Comparison of Two Different Rota-Flush Solutions in Patients Undergoing Rotational Atherectomy: A Randomized, Controlled, Triple-Blind Trial

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ABSTRACT

Introduction: This prospective study accessed the feasibility and safety of the heparin rota-flush solution in patients undergoing rotational atherectomy (RA).

Methods: Between August 2019 and November 2021, 200 patients who underwent RA were included in this study, among whom 103 (51.5%) were randomly allocated into the heparin rota-flush group and 97 (48.5%) into the traditional rota-flush group. The primary endpoint was the incidence of slow flow/no-reflow after RA; the secondary endpoints were procedural success, RA-related procedural complications, and in-hospital major adverse cardiovascular events (MACE).

Results: There were no significant differences in baseline clinical and angiographic characteristics between the two groups. Thirty patients (29.1%) in the heparin rota-flush group and nineteen patients (19.6%) in the traditional rota-flush groups developed slow flow/no-reflow \((P = 0.117)\), respectively, and procedural success was also comparable (97.1% vs. 93.8%, \(P = 0.320\)). Severe hypotension (systolic blood pressure < 90 mmHg) was not significantly different (15.5% vs. 16.5%, \(P = 0.841\)), but the incidence of coronary spasm was significantly higher in the heparin rota-flush group (42.7% vs. 22.7%, \(P = 0.003\)). MACE including stent-thrombosis (ST), target-lesion revascularization (TLR), and cardiac death were also comparable between the two groups; no stroke was observed.

Conclusions: The findings suggest that although continuous intracoronary infusion of heparin rota-flush solution does not increase the incidence of slow flow/no-reflow, traditional rota-flush solution without Rotaglide prevents coronary spasm more effectively compared to the heparin rota-flush without significant impact on severe hypotension. These results do not support a strategy of routine use of heparin rota-flush solution in patients receiving RA procedures.

Keywords: Coronary artery disease; Rotational atherectomy; Rota-flush solution; Slow flow/no-reflow
We did not find a significant difference in the rate of slow flow/no-reflow between the traditional rota-flush group and heparin rota-flush group (19.6% vs. 29.1%, \( P = 0.117 \)), and the procedural success was also comparable.

The incidence of coronary spasm was significantly higher in the heparin rota-flush group compared to the traditional rota-flush group (42.7% vs. 22.7%, \( P = 0.003 \)).

Although the incidence of systolic blood pressure (SBP) drop \( \geq 20 \) mmHg was significantly higher in the traditional rota-flush group, severe hypotension (SBP < 90 mmHg) was not significantly different \( (P = 0.841) \), indicating that vasodilators in the flush did not severely impact hemodynamic stability.

### INTRODUCTION

Rotational atherectomy (RA) was first utilized to treat obstructive coronary diseases by Jarome Ritchie and colleagues in 1987 [1], and thereafter has been widely applied to modify plaque compliance and allow smooth passage for stents in highly calcific lesions of the left main coronary artery, bifurcations, ostial side branches, and chronic total occlusions [2–6]. Despite the high efficacy for lesions not suitable for direct coronary angioplasty or stenting, severe complications including coronary perforation (0–1.5%), dissection (10–13%), severe spasm (0.6–1.6%), and slow flow/no-reflow (1.2–7.6%) may occur during the RA procedure [7]. Distal coronary spasm can lead to adverse events such as ventricular fibrillation, and complete atrioventricular block [8]. Moreover, RA has been associated with a higher incidence of slow flow/no-flow than other coronary intervention measures, a phenomenon, if not timely handled, that can result in serious ischemic complications such as myocardial infarction, cardiogenic shock, or even death [9]. Many factors influence the incidence of slow flow/no-reflow related to the RA procedure, including lesion length, lesion angulation, reference diameter, total ablation time, short single run (< 15 s), systolic blood pressure (SBP) > 140 mmHg, and initial burr-to-artery ratio [10]. Traditionally, a “cocktail” consisting of normal saline, unfractionated heparin, verapamil, nitroglycerin, and RotaGlide lubricant was utilized to prevent slow flow/no-reflow during RA. However, the use of RotaGlide is contraindicated in patients with known allergies to it and adds to the cost of the RA procedure. A retrospective study by Whiteside et al. reported that similar outcomes were achieved despite not using RotaGlide as a part of the rota-flush solution [11]. Additionally, vasodilators added to the rota-flush solution can lead to hemodynamic disturbances like hypotension, bradycardia, and transient atrioventricular block [12]. There is growing evidence supporting simplifying traditional rota-flush as a heparin saline rota-flush. Siddiqi et al. reported that combining modern procedural techniques with the routine use of heparin-only rota-flush solution, RA procedures were safe with low slow flow/no-reflow rates (2.2%) and high rates of procedural success (94.8%) [13]. The aforementioned study was limited by its retrospective nature and small sample size. We conducted this prospective randomized controlled trial to compare the feasibility and safety of the heparin rota-flush and traditional rota-flush in patients undergoing RA.

### METHODS

#### Study Design and Patient Selection

This single-center, randomized, triple-blind, parallel-group trial was conducted at the Department of Cardiology, the Affiliated Anhui Provincial Hospital of Anhui Medical University from August 2019 to November 2021. Patients older than 18 years, with an indication for RA were selected consecutively in the
catheterization laboratory. The inclusion criteria were as follows: (1) angiographically moderate or severe calcific lesions; (2) diffuse lesions expected to be difficult to stent; (3) ostial or bifurcation lesions; (4) intravascular ultrasound (IVUS) indicating a large arc of superficial calcium involving three or four quadrants; (5) RA as a secondary approach after unsuccessful attempt to dilate a lesion or failure to deliver stents. The exclusion criteria were (1) bradycardia (heart rate ≤ 60 bpm) or peripheral blood pressure ≤ 90/60 mmHg; (2) atrioventricular block; (3) target lesions were culprit vessels of acute myocardial infarction within 4 weeks; (4) the burr cannot cross the target lesion; (5) history of coronary artery bypass grafting (CABG); (6) lesion angulation > 90°; (7) inability to provide informed consent. The study conformed to the principles of the Helsinki Declaration and the institutional review board of the Affiliated Anhui Provincial Hospital of Anhui Medical University approved the study protocol. All patients provided written informed consent before procedures.

Randomization

Randomization was performed using a computer-generated list of random numbers; the allocation sequence was concealed from patients, the RA operators, and angiogram analysts in sequentially numbered, opaque, sealed, stapled envelopes. Patients included in the study were randomly allocated (1:1) into the heparin rota-flush and the traditional rota-flush groups. Patients in the former group received a rota-flush solution containing 10,000 U unfractionated heparin in 1 L saline, while patients in the latter group received a cocktail containing 10,000 U unfractionated heparin, 10 mg verapamil, and 4 mg nitroglycerin in 1 L saline.

Revascularization Protocol

A radical, brachial, or femoral approach was employed on the basis of peripheral vascular condition and procedural requirement. In the catheterization laboratory, all patients in this study were preloaded with dual antiplatelet therapy. RA was performed with the Rotablator system (Boston Scientific Corporation, Natick, MA, USA). The pressured rota-flush solution was continuously infused into the coronary artery through a 4Fr Teflon sheath of the Rotablator system. Initial RA burr size was either 1.25 or 1.5 mm according to the senior operator’s selection; the burr was subsequently advanced to a position proximal to the lesion, the initial rotational speed was set within the conventional range (140,000–180,000 rpm), and the burr was activated and moved forward with a slow pecking motion. Each run time was less than 30 s, and care was taken to avoid a decrease in rotational speed of more than 5000 rpm. Following RA, routine balloon dilatation to facilitate drug-eluting stent (DES) implantation or drug-coated balloon (DCB) employment was performed unless serious complications like coronary perforations happened. If the slow flow/no-reflow phenomenon occurred, an intracoronary infusion of verapamil and/or sodium nitroprusside was immediately administered to improve coronary flow, and an intravenous infusion of vasoactive drugs such as noradrenalin or atropine was administered to maintain hemodynamic stability if necessary. Furthermore, an intra-aortic balloon pump (IABP) was used in high-risk cases with severe left ventricular dysfunction, unprotected left main stenosis, and severe three-vessel diseases. IVUS use was left to the operator’s discretion.

Definitions and Endpoints

The primary endpoint of the study was the incidence of slow flow/no-reflow after RA. The secondary endpoints of the study were procedural success, RA-related procedural complications, and in-hospital major adverse cardiovascular events (MACE). Slow flow was defined as the diminution of coronary flow by 1–2 thrombolysis in myocardial infarction (TIMI) flow grades from the baseline antegrade flow, and no-reflow was defined as the cessation of blood flow into the distal coronary artery in the absence of dissection or thrombus immediately after RA. Procedural success was defined as
the achievement of a residual diameter stenosis less than 30%, TIMI flow grade 3, and in the absence of cardiac death, coronary perforation, stroke, stent-thrombosis (ST), and target-lesion revascularization (TLR). Vessel perforation (defined as any contrast extravasation) from the burr, burr entrapment, transection of the RA guidewire, and coronary dissection were included in RA-related complications. Coronary spasm was characterized by transient total or subtotal occlusion or severe diffuse vasoconstriction of an epicardial artery. According to National, Heart, Lung, and Blood Institute (NHLBI) criteria, dissection was defined as grades C to F [14]. Hypotension was defined as a drop of SBP ≥ 20 mmHg or SBP < 90 mmHg; bradycardia was heart rate < 60 bpm during the RA procedure. MACE was defined as the composite of TLR, ST, stroke, and cardiac death. Death was to be considered cardiac in origin unless a non-cardiac origin was confirmed. Thrombus of the target lesion on either angiography or autopsy examination was defined as ST according to the Academic Research Consortium [15]. TLR was defined as unplanned ischemia-driven percutaneous or surgical revascularization of the treated vessel.

Sample Size

On the basis of a clinical audit in our hospital and a literature review, we estimated that the incidence of slow flow/no-reflow during RA would be 4.0% [16] in the traditional rota-flush group and 15.0% [17, 18] in the heparin rota-flush group. A minimum of 194 patients (97 in each group) would provide 84.5% power to detect a difference between the two groups in the proportion of subjects with slow flow/no-reflow. The test statistic used was the one-sided Z test and the significance level of the test was 0.05.

Statistical Analysis

After randomization, we recorded baseline characteristics of enrolled participants including demographic data, cardiovascular risks, angiography, and interventional procedure characteristics. The TIMI grade of coronary flow was confirmed by injecting sufficient contrast medium immediately after the burr was removed. Detail lesion information was documented by two cardiologists facilitated by a quantitative coronary angiography analysis system using offline, computer-based QAngio XA 7.3 software (MEDIS Imaging Systems, Leiden, the Netherlands). Continuous and categorical variables were expressed as mean ± SD and frequencies, respectively. The Kolmogorov–Smirnov test was performed to determine if the continuous variables were normally distributed. Normally distributed continuous variables were compared using unpaired Student’s t test; otherwise, the Mann–Whitney U test was employed. The categorical variables were compared using chi-square test or Fischer’s exact test. Univariate and multivariate logistic regression analyses were used to evaluate the independent predictors of slow flow/no-reflow and coronary spasm. All variables with a P ≤ 0.1 in the univariate analysis were included to the
### Table 1 Patients and angiographic characteristics

| Variables                  | All (n = 200) | Heparin rota-flush (n = 103) | Traditional rota-flush (n = 97) | P value |
|----------------------------|---------------|------------------------------|---------------------------------|---------|
| Age, years                 | 71.8 ± 8.8    | 71.8 ± 9.1                   | 71.9 ± 8.6                      | 0.931   |
| Male                       | 114 (57.0)    | 61 (59.2)                    | 53 (54.6)                       | 0.513   |
| UA                         | 158 (79.0)    | 78 (75.7)                    | 80 (82.5)                       | 0.242   |
| Hypertension               | 148 (74.0)    | 74 (71.8)                    | 74 (76.3)                       | 0.474   |
| Diabetes mellitus          | 80 (40.0)     | 41 (39.8)                    | 39 (40.2)                       | 0.954   |
| Dyslipidemia               | 187 (93.5)    | 95 (92.2)                    | 92 (94.8)                       | 0.454   |
| Smoking                    | 72 (36.0)     | 42 (40.8)                    | 30 (30.9)                       | 0.147   |
| Chronic heart failure      | 49 (24.5)     | 25 (24.3)                    | 24 (24.7)                       | 0.938   |
| CKD                        | 9 (4.5)       | 2 (1.9)                      | 7 (7.2)                         | 0.093   |
| Dialysis                   | 3 (1.5)       | 1 (0.9)                      | 2 (2.1)                         | 0.612   |
| Pre-MI                     | 35 (17.5)     | 21 (20.4)                    | 14 (14.4)                       | 0.268   |
| Pre-PCI                    | 81 (40.5)     | 48 (46.6)                    | 33 (34.0)                       | 0.070   |
| Stroke                     | 67 (33.5)     | 35 (33.9)                    | 32 (32.9)                       | 0.882   |
| LVEF (%)                   | 58.3 ± 11.7   | 58.0 ± 11.9                  | 58.6 ± 11.7                     | 0.747   |
| Medication                 |               |                              |                                 |         |
| ACEI/ARB                   | 100 (50.0)    | 49 (47.6)                    | 51 (52.6)                       | 0.479   |
| CCB                        | 51 (25.5)     | 30 (29.1)                    | 21 (21.6)                       | 0.225   |
| Nitrates                   | 101 (50.5)    | 54 (52.4)                    | 47 (48.5)                       | 0.574   |
| β-blocker                  | 112 (56.0)    | 58 (56.3)                    | 54 (55.7)                       | 0.927   |
| SBP just before RA (mmHg)  | 138.6 ± 22.4  | 138.4 ± 22.0                 | 138.8 ± 22.9                    | 0.903   |
| DBP just before RA (mmHg)  | 72.3 ± 12.4   | 72.5 ± 11.8                  | 72.1 ± 13.0                     | 0.823   |
| Heart rate just before RA (bpm) | 76.2 ± 13.5 | 76.5 ± 13.1                 | 75.8 ± 13.9                     | 0.690   |
| Target coronary vessel     |               |                              |                                 |         |
| LAD                        | 165 (82.5)    | 84 (81.6)                    | 81 (83.5)                       | 0.712   |
| LCX                        | 13 (6.5)      | 6 (5.8)                      | 7 (7.2)                         |         |
| RCA                        | 22 (11.0)     | 13 (12.6)                    | 9 (9.3)                         |         |
| No. of diseased vessels    |               |                              |                                 |         |
| 1                          | 20 (10.0)     | 9 (8.7)                      | 11 (11.3)                       | 0.072   |
| 2                          | 49 (24.5)     | 19 (18.4)                    | 30 (30.9)                       |         |
| 3                          | 131 (65.5)    | 75 (72.8)                    | 56 (57.7)                       |         |
| CTO lesion                 | 9 (4.5)       | 5 (4.9)                      | 4 (4.1)                         | 1.000   |
| Calcification              |               |                              |                                 | 0.250   |
multivariate analysis model. The Hosmer–Hemeshow goodness-of-fit statistics showed that the model adequately fitted the data. All tests were two-tailed and \( P < 0.05 \) was considered statistically significant. All statistical analyses were performed using SPSS (version 26.0, IBM, Armonk, New York, USA).

**RESULTS**

A total of 220 patients met the inclusion criteria, and cases of acute myocardial infarction (ST-segment elevation myocardial infarction, STEMI \( n = 10 \); non-STEMI, NSTEMI \( n = 8 \)), history of CABG (\( n = 1 \)), and the burr would not cross (\( n = 1 \)) were excluded from the study. Thus, a total of 200 patients were randomly assigned to one of the two groups: 103 to the heparin rota-flush group and 97 to the traditional rota-flush group. A flowchart demonstrating patient recruitment for the study is shown in Fig. 1. There were no significant differences in baseline clinical and angiographic characteristics as shown in Table 1. Vital signs including heart rates and systolic and diastolic blood pressure just before the RA procedure were comparable in the two groups. No significant difference of procedural characteristics was observed in the two groups as shown in Table 2. Procedural success was comparable between the two groups (97.1% vs. 93.8%, \( P = 0.320 \)). A comparison of complications is presented in Table 3. A relatively higher incidence of slow flow/no-reflow was observed in the heparin rota-flush group without reaching statistical difference (29.1% vs. 19.6%, \( P = 0.117 \)). Fewer patients developed hypotension in the heparin rota-flush group compared to the traditional rota-flush group (54.4% vs. 69.1%, \( P = 0.033 \)), and the incidence of bradycardia tended to be less (20.4% vs. 24.7%, \( P = 0.461 \)). However, the incidence of coronary spasm was significantly higher in the heparin rota-flush group (42.7% vs. 22.7%, \( P = 0.003 \)). Other procedure complications were not different between the two groups. None of the 200 patients had transection of the RA guidewire. MACE including

| Variables               | All (\( n = 200 \)) | Heparin rota-flush (\( n = 103 \)) | Traditional rota-flush (\( n = 97 \)) | \( P \) value |
|------------------------|---------------------|-----------------------------------|-------------------------------------|--------------|
| None/mild              | 21 (10.5)           | 10 (9.7)                          | 11 (11.3)                           |              |
| Moderate               | 31 (15.5)           | 12 (11.7)                         | 19 (19.6)                           |              |
| Severe                 | 148 (74.0)          | 81 (78.6)                         | 67 (69.1)                           |              |
| Angulation > 45°       | 101 (50.5)          | 56 (54.4)                         | 45 (46.4)                           | 0.259        |
| Diffuse lesion         | 145 (72.5)          | 75 (72.8)                         | 70 (72.2)                           | 0.918        |
| Initial TIMI flow < 3  | 40 (20.0)           | 25 (24.3)                         | 15 (15.5)                           | 0.120        |
| Lesion length (mm)     | 32.0 ± 10.0         | 32.1 ± 9.8                        | 31.9 ± 10.4                         | 0.933        |
| Reference diameter (mm)| 2.86 ± 0.37         | 2.87 ± 0.36                       | 2.85 ± 0.38                         | 0.867        |
| MLD (mm)               | 0.51 ± 0.32         | 0.52 ± 0.31                       | 0.51 ± 0.34                         | 0.726        |
| Stenosis, %            | 81.8 ± 12.6         | 81.6 ± 13.4                       | 82.1 ± 11.6                         | 0.755        |

Data are shown as number (%) or mean ± standard deviation. \( UA \) unstable angina, \( CKD \) chronic kidney disease, \( MI \) myocardial infarction, \( PCI \) percutaneous coronary intervention, \( ACEI \) angiotensin-converting enzyme inhibitor, \( ARB \) angiotensin receptor blocker, \( CCB \) calcium channel blocker, \( SBP \) systolic blood pressure, \( DBP \) diastolic blood pressure, \( LAD \) left anterior descending artery, \( LCX \) left circumflex artery, \( RCA \) right coronary artery, \( LVEF \) left ventricular ejection fraction, \( MLD \) minimal luminal diameter, \( CTO \) chronic total occlusion.
cardiac death, TLR, and ST were not different between the two groups. None of the 200 patients developed stroke. The univariate and multivariate logistic regression analyses to investigate underlying factors of slow flow/no-reflow are shown in Table 4. Among 11 variables, SBP just before the RA procedure (OR 0.82, 95% CI 0.67–0.99, P = 0.040) and reference diameter (OR 0.12, 95% CI 0.02–0.59, P = 0.010) were inversely associated with slow flow/no-reflow, while lesion length (OR 1.05, 95% CI 1.01–1.09, P = 0.027) and lesion angulation greater than 45° (OR 2.15, 95% CI 1.01–4.62, P = 0.049) were significantly

| Table 2 Procedural characteristics |
|------------------------------------|
| Variables                          | All (n = 200) | Heparin rota-flush (n = 103) | Traditional rota-flush (n = 97) | P value |
| Access                             |              |                             |                                  |        |
| Radial artery                      | 147 (73.5)   | 70 (67.9)                   | 77 (79.4)                       | 0.068  |
| Brachial artery                    | 17 (8.5)     | 13 (12.6)                   | 4 (4.1)                         |        |
| Femoral artery                     | 36 (18.0)    | 20 (19.4)                   | 16 (16.5)                       |        |
| Guiding catheter                   |              |                             |                                  | 0.056  |
| 6Fr                                | 160 (80.0)   | 77 (74.8)                   | 83 (85.6)                       |        |
| 7Fr                                | 40 (20.0)    | 26 (25.2)                   | 14 (14.4)                       |        |
| IABP supported                     | 23 (11.5)    | 16 (15.5)                   | 7 (7.2)                         | 0.065  |
| IVUS guided                        | 26 (13.0)    | 13 (12.6)                   | 13 (13.4)                       | 0.870  |
| Primary RA                          | 128 (64.0)   | 64 (62.1)                   | 64 (65.9)                       | 0.571  |
| Burr number                        |              |                             |                                  | 0.690  |
| 1                                  | 187 (93.5)   | 97 (94.2)                   | 90 (92.8)                       |        |
| 2                                  | 13 (6.5)     | 6 (5.8)                     | 7 (7.2)                         |        |
| Final burr size                    |              |                             |                                  | 0.990  |
| 1.25 mm                            | 43 (21.5)    | 22 (21.4)                   | 21 (21.6)                       |        |
| 1.5 mm                             | 141 (70.5)   | 73 (70.9)                   | 68 (70.1)                       |        |
| 1.75 mm                            | 16 (8.0)     | 8 (7.8)                     | 8 (8.2)                         |        |
| Initial burr-to-artery ratio (%)   | 51.5 ± 7.0   | 51.7 ± 7.3                  | 51.3 ± 6.7                      | 0.670  |
| Total run time(s)                  | 39.0 (26.0, 62.0) | 38.0 (26.0, 62.0) | 40.0 (27.0, 64.0) | 0.478  |
| Mean run time(s)                   | 14.5 ± 4.2   | 14.1 ± 4.0                  | 14.9 ± 4.4                      | 0.217  |
| Mean rotational speed (× 10,000 rpm) | 14.9 ± 1.5  | 15.1 ± 1.5                  | 14.8 ± 1.4                      | 0.138  |
| DES                                | 194 (97.0)   | 101 (98.1)                  | 93 (95.9)                       | 0.434  |

Data are shown as number (%), median (Q1, Q4), or mean ± standard deviation

IABP intra-aortic balloon pump, IVUS intravascular ultrasound, RA rotational atherectomy, DES drug-eluting stent
associated with slow flow/no-reflow. After adjustment for the other 10 variables, the use of heparin rota-flush solution was not an independent factor for slow flow/no-reflow (OR 1.66, 95% CI 0.78–3.52, \( P = 0.186 \)). In addition, as shown in Table 5, utilizing of the heparin rota-flush solution (OR 2.68, 95% CI 1.43–5.05, \( P = 0.002 \)) was significantly associated with coronary spasm after adjusting for lesion length, reference diameter, mean RA speed, mean single run time, and initial burr-to-artery ratio.

### Table 3: Comparison of procedural success, complications, and MACE

| Variables                          | All \( (n = 200) \) | Heparin rota-flush \( (n = 103) \) | Traditional rota-flush \( (n = 97) \) | \( P \) value |
|------------------------------------|----------------------|------------------------------------|-----------------------------------|-------------|
| Procedural success                 | 191 (95.5)           | 100 (97.1)                         | 91 (93.8)                         | 0.320       |
| Complications                      |                      |                                    |                                   |             |
| Slow flow/no-reflow               | 49 (24.5)            | 30 (29.1)                          | 19 (19.6)                         | 0.117       |
| Slow flow                         | 28 (14.0)            | 16 (15.5)                          | 12 (12.4)                         | 0.519       |
| No-flow                            | 21 (10.5)            | 14 (13.6)                          | 7 (7.2)                           | 0.142       |
| Coronary spasm                    | 66 (33.0)            | 44 (42.7)                          | 22 (22.7)                         | 0.003       |
| Hypotension                        | 123 (61.5)           | 56 (54.4)                          | 67 (69.1)                         | 0.033       |
| SBP drop ≥ 20 mmHg                 | 112 (56.0)           | 50 (48.5)                          | 62 (63.9)                         | 0.029       |
| SBP < 90 mmHg                      | 32 (16.0)            | 17 (16.5)                          | 15 (15.5)                         | 0.841       |
| Vasopressor usage                  | 21 (10.5)            | 12 (11.7)                          | 9 (9.3)                           | 0.584       |
| Bradycardia                        | 45 (22.5)            | 21 (20.4)                          | 24 (24.7)                         | 0.461       |
| Atropine usage                     | 6 (3.0)              | 3 (2.9)                            | 3 (3.1)                           | 1.000       |
| Complete AV block                  | 2 (1.0)              | 2 (1.9)                            | 0 (0)                             | 0.498       |
| Sinus arrest                       | 2 (1.0)              | 2 (1.9)                            | 0 (0)                             | 0.498       |
| Dissection                         | 27 (13.5)            | 12 (11.7)                          | 15 (15.5)                         | 0.430       |
| Perforation                        | 6 (3.0)              | 2 (1.9)                            | 4 (4.1)                           | 0.434       |
| Burr entrapment                    | 1 (0.5)              | 0 (0)                              | 1 (1.0)                           | 0.485       |
| Transection of RA guidewire        | 0 (0)                | 0 (0)                              | 0 (0)                             | –           |
| MACE                               |                      |                                    |                                   |             |
| ST                                 | 1 (0.5)              | 0 (0)                              | 1 (1.0)                           | 1.000       |
| TLR                                | 5 (2.5)              | 2 (1.9)                            | 3 (3.1)                           | 0.675       |
| Stroke                             | 0 (0)                | 0 (0)                              | 0 (0)                             | –           |
| Cardiac death                      | 2 (1.0)              | 1 (1.0)                            | 1 (1.0)                           | 1.000       |

Data are shown as number (%)

*MACE* major adverse cardiovascular events, *ST* stent-thrombosis, *TLR* target lesion revascularization
DISCUSSIONS

The principal findings of this analysis are as follows:

1. Continuous intracoronary infusion of heparin rota-flush solution does not increase the incidence of slow flow/no-reflow compared to the traditional rota-flush solution.
2. Traditional rota-flush solution prevents coronary spasm more effectively compared to the heparin rota-flush solution.
3. Although the incidence of SBP drop ≥ 20 mmHg was significantly higher in the traditional rota-flush group, severe hypotension (SBP < 90 mmHg) was not significantly different (P = 0.841), and the usage of vasopressors and atropine was also similar between the two groups, indicating that vasodilators in the flush did not severely impact hemodynamic stability.

Several retrospective studies investigating the efficacy of heparin rota-flush in the RA procedure obtained similar findings to our study. A retrospective study aiming to evaluate the feasibility and safety of heparin rota-flush solution was performed by Lee et al. [19] and included 67 consecutive patients who underwent RA. As a result, procedural success was achieved in all patients, slow flow/no-reflow occurred in 7%, with subsequent resolution after intracoronary vasodilator therapy, indicating that the use of a heparin rota-flush solution was a feasible and reasonable alternative to a rota-flush solution that contains Rotaglide and vasodilators. More recently, in a retrospective study of 48 patients who underwent RA, procedural success was achieved in all patients with similar slow flow/no-reflow rates (12% vs. 4.3%, P = 0.330) [17]. The aforementioned two studies were both non-randomized and the sample size was relatively small. To the best of our knowledge, the present study was the first prospective randomized trial to compare the feasibility and safety of heparin rota-flush and traditional rota-flush solution in preventing slow flow/no-reflow followed by RA.

The statistically non-significant but numerically higher rates of slow flow/no-reflow in the heparin rota-flush group were likely due to four factors, absence of vasodilators, lower SBP before RA, more diffuse lesions, and lesion angulation greater than 45°. But after the multivariate logistic regression analysis, we found that the use of the heparin rota-flush solution was not independently associated with slow flow/no-reflow (OR 1.66, 95% CI 0.78–3.52, P = 0.186), suggesting that the addition of vasodilators did not have a statistically meaningful impact on slow flow/no-reflow. Note that the reported incidence of slow flow/no-reflow in the traditional rota-flush group was similar to that reported by Sakakura et al. (19.6% vs. 12%), but the incidence was significantly higher in the heparin rota-flush group (29.1% vs. 4.3%). The baseline clinical and procedural characteristics were comparable between the two groups in our study. The multivariate logistic regression analysis revealed additional elements involving the slow flow/no-reflow phenomenon; as was shown in Table 4, lesion length and lesion angulation greater than 45° were significantly associated with slow flow/no-reflow, whereas SBP just before the RA procedure and reference diameter were inversely associated with slow flow/no-reflow, which was consistent with the findings of Sakakura et al. [10].

Lesion length was a known risk factor for slow flow during RA [20], probably because the massive distal embolization of atheromatous debris would be greater in the cases of diffuse long lesions than that with short lesions. Vasodilator drugs like nitroglycerin and verapamil had theoretical benefit of reducing microvascular obstruction as evidenced by relatively lower rates of slow flow/no-reflow in the traditional rota-flush group (19.6% vs. 29.1%, P = 0.117). Angulation greater than 45° was also closely associated with slow flow/no-reflow, one possible explanation being that RA operators would have difficulty in advancing the burr beyond the angle [21], resulting in longer ablation time and subsequent slow flow. Systolic blood pressure was inversely associated with slow flow/no-reflow, since low systolic blood pressure might reflect poor cardiac function; it was important to keep systolic blood pressure ≥ 120 mmHg (at least 100 mmHg) as advised by clinical expert consensus [10].
Besides, since the most frequent burr size was 1.5 mm in the present study, small vessel size less than 2.5 mm would naturally have a high (0.6) burr-to-artery ratio, a known risk factor for slow flow [22], which accounted for the finding that reference vessel diameter was inversely associated with slow flow. All patients who experienced slow flow/no-reflow were reverted by intracoronary administration of nitroglycerin, verapamil, tirofiban, or nitroprusside, and angiography demonstrated TIMI 3 flow grade prior to departure from the catheterization laboratory.

Although the use of the heparin rota-flush solution did not result in statistically significant higher incidence of slow flow, coronary spasm was more frequently observed (42.7% vs. 22.7%, \( P = 0.003 \)). We performed the logistic regression analysis to identify the risk factors for coronary spasm in the heparin rota-flush group, and the results revealed that the use of heparin saline was significantly associated with coronary spasm (OR 2.68, 95% CI 1.43–5.05, \( P = 0.002 \)). Spasm of coronary arteries may occur spontaneously or following interventional provocation, e.g., RA was known to provoke coronary spasm occasionally, and intracoronary administration of nitroglycerin and calcium channel antagonists were feasible rationales for preventing or resolving coronary spasm [23, 24]. The spasmed coronaries were all resolved completely after intracoronary injection of nitroglycerin or verapamil in our study. Bradycardia and atrioventricular block were more prevalent in the intervention of the right coronary artery (RCA) and left circumflex (LCX) coronary artery. In our study, two patients in the setting of RCA intervention developed transient complete atrioventricular block and reverted to sinus rhythm after stopping the RA procedure. Sinus arrest was documented in two cases each in the setting of RCA and LCX intervention. Out of the 67 patients from the traditional rota-flush group who developed hypotension, 15 patients had associated episodes of bradycardia in the setting of RCA or LCX intervention. The other 52 developed hypotension in the setting of left anterior descending (LAD) intervention, which was likely attributed to vasodilators in rota-flush solution. Although the incidence of SBP drop \( \geq 20 \text{mmHg} \) was significantly higher in the traditional rota-flush group, severe hypotension (SBP < 90 mmHg) was not

| Table 4 Univariate and multivariate logistic regression analyses for slow flow/no-reflow |
|---------------------------------|----|----------------|----|----------------|
|                                | OR (95% CI) | \( P \) value | OR (95% CI) | \( P \) value |
| Angulation > 45°               | 2.24 (1.15–4.37) | 0.018 | 2.15 (1.01–4.62) | 0.049 |
| Lesion length                  | 1.06 (1.02–1.93) | 0.002 | 1.05 (1.01–1.09) | 0.027 |
| SBP just before RA             | 0.79 (0.68–0.92) | 0.003 | 0.82 (0.67–0.99) | 0.040 |
| Reference diameter             | 0.42 (0.16–1.07) | 0.068 | 0.12 (0.02–0.59) | 0.010 |
| Heparin rota-flush             | 1.69 (0.87–3.26) | 0.089 | 1.66 (0.78–3.52) | 0.186 |
| Initial TIMI flow < 3          | 2.57 (1.23–5.38) | 0.013 | 0.70 (0.29–1.65) | 0.418 |
| LVEF                           | 0.97 (0.95–0.99) | 0.044 | 0.98 (0.95–1.01) | 0.143 |
| Mean RA speed                  | 1.19 (0.98–1.47) | 0.100 | 1.01 (0.98–1.03) | 0.673 |
| Mean single run time           | 0.96 (0.92–1.00) | 0.056 | 0.94 (0.86–1.03) | 0.177 |
| Initial burr-to-artery ratio   | 0.89 (0.68–1.05) | 0.098 | 0.48 (0.22–1.04) | 0.064 |

RA rotational atherectomy, OR odds ratio
significantly different, and the usage of vaso-
pressors was similar between the two groups,
indicating that vasodilators in the flush did not
severely impact hemodynamic stability. RA
procedure failed in nine cases. Among three
failed cases in the heparin rota-flush group, two
cases developed coronary perforation in the
setting of severely calcified LAD intervention
and another case received emergent CABG after
severely LCX dissection. Six cases failed in the
traditional rota-flush group, four of them
developed coronary perforation in the LAD
intervention, one case experienced burr
entrapment in the fibrocalcific lesion of the
middle LAD, another failed case experienced
persistent angina following successful RA and
stent implantation, emergent coronary angi-
ogram (CAG) revealed 80% stenosis due to acute
stent thrombosis and the patient underwent
successful PCI. Two cases in the heparin rota-
flush group developed coronary perforation due
to high pressure balloon dilatation. Among four
cases in the traditional rota-flush group who
developed coronary perforation, two cases
resulted from high-speed RA of severely calcifi-
ced and eccentric lesion in the LAD, and
another two cases resulted from poor manage-
ment of the guidewire. There was no transec-
tion of RA guidewire in the present study. Burr
entrapment occurred in one case in the tradi-
tional rota-flush group and was removed suc-
cessfully. In total, there were two deaths in our
study population; both of the patients
developed coronary perforation and received
bailout CABG and died before discharge.

**Limitations**

This study was conducted at a single center with
relatively small sample size, and the duration of
follow-up was too short. The outcomes of our
study need validation in a larger population of
patients from multicenter and longer-term fol-
low-up. Besides, periprocedural myocardial
infarction (PMI) have been underdiagnosed, as
cardiac biomarkers were not routinely tested in
all patients. PMI, defined as an elevation of
creatine kinase (CK) levels at least two times the
upper limit of normal (ULN) with an elevation
of CK-myocardial band (MB) levels above the
ULN, was evaluated only in 154 patients in the
present study. Ten of 74 patients (13.5%) in the
heparin rota-flush group and 13 of 71 patients
(18.3%) in the traditional rota-flush group
developed PMI (\(P = 0.429\)), and the CK-MB level
after the procedure was relatively lower in the
former group without reaching statistical sig-
nificance (28.4 ± 21.5 IU/L vs. 31.7 ± 26.4 IU/
L, \(P = 0.407\)). Although a few studies suggested
the determinants of PMI in RA were complex
lesion features, such as diffuse lesion, severe
calcification, and larger lesion angle, whether
the rota-flush solutions correlate with the PMI is
still unknown and needs validation by more
studies in the future.

**Table 5** Univariate and multivariate logistic regression analyses for coronary spasm

|                          | Univariate analysis | Multivariate analysis |
|--------------------------|---------------------|-----------------------|
|                          | OR (95% CI)         | \(P\) value           | OR (95% CI)         | \(P\) value |
| Heparin rota-flush       | 2.54 (1.37–4.70)    | 0.003                 | 2.68 (1.43–5.05)    | 0.002      |
| Lesion length            | 1.03 (0.99–1.06)    | 0.068                 | 1.03 (0.99–1.06)    | 0.076      |
| Reference diameter       | 0.83 (0.37–1.06)    | 0.086                 | 1.12 (0.3–4.19)     | 0.864      |
| Mean RA speed            | 0.98 (0.81–1.01)    | 0.093                 | 0.99 (0.97–1.01)    | 0.492      |
| Mean single run time     | 1.07 (0.99–1.09)    | 0.054                 | 1.03 (0.95–1.11)    | 0.479      |
| Initial burr-to-artery ratio | 1.54 (0.95–1.74) | 0.083                 | 1.02 (0.60–2.36)    | 0.610      |

*RA* rotational atherectomy, *OR* Odds ratio
CONCLUSIONS

The findings suggest that although continuous intracoronary infusion of heparin rota-flush solution does not increase the incidence of slow flow/no-reflow, traditional rota-flush solution without RotaGlide prevents coronary spasm more effectively compared to heparin rota-flush without significant impact on severe hypotension. These results do not support a strategy of routine use of heparin rota-flush solution in patients receiving RA procedures.

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Authorship. Li-Kun Ma was responsible for the idea behind the paper, he was the main contributor to the design of the work. The acquisition and interpretation of data were fulfilled by Zhiqing Guo, he was also responsible for drafting and revising the manuscript. Hao Hu and Jin-sheng Hua contributed with the acquisition as well as interpretation of the work. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosures. Zhi-Qing Guo, Hao-Hu, Jin-sheng Hua, and Li-kun Ma all have nothing to disclose.

Compliance with Ethics Guidelines. The study conformed to the principles of the Helsinki Declaration and the institutional review board of the Affiliated Anhui Provincial Hospital of Anhui Medical University approved the study protocol. All patients provided written informed consent before procedures.

Data Availability. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest. The article is original, has not been published in its current form or a substantially similar form, it has not been accepted for publication elsewhere, and it is not under consideration by another publication. All authors have read and approved the paper, they have met the criteria for authorship and without any potential competing interests.

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