Impacts of smoking status on the clinical outcomes of coronary non-target lesions in patients with coronary heart disease: a single-center angiographic study

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Abstract

Background: Coronary atherosclerotic plaque could go through rapid progression and induce adverse cardiac events. This study aimed to evaluate the impacts of smoking status on clinical outcomes of coronary non-target lesions.

Methods: Consecutive patients with coronary heart disease who underwent two serial coronary angiographies were included. All coronary non-target lesions were recorded at first coronary angiography and analyzed using quantitative coronary angiography at both procedures. Patients were grouped into non-smokers, quitters, and smokers according to their smoking status. Clinical outcomes including rapid lesion progression, lesion re-vascularization, and myocardial infarction were recorded at second coronary angiography. Multivariable Cox regression analysis was used to investigate the association between smoking status and clinical outcomes.

Results: A total of 1255 patients and 1670 lesions were included. Smokers were younger and more likely to be male compared with non-smokers. Increase in percent diameter stenosis was significantly lower (2.7 [0.6, 7.1] % *vs.* 3.5 [0.9, 8.9]%) and 3.4 [1.1, 7.7]%, $P = 0.020$) in quitters than those in smokers and non-smokers. Quitters tended to have a decreased incidence of rapid lesions progression (15.8% [76/482] *vs.* 21.6% [74/342] and 20.6% [89/431], $P = 0.062$), lesion re-vascularization (13.1% [63/482] *vs.* 15.5% [53/432] and 15.5% [67/431], $P = 0.448$), lesion-related myocardial infarction (0.8% [4/482] *vs.* 2.6% [9/342] and 1.4% [6/431], $P = 0.110$) and all-cause myocardial infarction (1.9% [9/482] *vs.* 4.1% [14/342] and 2.3% [10/431], $P = 0.128$) compared with smokers and non-smokers. In multivariable analysis, smoking status was not an independent predictor for rapid lesion progression, lesion re-vascularization, and lesion-related myocardial infarction except that a higher risk of all-cause myocardial infarction was observed in smokers than non-smokers (hazards ratio: 3.00, 95% confidence interval: 1.04–8.62, $P = 0.042$).

Conclusion: Smoking cessation mitigates the increase in percent diameter stenosis of coronary non-target lesions, meanwhile, smokers are associated with increased risk for all-cause myocardial infarction compared with non-smokers.

Keywords: Smoking status; Coronary non-target lesion; Rapid progression; Re-vascularization; Myocardial infarction

Introduction

Coronary heart disease (CHD) is a major cause of death in both developed and developing countries. Smoking is one of the most important causes of CHD.[1] The number of smokers worldwide is currently estimated to be 1.3 billion, of which 82% are in developing countries, for example, China.[2] Cigarette use contributes to the initiation and progression of coronary atherosclerosis independently of other traditional risk factors.[3,4] However, smoking tends to have long-term adverse effects on coronary lesions, whether changes in smoking status affect clinical outcomes of coronary lesions in a relatively short period of time is still unknown. It has recently been noted that coronary atherosclerosis could progress in a short period of time over few months to 2 to 3 years.[5,6] Rapid progression of coronary lesion leads to acute myocardial ischemia and is usually unpredictable.[6-8] The aim of this study was to investigate the effects of smoking status on rapid progression of coronary lesions as well as the incidence of adverse outcomes due to this process in patients with CHD.

Methods

Ethical approval

The study complied with the principles of the *Declaration of Helsinki* and was approved by the Review Board of

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Fuwai Hospital (No. 2005-1516). Written informed consent was obtained from all participants.

Study population

This was a single center, retrospective study. A total of 1607 consecutive patients with CHD (acute coronary syndrome or stable angina) who underwent two serial coronary angiographies (CAGs) at Fuwai Hospital were enrolled from January 2010 to September 2014. Percutaneous coronary intervention (PCI) was performed at the operator's discretion after first CAG. Second CAG was conducted because of clinical symptoms or an abnormal stress test with myocardial ischemia or routine angiographic follow-up. Patients with the second CAG performed within 2 years after the first CAG were included. The 338 patients were excluded because there was no non-target lesion recorded at the first CAG. Patients were also excluded as follows: two patients had a history of coronary artery bypass graft surgery before first CAG; three patients had active malignant tumor; and nine patients had a follow-up period longer than 2 years. No patient had clinically significant valvular heart disease, serious conduction disturbances, significant arrhythmias, and renal dysfunction. Thus, 1255 patients were finally included in this study. Patients were grouped according to their smoking status as described below. A total of 1670 coronary non-target lesions were recorded at the first CAG. All study patients received standard medicine therapy including statins, aspirin, clopidogrel or ticagrelor, beta-blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers, calcium channel blockers, and oral nitrates after the initial admission. Data including demographic information, medical history, CHD risk factors, detailed coronary angiographic information, and biomarkers associated with coronary atherosclerosis were collected at two consecutive coronary angiographic procedures.

Process of coronary angiography and quantitative coronary angiography measurement

Selective CAG was performed following the administration of intracoronary glyceryl nitrate. The assessment of rapid angiographic lesion progression was achieved by comparing the data from quantitative coronary angiography (QCA) at both CAG procedures. Each pair of coronary angiograms was obtained in the same projection and quantitatively assessed by two independent cardiologists who were unaware of all other clinical data of the patients. During quantitative CAG, 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.

Definitions

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.[9,10] Rapid lesion progression was interpreted from the increase in percent diameter stenosis calculated using percent diameter stenosis at second CAG minus that at first CAG. Rapid progression was defined based on previous reported criteria[10] which included the presence of any of the following: ≥10% diameter reduction of a pre-existing stenosis ≥ 30%, ≥30% diameter reduction of a pre-existing stenosis <30%, or progression of any lesion to total occlusion at second CAG. When at least one lesion showed rapid progression, the patient was considered as a progressor. Lesion re-vascularization at the second CAG was performed in lesions which were responsible for ischemic symptoms or had positive results on functional ischemia study. Clinical outcomes including rapid lesion progression, lesion re-vascularization, lesion-related myocardial infarction, as well as all-cause myocardial infarction were documented at second CAG.

Smoking status

Patients were divided into three groups on the basis of smoking information provided by the patients at both CAG procedures. Smoking status was defined in accordance with previously reported definition.[11] Briefly, non-smokers were defined as patients who had never smoked before or after the CAG procedure. Quitters were defined as those who had quit smoking either before or instantly after the first CAG. Persistent smokers were defined as patients who smoked before the first CAG and continued to smoking till the second CAG. Patients with reduced cigarette consumption after the first CAG were regarded as persistent smokers.

Statistical analysis

The results are expressed as mean ± standard deviation, median (Q1, Q3), or number (percentage). Continuous variables were tested for normal distribution with the Kolmogorov-Smirnov test. Differences in continuous variables were initially evaluated by one-way analysis of variance, and then by Tukey post-hoc test if appropriate. If variables were not normally distributed, the Kruskal-Wallis H test was performed. Categorical data were analyzed using Chi-squared test or Fisher exact test when required. A multivariable Cox proportional hazards model was used to evaluate the association between smoking status and study end points. Variables were included because of their known clinical importance or because univariate comparisons showed $P < 0.15$. The variables included age, sex, ST-segment elevation myocardial infarction (STEMI), hypertension, diabetes mellitus, baseline low-density lipoprotein cholesterol, C-reactive protein (CRP), and erythrocyte sedimentation rate. A $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS version 19.0 (IBM, Armonk, NY, USA). A $P < 0.05$ was considered to be statistically significant.

Results

Clinical characteristics

A total of 1255 patients with CHD were evaluated in this study. Patients were divided into three groups according to their smoking manners: non-smokers (431 patients),

quitters (482 patients), and smokers (342 patients). Clinical characteristics among groups are summarized in Table 1. Smokers and quitters were younger, more likely to be male and had a less prevalence of hypertension compared with non-smokers. Compared with quitters and smokers, the prevalence of STEMI and history of myocardial infarction were lower in non-smoker. The proportions of patients with three-vessel disease were similar among groups. There was no significant difference in medication therapy at discharge. Non-smokers were associated with decreased levels of white blood cells and CRP and increased level of total cholesterol at both CAG procedures. There was no remarkable significance in levels of N-terminal pro-B-type natriuretic peptide and hemoglobin A1c among groups.

Angiographic studies of coronary non-target lesions

A total of 1670 non-target lesions were documented at the first CAG: 578 lesions in non-smokers, 625 lesions in quitters, and 467 lesions in smokers. Lesion distribution, location, and classification were not significantly different among three groups [Table 2]. Lesion characteristics such as lesion length, morphology, and contour as well as tortuosity, angulation, calcification, and bifurcation were also similar among three groups. QCA analysis showed that quitters had a larger reference diameter and minimal lumen diameter compared with non-smokers and smokers at both CAG procedures. Although percent diameter stenosis was not different among groups, the increase of percent diameter stenosis at second CAG was significantly

Table 1: Clinical characteristics of 1255 patients with CHD grouped by smoking status.

Characteristics	Non-smokers ($n = 431$)	Quitters ($n = 482$)	Smokers ($n = 342$)	Statistical values	P
Age (years)	60.3 ± 9.9	58.3 ± 9.5	54.8 ± 8.6	31.890^{*}	<0.001
Male	212 (49.2)	464 (96.3)	327 (95.6)	$386.395^{\dagger}$	<0.001
BMI (kg/m^2)	26.0 ± 3.0	26.5 ± 3.2	26.3 ± 3.2	6.749^{*}	0.035
Diabetes mellitus	155 (36.0)	162 (33.6)	108 (31.6)	$1.659^{\dagger}$	0.436
Hypertension	314 (72.9)	317 (65.8)	201 (58.8)	$17.020^{\dagger}$	<0.001
Dyslipidemia	292 (67.7)	314 (65.1)	229 (67.0)	$0.731^{\dagger}$	0.694
Family history of CHD	32 (7.4)	33 (6.8)	29 (8.5)	$0.774^{\dagger}$	0.679
STEMI	39 (9.0)	79 (16.4)	52 (15.2)	$11.576^{\dagger}$	0.003
NSTEMI	10 (2.3)	12 (2.5)	8 (2.3)	$0.033^{\dagger}$	0.983
Previous MI	69 (16.0)	112 (23.2)	66 (19.3)	$7.562^{\dagger}$	0.023
Peripheral vascular disease	44 (10.2)	51 (10.6)	28 (8.2)	$1.420^{\dagger}$	0.492
Previous stroke	40 (9.3)	49 (10.2)	29 (8.5)	$0.679^{\dagger}$	0.712
Previous PCI	74 (17.2)	110 (22.8)	69 (20.2)	$4.516^{\dagger}$	0.105
LVEF (%)	63.6 ± 6.5	61.8 ± 7.7	62.8 ± 6.8	7.247^{*}	0.002
Three-vessel disease	250 (58.0)	256 (53.1)	197 (57.6)	$1.843^{\dagger}$	0.515
Medication at discharge					
Aspirin	427 (99.1)	478 (99.2)	341 (99.7)	$0.104^{\dagger}$	0.877
P2Y12 receptor antagonist	376 (87.2)	423 (87.8)	302 (88.3)	$0.631^{\dagger}$	0.718
Statin	410 (95.1)	463 (96.1)	330 (96.5)	$0.548^{\dagger}$	0.733
Biochemistry examination (first CAG)					
White blood cell ($\times 10^9$/L)	6.5 ± 1.7	6.9 ± 1.9	7.3 ± 1.9	14.042^{*}	<0.001
CRP (mg/L)	2.4 (1.5, 4.5)	2.8 (1.8, 4.8)	2.9 (1.7, 5.1)	$8.696^{\ddagger}$	0.013
ESR (mm/H)	10.0 (5.0, 18.0)	6.0 (3.0, 11.0)	6.0 (2.0, 11.0)	$56.162^{\ddagger}$	<0.001
NT-pro BNP (pg/mL)	699.9 ± 368.5	709.5 ± 482.0	705.2 ± 499.1	0.048^{*}	0.946
TC (mmol/L)	4.5 ± 1.1	4.2 ± 1.0	4.4 ± 1.1	10.033^{*}	<0.001
LDL-C (mmol/L)	2.7 ± 1.0	2.5 ± 0.8	2.5 ± 0.9	6.608^{*}	0.005
TG (mmol/L)	1.9 ± 1.1	1.8 ± 0.9	2.1 ± 1.7	5.992^{*}	0.050
HbA1c (%)	6.4 ± 1.2	6.4 ± 1.1	6.4 ± 1.1	0.288^{*}	0.750
Biochemistry examination (second CAG)					
White blood cell ($\times 10^9$/L)	6.3 ± 1.5	6.5 ± 1.5	6.9 ± 1.7	32.027^{*}	<0.001
CRP (mg/L)	1.9 (1.3, 3.0)	1.8 (1.3, 3.3)	2.3 (1.4, 3.7)	$10.354^{\ddagger}$	0.006
ESR (mm/H)	7.0 (3.0, 14.0)	4.0 (2.0, 8.0)	4.0 (2.0, 7.5)	$72.224^{\ddagger}$	<0.001
NT-pro BNP (pg/mL)	618.7 ± 306.7	651.7 ± 445.2	623.4 ± 349.1	0.961^{*}	0.619
TC (mmol/L)	4.1 ± 1.1	3.8 ± 0.9	4.0 ± 1.0	14.516^{*}	0.001
LDL-C (mmol/L)	2.3 ± 0.9	2.2 ± 0.7	2.3 ± 0.8	4.032^{*}	0.133
TG (mmol/L)	1.7 ± 1.1	1.6 ± 0.8	1.9 ± 1.7	15.467^{*}	<0.001
HbA1c (%)	6.6 ± 1.1	6.5 ± 1.1	6.5 ± 1.0	1.011^{*}	0.603

Data are represented as mean ± standard deviation, median (Q1, Q3) or n (%). $^{*}F$ values. $^{\dagger}\chi^2$ values. $^{\ddagger}H$ values. CHD: Coronary heart disease; BMI: Body mass index; STEMI: ST-segment elevation myocardial infarction; NSTEMI: Non-ST-segment elevation myocardial infarction; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; LVEF: Left ventricular ejection fraction; CAG: Coronary angiography; 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: Hemoglobin A1c.

Table 2: Lesion characteristics and QCA analysis of non-target lesions among three groups.

Characteristics	Non-smokers (n = 578)	Quitters (n = 625)	Smokers (n = 467)	Statistical values	P
Lesion Distribution				7.101*	0.526
LM	1 (0.2)	1 (0.2)	0		
LAD	204 (35.3)	228 (36.5)	169 (36.2)		
LCX	158 (27.3)	140 (22.4)	129 (27.6)		
RCA	197 (34.1)	231 (37.0)	152 (32.5)		
DIA/OM	18 (3.1)	25 (4.0)	17 (3.6)		
Lesion location				7.681*	0.104
Proximal	258 (44.6)	286 (45.8)	188 (40.3)		
Mid	207 (35.8)	241 (38.6)	199 (42.6)		
Distal	113 (19.6)	98 (15.7)	80 (17.1)		
Lesion classification				1.372*	0.504
A + B1	212 (36.7)	242 (38.7)	165 (35.3)		
B2 + C	366 (63.3)	383 (61.3)	302 (64.7)		
Diffuse lesion	88 (15.2)	81 (13.0)	80 (17.1)	4.908*	0.297
Eccentric lesion	157 (27.2)	182 (29.1)	138 (29.6)	0.874*	0.646
Tortuosity	102 (17.6)	114 (18.2)	85 (18.2)	0.085*	0.958
Angulation	114 (19.7)	133 (21.3)	93 (19.9)	0.528*	0.768
Irregular contour	99 (17.1)	101 (16.2)	78 (16.7)	0.204*	0.903
Lesion calcification	47 (8.1)	43 (6.9)	27 (5.8)	2.214*	0.331
Ostial lesion	43 (7.4)	47 (7.5)	32 (6.9)	0.199*	0.905
Bifurcation	99 (17.1)	104 (16.6)	87 (18.6)	0.772*	0.680
QCA analysis (baseline)					
Reference diameter (mm)	2.8 ± 0.6	2.9 ± 0.6	2.8 ± 0.6	15.568†	0.001
Lesions length (mm)	12.8 ± 7.4	12.7 ± 7.2	13.4 ± 7.5	1.207†	0.289
Minimal lumen diameter (mm)	1.7 ± 0.4	1.8 ± 0.5	1.8 ± 0.4	3.237†	0.040
Percent diameter stenosis (%)	37.7 ± 8.9	38.0 ± 9.2	37.9 ± 9.2	0.191†	0.889
QCA analysis (follow-up)					
Reference diameter (mm)	2.8 ± 0.6	2.9 ± 0.6	2.8 ± 0.6	11.361†	0.003
Lesions length (mm)	14.8 ± 8.3	14.4 ± 8.1	15.0 ± 8.2	0.664†	0.727
Minimal lumen diameter (mm)	1.6 ± 0.5	1.7 ± 0.5	1.60 ± 0.5	5.771†	0.003
Percent diameter stenosis (%)	43.2 ± 12.6	41.8 ± 11.7	43.2 ± 13.4	2.509†	0.285
Increase in percent diameter stenosis (%)	3.4 (1.1, 7.7)	2.7 (0.6, 7.1)	3.5 (0.9, 8.9)	7.799‡	0.020
Rapid lesion progression	92 (15.9)	80 (12.8)	79 (16.9)	4.091*	0.129
Lesion re-vascularization	67 (11.6)	65 (10.4)	55 (11.8)	0.648*	0.723
Number of stents	1.3 ± 0.5	1.3 ± 0.6	1.3 ± 0.5	0.907†	0.635

Data are represented as mean ± standard deviation, median (Q1, Q3) or n (%). *χ^2 values. †F values. ‡H values. QCA: Quantitative coronary angiography; LM: Left main; LAD: Left anterior descending artery; LCX: Left circumflex artery; RCA: Right coronary artery; DIA: Diagonal branch; OM: Obtuse marginal branch.

decreased in quitters compared with smokers and non-smokers (2.7 [0.6, 7.1]% vs. 3.5 [0.9, 8.9]%) and 3.4 [1.1, 7.7]%, P = 0.020) [Figure 1]. A total of 251 lesions showed rapid progression at second CAG. At the lesion level, quitters tended to have a lower incidence of rapid lesion progression (12.8% [80/625] vs. 15.9% [92/578] and 16.9% [79/467], P = 0.129) and lesion re-vascularization (10.4% [65/625] vs. 11.6% [67/578] and 11.8% [55/467], P = 0.723) compared with non-smokers and smokers, but the results were not significantly different.

Impacts of smoking status on clinical outcomes

The clinical outcomes of coronary non-target lesions at the patient level were documented at the second CAG and are presented in Table 3. The incidence of rapid lesion progression in quitters were lower compared with smokers and non-smokers but results were not statistically significant (15.8% [76/482] vs. 21.6% [74/342] and 20.6% [89/431], P = 0.062). Quitters also had a lower incidence toward lesion re-vascularization, lesion-related myocardial infarction, and all-cause myocardial infarction compared with non-smokers and smokers though significant difference was not evident. The association between smoking status and clinical outcomes were investigated in Cox regression analysis [Table 4]. Results showed that smoking status was not an independent risk factor for clinical outcomes in univariable analysis (P > 0.05). Multivariable analysis showed that, after adjusting for age, sex, STEMI, hypertension, diabetes mellitus, baseline low-density lipoprotein cholesterol, CRP and erythrocyte sedimentation rate, smokers were at a higher risk for all-cause myocardial infarction compared to non-smokers (hazards ratio: 3.00, 95% confidence interval: 1.04–8.62, P = 0.042). Smoking status were not independent predictors for lesion progression, lesion re-vascularization, and lesion-related myocardial infarction (P > 0.05).

Discussion

In this study, impacts of smoking status on clinical outcomes of coronary non-target lesions were assessed angiographically in a single center. Our results showed that quitters had a significantly lower increase in percent

Figure 1: Changes in percent diameter stenosis of coronary non-target lesion at the second coronary angiography among groups with different smoking status.

diameter stenosis compared with smokers and non-smokers. Quitters also had lower incidence of rapid lesion progression compared with non-smokers and smokers both at lesion level and patient level though significant difference was not evident. Smoking status was not an independent risk factor for rapid lesion progression, lesion re-vascularization and lesion-related myocardial infarction in multivariable analysis but smokers were at a higher risk for all-cause myocardial infarction than non-smokers.

A plenty of evidence had showed that coronary plaques would go through a period of rapid progression weeks to months before developing to myocardial infarction.[12] 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-year follow-up, there was rapid progression from a mean angiographic diameter stenosis of $32 \pm 21\%$ to $65 \pm 16\%$ at the time of acute events. In our study, two serial CAGs were all performed within 2 years. Changes of coronary lesions stenosis during this time course could be defined as rapid progression according to previous studies.[14] The onset of new lesions was not included because previous study showed that more than 95% of re-vascularization in non-target lesions was driven by preexisting lesions rather than new onset lesions.[15]

Identifying modifiable clinical factors resulting in rapid coronary lesion progression is of great importance. Smoking promotes coronary atherosclerosis and is one of the most important risk factors for CHD.[1,2] Previous
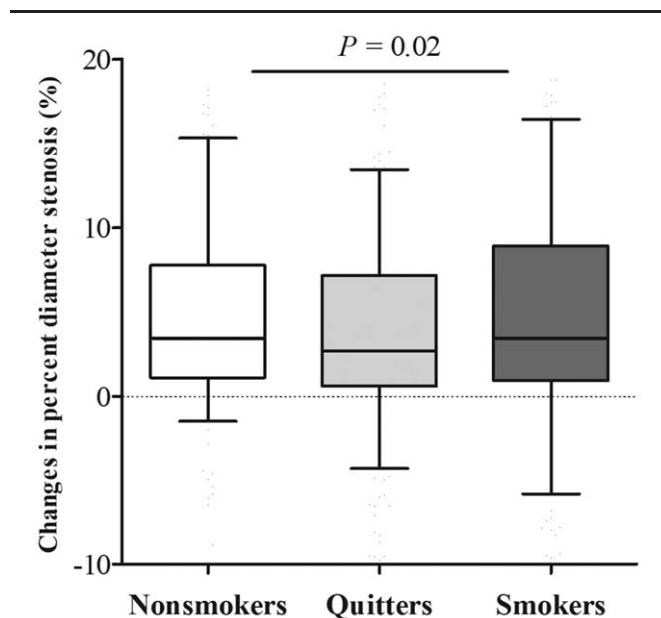
Table 3: Clinical outcomes at the time of follow-up among three groups.

Clinical outcomes	Non-smokers ($n = 431$)	Quitters ($n = 482$)	Smokers ($n = 342$)	Statistical values	P
Follow-up interval (months)	14.2 ± 4.4	14.9 ± 5.3	14.0 ± 4.5	3.891[*]	0.036
Rapid lesion progression	89 (20.6)	76 (15.8)	74 (21.6)	5.569[†]	0.062
Lesion re-vascularization	67 (15.5)	63 (13.1)	53 (15.5)	1.435[†]	0.488
Lesion-related myocardial infarction	6 (1.4)	4 (0.8)	9 (2.6)	4.421[†]	0.110
All-cause myocardial infarction	10 (2.3)	9 (1.9)	14 (4.1)	4.118[†]	0.128

[*] F values. [†] χ^2 values. Data are represented as mean ± standard deviation or n (%).

Table 4: Univariable and multivariable analyses of the association between smoking status and outcomes.

Outcomes	Smoking Status	Crude HR (95% CI)	Crude P	Adjusted HR (95% CI)	Adjusted P
Rapid lesion progression	Non-smokers	Reference	–	Reference	–
	Quitters	0.93 (0.68–1.27)	0.641	0.92 (0.64–1.32)	0.640
	Smokers	1.14 (0.84–1.55)	0.415	1.06 (0.73–1.53)	0.760
Lesion re-vascularization	Non-smokers	Reference	–	Reference	–
	Quitters	0.99 (0.70–1.40)	0.946	0.93 (0.62–1.38)	0.708
	Smokers	1.08 (0.76–1.54)	0.676	0.99 (0.66–1.50)	0.970
Lesion-related myocardial infarction	Non-smokers	Reference	–	Reference	–
	Quitters	0.58 (0.14–2.31)	0.436	1.15 (0.25–5.38)	0.861
	Smokers	2.12 (0.75–6.00)	0.155	3.30 (0.84–13.00)	0.088
All-cause myocardial infarction	Non-smokers	Reference	–	Reference	–
	Quitters	0.94 (0.37–2.40)	0.901	1.46 (0.48–4.46)	0.502
	Smokers	2.01 (0.89–4.55)	0.093	3.00 (1.04–8.62)	0.042

HR: Hazard ratio; CI: Confidence index; –: No data.

studies showed that smoking was significantly associated with the severity of coronary arterial stenosis.[16,17] However, in our study, the increase in percent diameter stenosis, the incidence of rapid lesion progression as well as lesion re-vascularization was not different between smokers and non-smokers. There were reasons that might explain the results. First, smoking usually influence the progression of atherosclerosis in a long-term manner. Smokers often started cigarette use from a young age and the influence of smoking persisted for decades before the occurring of coronary lesions with significant stenosis. While in our study, the two serial CAGs were all performed within 2 years, which was a relative short time course compared with the duration of smoking. Second, other risk factors, such as systemic inflammatory responses, might also participated in lesion progression. Inflammation plays a pivotal role in the formation and progression of atherosclerosis.[10,18-20] In this study, levels of white blood cells and CRP were significantly higher in smokers compared with non-smokers at both procedures indicating persistent elevation of inflammatory responses. Even though results were insignificant between smokers and non-smokers concerning rapid lesion progression, smoking cessation was shown to alleviate the progression of coronary arterial stenosis in our study. Results showed that the increase in percent diameter stenosis was significantly lower in quitters compared with that in smokers and non-smokers. Additionally, quitters tended to have a lower incidence of rapid progression and re-vascularization of coronary non-target lesions compared with smokers and non-smokers. Similar to our results, the benefits of smoking cessation have been reported in patients with CHD before. Conroy et al showed that cessation before the age of 40 years reduces the risk of cardiovascular death associated with continued smoking by about 90% and the relative risk of major adverse cardiac and cerebrovascular events were approximately three-fold greater in persistent smokers than in quitters.[21] In addition, inflammatory markers associated with CHD were shown to return to the similar level of a non-smoker at 5 years after quitting smoking.[22] In accordance with previous studies, our results indicated that smoking cessation is beneficial for the progression of coronary lesions even in a relatively short period of less than 2 years.

The prognosis of CHD in smokers is still debating. Prior studies have found that smokers have lower mortality than non-smokers after the onset of acute coronary syndrome or post-PCI procedure, a phenomenon known as "smoking paradox."[23-25] Possible explanations for the higher mortality rate in non-smokers are that non-smokers are older and have a higher prevalence of comorbid factors such as hypertension and impaired left ventricle function.[11] In our study, smoking status was not an independent predictor for lesion re-vascularization and lesion-related myocardial infarction. Therefore, the phenomenon of "smoking paradox" was not observed concerning clinical outcomes of coronary non-target lesions. Furthermore, multivariable analysis showed that smokers were at a higher risk of all-cause myocardial infarction compared with non-smokers. In accordance with our results, Zhang et al[26] showed that smoking is associated with a higher incidence of recurrent myocardial infarction in patients underwent PCI treatment.

We proposed that smoking aggravate the instability of coronary plaque which resulting in plaque rupture and subsequently myocardial infarction. As the smoking rate in China was reported to be 27.7% at 2015,[27] it is of great challenge for our government to implement stricter tobacco control policies.

This study had several limitations. First, our study was a retrospective single center study, only patients who underwent serial CAGs were enrolled. These patients might take more serious of their health and be more likely to seek for medical assistances when symptoms occur. This selection bias might have influence on the final results. Second, it is limited to evaluate lesion progression only by CAG, combined modalities such as intravascular ultrasound and optic coherence tomography should be useful to evaluate rapid lesion progression in the future studies. Third, the results needed to be confirmed in large, prospective studies.

In conclusion, the present study showed that the increase of percent diameter stenosis of coronary non-target lesions is significantly lower in quitters compared with that in smokers and non-smokers. Smoking status were not independent risk factors for lesion progression, lesion re-vascularization and lesion-related myocardial infarction but smokers were at a higher risk for all-cause myocardial infarction compared with non-smokers. Our study places further emphasis on efforts at smoking cessation to improve clinical outcomes of coronary non-target lesions.

Conflicts of interest

None.

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