

# The association of procedural variables and lipid parameters with coronary rotational atherectomy outcomes

Shuang Zhang<sup>1,†</sup>, Wen-Jia Zhang<sup>1,†</sup>, Hui-Wei Shi<sup>1</sup>, Zhi-Fan Li<sup>1</sup>, Yong-Gang Sui<sup>1</sup>, Jie Qian<sup>1</sup>, Na-Qiong Wu<sup>1,\*</sup>

<sup>1</sup>Cardiometabolic Center, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Science & Peking Union Medical College, 100037 Beijing, China

\*Correspondence: [fuwainaqiongwu@163.com](mailto:fuwainaqiongwu@163.com) (Na-Qiong Wu)

† These authors contributed equally.

DOI: [10.31083/j.rcm2204172](https://doi.org/10.31083/j.rcm2204172)

This is an open access article under the CC BY 4.0 license (<https://creativecommons.org/licenses/by/4.0/>).

Submitted: 4 August 2021 Revised: 22 October 2021 Accepted: 26 October 2021 Published: 22 December 2021

The aim of our study is to evaluate the association of rotational atherectomy (RA) operation procedural indices and baseline lipid parameters with the prognosis of the patients with severe coronary calcification who underwent RA. Our study population consists of 287 patients treated with RA in Fuwai Hospital from January 2013 to December 2019. We analyzed the patients' rotation procedural indices including the number of burrs, the size of burrs, approach site, the size of guiding catheter, along with the baseline level of lipoprotein(a) (Lp(a)), low-density lipoprotein-cholesterol (LDL-C) and high-sensitivity C-reactive protein (hs-CRP) to examine the association of these measurements with the prognosis of these patients using Cox regression analysis and Kaplan-Meier survival analysis. We find that during the follow-up period of 56.7 months with the median, the use of single burr in the patients who underwent RA was significantly associated with the occurrence of cumulative major adverse cardiac events (MACE) when compared with using non-single burrs [Hazard Ratio (HR) 0.43, 95% confidence interval (95% CI) 0.24–0.77,  $p = 0.004$ ] from univariate Cox regression analysis; (HR 0.36, 95% CI 0.20–0.66,  $p = 0.001$ ) from multivariate Cox regression analysis. In addition, we find a higher event-free survival rate in the single-burr group after Kaplan-Meier survival analysis (Log rank  $p = 0.0033$ ). However, there was no significant association of the size of burrs with the occurrence of MACE (HR 0.90, 95% CI 0.47–1.73,  $p = 0.76$ ). Similarly, we find no significant associations between the approach site and the occurrence of MACE (HR 0.79, 95% CI 0.24–2.53,  $p = 0.69$ ), the baseline Lp(a) (HR 1.07, 95% CI 0.76–1.49,  $p = 0.71$ ), the level of LDL-C (HR 0.83, 95% CI 0.55–1.26,  $p = 0.38$ ) or hs-CRP (HR 0.85, 95% CI 0.45–1.58,  $p = 0.60$ ). We find that the patients who receive RA with a single burr have better outcomes than those who receive RA with non-single burrs. Moreover, we find that the number of burrs used in RA instead of the size of burrs, approach site, the size of guiding catheter, or baseline levels of Lp(a), LDL-C or hs-CRP had significant association with the prognosis of RA patients.

## Keywords

Coronary artery calcification; Rotational atherectomy; Rotation procedural indices; Lipoprotein(a)

## 1. Introduction

Coronary heart disease (CHD) is the leading cause of mortality and morbidity worldwide, and arterial calcification is strongly associated with poor prognosis of CHD [1, 2]. Previous studies have shown that the higher coronary artery calcification (CAC) was associated with the higher risk for atherosclerotic cardiovascular disease, and the CAC score has been regarded as an effective tool for predicting cardiovascular risk [1, 3–5].

Percutaneous coronary intervention (PCI) is one important treatment for CHD, but calcified lesions have been found to increase the possibility of failure in stent delivery [2]. To avoid this problem, the rotational atherectomy (RA) adopted differential cutting to ablate atherosclerotic plaques by forward advancement of a rotating abrasive diamond-encrusted burr [6]. RA can effectively reduce the plaque volume and enlarge the lumen, which allows easier stent deployment [7–9], and plaque modification has been shown to decrease the risk of stent restenosis and malapposition [10–13]. RA has been traditionally performed via the transfemoral approach, mostly utilizing large guide catheters [ $\geq 7$  French (Fr)], which can accommodate the passage of large burrs ( $\geq 1.75$  mm). However, contemporary data show that using smaller sheath and catheter sizes reduces the risk of procedural access-site related complications [6]. We seek to clarify further factors that might be associated with the RA patient prognosis, such as procedural indices including the number of burrs, the size of burrs, approach site, the size of guiding catheter.

Many studies have also examined the relationship between heart patients' blood chemistry and their prognosis. Plasma lipoprotein(a) [Lp(a)], low density lipoprotein cholesterol (LDL-C), and inflammatory factor high sensitivity C-reactive protein (hs-CRP) have all been shown to be related to the prognosis of patients with atherosclerotic cardiovascular disease (ASCVD) [1, 14, 15]. Importantly, Lp(a) has been shown to be a causal risk factor for CAC [16–19]. However, it remains uncertain whether the level of Lp(a), LDL-C or hsCRP is related to the prognosis of patients who undergo RA, a relationship we aim to clarify in our study.

## 2. Methods

### 2.1 Study design and population

In our study, we examine the prognosis and contributing factors in 287 individuals who underwent RA from January 2013 to December 2019 at Fuwai Hospital. According to the RA procedural routine of our hospital, the characteristics of lesion calcification were generally as ring with 360°, which indicated to undergo RA. For every patient, we collected medical history and RA procedural indices. In the study, we define the single-burr group as the patients who received single burr rotation during RA, and non-single burr group as the patients who received at least two burrs during RA. We additionally categorize the size of burrs used as “small” for any burr no more than 1.5 mm and “large” for all burrs greater than 1.5 mm. To classify whether a patient had hypertension, we use thresholds of systolic blood pressure (SBP)  $\geq 140$  mmHg and/or diastolic blood pressure (DBP)  $\geq 90$  mmHg for at least 3 consecutive readings, or if the patient is on antihypertensive drugs therapy. We consider a patient to have had diabetes if the patient's fasting plasma glucose was at least 7.0 mmol/L, the patient was currently using hypoglycemic drugs or insulin, if the patient's two-hour plasma glucose from the oral glucose tolerance test was at least 11.1 mmol/L or the patient had a history of clinically diagnosed diabetes. To compute body mass index (BMI) we divide weight by height squared ( $\text{kg}/\text{m}^2$ ). This study complied with the Declaration of Helsinki and was approved by the Fuwai Hospital's ethical review board.

### 2.2 Laboratory tests

We collected fasting plasma samples in the morning from all the patients, and measured plasma levels of total cholesterol (TC), triglyceride (TG), LDL-C, high-density lipoprotein cholesterol (HDL-C), and hsCRP using an automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan). And the serum Lp(a) levels using an immune-turbidimetry assay (LASAY Lp(a) auto; SHIMA laboratories, Tokyo, Japan).

### 2.3 Follow up

All patients received follow-up examinations regularly, with a median period of follow-up of 56.7 months (30–73 months). We defined MACE as the composite of cardiac death, nonfatal myocardial infarction (MI), nonfatal stroke, unstable angina pectoris and target lesion revascularization (TLR) and hospitalization with unstable angina (UA). For the dead patients, the events were reported by their relatives. Our definition for a diagnosis of nonfatal myocardial infarction (MI) was positive cardiac troponins with typical chest pain or typical electrocardiogram (ECG) serial changes, and we defined stroke as persistent neurological dysfunction with documentation of acute cerebral infarction on computed tomography and/or magnetic resonance imaging. Finally, we use PCI or coronary artery bypass graft (CABG) during the follow-up period to indicate TLR.

### 2.4 Procedural details

According to the PCI guidelines, procedures were performed via the radial or femoral route by experienced operators. The indications for RA included (1) severe calcification lesions with 360° calcification as a ring observed on intravascular ultrasound (IVUS) or linear calcium density images on both sides of the target lesion visible under fluoroscopy, and (2) calcified lesions making the passage of imaging probes difficult, where inadequate stent delivery or expansion was to be expected. The burr size of the rotablator was selected to reach a burr to vessel ratio of between 0.5 and 0.7, and its rotational speed was set between 150,000 and 170,000 rpm. All patients received a continuous intracoronary infusion of verapamil, nitroglycerin, and unfractionated heparin and pretreatment of dual antiplatelet therapy. Intraprocedural intrarterial unfractionated heparin bolus (70–100 IU/kg) was administered to maintain the activated clotting time at  $\geq 250$  seconds or longer. According to the operators' experience and the routine of our hospital, the operators checked the calcification lesion by IVUS before RA, or they decided to perform RA procedure after they failed to dilate the lesion by post-dilated balloon or cutting balloon. And they usually used cutting balloon or post-dilated balloon to dilate the lesion fully after RA. Successful stent implantation signified RA procedural success.

### 2.5 Statistical analysis

We perform statistical analyses using the R language (version 4.0.4, Feather Spray; The R Foundation for Statistical Computing, Vienna, Austria) and measure statistical significance as any  $p$ -value  $< 0.05$ . Specifically, to test the distribution pattern, we employ a Kolmogorov-Smirnov test, and use Student's  $t$  test or Mann-Whitney U tests to test differences between the single-burr and non single-burr groups. We express continuous data as mean  $\pm$  standard deviation or median (interquartile range) as appropriate and present categorical variables as  $n$  (%) and compare them with the chi-square test or Fisher exact tests. Additionally, we perform univariate and multivariate Cox regression analysis to evaluate the factors that might be associated with the occurrence of MACE, and estimate event-free survival rates using the Kaplan-Meier method and compared by the log-rank test. Finally, we use univariate and multivariate Cox regression analyses to calculate hazard ratios (HRs) and 95% confidence intervals.

## 3. Results

### 3.1 Baseline characteristics

Table 1 shows the baseline characteristics of the study population. We find no significant differences in the single-burr group and non-single burr group in ages ( $67.73 \pm 7.98$  vs  $67.28 \pm 8.76$  years old,  $p = 0.65$ ), BMI ( $24.74 \pm 3.10$   $\text{kg}/\text{m}^2$  vs  $24.81 \pm 3.05$   $\text{kg}/\text{m}^2$ ,  $p = 0.85$ ), the proportion of males (69.05% vs 63.03%,  $p = 0.35$ ), hypertension (74.40% vs 68.07%,  $p = 0.30$ ), hyperlipidemia (85.71% vs 80.67%,  $p = 0.33$ ), diabetes mellitus (44.64% vs 37.82%,  $p = 0.30$ ), smok-

ers (50.60% vs 43.70%,  $p = 0.30$ ). Similarly, we find no significant differences between the single-burr group and the non-single-burr group in Left Ventricular Ejection Fractions (LVEF) (60.98% vs 59.45%,  $p = 0.25$ ), glycated hemoglobin [glycosylated hemoglobin (HbA1C) (6.77% vs 6.59%,  $p = 0.29$ ), Lp(a) (120.9 mg/L vs 172.83 mg/L,  $p = 0.08$ ), LDL-C ( $2.19 \pm 0.77$  mmol/L vs  $2.12 \pm 0.68$  mmol/L,  $p = 0.43$ ), hs-CRP (1.18 mg/L vs 1.37 mg/L,  $p = 0.24$ ), glomerular filtration rate (eGFR) ( $79.07 \pm 20.96$  mL/min·1.73 m<sup>2</sup> vs  $76.56 \pm 18.79$  mL/min·1.73 m<sup>2</sup>, burr to artery ratio ( $0.52 \pm 0.10$  vs  $0.51 \pm 0.09$ ,  $p = 0.46$ ), guiding catheter size (6F: 61.31% vs 60.50%,  $p = 0.99$ ), or approach site (Radial or Brachial: 91.07% vs 92.44%,  $p = 0.85$ ). The proportion of stent implantation was similar in both the groups (0 stent: 17.86% vs 13.45%, 1 stent: 16.67% vs 29.41%, 2 stents: 50.60% vs 38.66%, 3 stents: 13.10% vs 15.97%; 4 stents: 1.79% vs 2.52%,  $p = 0.07$ ). We could not reject the null hypothesis that the values for both groups were equal for any of the remaining baseline characteristics using the 0.05 level for the  $p$ -value.

### 3.2 Association between rotation operation procedural indices and MACE

We find that the use of a single burr in RA patients significantly associated with the occurrence of MACE when compared to using non-single burr produces (HR 0.43, 95% CI 0.24–0.77,  $p = 0.004$  from univariate Cox regression analysis; HR 0.36, 95% CI 0.20–0.66,  $p = 0.001$  from multivariate Cox regression analysis, Table 2). Furthermore, we find that there was higher event-free survival probability in the single-burr group after Kaplan-Meier survival analysis (Log-rank  $p = 0.0065$ , Fig. 1). However, there we find no significant association of the size of burrs with the occurrence of MACE (HR 0.9, 95% CI 0.47–1.73,  $p = 0.76$ , Table 2).

For the approach site, and guiding catheter size, we find no significant association between the approach site (transradial or transfemoral) and occurrence of MACE after univariate or multivariate Cox regression analysis (HR 0.79, 95% CI 0.24–2.53,  $p = 0.69$ , Table 2) and similarly, find no significant association between guiding catheter size (6F or 7F) (HR 1.43, 95% CI 0.78–2.6,  $p = 0.25$ , Table 2). In addition, our univariate Cox regression analysis shows no statistically significant association of burr-to-artery ratio with the occurrence of MACE (HR 1.88, 95% CI 0.11–3.26,  $p = 0.67$ , Table 2).

### 3.3 Association between lipid parameters and MACE

We divide all patients into three groups according to the tertile of Lp(a) level. The low-level group includes patients with Lp(a) <72 mg/L, the medium-level group includes patients with Lp(a) between 72 and 244.23 mg/L, and the high-level group includes patients with Lp(a) >244.23 mg/L. In addition, we divide the patients into two groups depending on whether hs-CRP <2 mg/L or  $\geq 2$  mg/L.

We find no statistically associations between the level of Lp(a) and the occurrence of MACE after univariate Cox regression analysis ( $p > 0.05$ , Table 2). Similarly, we find no any statistically significant association between the level of LDL-C and the occurrence of MACE (HR 0.83, 95% CI 0.55–

1.26,  $p = 0.38$ , Table 2) or the level of hs-CRP with the occurrence of MACE from univariate Cox regression analysis either (HR 0.85, 95% CI 0.45–1.58,  $p = 0.60$ , Table 2).

## 4. Discussion

CAC was defined as mineral deposition in the coronary artery wall, which was very common in the aging population of the world [20, 21]. In routine PCI procedure, CAC could impair stent delivery and expansion. Importantly, it was highly predictive for MACE. So heavily calcified lesions need to be treated by RA to facilitate subsequent procedures [1, 2]. In the European expert consensus on RA, they recommended during RA, the operators could choose burrs step by step through burrs upsizing or downsizing [6]. However, there is scant data on whether the number or size of burrs is associated with long-term outcomes for the patients who underwent RA.

In this study, we analyzed the association between RA operation procedural indices and the prognosis of patients undergoing RA after a median of 56.7 months follow-up period. In our study, RA procedures were performed according to the operators' experience and the routine about RA of our hospital in both the groups, including that the operators checked the calcification lesion by IVUS before RA, or they decided to perform RA procedure after they failed to dilate the lesion by post-dilated balloon or cutting balloon. And they usually used cutting balloon or post-dilated balloon to dilate the lesion fully after RA. Under the abovementioned background about procedural details, the analysis showed that using single burr during RA was related with lower rate of MACE and higher event-free survival rate (Log-rank  $p = 0.0065$ ). We speculated that the possible explanations included that optimization of choosing the single burr during RA was enough to facilitate the procedure of intervention about severe calcification lesions, and in addition, choosing the optimal single burr, not 2 or more burrs could shorten the whole procedural time, and had more possibility to choose transradial access and less puncture-site related complications. In previous studies, using large burrs, which was more possible in non-single-burr group, didn't improve the outcomes of the patients undergoing RA. Moreover, the experience from Taiwan local hospital supplied convincing evidence supporting the use of a single-burr strategy for RA to treat complex calcified coronary lesions rather than a routine step-by-step strategy for RA [22].

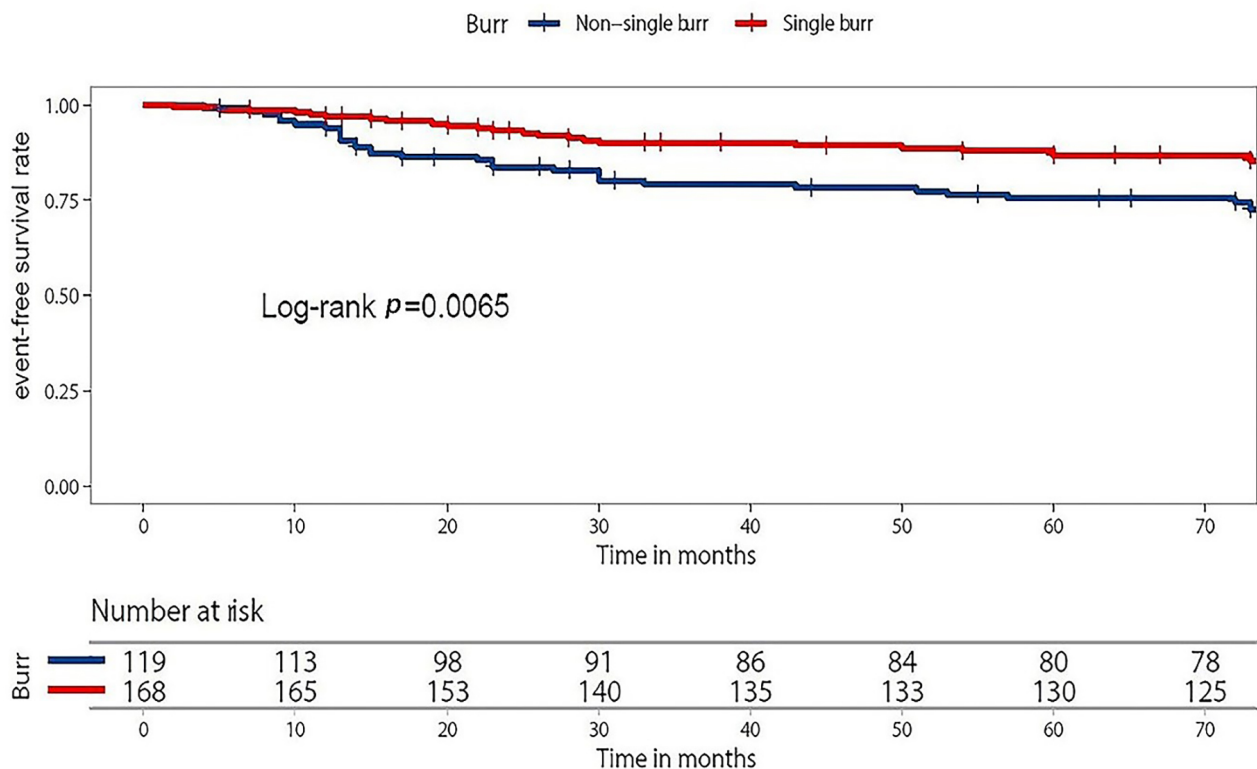
This study finds that appropriate burr size is vital for treatment of CAC during RA. We divided burrs into small (1.25 mm and 1.5 mm) and large (1.75 mm and 2.0 mm) groups and saw that, a burr-to-artery ratio <0.7 was recommended. In our study, we found that the burr-to-artery ratio was similar between the single-burr group and the non-single burr group ( $0.52 \pm 0.1$  vs  $0.51 \pm 0.09$ ,  $p = 0.46$ , Table 1), and the burr to artery ratio was not associated with the occurrence of MACE (HR 1.88, 95% CI 0.11–3.26,  $p = 0.46$ , Table 2). Burr upsizing and burr downsizing was also beneficial for the lesions

**Table 1. Baseline characteristics of both single-burr group and non-single burr group.**

	Single burr group (n = 168)	Non-singleburr group (n = 119)	p
Age (y)	67.73 ± 7.97	67.28 ± 8.76	0.65
Male, n (%)	116 (69.05)	75 (63.03)	0.35
BMI (kg/m <sup>2</sup> )	24.74 ± 3.10	24.81 ± 3.05	0.85
Hypertension, n (%)	125 (74.40)	81 (68.07)	0.30
Hyperlipidemia, n (%)	144 (85.71)	96 (80.67)	0.33
Diabetes mellitus, n (%)	75 (44.64)	45 (37.82)	0.30
Smokers, n (%)	85 (50.60)	52 (43.70)	0.30
Previous CABG, n (%)	6 (3.57)	2 (1.68)	0.55
SBP (mmHg)	135.51 ± 19.98	135.87 ± 18.58	0.88
DBP (mmHg)	74.75 ± 11.28	74.60 ± 10.75	0.91
LVEF (%)	60.98 ± 10.52	59.45 ± 12.00	0.25
HbA1c (%)	6.77 ± 1.31	6.59 ± 1.53	0.29
Lp(a) (mg/L)	120.9 [53.98–311.67]	172.83 [52.2–418.45]	0.08
TC (mmol/L)	4.17 ± 2.89	4.02 ± 0.95	0.60
TG (mmol/L)	2.15 ± 7.83	1.56 ± 1.44	0.41
HDL-C (mmol/L)	1.26 ± 0.31	1.27 ± 0.370	0.86
LDL-C (mmol/L)	2.19 ± 0.77	2.12 ± 0.68	0.43
hs-CRP (mg/L)	1.18 [0.48–2.20]	1.37 [0.63–3.41]	0.24
eGFR (mL/min·1.73 m <sup>2</sup> )	79.07 ± 20.96	76.56 ± 18.79	0.30
Clinical diagnosis			0.015
Stable angina, n (%)	86 (72.3)	146 (86.9)	
Unstable angina, n (%)	3 (2.5)	1 (0.6)	
NSTEMI, n (%)	22 (18.5)	17 (10.1)	
STEMI, n (%)	8 (6.7)	4 (2.4)	
Medications at follow-up, n (%)			
Aspirin	167 (99.40)	119 (100.00)	-
ACEI/ARB	31 (18.45)	24 (20.17)	0.83
β-blockers	123 (73.21)	95 (79.83)	0.25
Clopidogrel	144 (85.71)	100 (84.03)	0.82
Statins	163 (97.02)	118 (99.16)	0.41
Stent implantation, n (%)			0.07
0	30 (17.86)	16 (13.45)	
1	28 (16.67)	35 (29.41)	
2	85 (50.60)	46 (38.66)	
3	22 (13.10)	19 (15.97)	
4	3 (1.79)	3 (2.52)	
Approach site			0.85
Radial (brachial)	153 (91.07)	110 (92.44)	
Femoral	15 (8.93)	9 (7.56)	
Burr:artery ratio	0.52 ± 0.1	0.51 ± 0.09	0.46
Guiding catheter size, n (%)			0.99
6F	103 (61.31)	72 (60.50)	
7F	65 (38.69)	47 (39.50)	
Size of burrs, n (%)			
small <sup>#</sup>	136 (80.95)	90 (75.63)	0.35
large <sup>#</sup>	32 (19.05)	29 (24.37)	
Target vessel, n (%)			0.85
LAD	122 (72.62)	92 (77.31)	
LCX	13 (7.74)	5 (4.20)	
RCA	33 (19.64)	22 (18.49)	
Cumulative MACE, n (%)	24 (14.29)	31 (26.05)	0.02*
TLR	2 (1.19)	3 (2.52)	0.70
Cardiac death	9 (5.36)	6 (5.04)	1.00
Stroke	4 (2.38)	11 (9.24)	0.02*
Nonfatal MI	2 (1.19)	1 (0.84)	1.00
Hospitalization with UA	7 (4.17)	10 (8.40)	0.21

BMI, body mass index; CABG, coronary artery bypass graft; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery; TLR, target lesion revascularization; MI, myocardial infarction, UA, unstable angina. \* indicates  $p < 0.05$ . <sup>#</sup> Small size included 1.25 mm, 1.5 mm burrs, large size included 1.75 mm, 2.0 mm burrs.





**Fig. 1. Kaplan-Meier curve in the single-burr group and non-single-burr group.** Overall 287 patients were categorized into non-single burr group ( $n = 119$ ) and single burr group ( $n = 168$ ). During the median period of follow-up of 56.7 months (30–73 months), the single-burr group had higher event-free survival probability (Log-rank  $p = 0.0065$ ).

which could not be treated by one burr. The aforementioned European expert consensus suggested the step-up approach starting with 1.25 mm up to 1.5 mm or 1.75 mm burr [6, 7]. Given that RA has changed from merely a debulking tool to now lesion modification before stent implantation, a single-burr strategy could be improved to disrupt the continuity of calcium rings and flatten the vessel lumen in order to enable balloon dilatation and stent implantation [6, 7].

Chiou *et al.* [22] find that the single-burr strategy had the same result compared to the step-up approach pursuant to its advantages of less procedure time and complications. Levi *et al.* [23] report that 151 patients with small burrs achieve successful procedure, in comparison with 58 patients received the large burr (93% vs 100%,  $p = 0.07$ ). In a long-term of 2616 days follow-up study about RA from a single center, Bartus *et al.* [24] found that both high-risk category and mean stent(s) length were identified as independent predictors of MACCE. EuroSCORE II was confirmed to be the only independent predictor of MACE after RA [24].

However, approach site also plays an important role in the RA procedure. As reported previously, the procedural success rate and long-term prognosis were found to be similar between the transfemoral approach (TFA) and transradial approach (TRA) in routine PCI without RA procedures, but radial access had a lower risk of in-hospital major bleeding, major access site complications and longer hospital stay [6, 25]. Watt *et al.* [25] find TRA has the same procedural

success as TFA (95.2% vs 94.9%,  $p = 0.56$ ) and that TRA has a lower incidence of major access site complications than TFA (0.04% vs 1.3%,  $p = 0.004$ ). Similarly, Kübler *et al.* [26] suggest that TRA is associated with equivalent procedural success compared to TFA (95% vs 87%,  $p = 0.07$ ). However, they find that TFA is prone to have major access site bleedings (13% vs 1%,  $p = 0.001$ ). After 1 year, however they find that TRA maintains the same results in comparison to TFA ( $p = 0.41$ ) [26]. In our study, we also find that there was no statistical significance for the long-term prognosis between TRA and TFA group ( $p = 0.69$ , Table 2), providing evidence that TRA is a useful alternative method to avoid vascular complications. Using a 7F system offers the availability of larger burr sizes, when it comes to plaque preparation, operators in our study found it adequate to use a maximum burr size of 1.75 mm, which can be accommodated in a 6F guide. And 6F guide, which were themselves usually used in transradial procedures. Larger guide catheter offers the more support for complex bifurcation [7, 27]. In our study, there was no difference in prognosis between the two catheter-size groups ( $p = 0.25$ , Table 2).

In previous studies, Lp(a) was found to be associated with CAC in patients with or without familial hypercholesterolemia [17, 28]. Pechlivanis *et al.* [18] find that both log-transformed Lp(a) and categories of Lp(a) ( $\text{Lp(a)} \geq 54.3$  mg/dL and  $\text{Lp(a)} < 54.3$  mg/L) have statistically significant links with CAC (beta per log unit increase in  $\text{Lp(a)} = 0.11$ ,

**Table 2. Univariate and multivariate Cox regression analysis for MACE and the relative factors.**

	Univariate Cox regression analysis			Multivariate Cox regression analysis		
	HR	95% CI	<i>p</i>	HR	95% CI	<i>p</i>
Male	1.16	0.63–2.13	0.64			
Age	1.03	0.99–1.07	0.11	1.04	1.00–1.07	0.07
ACS	1.24	0.58–2.64	0.58			
BMI	0.96	0.87–1.05	0.37			
Hypertension	0.88	0.48–1.6	0.67	0.79	0.41–1.50	0.47
smoking	0.97	0.56–1.71	0.93	1.25	0.68–2.29	0.47
DM	1.14	0.65–2.01	0.64	1.23	0.67–2.26	0.50
LDL-C	0.83	0.55–1.26	0.38	0.81	0.53–1.24	0.34
hs-CRP	0.85	0.45–1.58	0.60	0.69	0.37–1.31	0.26
eGFR,	0.79	0.37–1.68	0.54			
LVEF	1.02	0.99–1.05	0.27			
Lp(a)						
low-level	Ref					
medium level	0.81	0.4–1.64	0.56			
high level	1.07	0.76–1.49	0.71			
Single burr	0.43	0.24–0.77	0.004*	0.36	0.20–0.66	0.001*
Guiding catheter size	1.43	0.78–2.6	0.25			
Approach site	0.79	0.24–2.53	0.69			
Burr/artery ratio	1.88	0.11–3.26	0.67			
Size of burrs	0.90	0.47–1.73	0.76			

ACS, acute coronary syndrome; BMI, body mass index; DM, diabetes mellitus; LDL-C, low-density lipoprotein-cholesterol; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; Lp(a), lipoprotein(a); \* indicates  $p < 0.05$ .

95% CI 0.04–0.18,  $p = 0.002$ ; Lp(a)  $\geq 54.3$  mg/dL vs Lp(a)  $< 54.3$  mg/L: 0.23, 95% CI 0.005–0.45,  $p = 0.05$ ). Prior studies had found that Lp(a)  $> 30$  mg/dL could result in 5.51-fold increased risk for CAC progression  $> 100$ , after adjustment for other potential covariates ( $p = 0.02$ ) [29]. Patients with Lp(a) level  $\geq 50$  mg/dL were found to be more prone to having CAC progression than those with Lp(a)  $< 50$  mg/dL (odds ratio 1.333) [30]. Furthermore, except for the calcification, Lp(a) had an association with ASCVD. In particular, the mortality of patients with a high level of the Lp(a) increased than those with low-Lp(a) after PCI [16, 31]. However, we didn't observe this association between Lp(a) and the prognosis of patients who underwent RA. Previous studies have also shown that patients with lower LDL-C will have lower rates of major coronary events [15]. Wada *et al.* [15] report that after an average of 6.5 years of follow-up, hs-CRP has a great association with the MACE [HR 1.1 (1.04–1.16),  $p < 0.001$ ] and all-cause mortality [HR 1.14 (1.06–1.22),  $p = 0.001$ ]. However, we find no statistical significance in the relationship between the baseline level of LDL-C or hs-CRP with the prognosis of patients who underwent RA in our study.

## 5. Limitations

There are several limitations to this study. First, the rotation operation strategies were decided by the cardiovascular intervention specialist based on experience, which might induce selection bias compared with randomized controlled

trials. Although we adjust the comparison between groups for possible confounders, the selection bias might still exist because of unknown confounders. Second, the sample size of our study was small. For Lp(a), large scale prospective randomized controlled trials are needed to determine the role of Lp(a) in the prognosis of patients who undergo RA. Finally, our results are tempered by the fact that all of the data we collected came from a single medical center.

## 6. Conclusions

In summary, we provide evidence that patients who undergo RA with a single burr may have better outcomes than patients who receive more than one burr. We find no significant association between the occurrence of MACE with the other issues of RA procedural indices including the size of burrs, approach site and guiding catheter size. Moreover, we find that baseline levels of Lp(a), LDL-C and hs-CRP have no significant predictive value for the prognosis of RA patients.

## Abbreviations

RA, rotational atherectomy; MACE, major adverse cardiac events; Lp(a), lipoprotein(a); LDL-C, low density lipoprotein cholesterol; hs-CRP, high sensitivity C-reactive protein; CHD, coronary heart disease; CAC, coronary artery calcification; PCI, percutaneous coronary intervention; ASCVD, atherosclerotic cardiovascular disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL-C,

high-density lipoprotein cholesterol; MI, myocardial infarction; TLR, target lesion revascularization; CABG, coronary artery bypass graft; HRs, hazard ratios; TFA, transfemoral approach; TRA, transradial approach.

## Author contributions

NQW designed the study; SZ and WJZ collected the medical records, followed up the patients and performed statistical analysis, and wrote this manuscript; HWS, ZFL, YGS participated in collecting the data and data management; JQ was the consultant of this study. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Fuwai Hospital (Approval Number 2018-1086).

## Acknowledgment

We would like to express our gratitude to all those who helped us during the writing of this manuscript. Thanks to all the peer reviewers for their opinions and suggestions.

## Funding

This research received no external funding.

## Conflict of interest

The authors declare no conflict of interest.

## References

- [1] Greenland P, Blaha MJ, Budoff MJ, Erbel R, Watson KE. Coronary Calcium Score and Cardiovascular Risk. *Journal of the American College of Cardiology*. 2018; 72: 434–447.
- [2] Madhavan MV, Tarigopula M, Mintz GS, Maehara A, Stone GW, Généreux P. Coronary artery calcification: pathogenesis and prognostic implications. *Journal of the American College of Cardiology*. 2014; 63: 1703–1714.
- [3] Blaha MJ, Budoff MJ, Tota-Maharaj R, Dardari ZA, Wong ND, Kronmal RA, *et al*. Improving the CAC Score by Addition of Regional Measures of Calcium Distribution: Multi-Ethnic Study of Atherosclerosis. *JACC: Cardiovascular Imaging*. 2016; 9: 1407–1416.
- [4] Yerramasu A, Lahiri A, Venuraju S, Dumo A, Lipkin D, Underwood SR, *et al*. Diagnostic role of coronary calcium scoring in the rapid access chest pain clinic: prospective evaluation of NICE guidance. *European Heart Journal Cardiovascular Imaging*. 2014; 15: 886–892.
- [5] Sharma SK, Tomey MI, Teirstein PS, Kini AS, Reitman AB, Lee AC, *et al*. North American Expert Review of Rotational Atherectomy. *Circulation: Cardiovascular Interventions*. 2019; 12: e007448.
- [6] Barbato E, Carrié D, Dardas P, Fajadet J, Gaul G, Haude M, *et al*. European expert consensus on rotational atherectomy. *EuroIntervention*. 2015; 11: 30–36.
- [7] de Belder AJ. Rotational atherectomy: re-emergence of an old technique. *Heart*. 2018; 104: 440–448.
- [8] Abdel-Wahab M, Richardt G, Joachim Büttner H, Toelg R, Geist V, Meinertz T, *et al*. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) trial. *JACC: Cardiovascular Interventions*. 2013; 6: 10–19.
- [9] Hachinohe D, Kashima Y, Kanno D, Kobayashi K, Sugie T, Kaneko U, *et al*. Rotational atherectomy and new-generation drug-eluting stent implantation. *Catheterization and Cardiovascular Interventions*. 2019; 91: 1026–1034.
- [10] Baber U, Kini AS, Sharma SK. Stenting of complex lesions: an overview. *Nature Reviews. Cardiology*. 2010; 7: 485–496.
- [11] Tian W, Lhermusier T, Minha S, Waksman R. Rational use of rotational atherectomy in calcified lesions in the drug-eluting stent era: Review of the evidence and current practice. *Cardiovascular Revascularization Medicine*. 2015; 16: 78–83.
- [12] Attizzani GF, Capodanno D, Ohno Y, Tamburino C. Mechanisms, pathophysiology, and clinical aspects of incomplete stent apposition. *Journal of the American College of Cardiology*. 2014; 63: 1355–1367.
- [13] Bäck M, Yurdagül A, Jr., Tabas I, Öörni K, Kovanen PT. Inflammation and its resolution in atherosclerosis: mediators and therapeutic opportunities. *Nature Reviews Cardiology*. 2019; 16: 389–406.
- [14] Nguyen MT, Fernando S, Schwarz N, Tan JT, Bursill CA, Psaltis PJ. Inflammation as a Therapeutic Target in Atherosclerosis. *Journal of Clinical Medicine*. 2020; 8: 1109.
- [15] Wada H, Dohi T, Miyauchi K, Shitara J, Endo H, Doi S, *et al*. Preprocedural High-Sensitivity C-Reactive Protein Predicts Long-Term Outcome of Percutaneous Coronary Intervention. *Circulation Journal*. 2016; 81: 90–95.
- [16] Greif M, Arnoldt T, von Ziegler F, Ruemmler J, Becker C, Wakili R, *et al*. Lipoprotein (a) is independently correlated with coronary artery calcification. *European Journal of Internal Medicine*. 2013; 24: 75–79.
- [17] Sung K-, Wild SH, Byrne CD. Lipoprotein (a), metabolic syndrome and coronary calcium score in a large occupational cohort. *Nutrition, Metabolism and Cardiovascular Diseases*. 2013; 23: 1239–1246.
- [18] Pechlivanis S, Mahabadi AA, Hoffmann P, Nöthen MM, Broecker-Preuss M, Erbel R, *et al*. Association between lipoprotein(a) (Lp(a)) levels and Lp(a) genetic variants with coronary artery calcification. *BMC Medical Genetics*. 2020; 21: 62.
- [19] Clemente A, Traghella I, Mazzone A, Sbrana S, Vassalle C. Vascular and valvular calcification biomarkers. *Advances in Clinical Chemistry*. 2020; 8: 73–103.
- [20] Lee SJ, Lee IK, Jeon JH. Vascular Calcification-New Insights Into Its Mechanism. *International Journal of Molecular Sciences*. 2020; 21: 2685.
- [21] Sakakura K, Taniguchi Y, Yamamoto K, Wada H, Momomura S, Fujita H. When a Burr can not Penetrate the Calcified Lesion, Increasing Burr Size as well as Decreasing Burr Size can be a Solution in Rotational Atherectomy. *International Heart Journal*. 2017; 58: 279–282.
- [22] Chiou WR, Liao FC, Su MI, Cheng HY, Chen YT, Lin WH, *et al*. The Use and Clinical Outcomes of Single-Burr Rotational Atherectomy: The Experience of a Local Hospital in Taiwan. *Acta Cardiologica Sinica*. 2020; 36: 233–239.
- [23] Levi Y, Lavi S, Solomonica A, Israeli Z, Bagur R. Small-Size vs Large-Size Burr for Rotational Atherectomy. *Journal of Invasive Cardiology*. 2019; 31: 183–186.
- [24] Bartuś S, Januszek R, Legutko J, Rzeszutko Ł, Dziewierz A, Dudek D. Long-term effects of rotational atherectomy in patients with heavy calcified coronary artery lesions: a single-centre experience. *Kardiologia Polska*. 2017; 75: 564–572.
- [25] Watt J, Austin D, Mackay D, Nolan J, Oldroyd KG. Radial Versus Femoral Access for Rotational Atherectomy: A UK Observational Study of 8622 Patients. *Circulation: Cardiovascular Interventions*. 2017; 10.

- [26] Kübler P, Zimoch W, Kosowski M, Tomasiewicz B, Telichowski A, Reczuch K. In patients undergoing percutaneous coronary intervention with rotational atherectomy radial access is safer and as efficient as femoral access. *Journal of Interventional Cardiology*. 2018; 31: 471–477.
- [27] Alonso R, Mata P, Muñiz O, Fuentes-Jimenez F, Díaz JL, Zambón D, *et al*. PCSK9 and lipoprotein (a) levels are two predictors of coronary artery calcification in asymptomatic patients with familial hypercholesterolemia. *Atherosclerosis*. 2016; 254: 249–253.
- [28] Miyoshi T, Kotani K, Doi M, Nakamura K, Kohno K, Koyama Y, *et al*. High baseline lipoprotein(a) Level as a risk factor for coronary artery calcification progression: Sub-analysis of a prospective multicenter trial. *Atherosclerosis*. 2018; 275: e17.
- [29] Cho JH, Lee DY, Lee ES, Kim J, Park SE, Park C, *et al*. Increased risk of coronary artery calcification progression in subjects with high baseline Lp(a) levels: the Kangbuk Samsung Health Study. *International Journal of Cardiology*. 2016; 222: 233–237.
- [30] Feng Z, Li H, Bei W, Guo X, Wang K, Yi S, *et al*. Association of lipoprotein(a) with long-term mortality following coronary angiography or percutaneous coronary intervention. *Clinical Cardiology*. 2017; 40: 674–678.
- [31] Silverman MG, Ference BA, Im K, Wiviott SD, Giugliano RP, Grundy SM, *et al*. Association between Lowering LDL-C and Cardiovascular Risk Reduction among Different Therapeutic Interventions. *The Journal of the American Medical Association*. 2016; 316: 1289.