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# Catlet scoring system as a new predictor for in-stent restenosis in patients with chronic coronary artery disease undergoing percutaneous coronary intervention with drug-eluting stent

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## Abstract

**Background** He's team have recently developed a new Coronary Artery Tree description and Lesion EvaluaTion (CatLet) angiographic scoring system, which is capable of accounting for the variability in coronary anatomy, and risk-stratifying patients with coronary artery disease. Preliminary studies have demonstrated its superiority over the the Synergy between percutaneous coronary intervention with Taxus and Cardiac Surgery (SYNTAX) score with respect to outcome predictions for acute myocardial infarction (AMI) patients. However, there are fewer studies on the prognostic in chronic coronary artery disease(CAD). This study aimed to clarify whether the CatLet score had a predictive value for in-stent restenosis(ISR) in patients with chronic coronary artery disease undergoing percutaneous coronary intervention with drug-eluting stent(DES).

**Methods** A total of 260 patients who were diagnosed with chronic CAD and underwent coronary DES implantation at the second affiliated Hospital of Wannan medical college in China were consecutively enrolled from January 2020 to June 2021. Finally, 164 patients underwent the second angiography after 2 years. According to whether ISR was detected at follow-up angiography, patients were divided into the ISR group (n = 26) and the non-ISR group (n = 139).

**Results** A total of 165 patients (46 women and 119 men) with a mean ages of 66.19±10.54 years were finally enrolled in this study. Of these, ISR occurred in 26/165 chronic CAD patients (15.76%) by follow-up angiography. Univariate analysis showed that most baseline characteristics of the ISR and non-ISR group were similar. Patients in the ISR group had significantly the history of chronic obstructive pulmonary disease(COPD), adverse lesion characteristic, higher Catlet score compared with patients in the non-ISR group.The CatLet score was capable of predicting in-stent

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restenosis after adjustment for risk factors; The Multivariable-adjusted model showed good calibration and good discrimination (area under ROC curve = 0.7164) for ISR.

Conclude CatLet score is a new predictor of ISR in patients with chronic CAD after coronary DES implantation.

Keywords In-stent restenosis, Uric acid, CatLet score, Coronary artery disease

## Introduction

Coronary heart disease has become the most major factors endangering people's health.Currently, Percutaneous coronary intervention(PCI) therapy has been the major therapeutic procedure for coronary artery disease (CAD) [1, 2]. With the innovation of stent technology, the restenosis rate of new-generation drug-eluting stents has significantly decreased [3].However, several large-scale clinical trials have confirmed that even in the era of drugeluting stents (DES), in-stent restenosis (ISR) occurs in 3–20% of patients after coronary stenting implantation [4], which remains an unresolved clinical problem in clinical practice.Therefore, exploring the reliable risk factors for predicting ISR would be of great significant for patients risk assessment.

The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score, an anatomic coronary scoring system, has been developed to grade the severity and complexity of coronary artery disease (CAD) [5]. However, the SYNTAX score, solely based on the dichotomized left or right coronary dominance, has failed to adequately describe the variability of coronary anatomy [6, 7]. Recently, a new Coronary Tree Description and Lesion Assessment CatLet Coronary Scoring System has been developed, which is unique in that it can interpret coronary variants, record the severity of diseased coronary arteries, and semiquantify the range of blood supply to diseased vessels [8]. And previous studies have shown that the CatLet score has a good predictive value for the risk assessment of patients with acute myocardial infarction [9, 10]. However, the risk predictors of ISR in chronic CAD patients had not been well characterized.

Therefore, our study aims to explore whether the Cat-Let score had a predictive value for in-stent restenosis in patients with chronic coronary artery disease undergoing percutaneous coronary intervention with drug-eluting stent.

## Methods

## Study patients

A total of 260 patients who were diagnosed with chronic CAD and underwent coronary DES implantation at the second affiliated Hospital of Wannan medical college in China were consecutively enrolled from January 2020 to June 2021.Of these, 200 of these patients who met the inclusion and exclusion criteria were followed up

by angiography after baseline PCI.Finally, 164 patients underwent the second angiography after 2 years. Exclusion criteria as follow: (1)patients who died during follow-up(n = 2);(2) patients with myocardial infarction (MI) within one month of baseline PCI (to exclude potential subacute stent thrombosis of the intervened arterial segment)(n = 1);(3) patients without sufficient clinical and angiographic data at baseline and follow up (n = 92). 26 patients with 46 lesions were treated with repeat DES (re-DES) or DCB implantation after the occurrence of ISR in the target vessels.Maintenance drug therapy was routinely administered unless otherwise contraindicated. Dual antiplatelet treatments were strongly recommended for at least 6 months.

This study was approved by the Clinical Research Ethics Committee of the second affiliated Hospital of Wannan medical college, and All patients gave written informed consent.

## The CatLet score and the lesion evaluation

The CatLet angiographic scoring system has been described elsewhere in detail [8].Its tutorial is available at http://www.Catletscore.com (Internet Explorer or Microsoft Edge browser is required). In short, this novel angiographic scoring system has adequately accounted for the variability in the coronary trees, where six types of the right coronary artery (RCA), three types of the left anterior descending artery (LAD), and three types of the diagonal branch were reclassified, resulting in a total of 54 ( $6 \times 3 \times 3$ ) types of coronary artery depends on the myocardial territory subtended by the coronary artery. The lesion is defined as >50% diameter stenosis on vessels  $\geq 1.5$  mm in diameter. The lesion scoring is a product of the stenosis.

degree and the weighting of the coronary artery involved. Scoring points for multiple lesions were added to derive the total score for a patient. The adverse characteristics pertinent to those lesions were not scored anymore, but rather recorded qualitatively. Non-occlusive lesions were scored straightforward; for a total occlusive lesion, wiring/small ballooning was used to improve the blood flow to evaluate the severity of the lesion (scored as a non-occlusive lesion) while persistently poor blood flow that failed to allow adequate visualization of the lesion was scored as a total occlusive one [11]. A multiplication factor of 2.0 is used for non-occlusive lesions and 5.0. for occlusive lesions. The CatLet score was calculated from the final angiographic results after elective percutaneous revascularization procedures. Two experienced observers reviewed the angiograms. The view of a third analyst was sought in the event of disagreement, and the final decision was made by consensus. The observers were blinded to patients' clinical characteristics and outcomes.

## **Disease definitions and endpoints**

The primary end point of the study was the occurrence of ISR. ISR was defined as a diameter stenosis of  $\geq$  50% occurring in the segment inside the stent or a 5 mm proximal or distal to the stent at follow-up angiography [12, 13].According to whether ISR was detected, patients were classified into two groups: the ISR group and the non-ISR group. Target lesion was considered the most severe narrowing, identified by angiographic appearance with Electrocardio-.

graph (ECG) changes. Multivessel disease (MVD) was defined as a diameter stenosis of  $\geq$  50% occurring in two or more vessels.

Diabetes mellitus was defined as either a previous diagnosis of DM treated with diet, oral agents or insulin or a new diagnosis of DM if FBG  $\geq$  7.0mmol/L on two occasions during hospitalization [14]. Hypertension was defined by systolic blood pressure (SBP)  $\geq$  140 mmHg and/or diastolic blood pressure (DBP)  $\geq$  90 mmHg, and/ or the use of antihypertensive treatment in the past two weeks [15]. Low.

levels of HDL-C were defined as 1.04 mmol/L [16]. Chronic obstructive pulmonary disease (COPD) was defined as after Inhalation of bronchodilators, FEV1/ FVC < 70% indicates the presence of persistent airflow limitation [17]. The severity of coronary artery lesions was quantified with Coronary Artery Tree description and Lesion EvaluaTion (CatLet) score, which was calculated using the online calculator for CatLet score.

## Data collection

We use a standard case report form to collect patients' clinical and demographic characteristics, including age, gender, smoking, alcohol consumption, CAD risk factors, medical history, and coronary angiography information at baseline PCI and follow-up. Body measurements such as blood pressure (BP) was taken upon admission. Neutrophil-lymphocyte ratio (NLR) is calculated by neutrophils divided by lymphocyte counts. Coronary angiography data such as CatLet score, minimum stent diameter, average stent length, and stent narrowing percentage, were also recorded by two experienced researchers at baseline and follow-up for coronary angiography analysis.

#### Sample size estimation and statistical analysis

Statistical analyses and graphics were completed with STATA 15.1 (State Corp LP, College Station, TX, USA). The enrolled sample size calculation has been provided in detail elsewhere [9]. Briefly, according to the published data, the CatLet score is associated with a 1.05-fold increased risk of adverse cardiovascular events per 1 unit higher, and its standard deviation is 12; previously similar study has reported that the failed probability is around 15% at 1.5-year follow-up [18].

Continuous variables following a normal distribution are represented by mean ± standard deviation. The t-test is used for comparing differences between two groups, while analysis of variance is used for comparing three or more groups. For continuous data that does not follow a normal distribution, the median (with the interquartile range P25, P75) is used, and the differences are compared using the rank sum test. Categorical variables are represented by frequency (rate), and differences between groups are compared using the chi-square test. We use a multiple logistic stepwise regression model using the stepwise method (entry,0.05; removal,0.05) to select the risk factors for ISR, adjusting for traditional risk factors and other confounding factors. The included variables are age, gender, history of COPD, smoking, alcohol consumption, creatinine, blood lipids, imaging indicators, Catlet score, and other biochemical indicators (uric acid, NLR), among others. The Odds ratio (OR) and 95% confidence intervals (95% CI) were calculated to estimate the adjusted risk of ISR in chronic CAD patients. The predictive value of the Logistic regression model was evaluated using Decision Curve Analysis(DCA) .Differences are considered statistically significant when P < 0.05.

## Results

Out of 260 patients initially enrolled in this study, 95 were excluded, and 165 patients were finally analyzed as shown in Fig. 1. The mean age was  $66.19 \pm 10.54$  years, and 71.95% (118/164) were male.The CatLet score ranged from 0 to 92, with a mean  $\pm$  SD of  $34.85 \pm 19.47$ . Angiography result showed that ISR occurred in 26/165 chronic CAD patients (15.76%). According to whether ISR was detected, patients were divided into an ISR group (n = 26) and Non-ISR group (n = 139).

#### **Baseline clinical characteristics**

The baseline clinical variables of the patients were listed in Table 1. There were no significant differences between the ISR group and non-ISR group in terms of age, gender, smoking, drinking, history of hypertension or diabetes, and history of chronic kidney disease. Patients in the ISR group had significantly the history of chronic obstructive pulmonary disease(COPD) (26.9% vs. 10.8%, P=0.026).

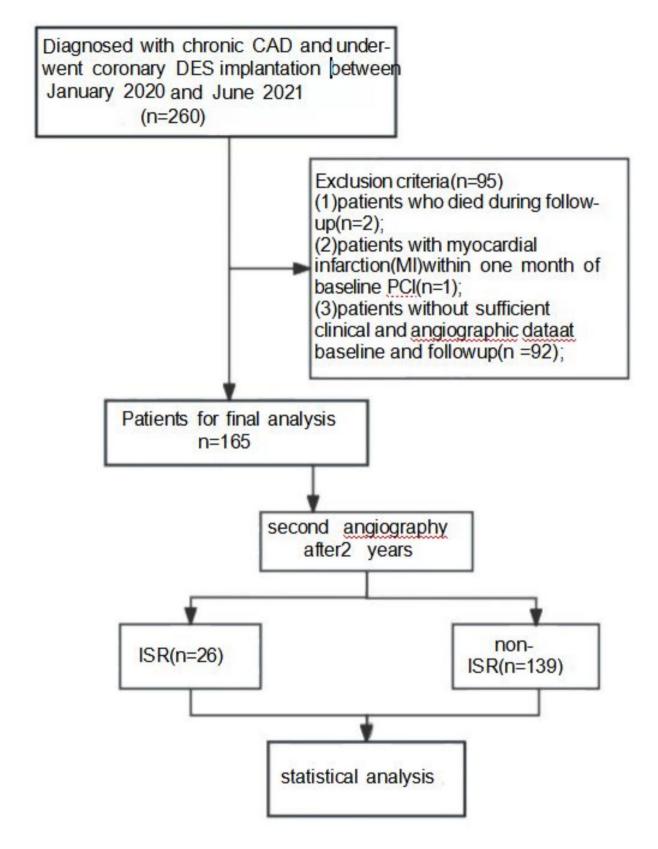


Fig. 1 Flow chart of patient selection. CAD: coronary artery disease, DES: drug-eluting stent, ISR: in-stent restenosis. 139)

**Table 1** Baseline clinical characteristics of study population

Variables	ISR(n=26)	non-ISR( <i>n</i> = 139)	<i>p</i> -values
Age(years)	67.15±11.32	66.01±10.43	0.61
Male	99 (71.2%)	20 (76.9%)	0.55
Medical history			
Diabetes	5 (19.2%)	41 (29.5%)	0.28
Hypertension	18 (69.2%)	100 (71.9%)	0.78
COPD	7 (26.9%)	15 (10.8%)	0.026
CKD	1 (3.8%)	9 (6.5%)	0.61
Smoking			0.42
Current	12 (46.2%)	58 (41.7%)	
Never	8 (30.8%)	63 (45.3%)	
Past	6 (23.1%)	18 (12.9%)	
Alcohol consumption			0.84
Current	5 (19.2%)	33 (23.7%)	
Never	20 (76.9%)	99 (71.2%)	
Past	1 (3.8%)	7 (5.0%)	
Laboratory results			
LVEF	0.56±0.11	0.57±0.10	0.48
Creatinine, umol/L	138.28±131.38	111.01 ± 57.83	0.087
UA, umol/L	399.98±101.31	379.33±114.88	0.39
TG, mmol/L	1.51±0.60	1.79±1.11	0.20
TC, mmol/L	4.13±1.02	$4.50 \pm 1.04$	0.091
HDL-C, mmol/L	$1.05 \pm 0.45$	1.10±0.31	0.55
LDL-C, mmol/L	2.43±0.83	2.59±0.81	0.36
FBG, mmol/L	$6.01 \pm 1.60$	6.58±2.86	0.33
apob/apoa1,mmol/L	0.66±0.23	0.63±0.18	0.50
NLR	$3.40 \pm 1.73$	3.72±3.92	0.68

Data are expressed as mean ± SD or n (%). COPD: chronic obstructive pulmonary disease; CKD: Chronic kidney disease; HDL-C: High density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; FBG: fasting blood glucose; ISR: in-stent restenosis; TC: total cholesterol; TG: triglyceride; UA: uric acid; NLR: neutrophil to lymphocyte ratio

The levels of Cr, TG, LDL-C, HDL-C, FBG, apob, NLR, and LVEF were similar in both groups.

## **Baseline angiographic characteristics**

The baseline angiographic and procedural characteristics of the patients were shown in Table 2. Within bifurated lesions, as Medina110 and Medina011 types was higher in the ISR group than in the non-ISR group (11.5% vs. 2.9%, P=0.044) (26.9% vs. 10.8%, P=0.026). The Catlet score in the ISR group was also significantly higher than in the non-ISR group (44.23±24.53 vs. 33.09±17.94, P=0.007). Other basic vascular imaging information, such as target vessels, coronary artery classification, advere lesion characteristic, minimum stent diameter, and stent length, did not show significant differences between the two groups.

## Predictors of ISR in CAD

In the multivariate logistic regression analysis model, after adjusting for a history of COPD, stent number, Catlet score, and the bifurated lesions as Medina110 and Medina011,CatLet score remains to be a predictors associated with ISR in coronary heart disease patients as shown in supplementary Table 1. Adjusted CatLet score performed well in discrimination with respect to clinical outcomes as shown in Fig. 2. Areas under the receiver operating characteristic (ROC) curve ranged between 0.72.

#### Calibration

In terms of calibration, the model with the CatLet score and Adjusted Catlet score was robust as shown in Fig. 3.

#### Subgroup analysis

Subgroup analysis had demonstrated that the CatLet score was a consistent hazard risk for ISR although the CatLet score interacts with diabetes, which deserved further study as shown in Fig. 4.

## Discussion

The results of this study as follow: (a) the CatLet score in isolation independently predicted ISR clinical outcomes; (b) the CatLet score remained significantly predictive of ISR even after adjustment for important clinical explaining variables,

 Table 2
 Baseline angiographic characteristics of study population

Variables	ISR( <i>n</i> = 26)	non-ISR( <i>n</i> = 139)	<i>p</i> -values
Diagonal size			0.38
Small	0 (0.0%)	10 (7.2%)	
Large	20 (76.9%)	85 (61.1%)	
Inter	6 (23.1%)	44 (31.7%)	
LAD length			0.28
Short	7 (26.9%)	32 (23.0%)	
Average	8 (30.8%)	51 (36.7%)	
Long	10 (38.5%)	56 (40.3%)	
RCA dominance			0.64
PDA zero	0 (0.0%)	6 (4.3%)	
PDA only	1 (3.8%)	13 (9.4%)	
Small RCA	9 (34.6%)	36(25.9%)	
Average RCA	15 (57.7%)	65 (47.8%)	
Large RCA	1 (3.8%)	18 (12.9%)	
Super RCA	0 (0.0%)	1 (0.7%)	
Coronary artery treated			
LM	2 (7.7%)	2 (1.4%)	0.057
LAD	17 (65.4%)	93 (66.9%)	0.88
LCX	6 (23.1%)	23 (16.5%)	0.42
RCA	8 (30.8%)	31 (22.3%)	0.35
Culprit vessels			
LAD	16 (61.5%)	84 (60.4%)	0.92
LCX	2 (7.7%)	16 (11.5%)	0.57
RCA	7 (26.9%)	33 (23.7%)	0.73
Lesion characteristics			
Medina1,1,1	5 (19.2%)	16 (11.5%)	0.28
Medina1,1,0	3 (11.5%)	4 (2.9%)	0.044
Medina1,0,1	1 (3.8%)	9 (6.5%)	0.61
Medina1,0,0	0 (0.0%)	11 (7.9%)	0.14
Medina0,1,1	7 (26.9%)	15 (10.8%)	0.026
Medina0,1,0	4 (15.4%)	30 (21.6%)	0.47
Medina0,0,1	1 (3.8%)	3 (2.2%)	0.61
Tortuosity	12 (46.2%)	57 (41.0%)	0.63
calcification	2 (7.7%)	12 (8.6%)	0.87
Dilation	15 (57.7%)	87 (62.6%)	0.64
lesion length > 20 mm	19 (73.1%)	104 (74.8%)	0.85
Angulation < 70	15 (57.7%)	71 (51.1%)	0.54
ostial lesion	3 (11.5%)	21 (15.1%)	0.64
Catlet score	44.23±24.53	33.09±17.94	0.007
Minimal stent diameter, mm	$2.90 \pm 0.41$	2.99±0.45	0.33
total stent number	$1.31 \pm 0.47$	1.37±0.61	0.67

Data are presented as mean ± SD or n (%).ISR: in-stent restenosis; LAD: left anterior descending; LCX: left circumflex artery; LM: left main; RCA: right coronary artery; CatLet: Coronary Artery Tree description and Lesion EvaluaTion; PDA: Posterior descending artery;

Percutaneous coronary intervention(PCI) had become the major theraputic procedure for coronary artery disease(CAD), and with the improvement and advancement of stent technology, studies have shown that the incidence of in-stent restenosis (ISR) with third-generation drug-eluting stents (DES) is less than 10% [19].However, with the increasing complexity of procedures (such as more complex patients and coronary lesions), the incidence of in-stent restenosis (ISR) is also on the rise.The study shed light on that ISR occurred in 26/165 chronic CAD patients (15.76%) by follow-up angiography.It may be due to: ① the research results bias caused by a relatively small sample size; ② the patients enrolled with more complex lesions, such as a higher proportion of bifurcation lesions and long lesions, which could increase the intraoperative injury to the vascular endothelium during PCI and thereby increase the risk of ISR.

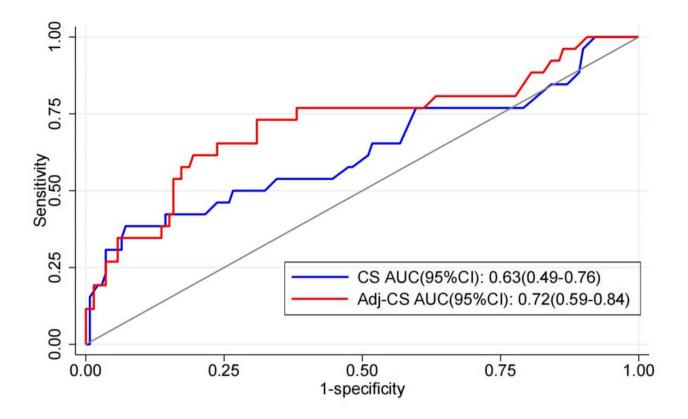


Fig. 2 The ROC curves of Catlet alone and adjusted Catlet models for ISR; AUC, Receiver Operating Characteristic (ROC) curve; and Cl, confidence interval. CS: Catlet score, Adj-CS: adjusted Catlet score

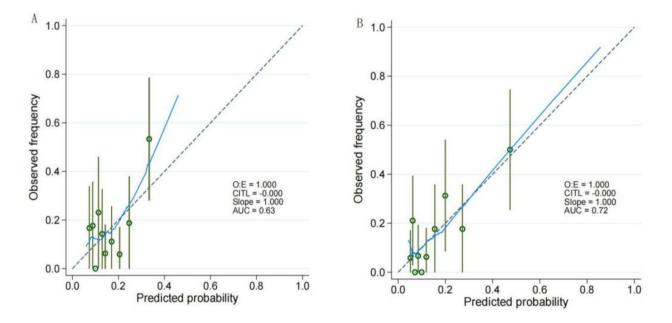


Fig. 3 Calibration plots of CatLet score and adjusted CatLet score at cross-validation with respect to ISR for CatLet score (A) and adjusted CatLet score (B). A blue lowess smoothing curve was added to each calibration plot. Intercept of 0 and slope of 1 indicate perfect prediction. Negative and positive intercepts indicate overestimation and underestimation, respectively

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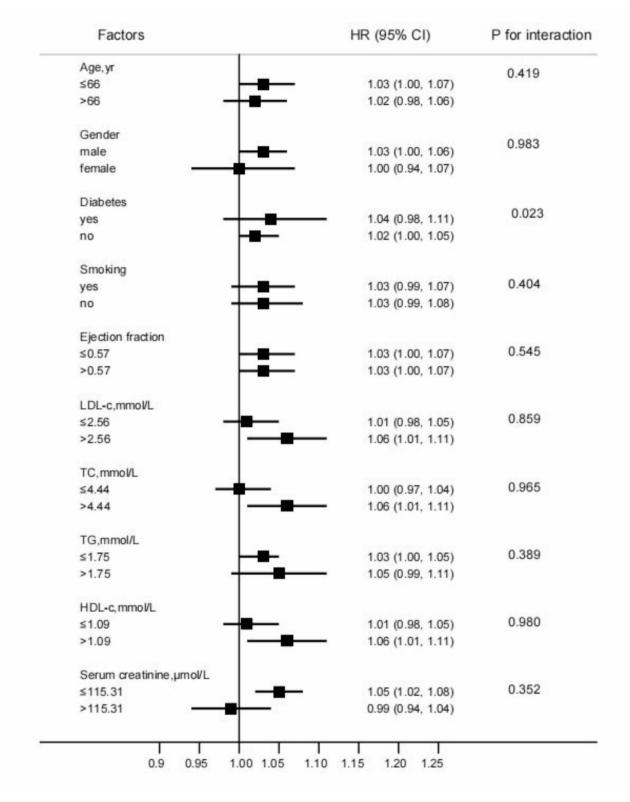


Fig. 4 Hazard ratios for ISR per 1 units higher CatLet score stratified by risk factors, categorically or medially, adjusted for meaningful factors. LDL-c, low density lipoprotein cholesterol; HDL-c, high density lipoprotein cholesterol; TG, triglycerides; and TC, total cholesterol

Research showed that individuals diagnosed with COPD are at a higher risk of developing adverse cardiovascular outcomes [20].Chronic inflammation in COPD has been found to involve both innate and adaptive immunity [21]. Previous studies found that patients with a history of COPD have an increased risk of ISR after receiving drug-eluting stent implantation(OR = 2.44, 95% CI: 1.33–4.49, P=0.004) [22, 23]. In the current study, A history of COPD manifested as the strongest predictor of clinical outcomes to be incorporated to construct the final multivariate adjusted models.

A lesion that causes coronary artery flow limitation has been considered as an important prognostic factor [24]. The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score, an anatomic coronary scoring system, has been developed to grade the severity and complexity of coronary artery disease (CAD). However, the SYNTAX score, solely based on the dichotomized left or right coronary dominance, has failed to adequately describe the variability of coronary anatomy. Although the SYNTAX score has been widely used in risk stratification and selection of revascularization strategies, there are studies questioning its predictive value in CAD patients.He's team developed a novel Coronary Artery Tree description and Lesion EvaluaTion (CatLet) angiographic scoring system, which can be utilized to account for the variability in coronary anatomy, and to risk-stratify patients with CAD [8]. In previous studies, various model designs have shown that the CatLet score is better than the SYNTAX score for the long-term prognosis of patients with acute coronary syndrome [25, 26]. In the current study, higher CatLet scores were associated with a higher incidence of ISR(Odds ratio/unit higher score were 1.03,P<0.05).This is consistent with the results of our previous studies of Catlet scores in chronic coronary syndrome [27].

## Limitation

This study has several limitations. First, the CatLet score validation trial is observational in design, and the confounding is unavoidable. Thus, this finding should be considered hypothesis-generating. Second, a single-center study with a small sample size is still a concern, which would have weakened the statistical power of the conclusions. Third, like the SYNTAX score, lesions with diameter stenosis  $\geq$  50% were scored in the CatLet score.However, only 35% of the intermediate (50–70%) angiographic.

stenosis was hemodynamically relevant as defined by fractional flow reserve (FFR)  $\leq$  0.80 [28]. Further studies are needed to clarify whether the FFR-guided CatLet score is a better predictor of prognosis than the one just based on the visual assessment.

## Conclusion

In the present study, we have demonstrated that the Cat-Let score has a predicting value for ISR in patients with CAD after coronary DES implantation.

#### Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s13019-025-03349-2.

Supplementary Material 1

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Not applicable.

#### Author contributions

JW and MCZ the co-first authors, developed treatment plan for the patient and wrote the manuscript. JYZ, WPG, MXX, performed follow-up for patient. LFY and YSK, the co-corresponding author, modify the manuscript, and made the illustrations. All authors read and approved the final manuscript. All authors agreed to their contribution.

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#### Data availability

Data is provided within the manuscript.

#### Declarations

#### Ethics approval and consent to participate

Ethical review and informed consent of patients have been obtained.

#### **Consent for publication**

Written informed consent was obtained from the patient for publication of this article and any accompanying images. A copy of written consent is available for review by the Editor this journal.

#### **Competing interests**

The authors declare no competing interests.

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