

Flow-mediated dilatation to relieve puncture-induced radial artery spasm: A pilot study

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Abstract

Background: Puncture-induced radial artery spasm (RAS) may extend the duration of coronary angiography (CAG) or cause transradial access failure. Flow-mediated dilatation (FMD), a widely-used noninvasive approach for assessing endothelial function, was reported to remove the entrapped radial sheath after percutaneous coronary intervention. Herein, the efficacy and safety of FMD in treating puncture-induced RAS before transradial CAG was investigated.

Methods: Ninety patients with puncture-induced RAS were randomized in a 1:1:1 ratio into three groups: FMD group was immediately treated with blockage of brachial artery blood for 5 min using a sphygmomanometric cuff and then rapid relief; nitroglycerin (NTG) group was administered with 0.5 mg sublingual NTG instantly; and the no-therapy group was treated with a wait-and-watch strategy. The time of radial pulse recovery, and regional and systemic complications were recorded.

Results: The rate of radial pulse recovery within 30 min in FMD group was significantly higher than that in no-therapy group (97% vs. 73%, $p = 0.026$). The median time to return of radial pulse in FMD group and NTG group was significantly shorter than that in no-therapy group (7 [6.5–9] min vs. 15 [12–18] min, 8 [7–9] min vs. 15 [12–18] min, respectively; both $p < 0.001$). Headache and decreased blood pressure were more prevalent in NTG group than those in FMD and no-therapy groups.

Conclusions: FMD is a feasible, noninvasive and nonpharmacological approach to relieve RAS and facilitate radial artery cannulation after an initial failed attempt. (Cardiol J 2018; 25, 1: 1–6)

Key words: coronary angiography, flow-mediated dilatation, transradial, radial artery spasm, nitroglycerin

Introduction

Radial artery access has been an increasingly widespread approach for coronary angiography (CAG) or percutaneous coronary intervention (PCI) [1] since Campeau [2] reported the first case in 1989 and its improvement was described by

Kiemeneij and Laarman in 1993 [3]. Compared with transfemoral access, transradial access decreases vascular-related and bleeding complications [4, 5], reduces in-hospital stay and hospitalization costs [6] while improving patient comfort [7] and preferred by patients. Moreover, the transradial approach significantly reduces all-cause mortality

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and major adverse cardiovascular events for patients with ST-elevated myocardial infarction undergoing PCI [8]. However, radial artery spasm (RAS) which happens during puncture, CAG/PCI or removal of the sheath after the procedure with an incidence of 3–10%, is an important reason for transradial approach failure and access site switch [9]. Some investigators have reported that nitroglycerin (NTG) given sublingually was effective in facilitating radial artery cannulation, although this approach may have a high risk of systemic side effects [10, 11].

Endothelial function is often noninvasively measured by flow-mediated dilatation (FMD) [12], which demonstrates shear stress-induced response of endothelium [13] and was first discovered by Schretzenmayr et al. [14]. Nitric oxide, as the endothelial-derived vasoactive mediator, plays a predominant role in FMD [15, 16]. However, FMD is rarely reported as a treatment despite the application for evaluation of the risk of coronary [17] and peripheral artery disease [18]. Two cases demonstrated that FMD was effective in removing entrapped radial sheath rapidly and successfully after the failure of administration of NTG, verapamil, and sedative therapy [19]. This study aimed at measuring the efficacy and safety of FMD as a nonpharmacological method for relieving RAS induced by puncture.

Methods

Patient population

This was a prospective, randomized, single-center, open-label, pilot study, consistent with the principles of the Declaration of Helsinki and local regulations, approved by the local Ethics Committee. Written informed consent was obtained from each patient before screening. Patients over 18 years old, scheduled to receive elective CAG or PCI via radial artery access and suffered from RAS during puncture in the First Affiliated Hospital of Nanjing Medical University were eligible for this study. RAS was defined as a spasm that resulted in weakness or loss of radial artery pulse, hardly meeting the demand for re-puncture. Diagnoses were made by one experienced operator according to palpation (Dr. L. or Dr. Y., who each had performed more than 300 cases of successful radial artery puncture per year). Before the procedure, patients with an abnormal Allen test, known contraindications to NTG (hypertrophic obstructive cardiomyopathy, severe aortic valve stenosis, heart rate < 50 bpm, systolic blood pressure [SBP]

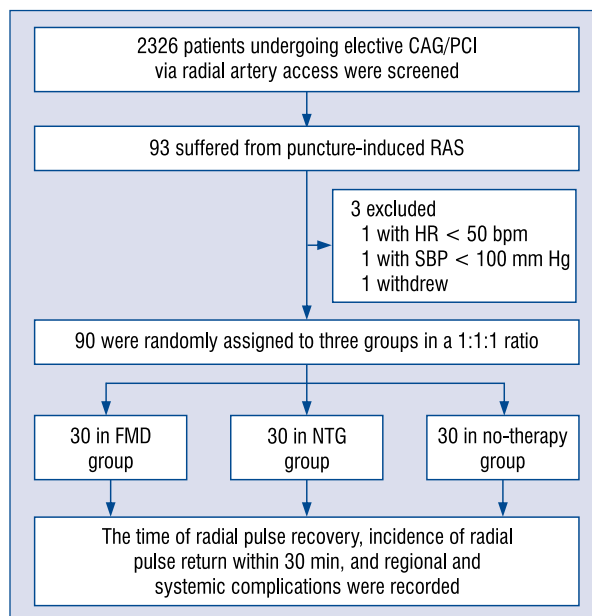


Figure 1. Study flow chart; CAG — coronary angiography; HR — heart rate; FMD — flow mediated dilation; NTG — nitroglycerin; PCI — percutaneous coronary intervention; RAS — radial artery spasm; SBP — systolic blood pressure.

< 100 mm Hg), and requiring emergency PCI were excluded.

Procedure

Patients were randomly assigned in a ratio of 1:1:1 to be treated by FMD, NTG or a wait-and-watch strategy (no-therapy) (Fig. 1). Patients in FMD group were immediately treated with blocking blood flow of the brachial artery for 5 min by a sphygmomanometric cuff wrapped around the upper arm with puncture, and the cuff was rapidly inflated over 50 mm Hg above SBP, releasing the air rapidly for fast recovery of blood flow, as recommended by the International Brachial Artery Reactivity Task Force [20]. Patients in NTG group were treated with sublingual administration of a single dose of NTG (0.5 mg) as soon as RAS was diagnosed. Patients in no-therapy group received no special treatment except waiting and watching for spontaneous recovery of the radial artery pulse. The pulse of the punctured radial artery was evaluated persistently by the same experienced operator starting from the diagnosis of RAS, and the pulse of adjacent ulnar artery was measured at the same time. Evaluation of radial pulse was suspended during the inflation of the cuff and restarted after loosening the cuff. Recovery of the radial artery

Table 1. Baseline clinical characteristics.

Variable	FMD (n = 30)	NTG (n = 30)	No-therapy (n = 30)	P
Age [years]	64.7 ± 10.5	63.1 ± 10.2	63.2 ± 9.9	0.88
Female gender	13 (43%)	14 (47%)	15 (50%)	0.86
Height [cm]	164.5 ± 8.4	162.9 ± 8.1	165.9 ± 8.2	0.37
Weight [kg]	65.9 ± 9.0	65.6 ± 10.5	67.8 ± 12.1	0.69
Body mass index [kg/m ²]	24.3 ± 2.3	24.7 ± 3.5	24.5 ± 2.9	0.91
Hypertension	9 (30%)	10 (33%)	14 (47%)	0.37
Diabetes	7 (23%)	8 (27%)	10 (33%)	0.68
Smoking	7 (23%)	8 (27%)	9 (30%)	0.84

Values are presented as mean ± standard deviation or numbers (percentages); FMD — flow mediated dilation; NTG — nitroglycerin

pulse was defined as the event that similar pulses were obtained from the radial and ulnar arteries. The duration of pulse recovery was calculated from the diagnosis of RAS to radial artery pulse recovery, including the time of NTG administration and compression by cuff. Femoral or contralateral radial artery access for CAG was used if no recovery of the radial artery pulse was achieved after 30 min of observation. Success of pulse recovery and the time of recovery were recorded before trying to cannulate the radial artery again. Blood pressure, heart rate, headache, and local adverse reaction of the upper limb with puncture, decreased blood pressure (defined as SBP decreasing by over 10% during the procedure) and bradycardia (defined as heart rate below 50 bpm during the procedure) were observed and recorded. Symptomatic hypotension was defined as SBP below 90 mm Hg with accompanying symptoms.

Statistical analysis

Analyses were performed using SPSS version 19.0 (IBM SPSS, Inc., Chicago, IL, USA) for Windows. The Shapiro-Wilk test was used to test normality of distribution. Continuous variables with normal distribution, continuous variables with non-normal distribution and categorical variables are presented as the mean ± standard deviation, median (interquartile range) and number of events (frequency or percentage), respectively. Comparisons among the three groups were tested by one-way ANOVA for continuous data with a normal distribution, Kruskal-Wallis H test for continuous data with a non-normal distribution or χ^2 test for categorical data. Comparisons between the two groups were tested by Kolmogorov-Smirnov test for continuous data with non-normal distribution. All hypothesis tests were two-sided with 0.05 significance levels.

Results

A total of 2326 patients between October 2015 and August 2016 were consecutively screened and 93 (4.0%) of the candidates suffered from RAS during puncture. Three patients were excluded for various reasons (1 patient with heart rate < 50 bpm, 1 patient with SBP < 100 mm Hg, another withdrew before enrollment). Ultimately, 90 patients in all and 30 participants in each group were enrolled in this study. The baseline characteristics included age, gender, height, weight, body mass index, hypertension, diabetes and smoking were well matched among the three groups (Table 1).

Primary endpoints are shown in Figures 2 and 3. Twenty-nine out of 30 patients in FMD group (97%), 28 out of 30 patients in NTG group (93%) and 22 out of 30 patients in no-therapy group (73%) had re-establishment of radial pulse and achieved radial artery cannulation successfully. The success rate of radial pulse recovery in FMD group was significantly higher than that in no-therapy group ($p = 0.026$); but the difference between NTG group and no-therapy group was not statistically significant ($p = 0.083$). The median recovery time was 7 (6.5–9) min in FMD group and 8 (7–9) min in NTG group; both were remarkably shorter than that in no-therapy group (15 [12–18] min; both $p < 0.001$). The incidence of successful recovery of radial artery pulse and the median recovery time presented no significant difference between FMD group and NTG group ($p = 1.000$ and 0.859 , respectively). In FMD group, 1 patient did not regain the radial pulse within 30 min, and the procedure was completed via contralateral radial access. In NTG group, 2 patients with unsuccessful recovery of the radial artery pulse were operated on transfemorally. In no-therapy group, failure of the radial artery pulse

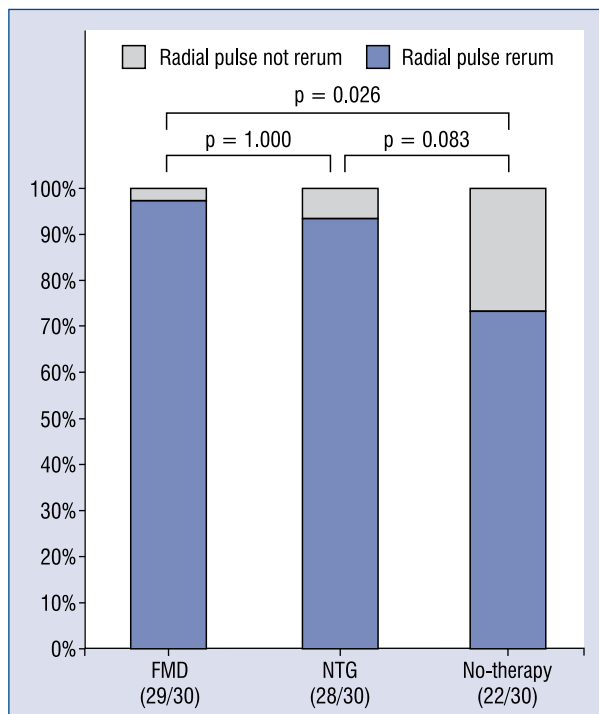


Figure 2. The success rate of radial pulse recovery; FMD — flow mediated dilation; NTG — nitroglycerin.

recovery occurred in 8 patients; contralateral radial access was obtained successfully in 4 of them, and the procedure was completed transfemorally in another 4 patients,

The secondary outcomes are shown in Table 2. During the procedure, decreased blood pressure was more frequent in NTG group compared with those in FMD group and no-therapy group (47% vs. 3%, $p < 0.001$; 47% vs. 3%, $p < 0.001$, respectively). One patient in NTG group underwent symptomatic hypotension and recovered after dopamine administration and fluid infusion treatment. A total of 40% patients in NTG group complained of headache; no other patients in the other groups reported headache. One patient in NTG group developed bradycardia. No adverse local reactions were observed in this study.

Table 2. Secondary outcomes.

Outcomes	FMD (n = 30)	NTG (n = 30)	No-therapy (n = 30)	P
Decreased blood pressure	1 (3%)	14 (47%)	1 (3%)	< 0.001
Bradycardia	0 (0%)	1 (3%)	0 (0%)	1.000
Headache	0 (0%)	12 (40%)	0 (0%)	< 0.001
Symptomatic hypotension	0 (0%)	1 (3%)	0 (0%)	1.000

FMD — flow mediated dilation; NTG — nitroglycerin

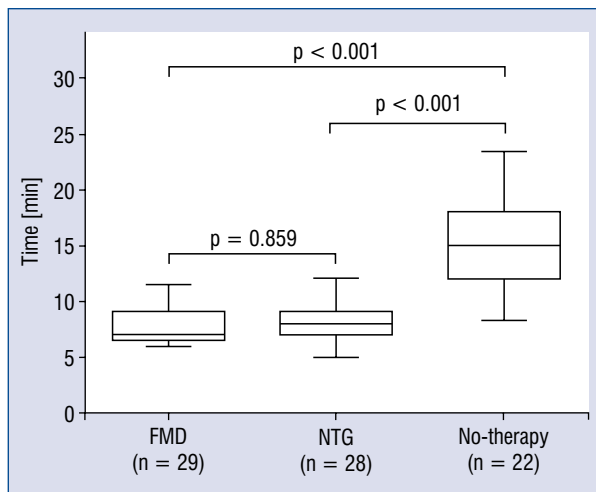


Figure 3. Time to return of radial pulse. The horizontal line in the middle of each box indicates the median. The top and bottom borders of each box indicate the interquartile range (IQR). The whiskers above and below the box indicate 5–95 percentiles, respectively; FMD — flow mediated dilation; NTG — nitroglycerin.

Discussion

According to available research, the present study was the first pilot study to evaluate the efficacy and safety of FMD as a treatment of puncture-induced RAS, and the results indicate that FMD is an effective noninvasive and nonpharmacological method with a higher success rate, reduced recovery time and few systemic complications.

Although transradial access is in widespread use due to fewer vascular-related and bleeding complications compared with transfemoral access, this benefit was eliminated by RAS in a small number of patients. Age > 75 years, a history of coronary artery bypass graft surgery and short stature were reported as independent predictors of failure of transradial access [21]. The RIVAL trial reported 5% of patients underwent switch of access site due to difficulty to treat spasm [22], and Schussler et al. [23] found bleeding complications were

increased with a switch to transfemoral approach. Unsuccessful puncture plays an important role in RAS, especially in patients with multiple failure of puncture or failure of delivering guidewire after puncture, which might result in pulse weakness or loss and difficulty of retrying puncture. Therefore, it is essential to develop an effective and accessible method for radial artery cannulation after RAS. FMD is endothelium-dependent vasodilation induced by elevated shear-stress caused by rapid blood flow and was developed as a noninvasive approach widely applied for the detection of endothelium function [13] and risk evaluation of coronary and peripheral artery disease [17, 18, 24]. FMD was applied for treating puncture-induced RAS, and the results indicated a high success rate (29/30, 97%), short time to return [7 (6.5–9) min] and few systemic complications. Similarly, Pancholy et al. [19] presented two successful cases using FMD for the removal of an entrapped radial sheath after PCI due to severe spasm after failure of NTG, verapamil, and sedative treatment. Moreover, a recent study by Collet et al. [25] showed that pressure-mediated dilatation (rapid injection with 10 mL of saline solution at a rate of 10 mL per second with a pressure of 400 pounds per square inch [PSI] through the radial sheath) was superior to vasodilators (intra-arterial NTG 100 μ g and verapamil 2.5 mg) for relieving RAS during the procedure, which showed the efficacy and safety of nonpharmacological methods based on shear stress-induced vasodilation.

The administration of vasodilators before puncture could reduce the incidence of RAS. Sublingual NTG before puncture was reported to reduce times and duration of puncture [10], and subcutaneously infiltrated NTG was used to increase the radial diameter, palpability and success rate of radial artery puncture [26]. Furthermore, a wait-and-watch strategy was applied for recovery from RAS in another study [11]. In the present study, three strategies (FMD, sublingual NTG and no-therapy) were compared, and FMD and sublingual NTG methods demonstrated similar effects for recovery from RAS with a higher success rate in 30 min, and less recovery time compared with the wait-and-watch strategy. Similar results were shown in a study performed by Pancholy et al. [11]; in the group treated by a wait-and-watch strategy, the success of radial cannulation occurred in 8 out of 11 (72%) patients and the average time to return of the radial pulse was 18 ± 5 min. Operators needed to wait for 8 ± 1 min to regain the palpability of the radial pulse in 18 out of 21 (90%) patients with sublingual NTG, with the risk of decreased

blood pressure and headache. Furthermore, a local subcutaneous injection of 1 mL NTG (200 μ g/mL) facilitated successful recovery of the radial pulse in 21 out of 21 patients (100%) within 3 ± 1 min without systemic adverse effects of NTG [11]. However, this strategy was not explored in the present study because local errhysis happened frequently after a failed radial artery puncture, and immediate compression was required to prevent local hematoma and then the local administration of NTG was delayed. Besides, bumps caused by subcutaneous injection might influence the palpability of radial artery pulse and re-puncture. These might be reasons why this method is not widely applied.

Limitations of the study

There are some limitations in this study. First, due to the wide use of transradial approach and improvement of medical instrumentation, the incidence of successful radial artery puncture is high and puncture-induced RAS is low (4.0% in our study). Also only 90 patients were included in this study. However, RAS is indeed an intractable phenomenon before CAG and PCI procedure, and the present aim was to develop a new noninvasive approach available for operators when RAS occurs. Second, without detection of blood flow and lumen diameter of radial artery by ultrasound, loss and recovery of radial artery pulse were assessed subjectively by operators. However, puncture of the radial artery is routinely based on palpation of the operators. Furthermore, the operator who assessed loss and recovery of pulse was experienced and was the same one in every case, and the adjacent ulnar artery pulse was also touched as a reference, thus the pulse evaluation is reliable in this study.

Conclusions

Conclusions herein are similar to the administration of sublingual NTG, FMD improves radial cannulation by alleviating puncture-induced RAS with a higher success rate in 30 min and shorter time of recovery compared with the wait-and-watch strategy. Moreover, systemic adverse effects caused by NTG, such as headache and decreased blood pressure were avoided and no local adverse reactions were observed. FMD is an effective, nonpharmacological and noninvasive method to relieve puncture-induced RAS and facilitates transradial cannulation after an initial failed attempt. Apart from this, the present study was designed as a pilot and open-labeled study because the three

treatments were entirely different and the operator who evaluated radial pulse immediately in the catheter lab was difficult to be blinded. Further study should be performed in an objective method under blind circumstances.

Conflict of interest: None declared

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