|---|
| Number of stents  | 1.73 (0.85)             | 2.10 (0.99)             | <.001| 1.96 (0.95)                     | 1.72 (0.91)                     | .103|
| Minimum diameter of stent, mm | 3.06 (0.39)             | 2.87 (0.34)             | <.001| 2.95 (0.37)                     | 2.98 (0.41)                     | .773|
| Diameter <3 mm (%) | 49 (30.3)                | 116 (58.9)              | <.001| 149 (46.1)                      | 16 (44.4)                       | .847|
| Length of stents, mm | 48.2 (26.6)              | 61.5 (31.4)             | <.001| 56.3 (30.4)                     | 48.3 (24.8)                     | .150|
| LM stenosis (%)    | 12 (7.41)                | 23 (11.7)               | .175 | 33 (10.2)                       | 2 (5.56)                        | .555|
| LAD stenosis (%)   | 157 (96.9)               | 194 (98.5)              | .476 | 315 (97.5)                      | 36 (100.0)                      | 1.000|
| LCX stenosis (%)   | 124 (76.5)               | 178 (80.4)              | <.001| 272 (84.2)                      | 30 (83.3)                       | .814|
| RCA stenosis (%)   | 125 (77.1)               | 168 (85.3)              | .048 | 259 (80.2)                      | 34 (94.4)                       | .040|
| **Gensini score**  | 101.2 (50.9)             | 124.5 (49.3)            | <.001| 113.1 (51.9)                    | 121.8 (45.4)                    | .333|
| Stenosed vessels  |                        |                        |      |                                |                                |    |
| 1                 | 22 (13.6)                | 9 (4.57)                |      | 29 (8.98)                       | 2 (5.56)                        |    |
| 2                 | 36 (22.2)                | 32 (16.2)               |      | 64 (19.8)                       | 4 (11.1)                        |    |
| 3                 | 104 (64.2)               | 156 (79.2)              |      | 230 (71.2)                      | 30 (83.3)                       |    |

DAPT = dual antiplatelet therapy, LAD = left anterior descending artery, LCX = left circumflex coronary artery, LM = left main coronary artery, RCA = right coronary artery.

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Figure 1. Gensini score according to quartiles of DAPT score and PRECISE-DAPT score.

Figure 2. Distribution of stenosed vessels according to quartiles of DAPT score and PRECISE-DAPT score.
3.3. Determinants of Gensini score

Then we performed multivariate step-wise regression analysis for determinants of Gensini score in Table 3. Age, gender, smoking, hypertension, DM, presentation of acute MI, WBC, hemoglobin, CrCl, TC, TG, HDL-C, LDL-C, ApoA1, and ApoB were included in 2 separate regression models if they were not components of DAPT score or PRECISE-DAPT score, and only significant results were presented. Results showed that smoking, DM, and ApoA1 were independently associated with Gensini score, and both DAPT score and PRECISE-DAPT score were proved to have a positive and independent relationship with Gensini score in separate regression model (P < .001 and P = .047, respectively).

3.4. Determinants of 3-VD

Finally, multivariate logistic regressions with different adjusting variables were performed to explore possible associations between DAPT score and PRECISE-DAPT score (both as continuous variables) with risk of 3-VD in Table 4. Results indicated that every point increase of DAPT score resulted in 43% increase of 3-VD risk without adjustment (odds ratio [OR]: 1.43, 95% confidence interval [CI]: 1.19–1.72, P < .001). The results were similar after adjusting for potential confounding factors and the risks of 3-VD were further increased by 51% (OR: 1.51, 95% CI: 1.19–1.91, P < .001). And the results for PRECISE-DAPT score were comparable with DAPT score. As shown in Table 4, each increment of 1 point in PRECISE-DAPT score resulted in 6% (OR: 1.06, 95% CI: 1.02–1.10, P = .003) increase of 3-VD risk, and every 5 points increase resulted with 34% (OR: 1.34, 95% CI: 1.11–1.62, P = .003) risk increase of 3-VD after adjustment.

4. Discussion

In the current study, we first evaluated the association between 2 DAPT decision-making tools, DAPT score and PRECISE-DAPT score, and the severity of coronary atherosclerosis in patients with ACS. Our results revealed that both DAPT score and PRECISE-DAPT score were independently and positively associated with Gensini score and risk of 3-VD. And every point increase in DAPT score and 5 points increment in PRECISE-DAPT score resulted with 89% and 46% increase of 3-VD risk after adjustment. Therefore, the current 2 recommended DAPT scoring tools had good ability in discriminating those with severe coronary stenosis.

Antiplatelet treatment remains an important integrant part of ACS treatment programs, and the optimized DAPT duration has great importance for patients' prognosis in addition to selection of antiplatelet medications. The contradiction between antiplatelet therapy and risk of bleeding is a longstanding issue which bothers both doctors and patients. However, there exited no consensus designing the plan of DAPT perfectly, especially the duration of DAPT. GRACE score was able to estimate the mortality risk in hospital and 6 months after discharge in patients with ACS. It was helpful in evaluating the overall prognosis and recognizing patients with extremely high risk whom need extensive medical care. Besides, it was reported that GRACE score was correlated with degree of coronary stenosis reflected by SYNTAX score. However, it did not concern the DAPT plan assignment. Another scoring tool, CRUSADE score, which was also derived from patients with ACS, could estimate bleeding risk and share several common indexes with GRACE score, such as heart rate, SBP, heart function, and renal function, indicating that patients with higher risk of coronary events might also have increased risk of bleeding. Besides, the HAS-BLED score also had capacity in risk stratifying patients in determining the continuation of DAPT beyond 12 months. Although the above scoring tools could provide advice in deciding the duration of DAPT to some extent, none of these were utilized widely and recommended in the guidelines.

In 2017, ESC guideline issued the official recommendations for DAPT and its uppermost importance was that it recommended 2 scoring systems, DAPT score and PRECISE-DAPT score, assisting in decision making of DAPT. DAPT score was proposed earlier, and its 8 items were described hereinbefore. For
DAPT score < 2, the risk of bleeding exceeds the risk of ischemia, and to the contrary, for DAPT score ≥ 2 points, the benefits of antiplatelet precedes the risk of bleeding.[6] With regard to PRECISE-DAPT score, which consists of 5 items, patients with PRECISE-DAPT score ≥ 25 are recommended a short DAPT duration while a standard or long DAPT duration should be considered for those < 25.[7] The most important clinical significance of the 2 scoring systems were that they both could discriminate patients with high risk of bleeding and low risk of ischemia or on the opposite with 1 single formula. Thus, they simplify greatly the process of decision making of DAPT and ensure the patients could receive the optimal regimens available, though lots of verifications in various groups of patients are still under demand.

In the current study, we were curious about the characteristics of the coronary stenosis in patients with ACS divided by 2 scoring tools with their suggested cut-offs. Our results showed that both DAPT score and PRECISE-DAPT score were independent influencing factors of Gensini score and 3-VD. And after adjustment, an increment of 1 point in DAPT score and 5 points in PRECISE-DAPT score were associated with 89% and 46% increase in risk of 3-VD, respectively. In patients whose DAPT score ≥ 2, their coronary atherosclerosis was more serious reflected by Gensini score and stenosed coronary arteries than the others; however, no statistical significant difference was found when classified by PRECISE-DAPT score; however, the highest Gensini score and 3-VD were found in the fourth quartile of both DAPT score and PRECISE-DAPT score.

Actually, we were not surprised that both DAPT score and PRECISE-DAPT score were examined to be correlated with the extent of coronary stenosis because they were calculated by summation of several clinical and procedural parameters, and most of the included parameters had been reported to be associated with coronary severity. It is well established that age, smoking, and DM were known risk factors of CAD and were reported to be associated with coronary severity.[12,13] WBC is an easily obtained surrogate marker of inflammation, which plays crucial role in the development and progression of atherosclerosis and was proved to be associated with coronary stenosis.[21] It was reported that low hemoglobin had an independent relationship with presence of CAD after adjusting for iron metabolic indexes.[24] In addition, anemia was associated with stenosed coronary arteries,[25] though the exact underlying mechanism was unclear. Renal dysfunction was also correlated with the occurrence and severity of CAD,[26] and possible mechanism may include low-grade inflammation and activation of the rennin angiotensin aldosterone system.[27] Nonetheless, we noticed that the associations between 2 scoring systems and coronary severity were independent of the influencing factors, which were not components of the 2 scores, indicating that both DAPT score and PRECISE-DAPT score could have an extra ability in estimating stenosis burden of coronary arteries.

To be mentioned, patients with advanced coronary stenosis tended to have increased scores of both scoring systems, but a higher DAPT score was associated with increased ischemic risk and a higher PRECISE-DAPT score was connected with elevated bleeding risk, inferring that these patients were combined with both high ischemic and bleeding risk based on 2 DAPT decision-making scores, and this finding was in accordance with real-world clinical outcomes.[10-14] It was reported that patients with high SYNTAX score, clinical SYNTAX score or residual SYNTAX score had increased risk of all-cause death, MI, repeat revascularization, target lesion failure, and major adverse cardiac events.[10-12] However, previous studies also inferred that elevated SYNTAX score was associated with increased risk of 30-day and 2-year major bleeding.[13,14] Therefore, the strategy of DAPT in patients with severe coronary stenosis still remained unclear and future investigations are rather required.

When we paid attention to the consistency of the clinical decisions according to the 2 independent scoring systems, 4.5% of the patients were recommended a long DAPT by DAPT score (≥ 2), while a short DAPT by PRECISE-DAPT score (≥ 25), leading to conflicting conclusions. Indeed, we were not astonished about this result, as in DAPT score system, long DAPT and standard DAPT were the 2 separated recommended decisions, while in PRECISE-DAPT score system, short DAPT and standard/long DAPT were the 2 recommendations. Neither of the 2 methods has a complete decision-making system covering short, standard, and long DAPT. And there were no suggestions available for the above inconsonant conditions in the current guideline.[15] We proposed a possible solution that PRECISE-DAPT score was calculated firstly to decide whether the patient should receive short DAPT, if not, DAPT score was obtained thereafter to discriminate whether long DAPT or standard DAPT was more appropriate. However, our method had not been verified in clinical practice.

There were several limitations in the present study. We only included patients diagnosed with ACS, and those with stable angina pectoris were not recruited, so the results in these patients were unavailable in our study. Besides, we stated in the methods section that none of our patients received paclitaxel-eluting stents or vein graft stents in our center, as paclitaxel-eluting stents were early generation stents and were seldom used in last few years, and patients received CAGB were few and PCI in vein grafts were even fewer. Thus, the DAPT score in our study might be somewhat lower than in other populations, but we did not consider this aspect could influence our results prominently. In addition, we discovered the inconsistency derived from 2 scoring systems in a small part of patients and which one had priority for clinical practice was still unknown. All these uncertainties need abundant future investigations to illuminate.

In conclusion, we first revealed that both DAPT score and PRECISE-DAPT score were independently associated with coronary severity assessed by Gensini score and 3-VD in patients with ACS. Besides, different suggestions were obtained in patients with severe coronary diseases derived from 2 decision-making tools, which need future study to solve.

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