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Comparative outcomes of invasive versus conservative strategy in stable coronary artery disease patients: a risk-stratification-based hypothesis-generative study

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Abstract

Background Whether percutaneous coronary intervention (PCI) can improve the long-term prognosis of patients with stable coronary artery disease (SCAD) in comparison to conservative treatment remains controversial. The present study sought to evaluate the impacts of initial invasive versus conservative strategy on long-term clinical outcomes for patients with SCAD stratified by risk scores.

Methods This was a sub-analysis of the multicenter, observational Optimal antiPlatelet Therapy for Chinese patients with Coronary Artery Disease (OPT-CAD) study. Clinical outcomes were compared in SCAD patients who initially received PCI (invasive strategy) or conservative treatment according to risk stratification by OPT-CAD score. The primary outcome was ischemic events at 5 years, composed of cardiac death, myocardial infarction, and ischemic stroke. Secondary outcomes included all-cause death, Bleeding Academic Research Consortium (BARC) types 2, 3, or 5, and 3 or 5 bleeding.

Results The conservative group comprised 1767 (58.0%) patients and the invasive group comprised 1278 (42.0%) patients. Overall, invasive strategy did not reduce the risk of ischemic events compared with conservative strategy but was associated with an increased risk of BARC 2, 3, or 5 bleeding (adjusted hazard ratio (HR), 1.59; 95% confidence interval (CI), 1.13–2.26; $P=0.009$). Similar results were observed in the low-risk patient subset ($N=2030$). While in the moderate-to-high-risk subset ($N=1015$), invasive strategy was associated with a reduced risk of ischemic events (HR, 0.67; 95% CI, 0.48–0.95; $P=0.02$) and all-cause death (HR, 0.73; 95% CI, 0.51–1.03; $P=0.07$), and with no excessive risk of bleeding.

Conclusions Invasive strategy could not confer additional clinical benefits in patients with SCAD compared to conservative strategy, except in patients at moderate-to-high risk. The OPT-CAD risk score may be valuable to the guidance of optimal treatment strategy in SCAD patients.

Keywords Stable coronary artery disease, Invasive strategy, Conservative strategy, Risk score

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Background

Percutaneous coronary intervention (PCI) is a widely accepted interventional procedure utilized to reduce the risk of ischemic events and alleviate clinical symptoms in patients with coronary artery disease (CAD) [1]. However, its role in treating patients with stable coronary artery disease (SCAD) remains controversial. Despite previous studies [2, 3] indicating that an invasive treatment is associated with greater improvement in angina-related health status in SCAD patients compared to a conservative strategy, evidence supporting the benefits of PCI in decreasing adverse cardiovascular events or extending survival remains limited [4–6], except in specific patient subsets. Therefore, it is imperative to establish a reliable algorithm to guide treatment strategy selection for SCAD patients.

Risk assessment is an essential prerequisite in developing personalized strategies for SCAD patients. However, the existing risk stratification tools often lack the sensitivity necessary to effectively differentiate the risk of ischemic events within this patient population. The Optimal antiPlatelet Therapy for Chinese patients with Coronary Artery Disease (OPT-CAD) risk score [7], derived from a real-world cohort study that enrolled a full spectrum of CAD patients, has demonstrated robust efficacy in predicting 1-year ischemic risk and death within the CAD population. A previous study has demonstrated the utility of OPT-CAD score in optimizing antiplatelet strategy after PCI [8]. However, the usefulness of the OPT-CAD risk stratification in identifying SCAD patients who might benefit from an invasive strategy was uncertain.

The present study aimed to evaluate potential gains in outcomes from invasive versus conservative strategy in SCAD patients stratified by OPT-CAD risk score in a large-scale, multicenter, real-world cohort study.

Methods

Study design

The OPT-CAD study is a multicenter, prospective, real-world observational study involving 14,032 CAD patients who received antiplatelet therapy and survived until hospital discharge from 109 centers in China (ClinicalTrials.gov Identifier: NCT01735305) [7]. The details of the inclusion and exclusion criteria of the OPT-CAD study have been reported previously [7] (Additional file 1: Supplemental Methods). The present study was a subanalysis of SCAD patients in the OPT-CAD study, which assessed clinical benefit from different treatment strategies in SCAD patients as stratified by the OPT-CAD score. Patients who suffered from left main disease had consent withdrawal or were unavailable to calculate an OPT-CAD score were excluded. The study was approved by the ethics committee of the General Hospital of Northern Theater Command and at each participating center. The study was performed in accordance with the principles of the Declaration of Helsinki. All enrolled patients provided written informed consent.

Definitions and outcomes

The OPT-CAD risk score [7] is a risk assessment tool derived from the OPT-CAD study, which could be used to predict the 1-year risk of ischemic events and all-cause death in CAD patients. The risk score consists of 10 independent risk factors, including age, heart rate, hypertension, prior myocardial infarction (MI), previous stroke, renal insufficiency, anemia, low ejection fraction, positive cardiac troponin, and ST-segment deviation (Additional file 1: Fig. S1). The OPT-CAD score is the sum of the scores of each variable in the model, with a score range of 0 to 257. According to the previous study, patients can be stratified as low risk (0–90), moderate risk (91–150), and high risk (≥151) according to the OPT-CAD score [7]. In the present analysis, patients were stratified as low risk (0–90) and moderate-to-high risk (≥91).

Invasive strategy was defined as PCI for coronary revascularization on top of the medical therapy, and conservative strategy was defined as medical therapy alone with or without coronary angiography. PCI procedure and post-discharge medications for secondary prevention were at physicians' discretion per contemporary guidelines.

The primary outcome was ischemic events occurring within 5 years, defined as a composite of cardiac death, MI, and ischemic stroke. Secondary endpoints included all-cause death, Bleeding Academic Research Consortium (BARC) [9] type 2, 3, or 5 bleeding, and BARC type 3 or 5 bleeding at 5 years. All patients were followed up by telephone or hospital visits at 3, 6, 9, and 12 months, and annually for up to 5 years by professional research staffs. All clinical events were adjudicated by an independent clinical events committee.

Statistical analysis

Categorical variables were expressed as frequencies and percentages, and the chi-square or Fisher exact test was used for the comparison between groups. Continuous variables were presented as mean ± standard deviation, and the differences between groups were assessed by the Student *t* test. To adjust for bias due to confounding across groups, propensity score matching (PSM) was performed when comparing the impacts of different treatment strategies with OPT-CAD risk score stratifications on clinical outcomes in a 1:1 ratio. Variables incorporated into the model included age, sex, body mass index, diabetes mellitus, hypertension, hyperlipidemia, smoking history, previous MI, previous PCI, previous stroke,

family history of CAD, estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), and anemia. We used inverse probability of treatment weighting (IPTW) analysis in addition to PSM to further adjust for confounding and test the consistency of our hypothesis. The PSM- and IPTW-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were determined from a Cox model. Time-to-event data, including ischemic events, all-cause death, and bleeding events were displayed using Kaplan–Meier curves, and between-group differences were analyzed by the log-rank test. Missing observations were imputed by using the most recent previous observation (the last observation carried forward). All tests were two-sided, and P values < 0.05 were considered statistically significant. Statistical analysis was performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

Results

A total of 3045 SCAD patients who completed the 5-year clinical follow-up were enrolled in the present study, consisting of 1767 (58.0%) who received medical therapy and 1278 (42.0%) who underwent PCI. According to the OPT-CAD risk score categorizations, 2030 (66.7%) patients were at low risk and 1015 (33.3%) were at moderate-to-high risk (Additional file 1: Fig. S2). The proportion of patients who had completed the 5-year clinical follow-up was 89.8%.

Invasive versus conservative strategy

As shown in the demographic data, patients in the conservative strategy group were older, had a higher proportion of previous MI or anemia, and the LVEF values were lower than patients treated with invasive strategy. For discharge medication, patients with conservative strategy used aspirin, clopidogrel, β-blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, statins, and proton pump inhibitors significantly less than those in the invasive strategy group (Additional file 1: Table 1). The procedure information for patients with invasive strategy was shown in Additional file 1: Table 2 that the average number of stents implanted was 1.8 ± 1.0, and the main type of stent was a durable polymer drug-eluting stent. The medication management at each annual visit for patients with conservative and invasive groups was shown in Additional file 1: Table 3.

Five-year clinical outcomes for patients in the invasive and conservative groups are demonstrated in Additional file 1: Table 4. After multivariate adjustment, the invasive strategy did not show a significant advantage over the conservative strategy in reducing the risk of ischemic events (adjusted hazard ratio (HR): 0.83, 95% confidence interval (CI), 0.67–1.04, P = 0.11), and all-cause death (adjusted HR: 0.88, 95% CI, 0.70–1.12, P = 0.31). Moreover, the invasive strategy was associated with an increased risk of BARC type 2, 3, or 5 bleeding events (adjusted HR, 1.59; 95% CI, 1.13–2.26; P = 0.009) compared with conservative strategy.

Performance of the OPT-CAD risk score in predicting 5-year adverse clinical events

Baseline characteristics of patients at different risks according to OPT-CAD risk stratification are demonstrated in Additional file 1: Table 5. As shown in Additional file 1: Table 6, the OPT-CAD risk score had good performance in discriminating the risk of ischemic events and bleeding events between patients at low risk and moderate-to-high risk. After multivariate adjustment, patients at moderate-to-high risk had significantly higher risk of ischemic events (HR: 3.23, 95% CI, 2.62–3.98, P < 0.0001), cardiac death (HR: 4.50, 95% CI, 3.38–5.99, P < 0.0001), MI (HR: 2.56, 95% CI, 1.75–3.74, P < 0.0001), ischemic stroke (HR: 2.33, 95% CI, 1.55–3.51, P = 0.0001), as well as all-cause death (HR: 4.61, 95% CI, 3.67–5.79, P < 0.0001), BARC type 2, 3, or 5 bleeding (HR: 1.46, 95% CI, 1.03–2.06, P = 0.03), and BARC type 3 or 5 bleeding (HR: 1.75, 95% CI, 1.03–2.96, P = 0.04) compared to patients at low risk.

Invasive versus conservative strategy in different OPT-CAD risk stratifications

Baseline characteristics, medications after discharge of patients who received invasive and conservative treatment in different OPT-CAD risk stratifications are demonstrated in Table 1 and Additional file 1: Table 7. Clinical outcomes of invasive versus conservative strategy according to OPT-CAD risk stratification before PSM were shown in Additional file 1: Table 8 and Additional file 1: Fig. S3. After PSM, in the low-risk cohort, the invasive strategy was associated with comparable risk of ischemic events (HR, 0.95; 95% CI, 0.66–1.37; P = 0.79), MI (HR, 0.95; 95% CI, 0.50–1.80; P = 0.87), and all-cause death (HR, 1.25; 95% CI, 0.82–1.91; P = 0.31), but significantly increased risk of BARC type 2, 3, or 5 bleeding (HR, 1.98; 95% CI, 1.20–3.27; P = 0.008) at 5 years when compared to the conservative strategy. While in patients at moderate-to-high risk, invasive strategy was associated with reduced risk of 5-year ischemic events (HR, 0.67; 95% CI, 0.48–0.95; P = 0.02) and MI (HR, 0.46; 95% CI, 0.24–0.90; P = 0.02), but with no excessive risks of BARC type 2, 3, or 5 bleeding when compared to the conservative strategy (Table 2, Fig. 1). Moreover, compared with conservative strategy, a numerically lower rate of 5-year all-cause death was seen in patients receiving invasive strategy with moderate-to-high risk (21.6% vs. 16.4%; HR, 0.73;

Table 1 Baseline characteristics between conservative and invasive group stratified by the OPT-CAD score after PSM

	Low risk			Moderate-to-high risk		
	Conservative strategy (*N* = 849)	**Invasive strategy (*N* = 849)**	***P* value**	**Conservative strategy (*N* = 342)**	**Invasive strategy (*N* = 342)**	***P* value**
Age, years	59.4 ± 9.8	59.6 ± 10.1	0.67	70.7 ± 8.9	70.5 ± 8.5	0.79
Male	663 (78.1%)	665 (78.3%)	0.91	232 (67.8%)	243 (71.1%)	0.36
BMI	24.6 ± 2.9	24.6 ± 3.0	0.58	24.2 ± 3.2	24.0 ± 3.1	0.48
Diabetes mellitus	213 (25.1%)	216 (25.4%)	0.87	122 (35.7%)	127 (37.1%)	0.69
Hypertension	465 (54.8%)	457 (53.8%)	0.70	281 (82.2%)	285 (83.3%)	0.69
Hyperlipidemia	158 (18.6%)	155 (18.3%)	0.85	57 (16.7%)	56 (16.4%)	0.92
Smoking history			0.15			0.24
None	470 (55.4%)	448 (52.8%)		208 (60.8%)	190 (55.6%)	
Current smoker	226 (26.6%)	262 (30.9%)		62 (18.1%)	79 (23.1%)	
Ex-smoker	153 (18.0%)	139 (16.4%)		72 (21.1%)	73 (21.3%)	
Previous MI	221 (26.0%)	217 (25.6%)	0.82	164 (48.0%)	163 (47.7%)	0.94
Previous PCI	439 (51.7%)	433 (51.0%)	0.77	208 (60.8%)	205 (59.9%)	0.82
Previous stroke	33 (3.9%)	28 (3.3%)	0.51	62 (18.1%)	64 (18.7%)	0.84
Family history of CAD	99 (11.7%)	104 (12.2%)	0.71	28 (8.2%)	25 (7.3%)	0.67
eGFR, mL/min/1.73 m^2	104.8 ± 30.0	106.1 ± 34.5	0.39	82.5 ± 35.7	82.2 ± 43.0	0.91
LVEF, %	60.6 ± 8.7	60.6 ± 8.3	0.92	54.7 ± 11.5	54.7 ± 11.5	0.98
Anemia	42 (4.9%)	33 (3.9%)	0.29	91 (26.6%)	88 (25.7%)	0.79
Medications at discharge						
Aspirin	821 (96.7%)	834 (98.2%)	0.04	311 (90.9%)	326 (95.3%)	0.02
Clopidogrel	493 (58.1%)	838 (98.7%)	< .0001	205 (59.9%)	331 (96.8%)	< .0001
β-blocker	699 (82.3%)	694 (81.7%)	0.75	274 (80.1%)	269 (78.7%)	0.64
ACEI/ARB	593 (69.8%)	585 (68.9%)	0.67	273 (79.8%)	271 (79.2%)	0.85
Statin	814 (95.9%)	819 (96.5%)	0.53	338 (98.8%)	335 (98.0%)	0.36
PPIs	164 (19.3%)	259 (30.5%)	< .0001	65 (19.0%)	117 (34.2%)	< .0001

Values are mean ± standard deviation or No. (%)

ACEI angiotensin-converting enzyme inhibitor, *ARB* angiotensin II receptor blocker, *BMI* body mass index, *CAD* coronary artery disease, *eGFR* estimated glomerular filtration rate, *LVEF* left ventricular ejection fraction, *MI* myocardial infarction, *PCI* percutaneous coronary intervention, *PPIs* proton pump inhibitors, *PSM* propensity score matching

Table 2 Clinical outcomes between conservative and invasive group stratified by the OPT-CAD score after PSM

	Low risk				Moderate-to-high risk			
	Conservative strategy (*N* = 849)	**Invasive strategy (*N* = 849)**	**HR (95% CI)**	***P* value**	**Conservative strategy (*N* = 342)**	**Invasive strategy (*N* = 342)**	**HR (95% CI)**	***P* value**
Ischemic events[†]	60 (7.1%)	58 (6.8%)	0.95 (0.66–1.37)	0.79	79 (23.1%)	56 (16.4%)	0.67 (0.48–0.95)	0.02
Cardiac death	21 (2.5%)	32 (3.8%)	1.51 (0.87–2.61)	0.14	52 (15.2%)	37 (10.8%)	0.69 (0.45–1.05)	0.08
MI	19 (2.2%)	18 (2.1%)	0.95 (0.50–1.80)	0.87	27 (7.9%)	13 (3.8%)	0.46 (0.24–0.90)	0.02
Ischemic stroke	25 (2.9%)	15 (1.8%)	0.60 (0.32–1.13)	0.12	16 (4.7%)	12 (3.5%)	0.72 (0.34–1.52)	0.39
All-cause death	38 (4.5%)	48 (5.7%)	1.25 (0.82–1.91)	0.31	74 (21.6%)	56 (16.4%)	0.73 (0.51–1.03)	0.07
BARC type 2, 3, or 5 bleeding	23 (2.7%)	45 (5.3%)	1.98 (1.20–3.27)	0.008	18 (5.3%)	21 (6.1%)	1.15 (0.61–2.16)	0.66
BARC type 3 or 5 bleeding	12 (1.4%)	15 (1.8%)	1.24 (0.58–2.65)	0.58	7 (2.0%)	12 (3.5%)	1.65 (0.65–4.20)	0.29

Values are No. (%)

BARC, Bleeding Academic Research Consortium; *CI*, confidence interval; *HR*, hazard ratio; *MI*, myocardial infarction; *PSM*, propensity score matching

[†] Ischemic events were defined as a composite of cardiac death, MI, and ischemic stroke

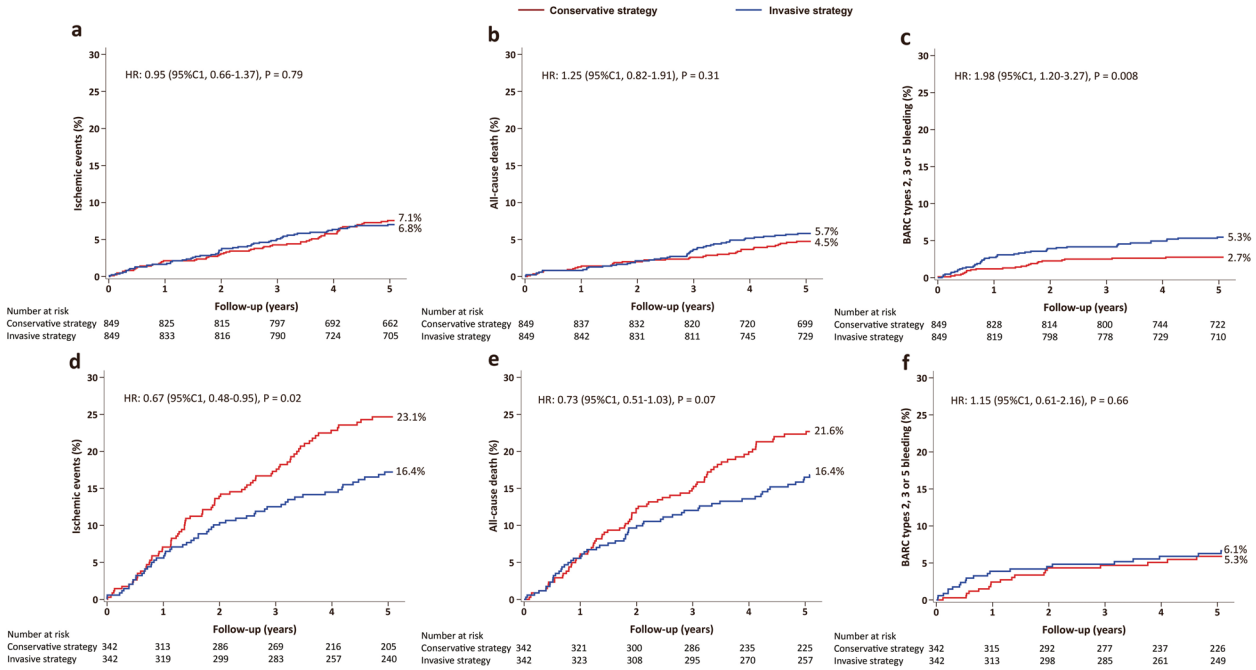

Fig. 1 Kaplan–Meier curves for clinical outcomes in low-risk or moderate-to-high-risk patients after PSM. Cumulative incidences according to follow-up time between conservative group and invasive group after multivariate adjustment for **a** primary outcome-ischemic events (defined as a composite of cardiac death, MI, and ischemic stroke) in low-risk patients, **b** all-cause death in low-risk patients, **c** BARC type 2, 3, or 5 bleeding in low-risk patients, **d** primary outcome-ischemic events in moderate-to-high-risk patients, **e** all-cause death in moderate-to-high-risk patients, and **f** BARC type 2, 3, or 5 bleeding in moderate-to-high-risk patients. BARC, Bleeding Academic Research Consortium; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; PSM, propensity score matching

95% CI, 0.51–1.03; $P=0.07$). As shown in Additional file 1: Table 9, the results were also consistent in the findings derived from the IPTW analysis.

Discussion

In this multicenter, real-world cohort study, we found that (a) an invasive strategy was not significantly associated with a lower incidence of ischemic events in patients with SCAD, compared with conservative strategy separately, but rather with an increased risk of BARC types 2, 3, and 5 bleeding during the 5-year follow-up period; (b) the OPT-CAD score demonstrated excellent in discriminating the risk of long-term adverse events in SCAD patients, especially the risk of ischemic events and all-cause death; (c) according to the OPT-CAD score categorization, moderate-to-high-risk SCAD patients could benefit from an invasive strategy in reducing the 5-year risk of ischemic events without increased bleeding risk.

Clinical guidelines recommend conservative treatment as the initial strategy for SCAD patients, with revascularization considered as an adjunct to medical therapy [10]. Our analysis indicated that an invasive strategy was not associated with a reduced risk of ischemic events compared to a conservative strategy. Such a conclusion aligns with previous clinical studies that focused on initial invasive strategy versus conservative strategy regarding the impacts on clinical outcomes [5, 6, 11–13]. Indeed, available evidence has shown potential effects in symptom relief and exercise tolerance improvement from an invasive strategy [2, 14], and a proven prognostic benefit has been found in SCAD patients with LVEF > 35% involving functionally significant left main stem stenosis [15], three-vessel disease [16] or proximal left anterior descending [17, 18], and patients with functionally significant multivessel disease and LVEF ≤ 35% [19]. Hence, it is important to emphasize that invasive strategy or conservative strategy options should not be seen as competing alternatives but rather as complementary strategies working together to enhance patient-centeerd outcomes. Moreover, an increased risk of bleeding in patients treated with invasive strategy was found in our analysis, possibly due to the higher proportion of unavoidable dual antiplatelet therapy after stent implantation. The consideration of both the benefits and risks associated with available therapeutic strategies is imperative in the treatment decision-making process. Given that clinical outcomes can differ substantially among patients, it is essential to assess each individual's specific needs and characteristics.

With the aim of identifying patients who will benefit from revascularization beyond the amelioration of

symptoms, risk stratification performed by risk scores has been suggested for suspected or newly diagnosed CAD patients. However, the extent to which risk score benefits SCAD patients is still unclear. The OPT-CAD score, a risk stratification tool for CAD patients, has been confirmed to have good predictive value for ischemic events (C statistic for 0.76) and death (C statistic for 0.82) at 1 year in SCAD patients [7]. Our results indicated that the 5-year risk of ischemic events was significantly higher in patients with moderate or high risk than those with low risk, showing that the OPT-CAD score has the primary advantage of including a limited number of variables and being easy to calculate, while maintaining high discriminative ability. Stratification using the OPT-CAD score revealed that patients with low risk were more likely to experience hemorrhage after stent implantation, without a meaningful reduction in ischemic risk. Conversely, the invasive strategy was significantly associated with a lower risk of ischemic events in patients with moderate-to-high-risk scores but no significant increase in the risk of bleeding. It is crucial to emphasize that the invasive strategy was associated with a 5.2% absolute reduction in all-cause death among patients with moderate-to-high risk. While the limited sample size precluded the robust statistical significance, the clinical implications are encouraging. This noteworthy finding promotes physicians to reconsider the potential benefits of invasive interventions for SCAD patients at high ischemic risk. These results underscore the inadequacy of a traditional one-size-fits-all approach for SCAD patients, indicating the potential value of the OPT-CAD risk score in personalized clinical decision-making, which is worth for further investigation via randomized trials.

Recent studies have focused on the survival benefit of revascularization in specific SCAD populations [20–22]. Clinical outcomes appear to favor a conservative strategy for patients with non-hemodynamical significance coronary lesions [23, 24], while an invasive strategy should be considered on top of conservative treatment in certain cases of high-risk anatomical features or functionally significant stenoses determined by fractional flow reserve [25]. For patients with mild-to-moderate left ventricular dysfunction in the ISCHEMIA study [26], an invasive strategy is more beneficial than a conservative strategy with a 4-year event rate difference of − 12.1% (95% CI, − 22.6 to − 1.6%). Furthermore, anemia [27], previous MI [28], or cardiac troponin elevation [29] has been demonstrated to be predictive factors for the presence of angiographic complexity of CAD, with the results of higher risk in such populations. Besides, traditional cardiovascular risk factors, such as age and hypertension, also play a substantial role in the structural remodeling of coronary microcirculation [30]. As noted, advanced age, a significant independent risk factor for morbidity and death [31], is a heavily weighted factor in the OPT-CAD score as well as most conventional risk scores utilized in clinical practice [32, 33], which necessitates careful treatment decisions for older individuals. Therefore, it is crucial to systematically identify and effectively manage these risk factors to prevent disease progression and alleviate symptoms. Given that these clinical characteristics are included in the OPT-CAD score, it provides an explanation for the validity of the OPT-CAD score in SCAD patients in terms of its ability to predict risks and guide treatment strategies. Although the OPT-CAD risk score is capable of effectively distinguishing the risks of ischemic events and all-cause death, merely 2% of the patients are classified into the high-risk group. In order to ensure the robustness and reliability of the analysis, we merged the moderate-risk and high-risk groups. Overall, the OPT-CAD score enables quick, easy, and non-invasive identification of ischemic risk in SCAD patients, allowing for tailored primary and secondary prevention, in whom the risk of subsequent clinical events may vary considerably.

Limitations

Several limitations of this study should be noted. First, this was a post hoc analysis of an observational cohort, and study interventions were not randomly assigned. Although PSM was well done and the results seemed clinically and biologically plausible, the bias was inevitable. Therefore, all our findings should be considered hypothesis generating, and specifically designed trials are warranted to validate the findings. Given that newer drugs and devices are being employed in routine clinical practice to enhance the clinical prognosis of SCAD patients, further researches are warranted to assess the potential benefits from invasive strategy stratified OPT-CAD risk score in the contemporary era. Second, data for secondary prevention medication adherence were not collected and analyzed in the present study. Considering the different medication regimens between patients who received initial invasive and conservative treatment as shown in this study, further studies are needed to explore the impact of medication adherence on long-term prognosis in SCAD patients with respect to invasive and conservative strategy. Third, the study population comprised individuals from the OPT-CAD cohort, necessitating external validation of the findings. Nevertheless, given that the OPT-CAD score was established from a general CAD patient cohort, focusing on 1-year clinical outcomes, the present study provided valuable insights for the consistent performance of the OPT-CAD score in predicting 5-year clinical outcomes specially within the SCAD patient subset. Fourth, given that troponin levels are consistently negative in patients with SCAD,

and considering that troponin is one of the key components in the OPT-CAD scoring system, using a cut-off of 90 points may potentially underestimate the risk in these patients. Finally, the present study included exclusively East Asian patients which raised significant concerns regarding the generalizability of the results. Therefore, our findings necessitate further validation in a more extensive patient population.

Conclusions

Among SCAD patients, the initial invasive strategy was associated with an excessive risk of clinically relevant bleeding complications at 5 years, without demonstrating any benefits in terms of ischemic events and death compared to the initial conservative strategy. The OPT-CAD score showed good discrimination for ischemic events and all-cause death, potentially providing a reliable algorithm to support decision-making for the management of SCAD patients. Specially, in patients at moderate-to-high risk according to the OPT-CAD score, the invasive strategy reduced ischemic events without an excessive bleeding risk compared to the conservative strategy at 5 years.

Additional files.

Abbreviations

95% CI	95% Confidence interval
ACEI	Angiotensin-converting enzyme inhibitor
ARB	Angiotensin II receptor blocker
BARC	Bleeding Academic Research Consortium
CAD	Coronary artery disease
eGFR	Estimated glomerular filtration rate
HR	Hazard ratio
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
PCI	Percutaneous coronary intervention
PPIs	Proton pump inhibitors
SCAD	Stable coronary artery disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-04020-2.

Additional file 1: Supplemental Methods, Tables 1 – 10 and Figure S1 – S3. Supplemental Methods – The inclusion and exclusion criteria for the OPT-CAD study. Table 1 – Baseline characteristics and medication at discharge between conservative and invasive group. Table 2 – The procedure information for patients with invasive strategy. Table 3 – Medications management at each annual visit for patients with conservative and invasive strategy. Table 4 – Clinical outcomes between conservative and invasive group by Cox regression analysis. Table 5 – Baseline characteristics among low-risk, moderate-risk, and high-risk groups stratified by the OPT-CAD score. Table 6 – Clinical outcomes among groups stratified by the OPT-CAD score. Table 7 – Baseline characteristics between conservative and invasive group stratified by the OPT-CAD score before PSM. Table 8 – Clinical outcomes between conservative and invasive group stratified by the OPT-CAD score before PSM. Table 9 – Clinical outcomes between conservative and invasive group stratified by the OPT-CAD score after IPTW. Table 10 – Comparison of bleeding types in patients with low risk and moderate-to-high risk. Figure S1 – Algorithm of the OPT-CAD risk score. Figure S2 – Flowchart of the Study. Figure S3 – Kaplan–Meier curves for clinical outcomes in low-risk or moderate-to high-risk patients before PSM

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Authors' contributions

The data were analysed by MHQ, ZZQ and MHQ were major contributors to writing the manuscript. YX, KX, HWL, XZW, JL, BL, SLC, and JYC participated in data collection and editing the manuscript. YLH and YL conceptualized and designed the study and provided critical amendments to this article. All authors read and approved the final manuscript.

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Data availability

The datasets analysed in the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate.

The study was approved by the ethics committee of the General Hospital of Northern Theater Command and at each participating center (approval number: k [2012] 17).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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