Stumpless lesion improves the value of J-CTO score in predicting the antegrade procedure outcome of chronic total occlusion percutaneous coronary intervention

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Abstract

Background

Percutaneous coronary intervention (PCI) of coronary chronic total occlusion (CTO) is one of the most challenging procedures of interventional cardiology. Debate continues with regard to the predictors that influence the antegrade procedure outcome.

Methods

The CTO PCIs were prospectively registered from May 1, 2012 to August 22, 2017 in a single center. Variables of patients' characteristics, CTO morphology, PCI strategy, procedure materials and outcomes were recorded. Multivariable logistic regression model was adopted to identify predictors of procedure outcome.

Results

A total of 193 CTO PCIs were consecutively included, and 187 antegrade PCIs were finally analyzed. The antegrade technical and procedure success rates were both 67.91%. Multivariable logistic regression indicated that stumpless lesion (OR: 2.813; 95% CI: 1.120–7.062, p = 0.028) and occlusion length ≥ 20 mm (OR: 2.196; 95% CI: 1.087–4.437, P = 0.028) independently predicted the procedure outcome. The area under the receiver-operator characteristic (ROC) curve for discriminating failed CTO PCI was 0.621 (95% CI: 0.534–0.708, p = 0.008) for Japanese multicenter CTO registry (J-CTO) score, which significantly increased to 0.673 (95% CI: 0.592–0.755, p = 0.000) after modifying stumpless lesion score from 1 to 2 points.

Conclusions

Stumpless lesion and occlusion length ≥ 20 mm independently predict the antegrade CTO procedure failure. Scoring 2 points to stumpless lesion improves the value of J-CTO score in predicting the procedure outcome.

Background

Coronary chronic total occlusion (CTO) recanalization is still an extremely challenging procedure in cardiovascular intervention. Identifying predictors of the procedure outcome of CTO intervention is critical for assessing benefit/risk and screening suitable cases to be treated. The Japanese multicenter CTO registry (J-CTO) score was established for assessment of lesion severity and prediction of antegrade guidewire crossing within 30 minutes[1]. However, the predictive value of J-CTO score for the final procedure outcome is controversial [2–4]. The objective of the present study was to explore further predictors of the antegrade procedure outcome of CTO percutaneous coronary intervention (PCI).

Methods

Study population

This prospective observational study enrolled consecutive CTO PCIs from May 1, 2012 to August 22, 2017 in our center. Patients who presented with propensity to bleeding, severe renal insufficiency (serum creatinine > 2.5 mg/dL), or cancer were excluded. Of 193 consecutive CTO PCIs in 164 patients, six CTO interventions were excluded because the patients only received retrograde attempt (three procedures succeeded with primary retrograde approach, another three failed with primary retrograde approach without rescue antegrade attempt). A total of 187 CTO PCIs performed in 162 patients were finally analyzed. The study design and flow chart are shown in Fig. 1.

Definitions

The CTO was defined as an obstruction of a coronary artery with thrombolysis in myocardial infarction (TIMI) flow 0 and estimated occlusion duration of at least 3 months based on the patient's clinical history or previous coronary angiography[5]. The J-CTO score was calculated as described by Morino et al[1]. Stumpless CTO lesion was defined as the entry point of the occlusion was located at the bifurcation and the vessel course distal to the occlusion was hardly predictable (Fig. 2)[6]. Study outcomes were set as the technical and procedure successes. The technical success was defined as successful CTO revascularization with achievement of < 20% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 flow, and the procedure success was defined as achievement of technical success without in-hospital major adverse cardiac events (MACE). The in-hospital MACE was defined as a composite of the following adverse events before hospital discharge: death, myocardial infarction, urgent repeat target vessel revascularization with either PCI or coronary artery bypass graft surgery, tamponade requiring either pericardiocentesis or surgery, and stroke. Myocardial infarction was defined using the Third Universal Definition of Myocardial Infarction[7]. The urgent target vessel revascularization was characterized by urgent, clinically driven repeat percutaneous or surgical intervention of the treated vessel.

PCI

PCI procedure were performed according to the guideline[8]. The procedure strategy (antegrade or retrograde), the use of vascular access site, and the devices were left to the operator's discretion. All procedures were performed by a single operator. Before the procedure, all patients received dual antiplatelet treatment of aspirin combined with either clopidogrel or ticagrelor.

Statistical analysis

Continuous variables following normal distribution were expressed as mean ± standard deviation (SD) and those following non-normal distribution as median (interquartile range). The normally distributed variables were compared by Student's *t*-test and the non-normal distributed variables by Mann-Whitney *U* test. Categorical data were expressed as percentages, compared by Chi-square or Fisher's exact test analysis as appropriate. Variables related to procedure success ($P < 0.1$) in univariate analysis were selected to join the multivariate logistic regression model to identify predictors of procedure outcome. The statistical analyses were carried out by SPSS software (version 13.0, SPSS Inc. Chicago, IL, USA).

The discriminatory performance of scoring model was validated by receiver-operator characteristic (ROC) curve analysis. Integrated discrimination improvement (IDI) and category-free net reclassification improvement (NRI) were calculated by R software (package PredictABEL) to evaluate the accuracy of reclassification when new predictors were added to the J-CTO model. The comparison of ROC curves was generated using MedCalc software (version 18, MedCalc, Ostend, Belgium). A 2-tailed p value < 0.05 was set for statistical significance.

Results

Demographics and Clinical Characteristic *s*

The baseline characteristics are summarized in Table 1. Compared with the failed PCI group, the previous myocardial infarction was more frequently but not significantly presented in the succeeded PCI group (19.69 vs. 10.00%, $p = 0.096$). There were no significant differences between the two groups regarding the demographics, prevalence of conventional cardiovascular risk factors, clinical manifestation, left ventricular ejection fraction (LVEF), serum creatinine level, or CTO duration (Table 1).

Table 1
Baseline characteristics of the study patients

variables	Antegrade success, n = 127	Antegrade failure, n = 60	*P*
Age (year)	63.26 ± 11.60	64.93 ± 9.98	0.337
Male	103 (81.10)	52 (86.67)	0.346
Hypertension	90 (70.87)	42 (70.00)	0.903
Diabetes mellitus	26 (20.47)	17 (28.33)	0.233
Dyslipidemia	5 (3.94)	3 (5.00)	0.737
Stoke	14 (11.02)	3 (5.00)	0.181
Family history of CAD	6 (4.72)	1 (1.67)	0.433
Current smoking	45 (35.43)	16 (26.67)	0.233
Previous myocardial infarction	25 (19.69)	6 (10.00)	0.096
Previous PCI	42 (33.07)	20 (33.33)	0.972
Previous CABG	0 (0)	1 (1.67)	0.321
LVEF (%)	59.60 ± 9.56	58.26 ± 10.47	0.460
Creatinine (umol/L)	79.09 ± 22.11	77.01 ± 20.90	0.540
NYHA /	20 (15.75)	10 (16.67)	0.873
CCS /	72 (56.69)	39 (65.00)	0.280
ACS	76 (59.84)	34 (56.67)	0.680
CTO duration (month)	4(3,12)	6(3,12)	0.105

Sample size, n = 187. Data is expressed as number of patients (percentage), mean ± SD or median (interquartile range).

CAD: coronary artery disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society; ACS: acute coronary syndrome; CTO: chronic total occlusion.

Angiographic And Interventional Procedures

The overall technical and procedural success rates were both 73.06%. Antegrade technical and procedural successes were achieved in 127 (67.91%) interventions. The most common target vessel of CTO PCI was the left anterior descending artery (43.32%), followed by the right coronary artery (38.50%) and the left circumflex artery (18.18%).

There were significantly more stumpless lesions (50.00% vs. 22.83%, p = 0.000) and long lesions with occlusion length of ≥ 20 mm (61.67% vs. 37.01%, p = 0.002) in the failed than those in the succeeded cohort. The prevalence of blunt morphology of the entry site (73.33% vs. 60.63%, p = 0.090) and the side branch at the proximal cap (56.67% vs. 43.31%, p = 0.088) were slightly increased in the failed CTO PCI in comparison with the succeeded CTO PCI. As expected, the failed PCI cohort showed a higher average J-CTO score (2.35 ± 1.02 vs. 1.90 ± 0.91, p = 0.003). The presence of Werner's collateral connection (CC) score of 1 (55.91% vs. 38.33%, p = 0.025) was higher in the succeeded CTO PCIs but that of Werner's CC score of 2 (56.67% vs. 37.80%, p = 0.015) was higher in the failed CTO PCIs. Bilateral injection was more frequently performed in the failed interventions (58.33% vs. 37.80%, p = 0.008). There were no differences in terms of wire technique (antegrade wire escalation, paralleled wire or kissing wire), use of microcatheter or intravascular ultrasound (IVUS) between the two groups.

There was no in-hospital MACE presented in this study. However, there were 9 (4.8%) procedure complications occurred, among which type D coronary dissection developed in 5 patients, no reflow in 3 patients, and coronary perforation in 1 patient. The procedure complications occurred more frequently in the failed PCI group (10.00% vs. 2.36%, p = 0.032; Table 2).

Table 2
Angiographic and procedural findings

Variable	Antegrade success, n = 127	Antegrade failure, n = 60	*P*
Angiographic			
CTO target coronary artery			
Left anterior descending	58 (45.67)	23 (38.33)	0.345
Left circumflex	25 (19.69)	9 (15.00)	0.438
Right coronary artery	44 (34.65)	28 (41.67)	0.115
Calcification	25 (19.69)	17 (28.33)	0.186
Tortuosity	25 (19.69)	10 (16.67)	0.621
Blunt	77 (60.63)	44 (73.33)	0.090
Occlusion length ≧ 20 mm	47 (37.01)	37 (61.67)	0.002
Occlusion length (mm)	18 (15,38)	37 (16,53)	0.001
Previously failed attempt	23 (18.11)	13 (21.67)	0.565
Stumpless	29 (22.83)	30 (50.00)	0.000
J-CTO score	1.90 ± 0.91	2.35 ± 1.02	0.003
modified J-CTO score	2.11 ± 1.13	2.80 ± 1.13	0.000
Side branch at the proximal cap	55 (43.31)	34 (56.67)	0.088
In-stent restenosis	8 (6.30)	0 (0)	0.056
Werner’s CC score			
0	8 (6.30)	3 (5.00)	1.000
1	71 (55.91)	23 (38.33)	0.025
2	48 (37.80)	34 (56.67)	0.015
Procedural			
Antegrade wire escalation	96 (75.59)	45 (75.00)	0.930
Parallel wire	23 (18.11)	13 (21.67)	0.565
Kissing wire	8 (6.30)	2 (3.33)	0.505
Bilateral injection	48 (37.80)	35 (58.33)	0.008
Microcatheter	105 (82.68)	48 (80.00)	0.658
IVUS-guided	10 (7.87)	8 (13.33)	0.237

Variable	Antegrade success, n = 127	Antegrade failure, n = 60	*P*
Procedural complication	3 (2.36)	6 (10.00)	0.032

Sample size, n = 187. Data is expressed as number of patients (percentage), mean ± SD or median (interquartile range).

CTO: chronic total occlusion, J-CTO: Japanese multicenter CTO registry, CC: collateral connection, IVUS: intravascular ultrasound.

Predictors Of Procedure Outcome

Nine variables were statistically correlated with procedure outcome by univariate analysis ($p < 0.1$), including previous myocardial infarction (Odds ratio [OR]: 0.453; 95% confidence interval [CI]: 0.175–1.172, p = 0.096), in-stent restenosis (OR: 0.000; 95% CI: 0.000-0.031, p = 0.056), stumpless lesion (OR: 3.379; 95% CI: 1.757–6.499, p = 0.000), blunt morphology (OR: 1.786; 95% CI: 0.910–3.503, p = 0.090), occlusion length ≥ 20 mm (OR: 2.738; 95% CI: 1.454–5.156, p = 0.002), side branch at the proximal cap (OR: 1.712; 95% CI: 0.921–3.181, p = 0.088), Werner’s CC score of 2 (OR: 2.152; 95% CI: 1.153–4.017, p = 0.015), Werner’s CC score of 1 (OR: 0.490; 95% CI: 0.262–0.918, p = 0.015) and bilateral injection (OR: 2.304; 95% CI: 1.232–4.310, p = 0.008).

Multivariable logistic regression indicated that stumpless lesion (OR: 2.813; 95% CI: 1.120–7.062, p = 0.028) and occlusion length ≥ 20 mm (OR: 2.196; 95% CI: 1.087–4.437, P = 0.028) independently predicted the procedure failure, as shown in Table 3.

Table 3
Univariate and multivariate analysis of predictors for procedural success

Variables	Univariate analysis			Multivariate analysis			
	OR	95% CI	*P* value	OR	95% CI	beta coefficient	*P* value
Previous myocardial infarction	0.453	0.175–1.172	0.096	0.395	0.135-0.1.159	− .928	0.091
In-stent CTO	0.000	0.000-0.031	0.056	0.000	0.000	-20.164	0.999
Stumpless	3.379	1.757–6.499	0.000	2.813	1.120–7.062	1.034	0.028
Blunt	1.786	0.910–3.503	0.090	1.601	0.689–3.718	0.471	0.274
Occlusion length ≥ 20mm	2.738	1.454–5.156	0.002	2.196	1.087–4.437	0.787	0.028
Side branch	1.712	0.921–3.181	0.088	0.813	0.326–2.029	− .207	0.657
Werner’s CC score 2	2.152	1.153–4.017	0.015	1.029	0.220–4.804	0.029	0.971
Werner’s CC score 1	0.490	0.262–0.918	0.025	0.568	0.126–2.561	− .565	0.462
Bilateral injection	2.304	1.232–4.310	0.008	1.408	0.676–2.937	0.343	0.361

CTO: chronic total occlusion, J-CTO: CC: collateral connection.

Statistically, the score of variable should be proportional to its beta coefficient in a score system[1]. Considering the beta coefficient of stumpless morphology was approximately 2 times of the blunt morphology (1.034 and 0.471 respectively), we scored 2 points, instead of pre-defined 1 point, to stumpless lesion referring to the J-CTO score[1]. By scoring 2 points to stumpless lesion, the modified J-CTO score was significantly higher in the failed PCI group compared with the succeeded PCI group (2.80 ± 1.13 vs. 2.11 ± 1.13, p = 0.000; Table 2). The area under the ROC curve (AUC) for predicting procedure failure was 0.621 (95% CI: 0.534–0.708, p = 0.008) for the current J-CTO score and 0.673 (95% CI: 0.592–0.755, p = 0.000) for the modified J-CTO score. The modified J-CTO score significantly increased the AUC (△AUC: 0.052, 95% CI: 0.012–0.092, p = 0.010) with a positive IDI (0.026; 95% CI: 0.009–0.043) and category-free assessment of NRI (0.459; 95% CI:0.169–0.749; Table 4 and Fig. 3).

Table 4
Comparison of predictive value for CTO recanalization assessment

	AUC	*p* value	△AUC (95% CI)	*p* value	IDI (95% CI)	*p* value	Category-free NRI (95% CI)	*p* value
J-CTO score	0.621	0.008						
J-CTO + stumpless score	0.673	0.000	0.052 (0.012–0.092)	0.010	0.026 (0.009–0.043)	0.003	0.459 (0.169–0.749)	0.002

AUC: area under the receiver operating characteristic curve; IDI: integrated discrimination improvement; NRI: net reclassification improvement, J-CTO: Japanese multicenter CTO registry.

Discussion

The results of this study indicated that stumpless lesion was an independent predictor of failed antegrade PCI. Scoring 2 points to stumpless lesion improves the value of the current J-CTO score in predicting the procedure outcome. To the best of our knowledge, this might be the first study suggesting a modified J-CTO score by stumpless lesion.

CTO accounts for one third of the lesions confirmed by coronary angiography[9]. Compared with failed PCI of CTO, succeeded CTO PCI has been associated with improvement in angina, left ventricular function and survival[10, 11]. Although new devices, increased operator experience and new crossing techniques have helped to improve the procedure success rate in the past decade[12], CTO recanalization is still an extremely challenging procedure in cardiovascular intervention. Studies have reported that the blunt stump [1, 13, 14], presence of bridging collaterals[15], side branch at the proximal cap [5, 16], severe tortuosity and moderate/severe calcification[1, 13, 14, 17], occlusion length[1, 18], and previous failed attempt[1] were associated with the procedure outcome. However, results from different studies were not fully consistent with each other [2–4]. The entry point of stumpless lesion was located at the bifurcation and the vessel course distal to the occlusion was hardly predictable by conventional angiography. The guidewire often slipped into the side branch or broke into a false lumen, which consequently caused PCI failure[19]. In J-CTO score, stumpless lesion was classified as blunt stump and scored 1 point, which might underestimate its value in predicting the antegrade procedure outcome. In this study, the procedure success rate of stumpless CTO was remarkably lower than that of non-stumpless CTO (49.15 vs. 76.56%, $p = 0.000$; data not shown). Scoring 2 points to stumpless lesion remarkably increased the area under the ROC curve of the J-CTO score for discriminating failed CTO PCI. Thus, we suggest that the current J-CTO score should be modified by scoring 2 points, instead of 1 point, to stumpless lesion.

CTO with stumpless morphology can be approached using the retrograde approach [20, 21], IVUS-guided wiring[22] or the “move-the-cap” subintimal crossing techniques, such as balloon-assisted subintimal entry or scratch and go[23]. The retrograde approach requires experienced operators, specific guidewires and appropriate interventional collaterals[24]. It could be the initial crossing strategy in cases of stumpless lesion without an appropriate side branch for IVUS but with excellent collateral vessels. Retrograde approaches were attempted in 18 stumpless lesions and succeeded in 6 interventions (33%) in the present study. In the 12 failed lesions, the mean diameter of distal CTO segment was 1.3 mm and tortuous collaterals presented in 8 lesions, both of which could have contributed to the procedure failure[25]. The IVUS-guided wiring technique could provide real-time images during the procedure with a favorable side branch. Park et al reported that the real-time IVUS-guided wiring technique was useful and safe for the recanalization of stumpless CTO lesions with procedural success rate being 81%[6]. IVUS was used in 15 stumpless CTO PCIs in our study and 10 lesions were reopened (67%). The relatively low success rate might be ascribed to the following factors: 1) the prevalence of calcification was higher in the present study compared to Park's study (20.00% vs. 3.23%). Heavy calcification can cause signal drop-out and posterior acoustic shadow; therefore, target lesions adjacent to the calcified plaques can be missed. 2) Real-time guidance had not been adopted in this study due to limited guiding catheter size as the procedures were accessed mostly through the radial artery. The "move-the-cap" techniques could be used if there are no significant side branches and should be avoided in patients with small and diffusely diseased distal vessels in whom re-entry into the distal true lumen may be challenging[26].

Some well-recognized predictors, including calcification, tortuosity and previously failed attempt, were not related to the procedure success in our study. The potential explanation may include: 1) the prevalence of calcification and tortuosity were lower in this study than that in the Japanese CTO registry (22.5% vs. 54.7% and 18.7% vs. 43.5% respectively) [1], which made it underpower to assess their impacts on procedure outcomes; besides, the difficulties caused by calcifications would also depend on their locations (intima or adventitia) and characteristics (eccentric or concentric); 2) a small sample size of previous CTO PCI failure in our study may unavoidably cause bias. However, our result was consistent with some of the previous studies[2, 27, 28]. We believe previous CTO PCI failure may not predict subsequent PCI outcome if the initial procedure was performed by doctors with very limited experience and there was no severe complications (e.g. severe dissection or intimal hematoma) occurred in the first attempt.

Several limitations of this study should be pointed out. First, all procedures were performed by single experienced operator (Chunjian Li). The single-operator nature of the study may prevent its external applicability, and large sample size is warranted to validate the score index for stumpless lesions. However, the antegrade success rate of CTO procedure in this study was consistent with the previous single- and multi-center studies[29, 30], and we believe that this result would represent the status of centers where only antegrade procedures are performed or less experienced doctors are performing CTO interventions, which make the result more close to the real-world condition. Second, the antegrade dissection and re-entry technique was not used in the study as our center was not equipped with Crossboss and Stingray system during the study period. Third, the study focused on the antegrade procedure, so the result cannot be extrapolated to retrograde or hybrid procedures.

Conclusions

In summary, the present study indicates that stumpless lesion and occlusion length ≥ 20 mm are independent predictors for antegrade procedure outcome of CTO PCI. Scoring 2 points to stumpless lesion improves the value of J-CTO score in predicting the procedure outcome. The results would be helpful for selecting optimal therapeutic strategy for CTO intervention. Further multicenter, large-sized studies are warranted to validate the present results.

Abbreviations

PCI: Percutaneous coronary intervention

CTO: coronary chronic total occlusion

ROC: receiver-operator characteristic

J-CTO: Japanese multicenter CTO registry

TIMI: thrombolysis in myocardial infarction

MACE: major adverse cardiac events

IDI: Integrated discrimination improvement

NRI: net reclassification improvement

LVEF: left ventricular ejection fraction

CAD: coronary artery disease

CABG: coronary artery bypass graft

NYHA: New York Heart Association

CCS: Canadian Cardiovascular Society

ACS: acute coronary syndrome

CC: collateral connection

IVUS: intravascular ultrasound

AUC: area under the receiver operating characteristic curve

Declarations

Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations. Written informed consent was obtained from individual or guardian participants. This study followed the principles outlined in the Declaration of Helsinki. The protocol was approved by Institutional Ethics Committee of the First Affiliated Hospital of Nanjing Medical University.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Dr. Xianqing Hu, Wenhao Zhang and Rui Hua contributed equally to this work. Xianqing Hu, Wenhao Zhang and Rui Hua: concept, design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review; Ran Li, Zhou Dong, Jianzhen Teng, Jiazheng Ma, Jiaxing Zong, Chen Li and Zhan Lv: design, definition of intellectual content, data acquisition, data analysis, manuscript review; Hui Yong, Tong Wang, Chunyue Tang, Inam Ullah and Xiaoxuan Gong: concept, definition of intellectual content, manuscript editing and manuscript review; Chunjian Li: concept, design, definition of intellectual content, literature search and manuscript review.All authors reviewed the manuscript.

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Figures

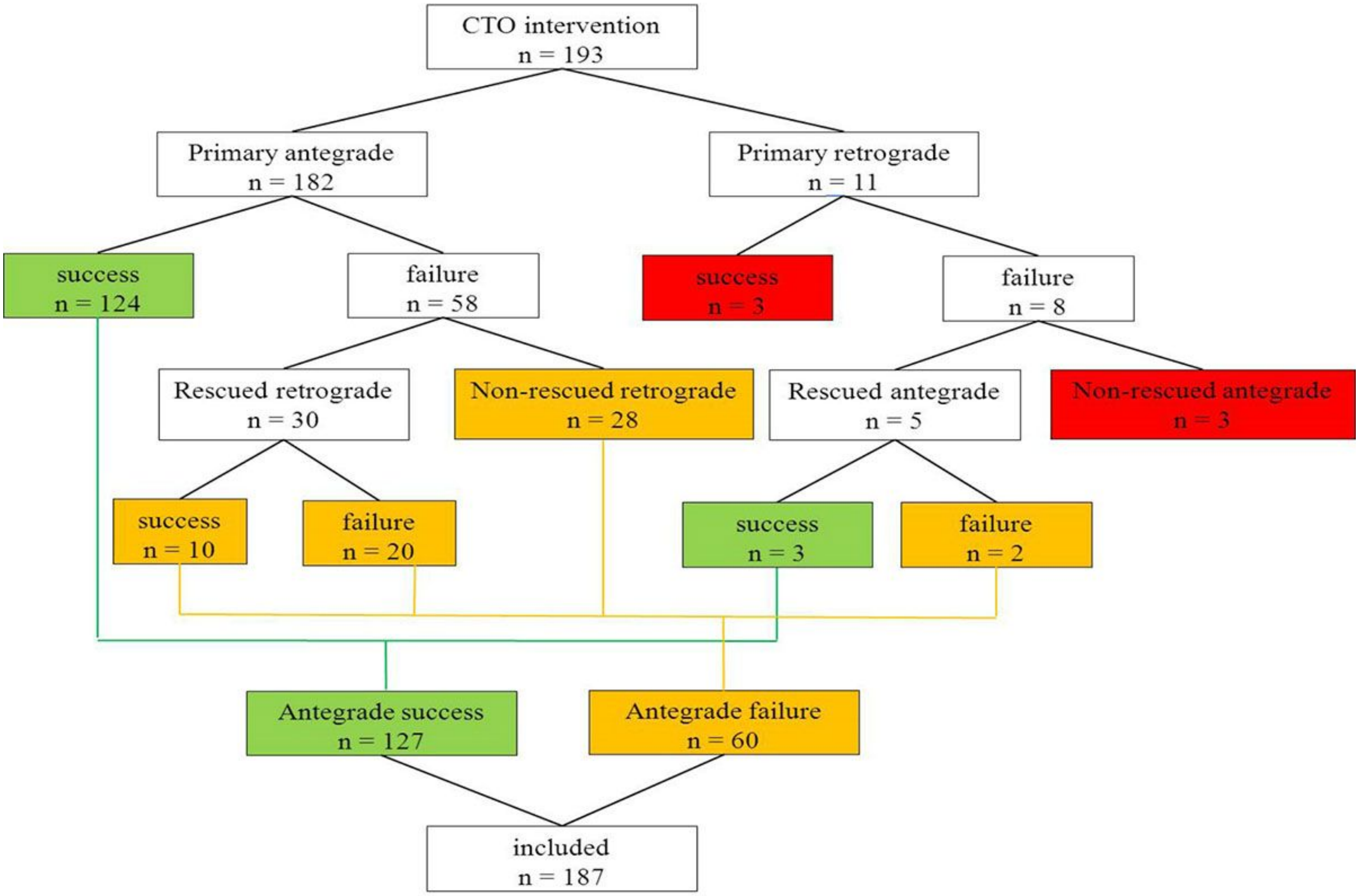
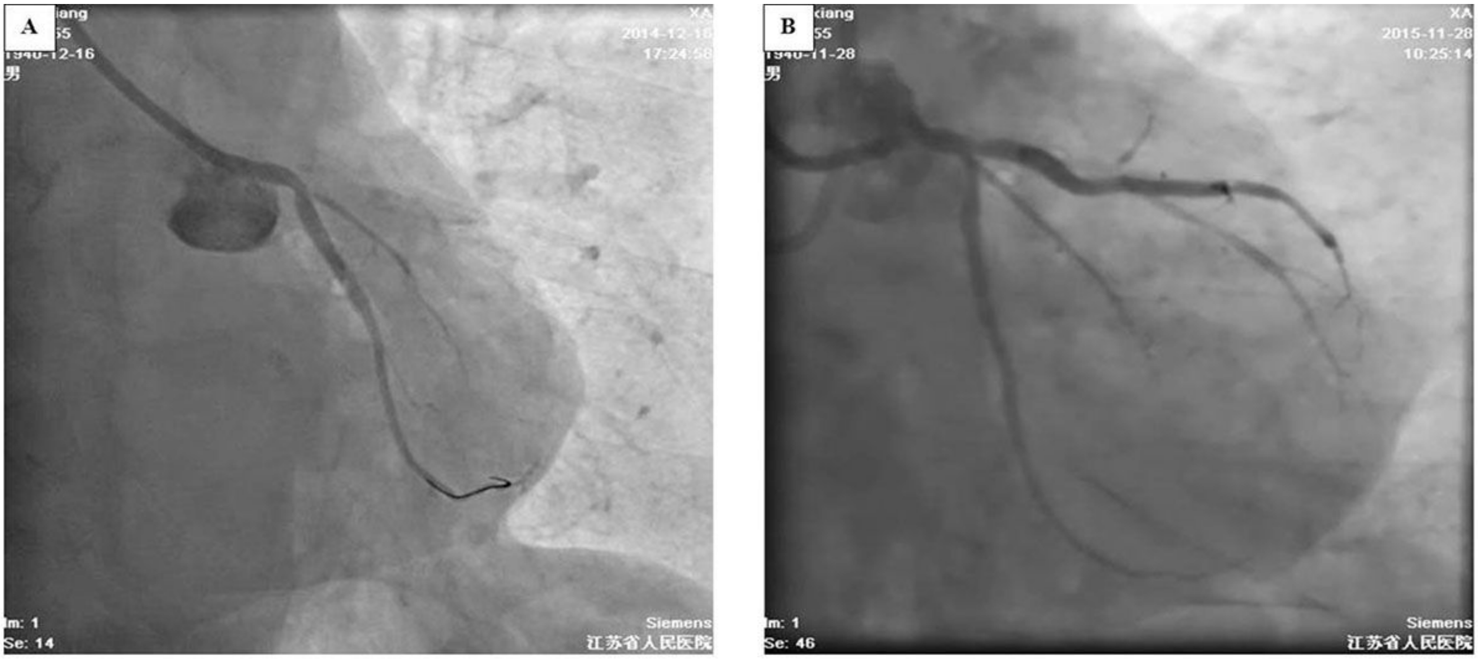


Figure 1

Flow diagram of the study



A : Chronically occluded left anterior descending artery with a blunt stump and a left circumflex artery adjacent to the occlusion (i.e., a stumpless lesion). The vessel course distal to the occlusion is hardly predictable.

B : Post-recanalization of the stumpless occlusion of the left anterior descending artery.

Figure 2

Example of stumpless CTO lesion

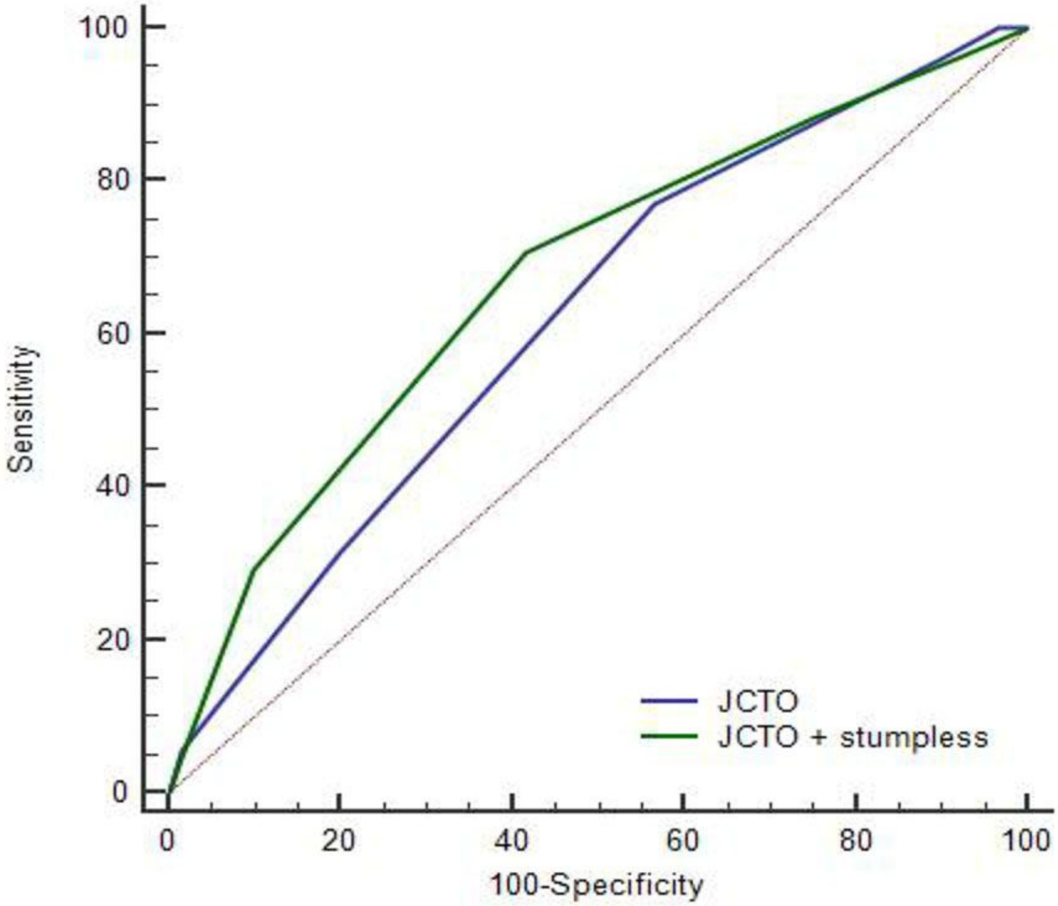


Figure 3

Comparison of receiver-operator characteristic curve