Effect of transradial catheterization and nifedipine on flow- and nitroglycerin-mediated dilations of distal and proximal radial artery

Xile Bi*, Qianghua Guo*, Hongdan Jia, Tingting Song, Jianshuang Feng, Min Li and Qingsheng Wang

Objective **Radial artery (RA) dysfunction after transradial access intervention is not limited to the distal portion but can also occur in the proximal portion of RA. The aim of the present study was to assess the effect of sublingual nifedipine administrated prior to puncture on the endothelial function of distal and proximal RA.**

Methods **Eighty-nine patients who underwent coronary angiography (CAG) were randomly assigned to the nifedipine group ($n = 45$) or control group ($n = 44$). The flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NMD) of distal and proximal RA were measured at baseline, 24 h, and 48 h after transradial angiography.**

Results **Compared with the control group, the nifedipine group only limited the reduction of FMD in the distal RA at 24 and 48 h [6.52 ± 1.40% (24 h) vs. 5.85 ± 1.38% (24 h), $P = 0.03$; 7.41 ± 1.30% (48 h) vs. 6.65 ± 1.25% (48 h), $P = 0.006$], whereas FMD alterations in the proximal RA were not restored by nifedipine. Both groups were still lower than baseline values (11.66 ± 2.35% and 11.24 ± 2.22%). We observed similar effects of nifedipine on the NMD of the distal RA.**

Conclusion **Although transradial angiography-induced dysfunction was reported in both distal and proximal RA, nifedipine could help restore the distal endothelial function of the cannulated RA.** *Coron Artery Dis* **33: 648–654**

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Keywords: flow-mediated dilation, nitroglycerin-mediated dilation, transradial

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Introduction

Transradial access cannulation, a widely used procedure in coronary intervention, has drawn considerable attention from interventionists due to causing radial artery (RA) dysfunction through damage or occlusion [1]. The most traditional hypothesis is that damage to the RA endothelial function only proceeds from the puncture site of RA. However, several studies have reported that due to the stimuli of the catheter advancing along the RA or being removed, the intima and medial dysfunction were not only limited to the distal portion but also observed in the proximal portion of the RA [2–7]. Although using sheath-injected nitroglycerin and diltiazem could protect endothelial function to a certain extent [8,9], the RA endothelial function is already damaged during puncturing. At present, clinical data that supports the administration of vasodilators before RA puncturing is scarce. Therefore, we evaluated whether an application of vasodilators prior to the puncture can improve RA dysfunction. Since it can be easily administered and has rapid onset of action, we chose sublingual nifedipine as drug prior to puncture and examined its effects on the endothelial function of distal and proximal RA.

Methods

Study population

From March to September 2017, patients that met the following inclusion criterion were eligible for enrollment: patients who were subjected to transradial cannulation with a 6F radial sheath for the first time and only underwent coronary angiography (CAG). The exclusion criteria were as follows: previous history of transradial artery cannulation, a negative Allen test, active inflammation, transradial cannulation with a sheath more than 6F, cross-over with other approaches (femoral, brachial, or ulnar arteries), left ventricular ejection fraction under 50%, allergy to contrast agent or nifedipine, previous use of calcium channel blocker within a month, RA occlusion after a transradial angiography, plan for percutaneous coronary intervention (PCI), or refusal to participate in the study. The study protocol was approved by the ethics committee of the first hospital of Qinhuangdao. Informed

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consent was obtained on admission. The study was conducted in accordance with the Declaration of Helsinki.

Enrolled patients were randomly assigned to nifedipine or control group. Ultrasound examination was performed before and after the procedure, but ultrasound was not used for sheath placement during procedure. Patients in the nifedipine group received 10 mg of sublingual nifedipine (Shijiazhuang Pharmaceutical Co Ltd, Shijiazhuang, China) 5 min before RA puncture. The optimal administration time was based on our previous study that reported the greatest effect on RA diameter 5 min after sublingual nifedipine [10]. A 16-cm-long 6F (external diameter 2.52 mm) hydrophilic sheath (Terumo Co., Tokyo, Japan) was used for transradial angiography. The overlying skin of RA was infiltrated with 2% lidocaine. RA was punctured with a 20G needle using the Seldinger technique. A small incision was made with a No. 11 surgical blade. The stylet was removed and a 0.025-inch guidewire and a 16-cm long 6Fr sheath were inserted. After sheath placement, a bolus of unfractionated heparin (3000 U) and nitroglycerin (200 ug) was administered through the sheath. Once the CAG ended, the sheath was immediately removed and a Transradial Band was deployed for hemostasis. The bladder was initially inflated with 12 ml of air and then deflated at a rate of 2 ml/h. The compression device was applied for 6 h. When applying band compression, we used a pulse oximeter sensor that was placed over the thumb to monitor the peripheral oxygen saturation curve to avoid excessive compression pressure.

The RA spasm was defined as severe local pain and discomfort during catheter movement compelling the operator to stop the procedure and confirmed by RA angiography. Local forearm hematomas were graded using the EASY classification as follows: type I, ≤5-cm diameter; type II, ≤10-cm diameter; type III, >10 cm but not above the elbow; type IV, extending above the elbow; and type V, anywhere with ischemic threat of the hand.

Ultrasound assessment of radial artery function

All measurements were performed in an air-conditioned room with constant temperature. Before the examination, patients were requested to rest for at least 15 min and to not ingest caffeine or tobacco during the previous 24 h. The images were acquired using an ultrasound system with a 5.0–12.0 MHz linear transducer (Philips iE-elite, Amsterdam, Netherlands). A schematic representation of measuring RA by ultrasound is shown in Fig. 1. The diameter of the distal RA was measured at a landmark 2–3 cm above the styloid process using ultrasound to evaluate the radial sheath insertion point. Similarly, the diameter of the proximal RA was measured at 2 cm below the cubital fossa to evaluate the outlet of radial sheath where there was no sheath protection. Measurements were taken across the three timepoints (preoperative baseline, 24 h, and 48 h after the procedure). At each timepoint, we assessed the distal and proximal of right RA (cannulated) functions as well as left RA (noncannulated) functions using flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NMD).

Measurement of flow-mediated dilation

FMD is a reliable measurement of the endothelium-dependent capability of RA dilation. In this study, the FMD (%) was defined as the percentage change in RA diameter from baseline to maximal dilation. As previously described [11], the steps to evaluate FMD were the following. First, we measured the distal and proximal RA diameter recorded in the initial rest period, along with the baseline heart rate and blood pressure. Second, the blood pressure cuff was inflated to suprasystolic pressures at the arm for 5 min. Third, the RA resumed hyperemia after cuff release and distal and proximal RA diameters were remeasured 60–90 s after cuff deflation. These parameters were recorded in the same way for the left arm.

Measurement of nitroglycerin-mediated dilation

NMD refers to the direct dilation of the RA by nitroglycerin, which is endothelium-independent. The NMD (%) was defined as the percentage change in RA diameter from baseline to maximal dilation after nitroglycerin was administered. In this case, the steps to measure NMD were as follows. First, 10 min after registering FMD measurements, patients received sublingual nitroglycerin (0.5 mg). Second, the distal and proximal of RA diameter measurements were recorded again for the right and left arms at 3 min.

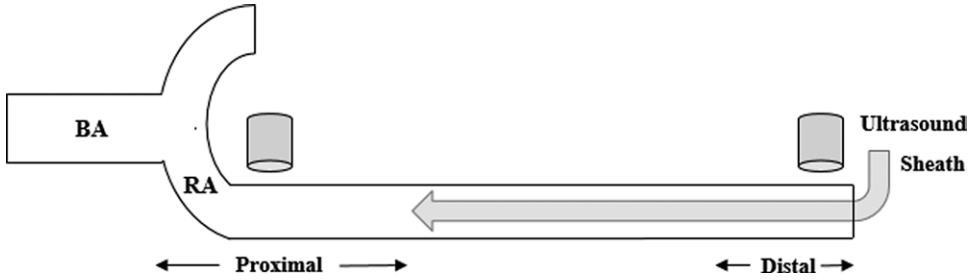
Statistical analysis

All calculations were performed using the SPSS statistical software (version 17.0, SPSS Inc., Chicago, Illinois, USA). The continuous variables were expressed as means ± SD or as median with interquartile range for normally and nonnormally distributed variables, respectively. In addition, the categorical variables were presented as percentages. Continuous variables were analyzed using Student's *t*-test for normally distributed values and the Mann–Whitney U test for those that were nonnormally distributed. Data from the three aforementioned timepoints (baseline, 24 h, and 48 h) were compared in both groups using repeated measurement analysis of variance. A P value <0.05 was considered statistically significant.

Results

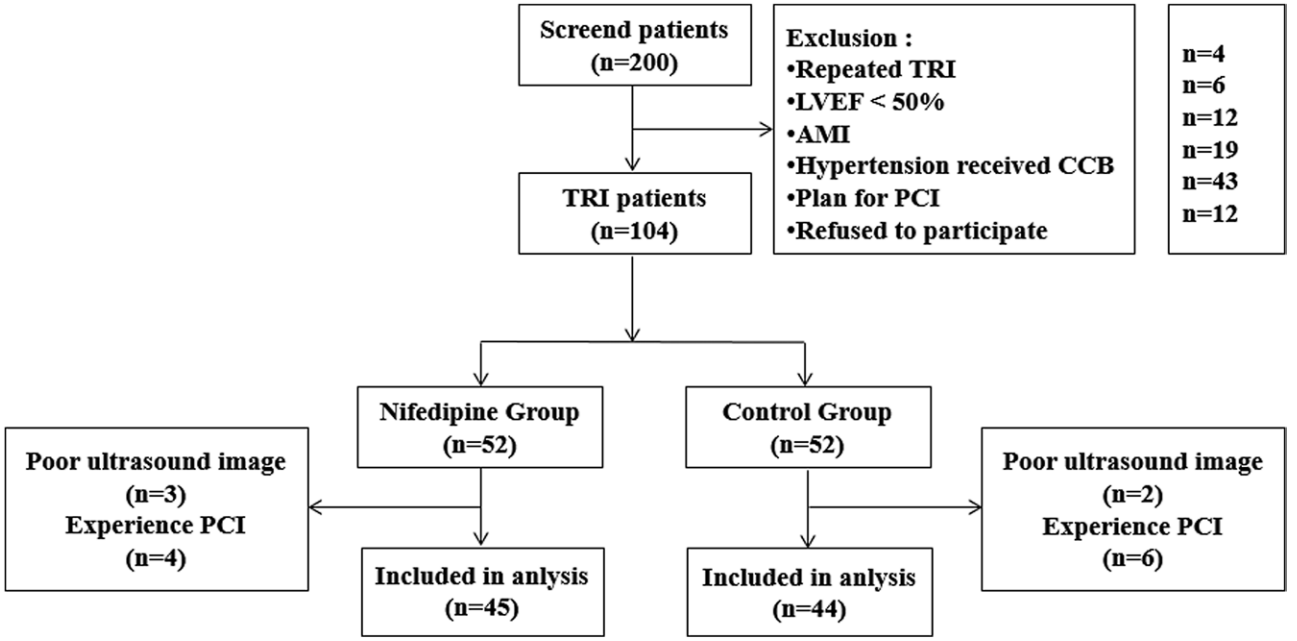
Of a total of 200 patients that were originally assessed, 96 patients were excluded based on the exclusion criteria. The excluded individuals comprised four patients who underwent repeated transradial angiography, six patients with heart failure NYHA III-IV, 12 patients who underwent emergency PCI for acute myocardial infarction, 19 hypertension patients who received CCB, 43 patients with plans for PCI, and 12 patients who refused to

Fig. 1



Schematic representation of measured radial artery by ultrasound.

Fig. 2



Trial profile.

participate. During the procedure and ultrasound measurements, 10 patients who experienced PCI and five who had poor ultrasound images were excluded as well. The resulting patients were randomized into the nifedipine group (n = 45) and the control group (n = 44) (Fig. 2).

Baseline characteristics

The baseline clinical and procedural characteristics are shown in Tables 1 and 2. No significant differences were found in risk factors of coronary artery disease, initial medication, or procedural data between the two groups. Additionally, no RA occlusion complications were observed in either of the patient groups. To evaluate the vascular dysfunction in the distal portion with sheath insertion and the proximal portion without sheath protection area, we divided the RA into two segments (distal and proximal), where we measured the diameter, FMD, and NMD.

Effect of transradial catheterization and nifedipine on distal and proximal radial artery diameters

In the distal RA of the cannulated arm, we observed a significant reduction in diameter at 24 h compared with the baseline in both groups (nifedipine group: 2.94 ± 0.42 vs. 2.76 ± 0.34, P = 0.02; control group: 2.91 ± 0.34 vs. 2.74 ± 0.34, P = 0.04). At 48 h, there was no difference in diameter in either group compared with baseline. In the proximal RA of the cannulated arm, there was also a significant decrease in diameter at 24 h compared with the baseline in both groups (nifedipine group: 3.46 ± 0.56 vs. 3.22 ± 0.51, P = 0.02; control group: 3.51 ± 0.52 vs. 3.25 ± 0.48, P = 0.03). At 48 h, there was no difference

Table 1 Baseline clinical characteristics of study patients

Variables	Nifedipine group ($n = 45$)	Control group ($n = 44$)	*P* value
Age (years)	61.3 ± 8.1	59.7 ± 9.4	0.39
Men, *n* (%)	32 (71.1)	34 (77.3)	0.67
BMI (kg/m^2)	25.2 ± 2.8	24.3 ± 3.1	0.15
Diabetes, *n* (%)	8 (17.8)	6 (13.6)	0.81
Hypertension, *n* (%)	19 (42.2)	23 (52.3)	0.46
Dyslipidaemia, *n* (%)	12 (26.7)	10 (22.7)	0.85
Smoking, *n* (%)	11 (24.4)	14 (31.8)	0.59
CAD, *n* (%)	37 (82.2)	39 (88.6)	0.58
Laboratory results			
Total cholesterol (mmol/l)	4.4 ± 1.1	4.6 ± 1.2	0.41
LDL cholesterol (mmol/l)	2.5 ± 0.6	2.7 ± 0.8	0.18
Glucose (mmol/l)	5.3 ± 1.1	5.6 ± 1.4	0.26
Hemoglobin (g/l)	136.9 ± 12.7	132.5 ± 14.8	0.14
Creatinine (μmol/l)	65.3 ± 16.1	68.8 ± 17.6	0.33
Medication, *n* (%)			
Aspirin	45(100.0)	44(100.0)	NS
Clopidogrel	43 (95.6)	41 (93.2)	0.98
Ticagrelor	2 (4.4)	3 (6.8)	0.98
Statins	39 (86.7)	41 (93.2)	0.50
Beta-blockers	34 (75.6)	31 (70.5)	0.76
Nitrate	5 (11.1)	7 (15.9)	0.72
ACEI/ARB	18 (40.0)	21 (47.7)	0.60

Data are presented as mean ± SD.
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CAD, coronary artery disease.

Table 2 Angiographic and procedural data

Variables	Nifedipine group ($n = 45$)	Control group ($n = 44$)	*P* value
Single puncture	40 (88.9)	37 (84.1)	0.72
Vessels with disease (≥50%)			
None	8 (17.8)	5 (11.4)	0.58
1	32 (71.1)	34 (77.3)	0.67
2	5 (11.1)	3 (6.8)	0.74
3	0 (0)	2 (4.6)	0.46
Diagnostic catheters used			
1	41 (91.1)	40 (90.9)	0.74
2	4 (8.9)	3 (6.8)	0.98
3	0 (0)	1 (2.3)	0.99
Radial artery spasm, *n* (%)	1 (2.2)	4 (9.1)	0.34
Forearm hematoma			
Type I	1 (2.2)	1(2.3)	0.48
Procedure time (min)	7.91 ± 1.64	8.49 ± 2.32	0.18
Compression time (h)	6.2 ± 1.6	6.5 ± 1.1	0.31
Volume of contrast medium (ml)	50 (40-50)	50 (40-57.5)	0.30

Data are presented as mean ± SD.

in diameter in either group compared with baseline. Conversely, in the noncannulated arm, no differences were observed in the diameter of distal and proximal RA at baseline, 24 h, and 48 h in either group (Table 3).

Effect of transradial catheterization and nifedipine on FMD and NMD of distal and proximal radial artery

Next, we measured the FMD, which represents the endothelium-dependent smooth muscle response of the RA. In the distal RA of the cannulated arm, the baseline FMD was 11.66 ± 2.35% and 11.24 ± 2.22% in the nifedipine and control groups, respectively. Compared with the baseline, FMD significantly decreased at 24 h in both groups [nifedipine group: 6.52 ± 1.40% (24 h) vs. baseline, $P < 0.001$; control group: 5.85 ± 1.38% (24 h) vs. baseline, $P < 0.001$]. At 48 h, the FMD of distal RA recovered

Table 3 Diameter of radial artery

Variables	Baseline	24 h	48 h
Distal RA (mm)			
Cannulated arm			
Nifedipine group	2.76 ± 0.34	2.94 ± 0.42*	2.89 ± 0.32
Control group	2.74 ± 0.34	2.91 ± 0.34*	2.87 ± 0.41
Noncannulated arm			
Nifedipine group	2.75 ± 0.42	2.77 ± 0.38	2.76 ± 0.32
Control group	2.77 ± 0.33	2.75 ± 0.32	2.78 ± 0.41
Proximal RA (mm)			
Cannulated arm			
Nifedipine group	3.22 ± 0.51	3.46 ± 0.56*	3.39 ± 0.42
Control group	3.25 ± 0.48	3.51 ± 0.52*	3.37 ± 0.59
Noncannulated arm			
Nifedipine group	3.20 ± 0.50	3.19 ± 0.45	3.24 ± 0.43
Control group	3.27 ± 0.38	3.20 ± 0.42	3.25 ± 0.48

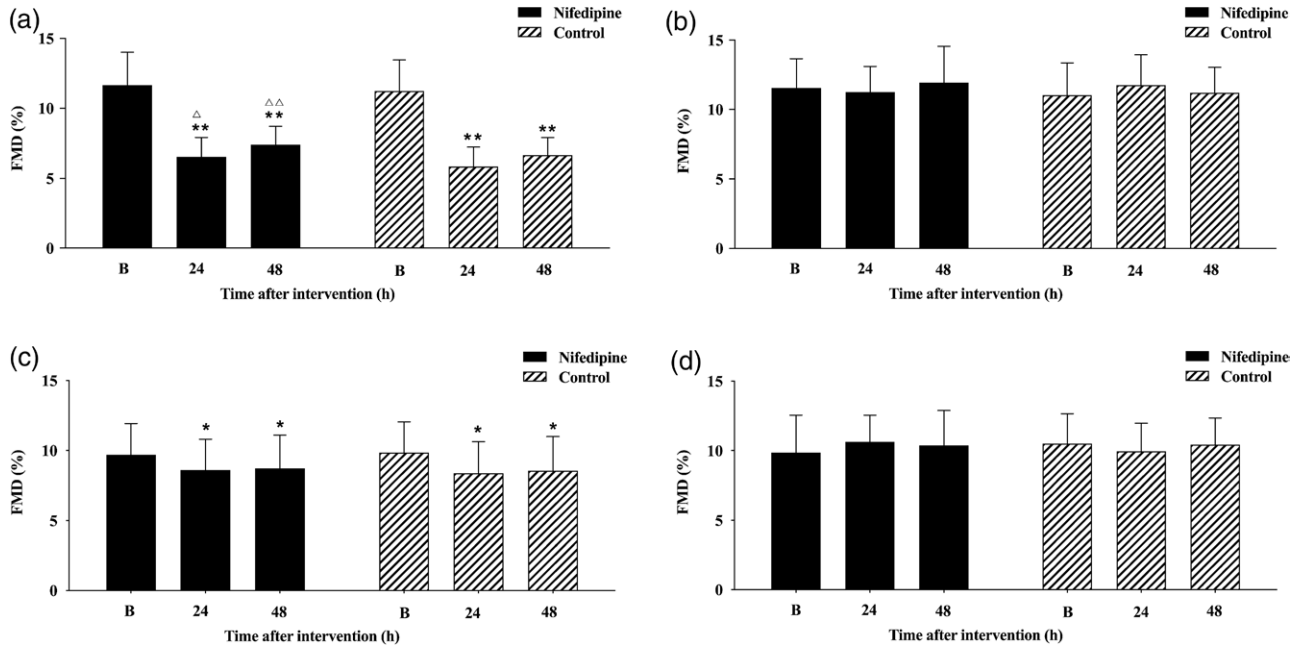
Data are presented as mean ± SD.
RA, radial artery.
*$P < 0.05$ versus baseline.

significantly but was still lower than baseline values in both groups [nifedipine group: 7.41 ± 1.30% (48 h) vs. baseline, $P < 0.001$; 48 h vs. 24 h, $P = 0.02$; control group: 6.65 ± 1.25% (48 h) vs. baseline, $P < 0.001$; 48 h vs. 24 h, $P = 0.03$]. The decrease in FMD of the distal RA at 24 and 48 h suggests that sheath insertion leads to RA dysfunction vs. baseline. Comparison of FMD between the nifedipine and control groups at equivalent timepoints revealed that the distal RA FMD was significantly higher in the nifedipine group than that in the control group at 24 and 48 h [6.52 ± 1.40% (24 h) vs. 5.85 ± 1.38% (24 h), $P = 0.03$; 7.41 ± 1.30% (48 h) vs. 6.65 ± 1.25% (48 h), $P = 0.006$] (Fig. 3a). FMD did not change in the distal RA of noncannulated arm across the three timepoints in either group (Fig. 3b).

In the proximal RA of the cannulated arm, the baseline FMD was 9.71 ± 2.22% in the nifedipine group and 9.85 ± 2.21% in the control group. Compared with the baseline, FMD significantly decreased at 24 h in both groups [nifedipine group: 8.60 ± 2.20% (24 h) vs. 9.71 ± 2.22% (baseline), $P = 0.02$; control group: 8.37 ± 2.26% (24 h) vs. 9.85 ± 2.21% (baseline), $P = 0.003$]. At 48 h, the FMD of proximal RA did not recover compared with that at 24 h and was still impaired compared with baseline values in both groups [nifedipine group: 8.73 ± 2.37% (48 h) vs. baseline, $P = 0.04$; 48 vs. 24 h, $P = 0.790$; control group: 8.55 ± 2.44% (48 h) vs. baseline, $P = 0.009$; 48 vs. 24 h, $P = 0.72$] (Fig. 3c). This decrease in proximal RA FMD was not prevented by nifedipine administration, because the values in this group remained unchanged compared with those in the control group at 24 and 48 h. In the case of the noncannulated arm, the FMD of the proximal RA did not change across the three timepoints in either group (Fig. 3d).

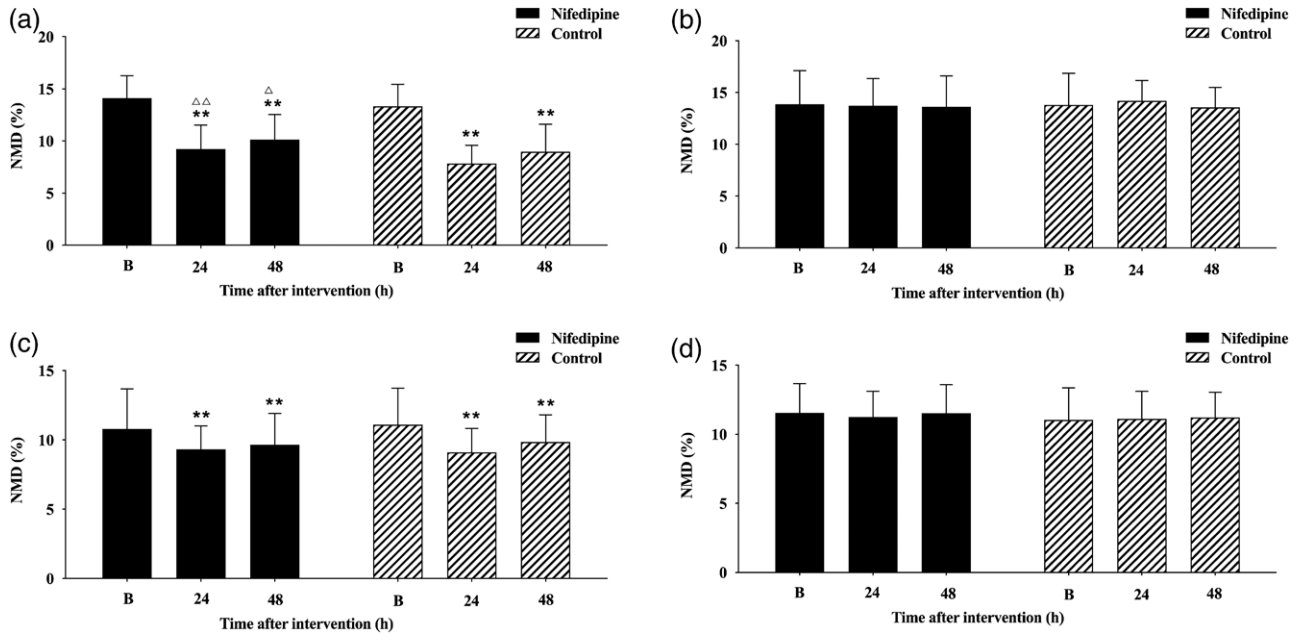
To determine the degree of endothelium-independent dysfunction of the distal and the proximal RA after catheterization, we measured the NMD response to sublingual nitroglycerin (0.5 mg). In the cannulated arm, NMD of both distal and proximal RA were significantly

Fig. 3



Comparisons of FMD across baseline, 24 and 48 h after transradial catheterization. *$P < 0.05$ vs. baseline; **$P < 0.01$ vs. baseline; $\Delta P < 0.05$ nifedipine vs. control; $\Delta\Delta P < 0.01$ nifedipine vs. control. (a) The FMD of distal RA in the cannulated arm. (b) The FMD of distal RA in the non-cannulated arm. (c) The FMD of proximal RA in the cannulated arm. (d) The FMD of proximal RA in the noncannulated arm. FMD, flow-mediated dilation; RA, radial artery.

Fig. 4.



Comparisons of NMD across baseline, 24 and 48 h after transradial catheterization. *$P < 0.05$ vs. baseline; **$P < 0.001$ vs. baseline; $\triangle P < 0.05$ nifedipine vs. control; $\triangle\triangle P < 0.01$ nifedipine vs. control. (a) The NMD of distal RA in the cannulated arm. (b) The NMD of distal RA in the noncannulated arm. (c) The NMD of proximal RA in the cannulated arm. (d) The NMD of proximal RA in the noncannulated arm. NMD, nitroglycerin-mediated dilation; RA, radial artery.

decreased at 24 and 48 h compared with the baseline in both groups ($P < 0.001$). The NMD of distal RA was significantly higher in the nifedipine group compared with that in the control group at both 24 h ($P = 0.002$) and 48 h ($P = 0.03$), whereas the NMD of the proximal RA did not differ between the nifedipine and the control group (Fig. 4a–d).

Discussion

We found that transradial angiography caused endothelial dysfunction in both distal and proximal RA and that sublingual nifedipine before RA puncture may improve FMD and NMD of the distal RA at 24 and 48 h. These findings may be due to increased compatibility of vessels with the sheath resulting in dysfunction reduction at the puncture site of RA.

Assessment of the endothelial function of distal and proximal radial artery

In this study, we measured the vasodilator function of distal and proximal RA after transradial angiography. Our results revealed that the FMD and NMD of distal RA in the nifedipine group recovered faster than those of the control group at 24 and 48 h. One possible explanation is that nifedipine can reduce the dysfunction of the distal RA endothelium during the process of puncture and sheath insertion by dilating the vessel, while another factor is that the endothelium of the distal RA is not stimulated by the angiographic catheter due to the protection of the sheath during the procedure. However, nifedipine administration was not found to improve proximal RA FMD and NMD, which may be related to the absence of sheath protection at proximal RA, as well as to the catheter-inducing endothelial dysfunction during the catheter movements, rotations, and exchange. This is consistent with the study by Heiss *et al.* [2], who showed that an increased number of catheter exchanges could lead to decreased FMD and endothelial function of the brachial artery, suggesting that the area without RA sheath protection is more likely to suffer vascular endothelial dysfunction.

Relationship between radial artery diameter and endothelial function

RA diameter is closely related to RA spasm and occlusion. Fukuda *et al.* [12] classified RA spasm into mild, moderate, and severe degrees and found that the spasm degree was associated with the initial diameter of the distal RA (severe spasm, 2.26 ± 0.60 mm; moderate spasm, 2.73 ± 0.47 mm; and mild spasm, 2.86 ± 0.7 mm). This author also reported that RA spasms can occur in vessels of any different diameter. Furthermore, Kim *et al.* [13] found that the incidence of RA spasm was as high as 51.3% by transradial angiography, which was much higher than our traditional understanding. When a RA spasm occurs, the diameter of the RA lumen decreases. Hence, puncture or sheath insertion could increase vascular endothelial dysfunction, which interacts with both RA spasm and vascular endothelial dysfunction [13–15]. Nagai *et al.* [16] found that when the RA diameter was smaller than the outer diameter of the sheath, the number of patients with diffuse stenosis and occlusion of the RA 3 months after the intervention significantly increased compared with those with RA diameters larger than the outer diameter of the sheath (38% vs. 14%; $P < 0.01$). In this study, we routinely used 6F sheaths without difficulty when the diameter of the RA was smaller than the outer diameter of the 6F radial sheath (2.52 mm), but excessive mechanical stretch increases vascular endothelial dysfunction. Therefore, the preventive application of nifedipine, especially in those patients with small lumen RA, could help reduce the RA endothelium dysfunction during the process of puncture and sheath insertion by dilating the vessel.

Impact of nifedipine on the recovery of radial artery endothelial function

Although nitroglycerin or diltiazem can protect the endothelial function to a certain extent, the dysfunction of RA endothelium has already appeared at the time of puncture and sheath insertion, whereas the tension of patients before the procedure can also induce an RA spasm. A study by Kiemeneij *et al.* [17] confirmed that a transradial sheath injection of verapamil and nitroglycerin mixture could reduce spasm occurrence compared with that in the control group and that drug injection significantly decreased maximum pullback force compared with the control group (0.53 ± 0.52 vs. 0.76 ± 0.45 kg; $P = 0.013$). Furthermore, a report by Deftereos *et al.* [18] demonstrated that RA spasm incidence was significantly lower when fentanyl and midazolam sedative drugs were administered preoperatively than in the control group (2.6% vs. 8.3%; $P < 0.001$), which could significantly reduce the rate of puncture cross-over and discomfort. In addition to preoperative sedation, vasodilators are commonly administered through the RA sheath after its implantation, but rarely before puncture. Our study found that a sublingual dose of 10 mg nifedipine administered 5 min before the procedure did not significantly alter the incidence of RA spasms compared with that in the control group (2.2% vs. 9.1%; $P = 0.34$). However, preventive nifedipine administration improved the postoperative FMD and NMD of distal RA. Spasm occurrence results from the interaction of multiple factors and is related to the proficiency of the interventionist and the intensity of radial pulse during the puncture procedure. Research to date is insufficient to support the feasibility of prophylactic use of vasodilator drugs before puncture due to a lack of clinical data. Our previous study found that the decrease in radial resistance index was most pronounced after 5 min of nifedipine action, with an evident increase in peak systolic flow velocity targeting the small

diameter RA due to dilation and a more subtle increase for larger diameter RA [10]. Nifedipine is a fast-acting drug and easy to administer in a controlled manner—its greatest advantage is that it can be administered with an onset of action immediately before puncture. Sublingual preoperative nifedipine could enhance the recovery of distal RA endothelial function in certain patients due to increased compatibility of vessels with the sheath by dilating the vessel.

This study has several inherent limitations. First, due to ethical constraints, in this study nifedipine was only applied prophylactically before procedure, but not continuously during the postoperative period. Second, FMD changes were not observed in the initial 24 h postoperatively because the cuff pressure needed to reach suprasystolic pressures for 5 min when measuring FMD, thus causing a potential bleeding risk at the puncture point hypertension patients. Third, few drugs can be employed before RA puncture; therefore, nifedipine is more convenient to use due to its short half-life and more suitable for preoperative sublingual administration.

In summary, our study demonstrated that despite the dysfunction induced in both distal and proximal RAs after transradial angiography, nifedipine could promote the recovery of distal RA endothelial function of the cannulated RA.

Acknowledgements

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The study was registered at ClinicalTrials.gov (NCT 02831322).

Conflicts of interest

There are no conflicts of interest.

References

1 Valgimigli M, Saia F, Guastaroba P, Menozzi A, Magnavacchi P, Santarelli A, *et al.*; REAL Registry Investigators. Transradial versus transfemoral intervention for acute myocardial infarction: a propensity score-adjusted and -matched analysis from the REAL (REgistro regionale AngiopLastiche dell'Emilia-Romagna) multicenter registry. *JACC Cardiovasc Interv* 2012; **5**:23–35.

2 Heiss C, Balzer J, Hauffe T, Hamada S, Stegemann E, Koeppel T, *et al.* Vascular dysfunction of brachial artery after transradial access for coronary catheterization: impact of smoking and catheter changes. *JACC Cardiovasc Interv* 2009; **2**:1067–1073.

3 Wakeyama T, Ogawa H, Iida H, Takaki A, Iwami T, Mochizuki M, Tanaka T. Intima-media thickening of the radial artery after transradial intervention. An intravascular ultrasound study. *J Am Coll Cardiol* 2003; **41**:1109–1114.

4 Yonetsu T, Kakuta T, Lee T, Takayama K, Kakita K, Iwamoto T, *et al.* Assessment of acute injuries and chronic intimal thickening of the radial artery after transradial coronary intervention by optical coherence tomography. *Eur Heart J* 2010; **31**:1608–1615.

5 Bi X, Wang Q, Liu D, Gan Q, Liu L. Is the complication rate of ulnar and radial approaches for coronary artery intervention the same? *Angiology* 2017; **68**:919–925.

6 Bi XL, Fu XH, Gu XS, Wang YB, Li W, Wei LY, *et al.* Influence of puncture site on radial artery occlusion after transradial coronary intervention. *Chin Med J (Engl)* 2016; **129**:898–902.

7 Bi XL, Wang QS. Lessons from transulnar access for repeat percutaneous coronary intervention after radial artery occlusion. *Chin Med J (Engl)* 2020; **133**:1497–1498.

8 Dharma S, Shah S, Radadiya R, Vyas C, Pancholy S, Patel T. Nitroglycerin plus diltiazem versus nitroglycerin alone for spasm prophylaxis with transradial approach. *J Invasive Cardiol* 2012; **24**:122–125.

9 Park KH, Park DW, Kim MK, Kim HS, Park WJ, Cho GY, Choi YJ. Effects of sheath injury and trimetazidine on endothelial dysfunction of radial artery after transradial catheterization. *J Interv Cardiol* 2012; **25**:411–417.

10 Bi X, Jia H, Wang Q. The effect of pre-procedural sublingual nifedipine on radial artery diameter. *Coron Artery Dis* 2020;**31**:206–207.

11 Corretti MC, Anderson TJ, Benjamin EJ, Celermajer D, Charbonneau F, Creager MA, *et al.*; International Brachial Artery Reactivity Task Force. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. *J Am Coll Cardiol* 2002; **39**:257–265.

12 Fukuda N, Iwahara S, Harada A, Yokoyama S, Akutsu K, Takano M, *et al.* Vasospasms of the radial artery after the transradial approach for coronary angiography and angioplasty. *Jpn Heart J* 2004; **45**:723–731.

13 Kim SH, Kim EJ, Cheon WS, Kim MK, Park WJ, Cho GY, *et al.* Comparative study of nicorandil and a spasmolytic cocktail in preventing radial artery spasm during transradial coronary angiography. *Int J Cardiol* 2007; **120**:325–330.

14 Deftereos S, Giannopoulos G, Kossyvakis C, Driva M, Kaoukis A, Raisakis K, *et al.* Radial artery flow-mediated dilation predicts arterial spasm during transradial coronary interventions. *Catheter Cardiovasc Interv* 2011; **77**:649–654.

15 Zencirci E, Esen Zencirci A, Degirmencioglu A. A randomized trial of flow-mediated dilation to prevent radial artery spasm during transradial approach. *Minerva Cardioangiol* 2021. [Epub ahead of print]

16 Nagai S, Abe S, Sato T, Hozawa K, Yuki K, Hanashima K, Tomoike H. Ultrasonic assessment of vascular complications in coronary angiography and angioplasty after transradial approach. *Am J Cardiol* 1999; **83**:180–186.

17 Kiemeneij F, Vajifdar BU, Eccleshall SC, Laarman G, Slagboom T, van der Wieken R. Evaluation of a spasmolytic cocktail to prevent radial artery spasm during coronary procedures. *Catheter Cardiovasc Interv* 2003; **58**:281–284.

18 Deftereos S, Giannopoulos G, Raisakis K, Hahalis G, Kaoukis A, Kossyvakis C, *et al.* Moderate procedural sedation and opioid analgesia during transradial coronary interventions to prevent spasm: a prospective randomized study. *JACC Cardiovasc Interv* 2013; **6**:267–273.