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Role of pre-procedure CCTA in predicting failed percutaneous coronary intervention for chronic total occlusions

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ABSTRACT

Purpose: This study aimed to identify major lesion characteristics of chronic total occlusions (CTOs) that predict failed percutaneous coronary intervention (PCI) using pre-procedure coronary computed tomography angiography (CCTA) in combination with conventional coronary angiography (CCA).

Methods: Consecutive patients with at least one CTO of the native coronary arteries received CCTA and CCA-guided PCI, with computed tomography performed before or during PCI.

Results: A total of 76 patients with CTO were included in this study. 76 patients were divided into successful and failed PCI groups based on their PCI outcome. There were 62 (81.58 %) patients in the successful PCI group and 14 (18.42 %) in the failed PCI group. The occlusion length ≥20 mm, ostial or bifurcation lesions, negative remodeling, microchannels, and good collateral vessels were the CCTA morphologic parameters associated with PCI outcome ($P<0.05$). In addition, the blunt stump, occlusion length ≥20 mm, and ostial or bifurcation lesions, were the CCA morphologic parameters associated with PCI outcome ($P<0.05$). The multivariate regression model showed that the three independent negative predictors: blunt stump on CCA (OR: 0.63; 95 % CI: 0.23–0.98; $p=0.048$), occlusion length ≥20 mm on CCTA (OR: 0.37; 95 % CI: 0.32–0.71; $p<0.001$) and negative remodeling on CCTA (OR: 0.26; 95 % CI: 0.28–0.44; $p<0.001$).

Conclusion: Our study demonstrated that combining CCTA and CCA morphologic characteristics could improve PCI outcome prediction in patients with CTO compared to CCTA morphologic features alone.

1. Introduction

Coronary artery chronic total occlusion (CTO) refers to a situation where a vessel in the heart is blocked due to a lesion. This blockage prevents blood from flowing forward to fill downstream blood vessels. The term "chronic" describes lesions that have been occluded for over three months [1]. CTO is commonly observed in patients with coronary heart disease who undergo coronary vascular CCTA or percutaneous interventional angiography. All CTO lesions develop from an initial acute coronary event [2]. Pathologically, during the acute stage, there is a rupture of the atherosclerotic plaques in the coronary arteries, leading to thrombosis in the vascular lumen. This results in lumen stenosis and occlusion [3]. Over time, collagen gradually replaces cholesterol-laden plaques, and thrombi become organized and mixed with them to form a fibrotic structure. Some lesions become calcified, progressively evolving into fibrocalcific fibrosis mixed with loose, dense connective tissue-occlusion structure [4].

Current research shows that interventional therapy can reduce angina symptoms or improve long-term prognosis better than drug therapy; therefore, interventional therapy is of great significance in the treatment of coronary CTO lesions [5]. Compared with other non-occlusive coronary artery stenosis diseases, interventional treatment of CTO lesions is difficult, time-consuming, expensive, has a high risk of complications, low surgical success rate and controversial long-term effects, resulting in only 8 %-15 % of patients undergoing coronary intervention [6]. In recent years, with the development of interventional technology and the use of related new instruments, the success rate of interventional surgery for CTO lesions has been significantly improved, and the opening rate of occluded blood vessels is close to that of interventional surgery for non-occlusive coronary artery

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stenosis disease [7]. Furthermore, previous studies have shown that reopening occluded blood vessels can significantly improve left ventricular function and patient life [8].

Drug stents have become widely used in clinical practice and have significantly reduced the rate of stent restenosis and interventional complications. Recently, there has been increased interest in the interventional treatment of CTO lesions [9]. Although the success rate of CTO interventional treatment has improved with technological advancements and increased clinical experience, the procedure remains complex and challenging. It is often considered the "last fortress" of coronary interventional treatment [10]. Therefore, it is crucial to accurately evaluate the preoperative characteristics of CTO patients' lesions and predict the difficulty and success rate of interventional treatment. However, in this study, we aim to investigate whether morphological features of pre-procedural CCTA and CCA could serve as predictors of failed PCI and guide interventional treatment procedures.

2. Methods

2.1. General information

The clinical and imaging data of 76 cases (91 lesions) with chronic total occlusion of coronary arteries, confirmed through coronary computed tomography angiography (CCTA) in our hospital between January 2019 and October 2022, were analyzed retrospectively. Patients were included if (i) they underwent both CCTA and ICA examinations, with a time interval of less than one month between the two tests, (ii) CCTA confirmed the presence of CTO lesions in at least one coronary vessel, (iii) the CCTA image quality met the diagnostic standards, and the clinical data were completed. Patients were excluded if (i) they previously underwent coronary artery bypass graft surgery (CABG), (ii) they did not have intervention revascularization of CTO, (iii) they did not have undergone coronary CCTA before PCI, (iv) the period between CCTA and PCI was more than 30 days, and (v) the image quality of the coronary CCTA was poor. Finally, among the 76 patients, there were 91 chronically occluded blood vessels, 64 of whom were male and 12 were female, aged 30–88 years (65.2±13.1). Additionally, 52 patients had hypertension, 19 had hyperlipidaemia, and 31 had diabetes.

2.2. Definition

Blunt Stump refers to the morphological manifestation observed at the terminus of an occluded arterial segment. In imaging modalities, a blunt stump is distinguished by a sudden and definitive cessation of the arterial structure instead of a more gradual or funnel-like termination. This particular morphology presents additional challenges for interventional cardiologists to navigate and address the occlusion.

Negative Remodeling describes a pathological phenomenon in which the vessel wall experiences structural modifications, culminating in a decrease in the vessel's luminal diameter. Chronic inflammatory responses or other pathological mechanisms may induce this process of negative Remodeling. It frequently leads to arterial constriction, complicating interventional procedures such as percutaneous coronary intervention (PCI).

2.3. CCTA examination

The patient underwent a 256-slice CT machine inspection. Before the scan, they were required to undergo breathing training and were positioned lying on their back. The scanning method used a single heart rate axis scanning technique with a tube voltage of 120 kV and a tube current ranging between 350 and 600mAs. The layer thickness was 0.625 mm. During the enhanced scanning, a double-barrel high-pressure syringe was used to inject 10 ml of normal saline through the cubital vein. Following this, 50–60 ml of iohexol, with a concentration of 350 mg I/ml, was injected at a 4.0–4.5 ml/s rate. Then, 40 ml of normal saline was added at the same rate. The contrast agent concentration in the ascending aorta root was monitored using automatic tracking technology, and the threshold was set to 150HU to trigger the scan automatically. The scanning range included the subtracheal carina from 1 to 2 cm below the diaphragm. For image post-processing, the GE workstation was used, which included coronary artery freezing technology images such as volume rendering VR (Volume rendering VR), curve planar reformation CPR (Curve planar reformation CPR), and Maximum intensity projection (MIP) to reconstruct the coronary arteries.

2.4. ICA examination

The machine typically uses the right radial artery puncture for procedures related to the heart's coronary arteries. However, in case of arterial spasm, the contralateral radial artery or right femoral artery puncture can be used to perform left and right coronary angiography. At least two or more different projection positions can be used to examine each coronary artery. CTO lesions refer to complete occlusion of the coronary arteries, interrupting forward blood flow and leading to thrombolysis in myocardial infarction (TIMI) blood flow grade of 0. CTO lesions last for at least three months.

2.5. Classification of ICA and CCTA collateral channels

There are three grades of collateral connections between occluded and collateral blood vessels. Grade CC0 indicates no continuous connection. Grade CC1 indicates a thin and line-like connection. Grade CC2 indicates a connection similar to a branch vessel. The sources of collateral channels are divided into three categories: epicardial branch collaterals, bridge-like collaterals, and ventricular septal branch collaterals.

2.6. Statistical analysis

The statistical tool used in this study is the SPSS 26.0 software. Continuous variables were represented as mean ± standard deviation. Interobserver and intraobserver agreement were reported as percentages of agreement and Cohen k values for categorical variables. The Student t-test was used for normally distributed data, the Mann-Whitney U test for non-normally distributed data, and the chi-square test for categorical variables. Univariate statistical tests were initially carried out using a binary logistic regression model to identify coronary CCTA and CCA characteristics linked with failed PCI. A multivariate model was created to predict failed PCI by adding significant factors ($p < 0.05$) from the univariate analysis. For multivariate analysis, the continuous data were converted to categorical variables using Youden's criteria cut-off values. When the same characteristics from CCA and CCTA were predictive of failed PCI in univariate analysis, the better predictor was included in the multivariate analysis. A p-value of <0.05 is deemed statistically significant.

3. Results

3.1. Baseline patient characteristics

A total of 76 patients with CTO were included in this investigation after 44 patients were eliminated due to a previous history of CABG (3), a lack of PCI for CTO (16), a lack of CCTA before PCI (10), or an interval between CCTA, PCI of more than 30 days (9), and poor image quality (6) (Fig. 1). 76 patients were divided into a successful PCI and a failed PCI group according to their PCI outcome. There were 62 (81.58 %) patients in the successful PCI group (54 males, 8 females) and 14 (18.42 %) in the failed PCI group (10 males, 4 females). One of the 14 patients in the failed PCI group had two lesions, whereas the other 13 had one lesion each. The patients' age was the only demographic parameter associated with the PCI outcome ($P<0.05$). Other baseline characteristics,

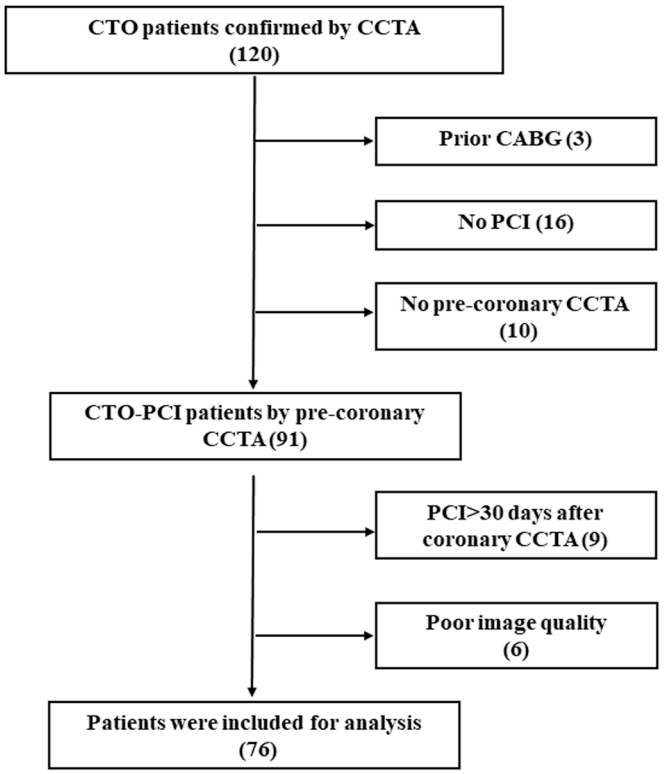

Fig. 1. A flowchart outlining the patient inclusion and exclusion procedure. CTO, coronary chronic total occlusion; ICA, invasive coronary angiography; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; CCTA, coronary computed tomographic angiography.

including body mass index (BMI), medical history and lesion site, were not significantly different between the two groups (P>0.05). Detailed baseline characteristics are presented in Table 1.

3.2. Outcomes analysis of the CCTA and PCI

CCTA identified 91 CTO lesions in 76 patients. The most prevalent site of CTO was the right coronary artery (RCA) (37/91, 40.66 %), followed by the left anterior descending artery (LAD) (30/91, 32.97 %) and the left circumflex artery (LCX) (24/91, 26.37 %). PCI was successfully achieved for 62 lesions of the 91 CTO lesions (62/91, 68.13 %) and failed PCI in 29 lesions (29/91, 31.87 %). Failure to pass through the guidewire was the leading reason for failed PCI (14/29, 48.28 %). PCI was discontinued in 15 patients due to significant procedure-related coronary dissection. No further major problems were reported in any of the patients, including wire perforation, cardiac tamponade, or acute myocardial infarction.

3.3. CCTA morphologic parameters

The morphologic parameters of CTO in the successful PCI group and the failed PCI group are represented in Table 2. The statistical analysis showed that the occlusion length ≥20 mm, ostial or bifurcation lesions, negative remodeling, microchannels, and suitable collateral vessels were the morphologic parameters associated with PCI outcome (P<0.05). Other morphologic parameters, including the calcification degree, blunt stump, tortuous course, CTO lesion calcium, bridging collateral vessel, retrograde collateral vessel, and good visualization of the occluded distal segment were not significantly different between the two groups (P>0.05). Interobserver agreement on CCTA morphological characteristics was good across all lesions (κ=0.86–0.90).

Table 1
Baseline patient characteristics.

Baseline/demographic characteristics	Total patients 76	Successful PCI 62	Failed PCI 14	p-value
Age, year (Mean ± SD)	65.2±13.1	64.0±13.5	70.5±10.0	0.052
BMI (kg/m^2)	24.81±2.98	24.61±2.88	24.93 ±3.06	0.613
Gender (%)				0.158
Male	64 (84.21 %)	54 (87.1 %)	10 (71.43 %)	
Female	12 (15.79 %)	8 (12.90 %)	4 (28.57 %)	
Medical History (%)				
Hypertension	52 (68.42 %)	40 (64.52 %)	12 (85.71 %)	0.743
Diabetes	31 (40.79 %)	23 (37.1 %)	8 (57.14 %)	0.439
Hyperlipidaemia	19 (25 %)	17 (27.42 %)	2 (14.29 %)	0.594
Prior Coronary artery disease	37 (48.68 %)	29 (46.77 %)	8 (57.14 %)	0.286
CKD/Renal failure	10 (13.16 %)	8 (12.90 %)	2 (14.29 %)	0.094
Smoking	26 (34.21 %)	22 (35.48 %)	4 (28.57 %)	0.217
Drink	23 (30.26 %)	21 (33.87 %)	2 (14.29 %)	0.781
Family history of CHD	7 (9.21 %)	6 (9.68 %)	1 (7.14 %)	0.599
Lesion site				0.765
RCA	37 (48.68 %)	20 (32.26 %)	17 (58.62 %)	0.192
LAD	30 (39.47 %)	22 (35.48 %)	8 (27.59 %)	0.957
LCX	24 (31.58 %)	20 (32.26 %)	4 (13.79 %)	0.177

Values are the mean ± standard deviation (SD), median (interquartile range), or percentage (%). Variables were compared using the Student's t-test, Mann-Whitney test, chi-squared test, or Fisher exact test. A P value less than 0.05 indicated statistical significance. PCI, percutaneous coronary intervention; CTO, coronary chronic total occlusion; BMI, body mass index; CKD, chronic kidney disease; CHD, coronary heart disease; RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery.

3.4. CCA morphologic parameters

Table 3 shows the morphologic characteristics of CTO in both the successful and failed PCI groups. The statistical analysis revealed that the blunt stump, occlusion length ≥20 mm, and ostial or bifurcation lesions were the morphologic parameters associated with PCI outcome (P<0.05). Other morphologic features, such as calcification, tortuous course, bridging collateral vessel, good visualization of the occluded distal segment, microvessels, and collateral vessels, did not vary substantially between the two groups (P>0.05). The interobserver agreement on CCA was good for all lesions (k= 0.73).

3.5. Independent predictors' analysis

The multivariate regression model showed three independent negative predictors: blunt stump on CCA (OR: 0.63; 95 % CI: 0.23–0.98; p =0.048), occlusion length ≥20 mm on CCTA (OR: 0.37; 95 % CI: 0.32–0.71; p <0.001) and negative remodeling on CCTA (OR: 0.26; 95 % CI: 0.28–0.44; p <0.001). The multivariate analysis revealed that ostial or bifurcation lesions on CCA and tortuous course on CCTA were not independent predictors (p > 0.05 for each) in between two groups (Table 4).

4. Discussion

Our investigations found that CCTA morphologic features of CTO lesions, such as a blunt stump, occlusion length ≥20 mm and negative remodeling, were independent predictors of PCI outcomes in patients

Table 2
Coronary computed tomography angiography (CTA) morphologic parameters characteristics.

	Total patients 76	Successful PCI 62	Failed PCI 14	p-value
Calcification degree				0.284
None	11 (14.47 %)	10 (16.30 %)	1 (7.14 %)	
Moderate	30 (39.47 %)	25 (40.32 %)	5 (35.71 %)	
Severe	35 (46.05 %)	27 (43.55 %)	8 (57.14 %)	
Occlusion length ≥20 mm	35 (46.05 %)	21 (33.87 %)	14 (100 %)	0.002
Ostial or bifurcation lesions	24 (31.58 %)	16 (25.81 %)	8 (57.14 %)	0.018
Blunt stump	16 (21.05 %)	4 (6.45 %)	12 (85.71 %)	0.138
Tortuous course	8 (10.53 %)	5 (8.06 %)	3 (21.43 %)	0.966
CTO lesion calcium	58 (76.32 %)	45 (72.58 %)	13 (92.85 %)	0.653
Bridging collateral vessel	8 (10.53 %)	4 (6.45 %)	4 (28.57 %)	0.160
Retrograde collateral vessel	67 (88.16 %)	56 (90.32 %)	11 (78.57 %)	0.522
Negative remodeling	11 (14.47 %)	1 (1.61 %)	10 (71.43 %)	<0.001
Microchannels	69 (90.79 %)	57 (91.94 %)	12 (85.71 %)	0.017
Good visualization of the occluded distal segment	37 (48.68 %)	24 (38.71 %)	13 (92.85 %))	0.485
Good collateral vessels	22 (28.94 %)	19 (30.65 %)	3 (21.43 %)	0.012

Values are the median (interquartile range) or n (%). Variables were compared using univariate logistic regression analysis. A P value less than 0.05 indicated statistical significance. CTO, coronary chronic total occlusion; PCI, percutaneous coronary intervention.

Table 3
Conventional coronary angiography (CCA) morphologic parameters characteristics.

	Total patients 76	Successful PCI 62	Failed PCI 14	p-value
Calcification	32 (42.11 %)	25 (40.32 %)	7 (50 %)	0.471
Blunt stump	43 (56.58 %)	30 (48.39 %)	13 (92.86 %)	0.029
Occlusion length ≥20 mm	27 (35.53 %)	18 (29.03 %)	9 (64.29 %)	0.038
Ostial or bifurcation lesions	25 (32.89 %)	17 (27.42 %)	8 (57.14 %)	<0.001
Tortuous course	23 (30.26 %)	15 (24.19 %)	8 (57.14 %)	0.241
Bridging collateral vessel	53 (69.74 %)	43 (69.35 %)	10 (71.43 %)	0.482
Good visualization of the occluded distal segment	58 (76.32 %)	48 (77.42 %)	10 (71.43 %)	0.622
Microvessels	41 (53.95 %)	34 (54.84 %)	9 (64.29 %)	0.703
Score for collateral vessels				0.759
0	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
1	4 (5.26 %)	3 (4.84 %)	1 (7.14 %)	
2	11 (14.47 %)	9 (14.52 %)	3 (21.43 %)	
3	61 (80.26 %)	50 (80.65 %)	11 (78.57 %)	

PCI, percutaneous coronary intervention.

with CTO. However, combining CCTA and CCA morphologic characteristics could improve PCI outcome prediction in patients with CTO compared to CCTA morphologic features alone.

Table 4
Multivariate analysis (MVA): Independent predictors' analysis.

	Odds Ratio (OR)	95 % CI	p-value
Blunt stump on CCA	0.63	0.23–0.98	0.048
Occlusion length ≥20 mm on CTA	0.37	0.32–0.71	<0.001
Ostial or bifurcation lesions on CCA	1.12	0.06–1.25	0.896
Tortuous course on CTA	0.82	0.25–1.33	0.652
Negative remodelling on CTA	0.26	0.28–0.44	<0.001

CTA, computed tomography angiography; CCA, conventional coronary angiography; CI, confidence interval.

CTO of the coronary artery remains a challenging condition for PCI. Despite impressive technical advancements and improvements in interventional procedures, the success rate of PCI for recanalization of CTO is much lower than that of non-occluded arteries. In our study, CTO-PCI had a success rate of around 68.13 % (62/91). In comparison, our study found a somewhat lower success rate for CTO-PCI than previously reported [11]. The degree of calcification, negative remodeling, and the presence of a necrotic core all correlate with the success rate of PCI for CTO [12]. Thus, the morphologic characteristics of the CTO may have influenced the success rate of PCI in the patients recruited. In addition, the limited availability of specialized equipment and the small number of cases from a single facility could be another reason for our study's comparatively lower success rates of the CTO-PCI.

Negative remodeling by CCTA, detected in 10 lesions (71.43 %) in the failed PCI group, was a predictor of PCI failure ($p < 0.001$). Ehara et al. [13] also reported this predictor. Chronic arterial occlusion leads to negative remodelling [14]. However, several variables can prevent the guidewire from crossing a negatively modified CTO. First, negative remodeling affects vessel diameter. A histological investigation of rabbit CTOs found that the arterial occlusion section reduced total artery size by around 80 % within 6 weeks, with the decline increasing with time [15]. Autopsies of human coronary arteries reveal that negative remodeling occurs in the late stages of CTO [15,16]. Second, negatively remodeled tissue is a kind of wound healing that involves replacing an originally proteoglycan-rich extracellular matrix with a collagen-rich scar, resulting in a stiff vessel lumen [12]. In addition, the presence of a "proximal fibrous cap," a thicker structure near the entry of the CTO with tightly packed collagen, makes it more difficult for a guidewire to overcome the occlusion[16] and simpler to perforate the vessel.

CTO calcification has long been related to revascularization failure [17,18]. Our investigation found no significant difference in calcification between failed and successful PCI groups. However, the proportion of CTOs with severe calcification was similar to prior publications [19]. This finding might be explained in a variety of ways. First, the calcification in our instances was typically dispersed, irregular, or sandwich biscuit-like. Successful recanalization requires a small amount of non-calcified remnant in the lumen, even in highly calcified CTOs. The enhanced resolution of 256-slice CT for CCTA allows for more sensitive identification of non-calcified residue lumens in blocked arteries [17,18], and the operator may readily locate the best anchor point and route to avoid calcification [19].

Previous studies have suggested that a longer occlusion length is associated with lower success rates in PCI procedures [20]. Our study confirmed this finding, with a lesion length cut-off value of ≥20 mm, which is consistent with previous reports [21,22]. However, unlike previous studies that identified other factors as significant predictors of antegrade CTO success, our study did not find any such predictors [17,18]. This could be partly explained by the recent development of interventional devices that are specifically designed for CTO lesions. In addition, our study utilized CCTA and CCA, which could have contributed to these findings [17,21,22].

5. Limitations

Our study has a few drawbacks. First, this was a single-centre, retrospective research with potential patient selection biases. More research with bigger sample sizes is needed. Second, if extensive calcification obscures the lumen, the exact position of the CTO's proximal or distal edge may be obscured on CCTA. The CCTA may not accurately determine lesion length if there is 360° calcification at the proximal or distal CTO boundary. (No CTO in this series had 360° calcification). Third, Confounding factors like patient diabetes and renal disease, which may affect PCI outcomes, could not be controlled in the relatively small sample size of the study. Finally, with five possible factors, the multivariable model might be over fit. Whether the three risk factors for failed PCI identified in our investigation are the most relevant procedural predictors, and whether regular CCTA increases the overall PCI success rate for CTOs, must be confirmed in a larger multicentre trial. Similarly, the cut-off values for the continuous variables determined using post hoc ROC curve analysis in the current study should be validated in future studies.

6. Conclusion

Our study showed that the negative predictors of successful PCI were occlusion length ≥20 mm, negative remodeling on CCTA, and blunt stump on CCA. However, integrating CCTA and CCA morphologic characteristics may enhance PCI outcome prediction in patients with CTO compared to CCTA morphologic features alone. Future investigations will validate the current study outcomes using a large sample size.

Ethics statement

The Ethics Committee of Zhoupu Hospital Affiliated to Shanghai Medical and Health College conducted the study in accordance with the Declaration of Helsinki and approved (2023-C-004-E01). All participating patients provided their written consent to participate in this study.

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CRediT authorship contribution statement

Hua Zhou: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Xiaojun Fan:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Mingyuan Yuan:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Wei Wang:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Conceptualization. **Qiyuan Wu:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Wu Qiyuan reports was provided by Zhoupu Hospital Affiliated to Shanghai Medical and Health College. Dr. Wu Qiyuan reports a relationship with Zhoupu Hospital Affiliated to Shanghai Medical and Health College that includes: employment. Dr. Wu Qiyuan has patent pending to N/A. N/A If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data Availability

The datasets used/analyzed during the present study are available from the corresponding author upon reasonable request.

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