Clinical predictors of the rapid progression and revascularization of coronary non-target lesions: a serial angiographic study

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Abstract

Rapid progression of coronary no-target lesions is essential for the induction of future cardiovascular events. We aimed to investigate clinical predictors of rapid progression and revascularization of coronary non-target lesions. Consecutive patients who underwent two serial coronary angiographies were included. All coronary non-target lesions were recorded and evaluated at both procedures. A total of 1255 patients and 1670 lesions were included. At the patient level, 239 (19%) had rapid progression and 186 (14.8%) underwent revascularization. The incidence of lesion revascularization and myocardial infarction was significantly higher in patients with rapid progression. In multivariable analyses, hypertension (hazards ratio [HR], 0.76; 95% confidence interval [CI], 0.58-1.00; *P* = 0.049), ST-segment elevation myocardial infarction (HR, 1.46; 95%CI, 1.03-2.07; *P* = 0.035), glycosylated hemoglobin (HR, 1.16; 95%CI, 1.01-1.33; *P* = 0.039) and lesion classification (B2/C versus A/B1) (HR, 1.73; 95%CI, 1.27-2.35; *P* = 0.001) were significant factors associated with rapid progression. The level of triglyceride (HR, 1.10; 95%CI, 1.00-1.20; *P* = 0.040) and lesion classification (B2/C versus A/B1) (HR, 1.53; 95%CI, 1.09-2.14; *P* = 0.014) were predictors of lesion revascularization. Clinicians should pay more attention to patients with these factors to prevent future cardiovascular events.

Introduction

Coronary heart disease (CHD) is a major cause of death in both developed and developing countries[1]. Although coronary atherosclerosis is believed to be a chronic process that would progress over many years, it has been increasingly noted to progress over few months to 1–2 years for accelerated atherosclerosis[2–4]. Serial studies in which angiographic data were available in the past have clarified that coronary lesions with mild or moderate stenosis progressively enlarged before the acute event occurred[5]. Yokoya et al. and Kaski et al. showed that acute coronary syndromes presented in 50–70% patients who had rapid progression of coronary lesions[6,7]. Therefore, identifying clinical predictors of the rapid progression of coronary lesions is of great importance.

Results from previous studies showed that risk factors such as cigarette smoking and high cholesterol levels contribute to rapid progression[8,9]. However, these studies were mainly conducted before 2010 and control of these risk factors was not as strictly compared with nowadays. Moreover, patients who receiving strictly risk factor control still had rapid lesion progression[10,11]. In order to provide strategies modifying the accelerated process, this study aim to identify clinical predictors of the rapid progression and revascularization of coronary non-target lesions. A total of 1255 patients who underwent two serial coronary angiographies from January 2010 to September 2014 were included. All coronary non-target lesions were recorded at the first coronary angiography (CAG) and measured by quantitative coronary angiography (QCA) at both procedures. Outcomes including rapid progression and revascularization of coronary non-target lesions and myocardial infarction were recorded at second CAG.

Results

Population characteristics and clinical outcomes

A total of 1255 patients were included in the analysis (Table 1). The mean interval between two CAGs was 14.8 months. According to the definition, 239 (19%) had rapid progression of coronary non-target lesions and were grouped into the progression group. Table 1 shows the baseline characteristics of the study population in the presence of rapid progression or not. Those in the progression group were younger, had a higher frequency of previous percutaneous coronary intervention and an elevated triglyceride level compared with non-progression group. There was no significant difference in clinical comorbidities, other biochemistry examinations, medication use and CAG interval between two groups. 186 (14.8%) had revascularization of coronary non-target lesions at the time of second CAG. There was no significant difference on population characteristics between patients with and without revascularization except for the elevated triglyceride level in revascularization group (Supplementary Table 1). The incidence of non-target lesion revascularization was significantly higher in progression group than in non-progression group (42.7% [102 in 239] versus 8.3% [84 in 1016], $P < 0.001$) (Fig. 1 and Table 2). Patients in progression group also had higher prevalence of non-target lesion related myocardial infarction and (3.3% versus 1.1%, $P = 0.010$) and all myocardial infarction (4.6% versus 2.2%, $P = 0.034$) compared with patients in non-progression group.

Table 1
Baseline characteristics of patients grouped by the presence of rapid progression of coronary non-target lesions.

Variables	Non-progression (n = 1016)	Progression (n = 239)	P-value
Age (years)	58.3 ± 9.6	56.9 ± 10.1	0.039
Male	817 (80.4)	186 (77.8)	0.360
BMI (kg/m^2)	26.3 ± 3.3	26.6 ± 3.9	0.274
Cigeratte use	674 (66.3)	150 (62.8)	0.295
Diabetes mellitus	389 (38.3)	97 (40.6)	0.512
Hypertension	678 (66.7)	154 (64.4)	0.499
Dyslipidemia	674 (66.3)	161 (67.4)	0.762
Peripheral vascular disease	106 (10.4)	17 (7.1)	0.120
STEMI	130 (12.8)	40 (16.7)	0.109
NSTEMI	26 (2.6)	4 (1.7)	0.420
Family history of CHD	78 (7.7)	16 (6.7)	0.604
Previous MI	191 (18.8)	56 (23.4)	0.105
Previous stroke	98 (9.6)	20 (8.4)	0.543
Previous PCI	186 (18.3)	67 (28.0)	0.001
LVEF (%)	62.7 ± 7.2	62.6 ± 6.6	0.614
Biochemistry examinations			
White blood cell (×10^9/L)	6.9 ± 1.8	7.1 ± 1.9	0.142
Platelet (×10^9/L)	205.8 ± 52.3	210.3 ± 54.4	0.228
CRP (mg/L)	5.7 ± 14.2	5.7 ± 9.7	0.995
ESR (mm/H)	10.4 ± 11.6	11.8 ± 11.7	0.093
NT-pro BNP (pg/ml)	701.4 ± 461.9	720.8 ± 403.5	0.560
TC (mmol/L)	4.4 ± 1.1	4.3 ± 1.0	0.485
LDL-C (mmol/L)	2.6 ± 0.9	2.5 ± 0.8	0.149
TG (mmol/L)	1.8 ± 1.0	2.1 ± 1.8	0.012
HbA1c (%)	6.4 ± 1.1	6.5 ± 1.3	0.095

Variables	Non-progression (n = 1016)	Progression (n = 239)	P-value
Medications between two CAGs			
Aspirin	1008 (99.2)	237 (99.0)	0.817
P2Y12 receptor antagonist	891 (87.7)	210 (87.9)	0.991
Statin	976 (96.1)	229 (95.8)	0.897
Interval between two CAGs (month)	14.7 ± 4.5	15.2 ± 4.6	0.100

Data were represented as mean ± standard deviation or n (%). BMI: body mass index; STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction; CHD: coronary heart disease; MI: myocardial infarction; PCI: percutaneous coronary intervention; LVEF: left ventricular ejection fraction; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; NT-pro BNP: N-terminal pro-B-type natriuretic peptide TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; HbA1c: glycosylated hemoglobin; CAG: coronary angiography.

Table 2
Clinical outcomes in patients grouped according to the presence of rapid progression at second CAG.

Variables	Non-progression (n = 1016)	Progression (n = 239)	*P*-value
Non-target lesion revascularization	84 (8.3)	102 (42.7)	< 0.001
Non-target lesion related myocardial infarction	11 (1.1)	8 (3.3)	0.010
All myocardial infarction	22 (2.2)	11 (4.6)	0.034
Data were represented as n (%).			
CAG: coronary angiography.			

Lesion characteristics and QCA analysis of coronary non-target lesions

A total of 1670 coronary non-target lesions were recorded at the first CAG. According to the definition, 251 (15.0%) lesions had rapid progression and 1419 (85.0%) showed no progression at the lesion level (Table 3). Lesions with rapid progression were more complex compared with that without progression (frequency of B2 + C type lesion was 72.9% versus 61.2% respectively, $P < 0.001$). QCA analysis showed that lesions with progression had both smaller reference diameter and minimal lumen diameter as well as longer lesion length at first CAG. The percent diameter stenosis was not different between groups. At the second CAG, minimal lumen diameter was significantly decreased and percent diameter stenosis was markedly increased in lesions with rapid progression (both $P < 0.001$). A total of 194 coronary non-target

lesions underwent revascularization at second CAG (Table 3). These lesions also showed significantly increased percent diameter stenosis compared with those without revascularization ($P < 0.001$). The incidence of revascularization was significantly higher in lesions with rapid progression group than those without (39.4% versus 6.7%, $P < 0.001$).

Table 3
Lesion characteristics and QCA analysis of non-target lesions grouped according to rapid progression or revascularization at the lesion level.

Variables	Non-progression (n = 1419)	Progression (n = 251)	P-value
Lesion Distribution			0.011
LM	2 (0.1)	0 (0.0)	
LAD	511 (36.0)	90 (35.9)	
LCX	346 (24.4)	81 (32.3)	
RCA	513 (36.2)	67 (26.7)	
Dia/OM	47 (3.3)	13 (5.2)	
Lesion location			0.949
Proximal	622 (43.8)	109 (43.4)	
Mid	547 (38.5)	100 (39.8)	
Distal	250 (17.5)	42 (16.7)	
Lesion classification			< 0.001
A + B1	551 (38.8)	68 (27.1)	
B2 + C	868 (61.2)	183 (72.9)	
QCA analysis (first CAG)			
Reference diameter (mm)	2.9 ± 0.6	2.8 ± 0.6	0.006
Lesion length (mm)	12.8 ± 7.1	13.8 ± 8.6	0.037
Minimal lumen diameter (mm)	1.8 ± 0.4	1.7 ± 0.4	< 0.001
Percent diameter stenosis (%)	37.9 ± 9.1	37.8 ± 8.4	0.912
QCA analysis (second CAG)			
Reference diameter (mm)	2.8 ± 0.6	2.8 ± 0.6	0.022
Lesions length (mm)	14.3 ± 7.8	17.1 ± 9.8	< 0.001
Minimal lumen diameter (mm)	1.7 ± 0.4	1.1 ± 0.5	< 0.001

Data were represented as mean ± standard deviation or n (%).

QCA: quantitative coronary angiograph; LM: left main; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; Dia: diagonal branch; OM: obtuse marginal branch; CAG: coronary angiography.

Variables	Non-progression (n = 1419)	Progression (n = 251)	P-value
Percent diameter stenosis (%)	40.3 ± 10.2	55.9 ± 15.7	< 0.001
Revascularization of non-target lesion	95 (6.7)	99 (39.4)	< 0.001
	Non-revascularization (n = 1476)	**Revascularization (n = 194)**	
Lesion Distribution			0.179
LM	2 (0.1)	0 (0.0)	
LAD	518 (35.1)	83 (42.8)	
LCX	388 (26.3)	39 (20.1)	
RCA	513 (34.8)	67 (34.5)	
Dia/OM	55 (3.7)	5 (2.6)	
Lesion location			0.058
Proximal	661 (44.8)	70 (36.1)	
Mid	555 (37.6)	92 (47.4)	
Distal	260 (17.5)	32 (16.5)	
Lesion classification			0.018
A + B1	562 (38.1)	57 (29.4)	
B2 + C	914 (61.9)	137 (70.6)	
QCA analysis (first CAG)			
Reference diameter (mm)	2.8 ± 0.6	2.8 ± 0.5	0.982
Lesions length (mm)	12.8 ± 7.2	14.2 ± 8.5	0.009
Minimal lumen diameter (mm)	1.8 ± 0.4	1.7 ± 0.4	0.001
Percent diameter stenosis (%)	37.7 ± 9.0	39.5 ± 9.0	0.006
QCA analysis (second CAG)			
Reference diameter (mm)	2.8 ± 0.6	2.8 ± 0.5	0.971

Data were represented as mean ± standard deviation or n (%).

QCA: quantitative coronary angiograph; LM: left main; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; Dia: diagonal branch; OM: obtuse marginal branch; CAG: coronary angiography.

Variables	Non-progression (n = 1419)	Progression (n = 251)	P-value
Lesions length (mm)	14.4 ± 7.8	17.2 ± 10.5	< 0.001
Minimal lumen diameter (mm)	1.7 ± 0.5	1.2 ± 0.5	< 0.001
Percent diameter stenosis (%)	41.2 ± 11.0	54.2 ± 16.6	< 0.001
Data were represented as mean ± standard deviation or n (%).			
QCA: quantitative coronary angiograph; LM: left main; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; Dia: diagonal branch; OM: obtuse marginal branch; CAG: coronary angiography.			

Association between clinical characteristics and rapid progression or revascularization

We then investigated the association between clinical characteristics and rapid progression in Table 4. Variables such as age, sex, body mass index, diabetes mellitus, hypertension, ST-segment elevation myocardial infarction (STEMI), family history of CHD, previous myocardial infarction, low-density lipoprotein cholesterol, triglyceride, glycosylated hemoglobin (HbA1c) and lesion classification were enrolled into analysis. In multivariable analyses, hypertension (hazards ratio [HR], 0.76; 95% confidence interval [CI], 0.58-1.00; $P = 0.049$), STEMI (HR, 1.46; 95%CI, 1.03–2.07; $P = 0.035$), HbA1c (HR, 1.16; 95%CI, 1.01–1.33; $P = 0.039$) and lesion classification (B2/C versus A/B1) (HR, 1.73; 95%CI, 1.27–2.35; $P = 0.001$) were significant factors associated with rapid progression. The receiver operating characteristics (ROC) curve for assessing the ability of these factors to identify rapid progression is shown in Fig. 2A. The area under the ROC curve (AUC) was 0.59 (95% CI, 0.55–0.63; $P < 0.001$). We then investigated the association between clinical characteristics and revascularization in Table 5. Results showed that level of triglyceride (HR, 1.10; 95%CI, 1.00-1.20; $P = 0.040$) and lesion classification (B2/C versus A/B1) (HR, 1.53; 95%CI, 1.09–2.14; $P = 0.014$) were significant factors associated with lesion revascularization. The ability of triglyceride and lesion classification to identify lesion revascularization was shown in Fig. 2B and the AUC was 0.58 (95% CI, 0.53–0.62; $P = 0.001$).

Table 4
Association between clinical variables and rapid progression of coronary non-target lesions.

Item	Variables	Univariable	*P*-value	Multivariable	*P*-value
Non-target lesion progression	Age	0.99 (0.97-1.00)	0.031		
	Male	1.02 (0.75–1.38)	0.914		
	BMI	1.01 (0.98–1.05)	0.469		
	Diabetes mellitus	1.02 (0.78–1.32)	0.906		
	Hypertension	0.79 (0.61–1.03)	0.081	0.76 (0.58-1.00)	0.049
	STEMI	1.53 (1.09–2.15)	0.014	1.46 (1.03–2.07)	0.035
	Family history of CHD	0.88 (0.53–1.46)	0.626		
	Previous MI	1.16 (0.86–1.57)	0.328		
	LDL-C	0.89 (0.77–1.03)	0.108		
	TG	1.10 (1.01–1.19)	0.025		
	HbA1c	1.08 (0.97–1.20)	0.152	1.16 (1.01–1.33)	0.039
	Lesion classification (B2/C versus A/B1)	1.74 (1.29–2.37)	< 0.001	1.73 (1.27–2.35)	0.001

Data are presented as hazards ratio (95% confidence interval). Variables listed in the univariable analysis were entered into multivariable analysis.

BMI: body mass index; STEMI: ST-segment elevation myocardial infarction; CHD: coronary heart disease; MI: myocardial infarction; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; HbA1c: glycosylated hemoglobin.

Table 5
Association between clinical variables and revascularization of coronary non-target lesions.

Item	Variables	Univariable	*P*-value	Multivariable	*P*-value
Non-target lesion revascularization	Age	0.99 (0.98–1.01)	0.204		
	Male	0.92 (0.65–1.32)	0.659		
	BMI	1.01 (0.97–1.06)	0.598		
	Diabetes mellitus	0.78 (0.58–1.06)	0.114		
	Hypertension	0.82 (0.61–1.11)	0.205		
	STEMI	1.33 (0.89–1.99)	0.168		
	Family history of CHD	0.84 (0.47–1.50)	0.547		
	Previous MI	0.96 (0.67–1.37)	0.802		
	LDL-C	0.99 (0.84–1.15)	0.851		
	TG	1.10 (1.01–1.20)	0.026	1.10 (1.00-1.20)	0.040
	HbA1c	0.97 (0.85–1.11)	0.688		

Data are presented as hazards ratio (95% confidence interval). Variables listed in the univariable analysis were entered into multivariable analysis.

BMI: body mass index; STEMI: ST-segment elevation myocardial infarction; CHD: coronary heart disease; MI: myocardial infarction; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; HbA1c: glycosylated hemoglobin.

Item	Variables	Univariable	*P*-value	Multivariable	*P*-value
	Lesion classification (B2/C versus A/B1)	1.55 (1.11–2.17)	0.010	1.53 (1.09–2.14)	0.014
Data are presented as hazards ratio (95% confidence interval). Variables listed in the univariable analysis were entered into multivariable analysis.					
BMI: body mass index; STEMI: ST-segment elevation myocardial infarction; CHD: coronary heart disease; MI: myocardial infarction; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; HbA1c: glycosylated hemoglobin.					

Discussion

The present study investigated the clinical predictors of the rapid progression and revascularization of coronary non-target lesions. Our results showed that 19.0% patients had rapid progression in a mean interval of 14.8 months and 42.7% of them underwent revascularization. In multivariate analysis, hypertension, STEMI, HbA1c and lesion classification were significant factors associated with rapid progression. In addition, triglyceride and lesion classification were significant factors associated with lesion revascularization.

It has been reported that coronary lesions would go through rapid progression in a short period of time and induce adverse cardiac events[7,12]. In our study, in a mean interval of 14.4 months between two serial CAGs, nearly one of five patients had lesion progression and 42.7% of them underwent revascularization. Patients with rapid progression also had higher prevalence of myocardial infarction. These results were in accordance with previous works and suggested that rapid progression was quite common and deserve more cautions. Previous studies showed that most acute coronary events result from the progression of mildly stenotic plaques, based on angiographic information available from many months to years before the event. Stone *et al.* [13] in the PROSPECT study found that among 106 non-culprit lesions in 697 patients resulting in subsequent acute coronary syndrome during median 3.4 years follow-up and the mean angiographic diameter stenosis of these progressed lesion was 32% ± 21% at first CAG. In our study, the progressed lesions had a mean percent diameter stenosis of 37.8% at the first CAG which was also in line with previous studies. These results suggested that screening clinical risk factors associated with rapid progression is of potential ability to improve clinical outcomes.

Traditional risk factors for lesion progression are cigarette use and high cholesterol level. The impacts of smoking cessation on the cardiovascular outcomes is still controversial[14]. Our previous work also revealed that smoking cessation was not associated with reduced frequency of rapid progression[15]. Several imaging studies using different modalities have uniformly demonstrated that intensive treatment with statins reduces total plaque burden and is able to halt progression[16]. In our study, the cholesterol level was not different between patients with and without progression at first CAG and the proportion of

statin use was also comparable. These results indicate that other factors might contribute to rapid progression.

In this study, multivariate analysis showed that hypertension, the presentation of STEMI, HbA1c and lesion classification (B2/C versus A/B1) were independent risk factors for rapid progression. The coefficients of these factors are all positive, except that hypertension was negatively associated with rapid progression. Studies from De Luca et al. and Yan et al. found that patients with CHD and hypertension were more likely to have future cardiovascular events[17,18]. In this case, the negative association between hypertension and rapid progression in our study might be results of relatively short CAG interval or just statistical significance but with limited clinical value. It has been showed earlier the presentation of STEMI accelerates non-culprit coronary lesion atherosclerosis[19]. Goldstein et al. reported that additional angiographic lesions are present in 39.5% of patients with AMI, and this subgroup of patients has an increased incidence of recurrent ischemia[20]. In our study, STEMI was independently associated with rapid progression which were consistent with previous studies. Therefore, more attention should be paid in patients with the presentation of STEMI and additional coronary lesions to prevent future cardiovascular events. We also found that the level of HbA1c was risk factor for rapid progression. Inaba *et al*. found that accelerated plaque progression was blunted in diabetic patients with HbA1c < 6.5%[21]. In addition, results from Ahmed *et al.* showed greater reductions in minimum luminal diameter in coronary lesions from diabetic patients with a baseline HbA1c ≥ 6.5%[22]. Meanwhile, our results showed that diabetes mellitus was not risk factor for rapid progression. These results indicated that the level of glycemic control was more important than the diagnosis of diabetes mellitus to the prevention of lesion progression.

Besides demographic features, our work also found that an angiographic feature, AHA/ACC lesion classification, was also risk factor for rapid progression. In our study, patients with B2/C type lesions were more likely to have rapid lesion progression. Theuerle et al. also showed that patients with more complex lesion classification such as B2 or C type had more major adverse cardiac events at one year follow-up[23]. In addition, Qiu et al. found that type C lesion was interpedently associated with worse prognosis[24]. Furthermore, we showed that lesion classification was not only risk factor for rapid progression but also independently associated with future revascularization. We postulated that clinicians also take the morphology characters into consideration when performing revascularization. Meanwhile, Pinilla-Echeverri et al. demonstrated that lesion angiographic morphology was closed related to lesion vulnerability as assessed by optical coherence tomography [25]. These results indicate that lesion morphology could predict clinical outcomes and enough attention should be paid in these patients during routine clinical management. Another risk factor we found for lesion revascularization was the level of triglyceride. High triglyceride as a component of cardiovascular metabolic abnormalities was shown to be associated with the risk of CHD[26] and poor clinical outcomes in patients with acute myocardial infarction[27]. In our study, the level of triglyceride was also significantly elevated in progression compared with non-progression group. These results suggested that abnormal lipid and glycemic metabolism together contribute to lesion progression and eventually revascularization.

This study had several limitations. First, the generalizability of our findings was limited by the retrospective nature and single center as well as the selection bias in study populations. Second, intravascular ultrasound and optic coherence tomography should be applied to evaluate lesion progression in the future studies. Third, we did not include target lesion-related events in our clinical outcomes because these events, such as in-stent restenosis or stent thrombosis, have different mechanisms compared with the progression of de novo coronary lesions. Fourth, the results needed to be confirmed in large, prospective studies.

In conclusion, our study showed that coronary non-target lesions rapid progressed and underwent revascularization in a short period of time. Risk factors including hypertension, STEMI, HbA1c and AHA/ACC lesion classification were useful to identify patients at high risk for rapid progression. Strictly medication and more attentions should be paid in these patients to prevent future cardiovascular events.

Material And Methods

Study populations

Consecutive patients with CHD (acute coronary syndrome or stable angina) who underwent two serial coronary angiographies from January 2010 to September 2014 at Fuwai Hospital were retrospectively enrolled. Patients were excluded as follows: history of coronary artery bypass graft surgery; active malignant tumor, clinically significant valvular heart disease, serious conduction disturbances, significant arrhythmias and renal dysfunction. A total of 1255 patients were finally included in this study. At the first CAG, percutaneous coronary intervention was performed at the operator's discretion. Second CAG was conducted because of clinical symptoms or an abnormal stress test with myocardial ischemia or routine angiographic follow-up. The serial CAGs were all performed within 2 years. Coronary non-target lesion was defined as a *de novo* stenotic lesion that was not responsible for ischemic symptoms or any positive functional ischemic test as previously described[28,29]. All coronary non-target lesions were recorded at first CAG. Revascularization of the non-target lesions at the second CAG was performed based on ischemic symptoms, positive results on functional ischemia study or at the operator's discretion. All study patients received standard medicine therapy between two CAGs. Data including demographic information, medical history, biochemistry data and detailed coronary angiography were collected. The study complied with the principles of the *Declaration of Helsinki* and was approved by the Review Board of Fuwai Hospital. Written informed consent was obtained from all participants.

Process of coronary angiography and quantitative coronary angiography measurement

Selective CAG was performed following the administration of intracoronary glyceryl nitrate. The assessment of angiographic lesion progression was achieved by comparing the data from QCA at both CAG procedures. Each pair of coronary angiograms was obtained in the same projection. Coronary angiograms were reviewed by 2 independent observers experienced in angiographic interpretation and blinded to the clinical data. During the analysis of QCA, the stem of the Judkins coronary catheter was

used for calibration to determine absolute measurements in millimeters, and correction was made for radiographic pincushion distortion. For each segment, measurements were carried out on end-diastolic frames in which the severity of the stenosis appeared maximal. Reference diameter, lesion length, minimal lumen diameter and percent diameter stenosis were measured.

Definition of rapid progression of coronary non-target lesion

Rapid progression was interpreted from the increase in percent diameter stenosis calculated using percent diameter stenosis at second CAG minus that at first CAG. The definition of rapid progression was described previously[29]. Coronary non-target lesion was considered to have rapid progression with the presence of any of the following: ≥10% diameter reduction with pre-existing stenosis ≥ 30% or ≥ 30% diameter reduction with pre-existing stenosis < 30%, or progression to total occlusion. Patients were grouped into the progression group when at least one lesion had rapid progression. Patients who had no rapid progression were grouped into the non-progression group.

Statistical analysis

The results are expressed as mean ± standard deviation or number (percentage). Continuous variables were tested for normal distribution with the Kolmogorov-Smirnov test. Differences of continuous variables between groups were compared using Student unpaired t test or Mann–Whitney U test, as appropriate. Comparison of categorical variables was performed using the χ^2 or Fisher exact test, as appropriate. A multivariable Cox proportional hazards model was used to evaluate the association between clinical variables and rapid progression or revascularization. Variables were included because of their known clinical importance or because univariate comparisons showed $P < 0.15$. The variables included age, sex, body mass index, diabetes mellitus, hypertension, ST-segment elevation myocardial infarction (STEMI), family history of CHD, previous myocardial infarction, low-density lipoprotein cholesterol, triglyceride, HbA1c, AHA/ACC lesion classification (B2/C versus A/B1). Results were expressed as HR and 95% CI. ROC curve and area under the ROC curve were used to assess the ability of the selected clinical variables to identify the rapid progression or revascularization. All reported probability values were 2-tailed, and a P value of < 0.05 was considered statistically significant. SPSS version 24.0 (IBM Corp., Armonk, NY) was used for calculations.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of Fuwai Hospital and was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. The written informed consent was provided by each participant.

Data availability

The data used and analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions

All the authors have participated in the study and manuscript preparation, and have approved the final version of the manuscript: J.W. and H.X. for data interpretation, manuscript drafting and revising; J.Y., C.G., F.H. and W.Y. for data collection and manuscript revising; L.S., X.L., and R.L. for statistical analysis and manuscript revising; J.Cui and S.L. for data interpretation. J.Chen and S.Q. for conception and design for the study and takes the responsibility of final approval for manuscript submitted.

Competing interests

The authors declare no competing interests.

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Figures

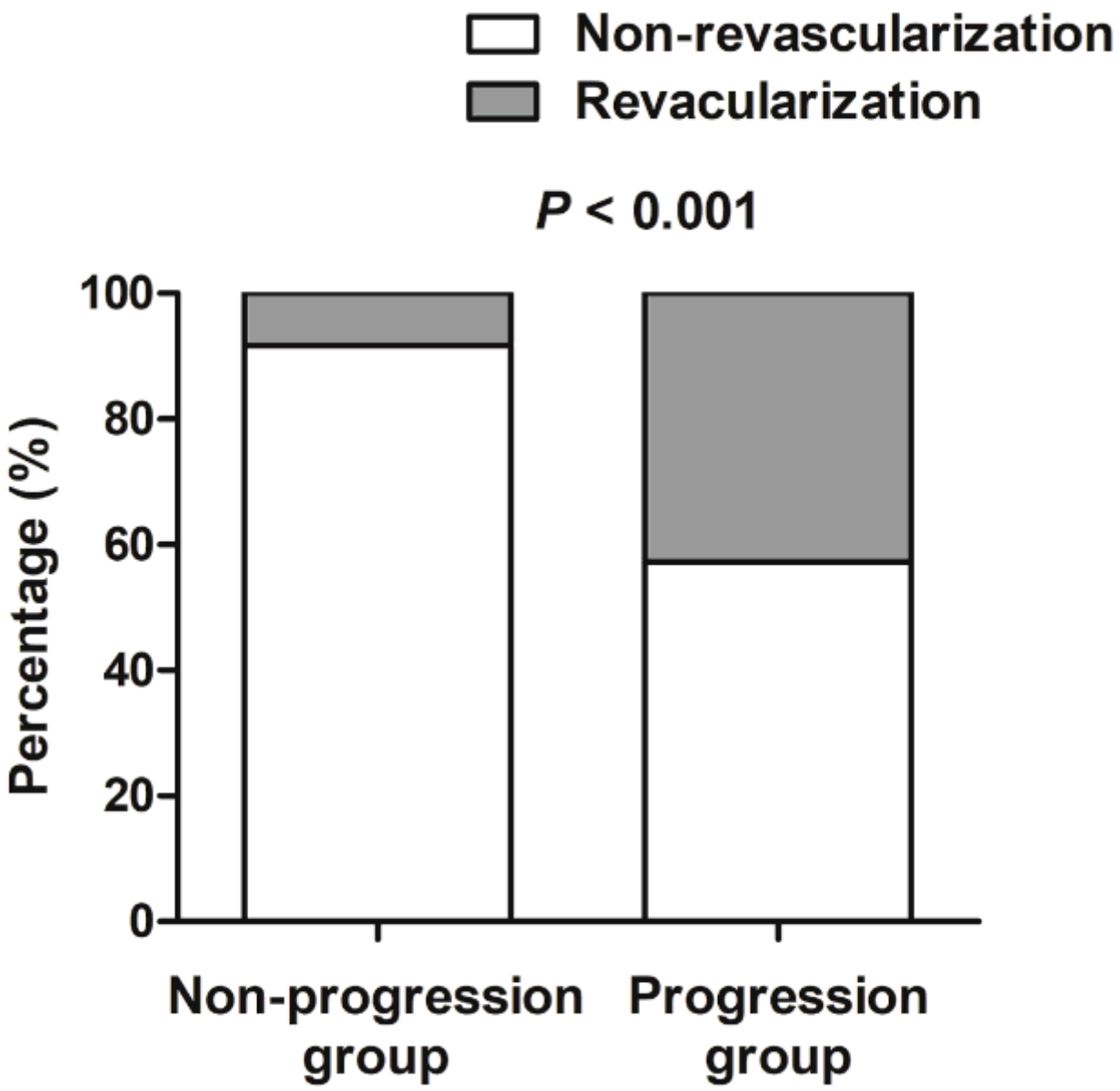

Figure 1

Incidence of non-target lesion revascularization in progression group and non-progression group.

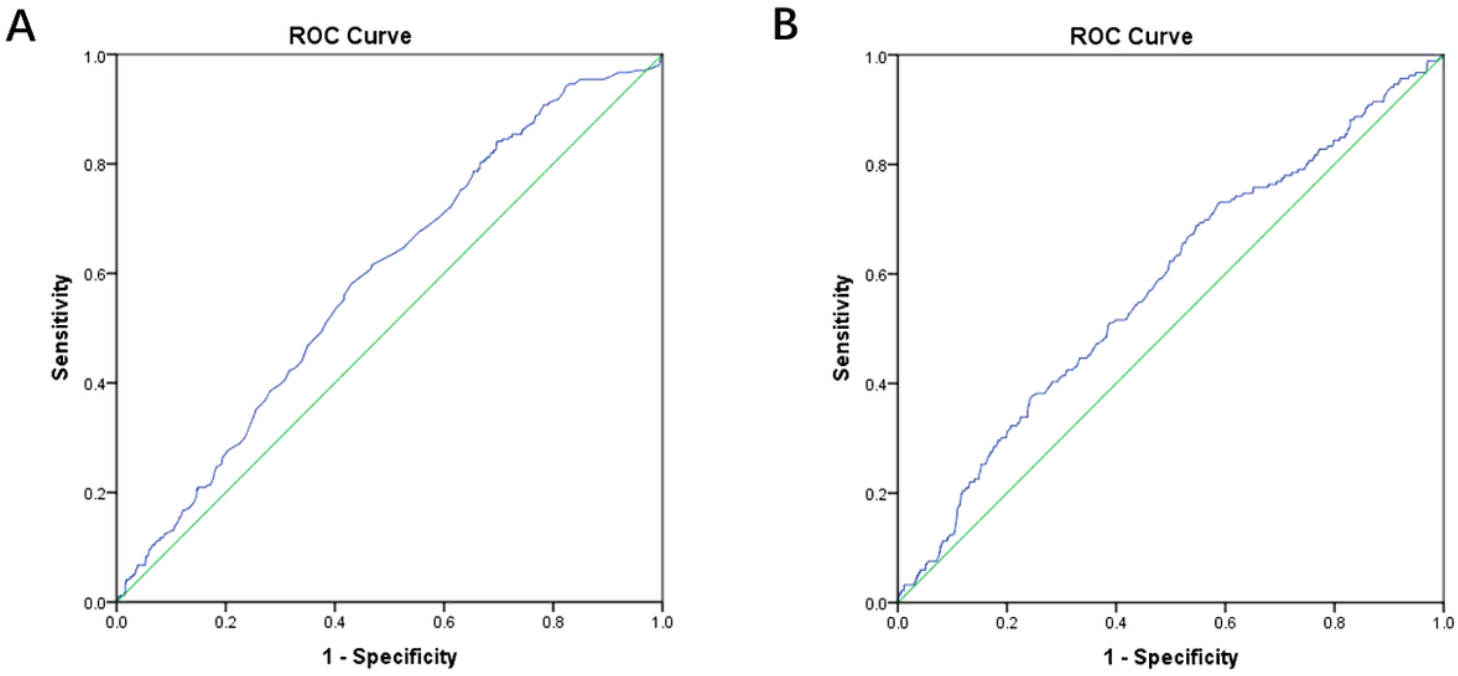

Figure 2

Receiver-operator characteristic (ROC) curve to identify rapid progression and revascularization of coronary non-target lesions. ROC curves for the clinical factors including hypertension, STEMI, glycosylated hemoglobin and lesion classification to identify rapid progression (A). ROC curves for triglyceride and lesion classification to identify revascularization (B).

Supplementary Files

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