Original Article

Vascular dysfunction and its recovery after transradial coronary angioplasty- A serial observational study

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ABSTRACT

Objective: To serially evaluate the effect of trans-radial coronary angioplasty (TRA) on the vascular function of radial artery (RA) and upstream brachial artery (BA) and to find out the relative contribution of endothelial dependent flow-mediated vasodilatation (FMD) and endothelial independent nitrate mediated dilatation (NMD).

Methods: Forty patients of chronic stable angina with successful TRA were studied. FMD and NMD of bilateral RA and BA were measured with high-resolution ultrasound, before and at 24 h and at 3 months, after catheterization.

Results: FMD as well as NMD were significantly decreased in right RA ($16.3 \pm 3.6\%$ to $5.7 \pm 1.8\%$; $p = 0.001$, and $24.1 \pm 5.3\%$ to $9.7 \pm 2.8\%$; $p = 0.001$, respectively) as well as in upstream BA ($17.0 \pm 1.6\%$ to $9.4 \pm 0.5\%$; $p = 0.001$,and $26.5 \pm 6.8\%$ to $20.5 \pm 3.7\%$; $p = 0.001$, respectively) at 24 h. FMD/NMD ratio was also decreased in RA ($70 \pm 10\%$ to $60 \pm 10\%$; $p = 0.04$) and as well as in BA ($70 \pm 20\%$ to $50 \pm 10\%$; $p = 0.03$). The endothelial dysfunctions returned to normal at 3 months. Control arm did not show any change in vascular function at any point of time. Radial artery diameter/sheath ratio <1 and catheter exchanges >2 were the independent predictors for >50% decrease in FMD.

Conclusions: TRA results in reversible depression in FMD as well as NMD in the radial artery as well as upstream brachial artery. These vascular dysfunctions are limited to the catheterized arm only and return to normal after 3 months.

1. Introduction

The transradial approach for coronary procedures is well established and is associated with fewer vascular complications than transfemoral approach.[1—4] It has been recommended as the standard approach, unless there are overriding procedural considerations.[5] The cannulation of relatively small radial artery (RA) may cause damage to its endothelial cell lining which may result into impaired arterial vascular functions and may promote intimal hyperplasia, thrombus formation, luminal loss and the development of atherosclerotic plaques.[6—8] It may potentially limit the quality of the RA as a bypass graft for future coronary artery bypass grafting (CABG) surgery.[9]

Vasodilator function of RA following transradial procedures has been studied extensively, most studies reporting a decline in endothelium dependent and endothelial independent vasodilatation in acute phase followed by some recovery in long term.[10—16] Whether the transradial catheterization also affects the upstream brachial artery (BA) is not very well established and neither it is known whether the endothelial dysfunction after transradial catheterization is localized or generalized. Furthermore, in all previous studies patients undergoing either diagnostic coronary angiography or angioplasty with the use of different sheath sizes had been included; no study has been conducted on patients with coronary angiography followed by angioplasty in the same sitting. Also, it is not known what proportion of endothelial dysfunction is caused by endothelial dependent mechanism versus endothelial independent mechanism.

In view of the above-mentioned limitations of previous studies, we serially studied the effect of transradial catheterization on endothelium dependent and endothelium independent

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vasodilatation of the RA and BA of both the arms in patients with chronic stable angina undergoing coronary angiography followed by angioplasty in the same sitting.

2. Material and methods

2.1. Study population

Over the last one year, 40 patients with chronic stable angina undergoing transradial coronary angiography followed by angioplasty at our tertiary care centre were enrolled in this prospective study. Only patients who had completed successful transradial coronary angioplasty were included. The exclusion criteria were as follows: patients with only diagnostic coronary angiography, previous trans-radial access, patients who developed any radial artery complication, acute coronary syndrome in the previous 3 months, post CABG, valvular heart disease, left ventricular ejection fraction <40%, heart failure NYHA functional class III to IV, chronic obstructive airway disease, renal or hepatic dysfunction, acute inflammation (C-reactive protein >0.5 mg/dl) and heart rhythm other than sinus rhythm. All patients gave written informed consent and all procedures followed institutional ethical standards and guidelines.

Data on demographics, medical history, and procedural characteristics was recorded for every patient. Routine hemogram, renal & hepatic function test, lipid profile, blood sugar levels, HbA1c and C-reactive protein (CRP) were measured in all patients. Left ventricular ejection fraction (LVEF) was measured by echocardiography in all patients. Other investigations were done as and when required.

2.2. Radial artery access and transradial catheterization

The access site was anaesthetized with lidocaine and then right radial arterial access was taken using a 6F radial sheath (Radifocus introducer II, Terumo, Japan). To reduce vasospasm and forearm discomfort, pre prepared mixture containing Nitroglycerine 100 μg, Diltiazem 5 mg and Lidocaine 21.3 mg was administered through the radial sheath. Unfractionated heparin was administered in all patients in doses of 100 units/kg.

Coronary angiograms were performed with 5 French (5F) diagnostic catheters (Optitorque, Terumo, Japan) followed by angioplasty using 6F standard coronary guiding catheters (Launcher, Medtronic Inc., Minneapolis, USA). Immediately after the procedure, the radial artery sheath was removed and haemaostasis was achieved by the application of haemaostasis device (TR band, Terumo, Japan) using patent haemaostasis technique.[17] Procedural details like catheter exchanges, angiographic severity of coronary artery disease, number of vessels stented, total number of stents used in each patient, procedure time and radiation dose were noted for each patient.

2.3. Vascular function assessment

Vascular function assessment including flow mediated dilatation (FMD) and nitrate mediate dilatation (NMD) of bilateral radial & brachial arteries was carried out as per international guidelines.[18] All the studies were done on high-resolution ultrasound (VIVID 7; GE Healthcare, USA) using 12-MHz linear probe. All patients were examined serially on three occasions: a day before transradial catheterization (basal), the day after catheterization (24 h), and 3 months after catheterization (3 months).

Patients were instructed to fast and abstain from caffeine, alcohol and tobacco for at least 12 h before the examination. Patients were rested in supine position for approximately 30 min before evaluation. Vascular probe was located 2–3 cm above puncture point for the evaluation of radial artery at the sheath insertion site. Brachial artery was scanned in the longitudinal sections 1–10 cm above the elbow, ensuring that the lumen diameter was maximized and the gain optimized to provide clear arterial wall interfaces. Heart rate and blood pressure were measured from an automated sphygmomanometer on the contral ateral arm. At each point of time, the left (non-cannulated) and right (cannulated) RA functions as well as left and right BA vasodilator functions were assessed with flow mediated dilatation (FMD) and nitrate mediated dilatation (NMD). All diameters were measured at peak of the R wave in ECG. For each recording, measurements were performed three times at one single peak in two different R waves, a total of six measurements. Mean value from these six measurements was used for final analysis. All the recordings were evaluated by two independent experienced investigators who were blinded to the data.

2.4. Measurement of FMD (endothelium-dependent NO-mediated function)

RA function was determined at a landmark 2–3 cm proximal to the sheath insertion point. Baseline measurements included RA diameter and RA flow velocity. Subsequently, a blood pressure cuff was inflated at the forearm to supra-systolic pressures for 5 min. Upon cuff release, the RA flow measurements were repeated to demonstrate hyperaemia. The RA diameter was measured 90 s after cuff deflation. The percentage rise in diameter from baseline diameter was taken as FMD [(Diameter$_{postischemia}$ − Diameter$_{baseline}$/Diameter$_{baseline}$) x 100]. FMD was also measured in the opposite arm and in the right BA, in the same fashion. The sequence was in random order.

2.5. Measurement of NMD (endothelium-independent NO-mediated function)

NMD was done after about 10 min of performing FMD measurements. Sublingual nitroglycerine (0.4 mg) was administered. Repeat flow and diameter measurements were recorded for both arms (RA as well as BA) at 4 min to assess the percentage rise in diameter, which is the NMD [(Diameter$_{post-nitroglycerine}$ − Diameter$_{baseline}$/Diameter$_{baseline}$) x 100].

2.6. Statistical analyses

All the study data were prospectively collected. Dichotomous variables are reported as numbers and proportions. Continuous variables were presented as mean ± standard deviations. Comparisons of data across the 3 time points (before the procedure, 24 h after the procedure, and 3 months after the procedure) were performed. Comparisons were made separately for the cannulated arm and for the non-cannulated arm. Paired samples t-test or Wilcoxon signed-rank test was used for comparison of pre- and post-procedural ultrasound findings. Predictors for FMD reduction were analyzed using binary logistic regression in the subset of patients who developed ≥50% reduction in FMD in comparison to the baseline. A two-tailed p-value of less than 0.05 was considered a statistically significant result. All statistical analyses were performed using SPSS, version 20.0 (SPSS Inc.).

3. Results

3.1. Study population characteristics

The characteristics of the study population are shown in Table 1. The mean age was 59.9 ± 5.3 years, and 70% of the patients were male. About half were hypertensive, half were dyslipidaemic and

Table 1
Characteristics of the study population ($n = 40$).

Age (years)	59.9 ± 5.3
Male gender	28 (70.0%)
BMI (kg/m^2)	25.4 ± 1.7
Diabetes mellitus	12 (30.0%)
Hypertension	22 (55.0%)
Smoker	16 (40.0%)
Dyslipidaemia	20 (50.0%)
SBP (mm Hg)	139.6 ± 10.9
DBP (mm Hg)	83.2 ± 7.1
Heart rate (beats/minute)	77.6 ± 9.8
Serum creatinine (mg%)	1.27 ± 0.2
Peripheral vascular disease	2 (5.0%)
Angina functional class	34 (85.0%)
NYHA class II	6 (15.0%)
NYHA class III	
Coronary artery disease	26 (65.0%)
1-vessel disease	9 (22.5%)
2-vessel disease	5 (12.5%)
3-vessel disease	
Multivessel stenting	10 (25.0%)
Catheter exchanges >2	8 (20.0%)
Procedure time (minutes)	68.2 ± 12.2
Radiation dose (Gy x cm^2)	128.2 ± 22.3

Abbreviations: SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; NYHA class = New York Heart Association class for angina.

about one-third were diabetic. Smokers were 40%. All patients had stable angina pectoris. All patients had successful transradial coronary angiography followed by angioplasty in the same sitting. All patients were taking aspirin, clopidogrel/ticagrelor, a statin, an angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB), and a beta-blocker. Efforts were made to avoid changes in the drug regimens throughout the study period. About two-third patients had single vessel disease. Multi-vessel stenting was done in 25% patients. Only 4 patients required 2 puncture attempts for radial artery access. In rest of the patients, access was taken in single attempt. Catheter exchanges >2 times were required in 20% procedures. Mean procedure time was 68.2 ± 12.2 min with the mean radiation dose of 128.2 ± 22.3 Gy x cm^2. Heart rate and blood pressure measured on each visit were not significantly different (Table 2).

3.2. Endothelial dysfunction after transradial coronary angioplasty

Basal mean diameter of right RA was 2.7 ± 0.3 mm and was increased significantly (2.9 ± 0.5 mm; p=<0.05) after 24 h of catheterization (Table 3). In a similar manner, diameter of right BA immediate post catheterization (24 h) was increased significantly from 4.2 ± 0.6 mm to 4.4 ± 0.4 mm (p=<0.05). In contrast, diameters of left RA and BA did not change post cannulation (Table 3).

Baseline FMD was 16.3 ± 3.6% in the right RA and 17.0 ± 1.6% in the right BA, which was decreased significantly after 24 h of catheterization to 5.7 ± 1.8% ($p = 0.001$) and 9.4 ± 0.5% (p=<0.001) respectively (Table 3 & Fig. 1). NMD response was also significantly decreased in both right RA & BA at 24 h [Right RA: 24.1 ± 5.3% (baseline) vs. 9.7 ± 2.8% (24 h), p=<0.001; right BA: 26.5 ± 6.8%

Table 2
Hemodynamic parameters ($n = 40$).

	Baseline	24 h	3 months
Heart rate (beats/minute)	77.6 ± 9.8	76.7 ± 22.3[a]	73.3 ± 20.2[a]
Mean arterial pressure (mm Hg)	108.3 ± 15.2	110.1 ± 20.9[a]	107.7 ± 17.5[a]

[a] p = NS in comparison to baseline.

(baseline) vs. 20.5 ± 3.7% (24 h), p=< 0.001 (Table 3 & Fig. 1). Control arm (left RA & BA) did not show any significant change in FMD and NMD at 24 h of catheterization (Table 3, Figs. 1 and 2,).

We also calculated the FMD/NMD ratio to determine the relative contribution of endothelium dependent to total nitrate mediated vasodilatation. This showed a significant decrease from 0.7 ± 0.1 (baseline) to 0.6 ± 0.1 (24 h); $p = 0.04$, in the right RA and from 0.7 ± 0.2 to 0.5 ± 0.1 ($p = 0.03$) in right BA. The FMD/NMD ratio was unaffected by the intervention in the control arm (Table 3 & Fig. 1).

3.3. Recovery of endothelial function

Vascular functions in bilateral RA & BA were re-evaluated after 3 months of procedure. The diameters of right RA as well as of right BA were decreased from the values at 24 h and became comparable to the basal values. Diameters of control arm RA and BA remained same throughout the study period (basal, at 24 h after and 3 months after transradial catheterization) (Table 3 & Fig. 1).

The FMD and NMD measurements of right RA as well as right BA at 3 months were improved significantly from the values at 24 h and became comparable to basal values (Table 3 & Fig. 1). In contrast FMD and NMD parameter of non-catheterized arm did not differ significantly at 3 months from basal and 24 h values (Table 3 and Fig. 1). Similarly, the ratio of FMD/NMD become normalized at 3-month follow-up in both the right RA and BA while that of control arm remain unchanged (Table 3 & Fig. 1).

3.4. Predictors affecting FMD

Univariate and multivariate logistic regression analysis for the predictors affecting right radial artery FMD are presented in Table 4 and 5. Of the 40 participating patients, 22 patients showed decrease in FMD >50% at 24 h as compared to the baseline FMD results. On univariate analysis; age, diabetes mellitus, smoking, radial artery dimeter <2.5 mm, radial artery diameter/radial sheath size <1 and catheter exchange >2 times were the predictors for >50% decrease in FMD (Table 4). On multivariate logistic regression analysis; radial artery diameter/radial sheath size <1 and catheter exchanges >2 (OR 3.4, 95% CI 0.5–16.3, $p = <0.01$, and OR 2.8, 95% CI 0.2–11.3, $p = 0.04$, respectively) have emerged as the independent predictors for >50% decrease in FMD after transradial coronary angioplasty (Table 5).

4. Discussion

Results of our study indicate that both FMD as well as NMD decreases in the catheterized arm after transradial angioplasty. This vascular dysfunction is not limited to the vascular sheath insertion site (right radial artery) but also involves the upstream right brachial artery. However; these vascular dysfunctions are limited to the catheterized arm only. Vascular functions return to normal after 3 months. Present study is the only study is which both FMD as well as NMD were serially evaluated not only in the radial artery but also in the upstream brachial artery with the contralateral radial & brachial arteries serving as the control. Additionally, present study is the only study done exclusively in the patients who underwent successful trans-radial coronary angioplasty.

In our study endothelial dysfunction was noted in right RA as well as in right BA, suggesting that not only the sheath insertion causes the mechanical damage to the artery but catheter manipulation is also equally responsible for the endothelial dysfunction. This had been previously shown by Heiss et al[19] that the transradial catheterization causes endothelial dysfunction in both RA and upstream BA, but they have done it in patients who underwent diagnostic coronary angiography with only 5 French (5F) sheath

Table 3
Serial changes in vessel diameter and vasomotor function after transradial catheterization (N = 40).

		Diameter (mm)			FMD (%)			NMD (%)			FMD/NMD ratio		
		Basal	24 h	3 months	Basal	24 h	3 months	Basal	24 h	3 months	Basal	24 h	3 months
Right arm (Catheterized arm)	RA	2.7 ± 0.3	2.9 ± 0.5*	2.6 ± 0.4	16.3 ± 3.6	5.7 ± 1.8*	15.7 ± 3.3	24.1 ± 5.3	9.7 ± 2.8*	23.3 ± 4.7	0.7 ± 0.1	0.6 ± 0.1*	0.7 ± 0.1
	BA	4.2 ± 0.6	4.4 ± 0.4*	4.1 ± 0.5	17.0 ± 1.6	9.4 ± 0.5*	16.9 ± 1.2	26.5 ± 6.8	20.5 ± 3.7*	26.4 ± 6.6	0.7 ± 0.2	0.5 ± 0.1*	0.7 ± 0.2
Left arm (Control arm)	RA	2.8 ± 0.3	2.8 ± 0.5	2.8 ± 0.4	17.1 ± 3.0	17.2 ± 3.2	17.0 ± 3.1	25.2 ± 4.9	25.1 ± 4.3	25.1 ± 4.4	0.7 ± 0.1	0.7 ± 0.3	0.7 ± 0.2
	BA	4.2 ± 0.4	4.2 ± 0.6	4.2 ± 0.5	15.6 ± 2.8	15.7 ± 3.6	16.2 ± 3.1	26.8 ± 6.8	26.4 ± 5.5	26.6 ± 6.1	0.6 ± 0.1	0.6 ± 0.4	0.6 ± 0.3

Abbreviations: RA = radial artery; BA = brachial artery; FMD = flow mediated dilatation; NMD = nitrate mediated dilatation.
Diameter are expressed in mm, FMD and NMD are expressed as percentage change in diameter from baseline, FMD/NMD ratio = relative contribution of FMD to NMD.
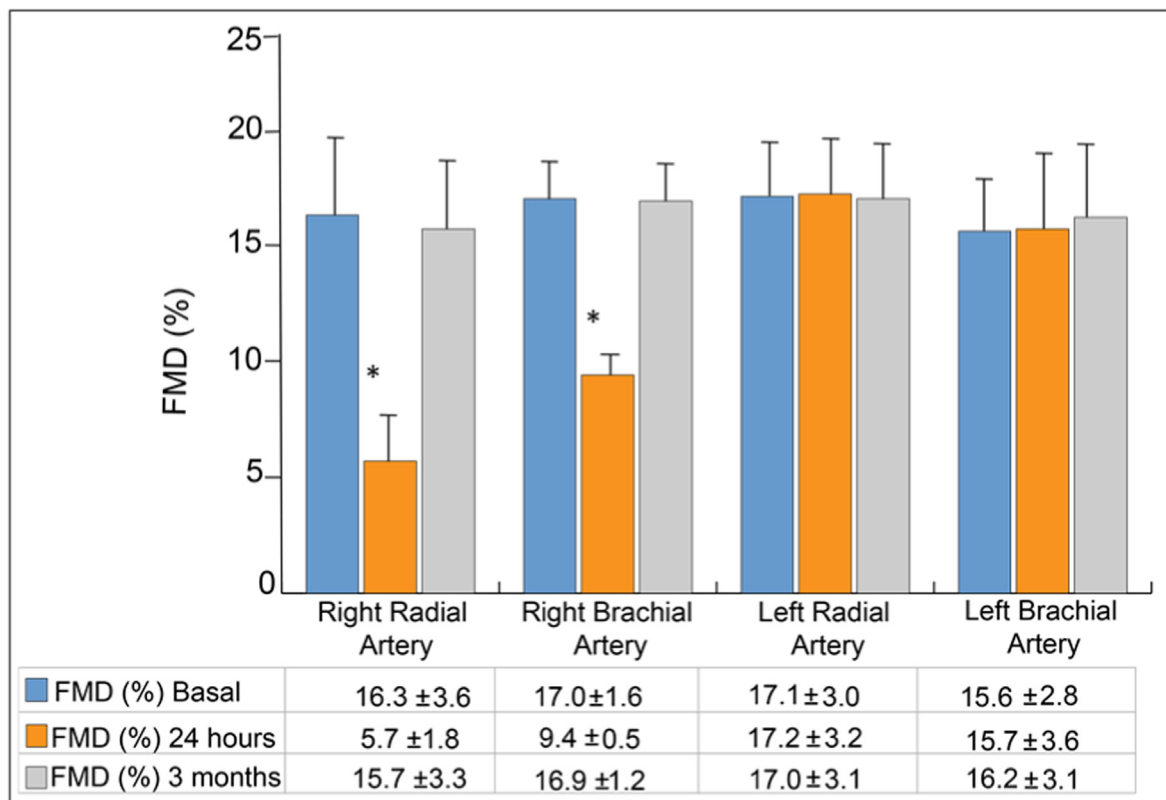*For all p values ≤ 0.05 versus basal reading before transradial catheterization———————

Fig. 1. Diagram showing serial changes in FMD in right radial, right brachial, left radial and left brachial arteries.

and catheter, whereas in our study all patients underwent coronary angiography followed by angioplasty in the same sitting using 6F sheath and catheter. In contrast to our findings, values were recovered after 12 h in non-smokers. Few other previous studies have also documented that transient vascular dysfunction occurs in upstream BA after transradial catheterization.[20,21]

In addition to the assessment of FMD (endothelial-dependent function), we also measured NMD (endothelial-independent NO mediated responses to GTN). As a NO donor, GTN provides a measure of the smooth muscle component of the vascular NO-dilator system. The decrease in the NMD along with FMD in the catheterized arm suggest that transradial sheath insertion and catheter manipulation, not only produces endothelial dysfunction but also produces vascular smooth muscle cell dysfunction. These findings are in concordance with the study done by Dawson et al and Heiss et al.[14,19]

The FMD/NMD ratio, which represents the relative contribution of FMD to total arterial smooth muscle cell mediated dilatation, normally is around 70% as shown by Heiss et al.[19] In our study, this ratio was decreased significantly both at the site of sheath insertion (right RA) and as well in the upstream right BA. However, the ratio was decreased more so at BA than RA. This may be because of the direct trauma to the relatively small caliber radial artery by the sheath insertion and by subsequent catheter manipulation leading to the endothelial denudation as well as injury to smooth muscle cells leading to an equal decrease in FMD as well as in NMD. On the other hand, catheter manipulation in the BA probably produces endothelial denudation by direct contact of catheters & wires to the endothelial lining but less irritation of smooth muscles because of its large diameter as a mechanism for relatively more reduction in FMD than NMD. Overall magnitude of decrease in FMD as well as in NMD was much greater in RA than in BA (decrease in FMD by 65.0% vs. 44.7% and in NMD by 59.8% vs. 22.7% in RA vs. BA respectively). Our results are in accordance to the study by Heiss et al; the FMD/GTN ratio in the BA only tended to decrease at 6 h but did not reach statistical significance during the whole study period, whereas the FMD/GTN ratio showed a significant decrease in the RA.[19]
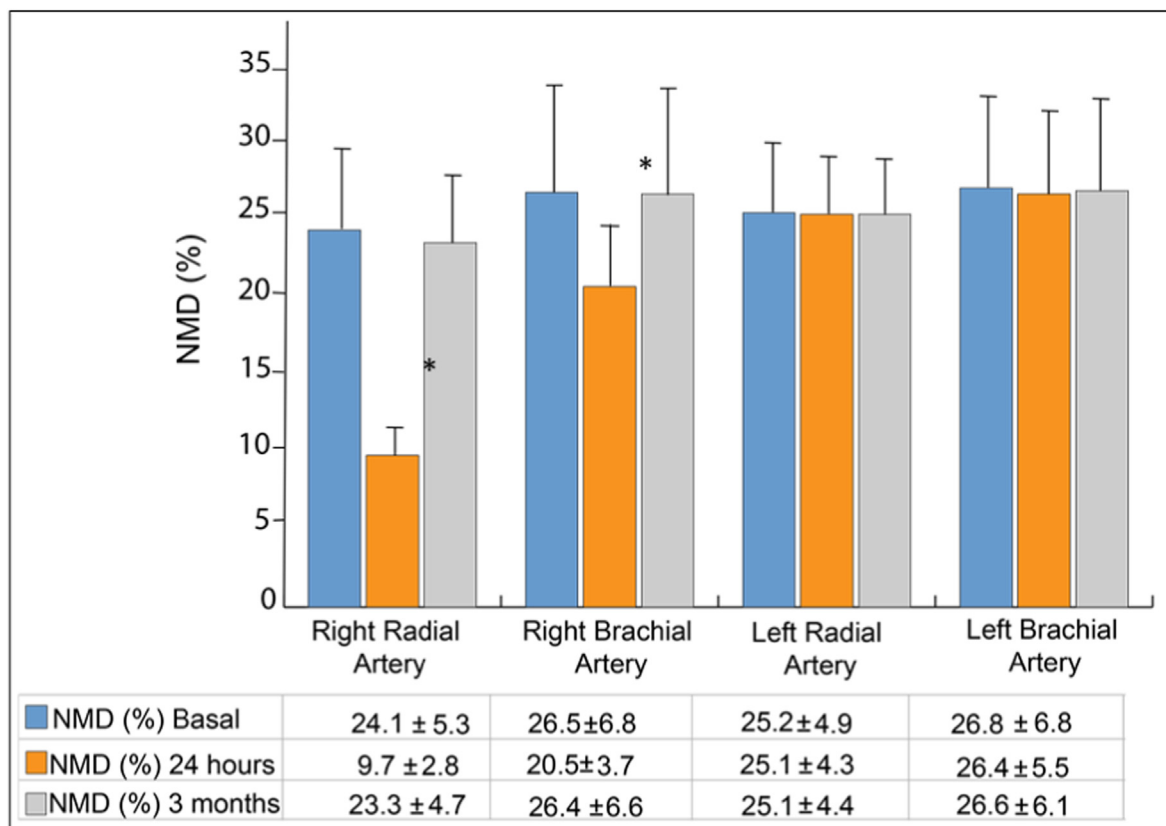
	Right Radial Artery	Right Brachial Artery	Left Radial Artery	Left Brachial Artery
■ NMD (%) Basal	24.1 ± 5.3	26.5±6.8	25.2±4.9	26.8 ± 6.8
■ NMD (%) 24 hours	9.7 ±2.8	20.5±3.7	25.1±4.3	26.4±5.5
■ NMD (%) 3 months	23.3 ±4.7	26.4 ±6.6	25.1±4.4	26.6±6.1

Fig. 2. Diagram showing serial changes in NMD in right radial, right brachial, left radial and left brachial arteries.

Table 4
Univariate Predictors for >50% fall in FMD at 24 h ($n = 22$).

Characteristics	OR (95% confidence interval)	p value
Age	2.2 (0.5–4.3)	0.04
Male gender	1.2 (0.7–1.9)	0.88
Body mass index (BMI)	1.0 (0.4–2.4)	0.75
Diabetes mellitus	1.9 (0.6–2.4)	0.03
Hypertension	1.1 (0.1–3.8)	0.99
Dyslipidemia	0.6 (0.2–1.6)	0.69
Smoking	3.4 (1.7–19.0)	0.03
Creatinine clearance <60 ml/min	0.8 (0.6–1.1)	0.63
Radial artery diameter <2.5 mm	2.1 (1.6–8.5)	0.04
Radial artery diameter/sheath size <1	4.5 (1.4–20.3)	<0.01
Catheter exchange >2 times	3.1 (1.2–15.6)	0.05
Procedure time	1.3 (0.9–3.8)	0.91

Throughout the study period the endothelial function of the non-catheterized arm remains normal, suggesting that the trans-radial catheterization causes only the localized endothelial dysfunction and a possibility of generalized impact of catheterization on vascular function, mediated via inflammation or oxidative stress, seems unlikely.

Interestingly, in our study FMD was significantly decreased but was not totally abolished. This is in agreement with previous experimental studies of FMD done after blocked NO function and studies done in eNOS knockout mice.[22] It has been postulated that some compensatory mechanisms, including the release of other endothelium-dependent vasodilators such as prostaglandins may come into play if the endothelial release of NO is impaired or absent. Our data raises a strong possibility of existence of some non-endothelium dependent vasodilatation during FMD.

Importantly, we found that transradial catheterization causes an increase in RA diameter as well as in upstream BA diameter in acute phase which can be explained by direct mechanical injury to arterial wall. At 3 months follow up, the diameter of right RA and BA returned to the basal level. These results are in agreement with Heiss et al[19] but in contrast to the results of study done by Wake-yama et al[8] which has shown that repeated transradial catheterization led to intimal thickening and luminal loss of the RA. Similarly, in a radial artery balloon angioplasty model study,

Table 5
Multivariate predictors for >50% fall in FMD at 24 h ($n = 22$).

Variable	Odds ratio (95% confidence interval)	p value
Age	1.1 (0.9–1.3)	0.47
Diabetes mellitus	1.1 (0.3–3.2)	0.23
Smoking	1.3 (0.3–15.8)	0.99
Radial artery diameter <2.5 mm	1.5 (1.1–5.5)	0.10
Radial artery diameter/sheath size <1	3.4 (0.5–16.3)	<0.01
Catheter exchange >2 times	2.8 (0.2–11.3)	0.04

damage induced by dilatation of radial artery triggered intimal hyperplasia and vascular remodelling.[23]

Our findings indicate that FMD as well as in NMD recovers completely after 3 months of the procedure. Previous studies in patients undergoing radial sheath insertion suggest a protracted recovery period. Recovery in endothelial dysfunction is expected to occur as early as 24 h of TRA and continue to occur up to 14 months after the procedure, although persistent impairment of RA function has also been reported.[10–15] Our results are in contrast to study by Burstein et al,[15] who noted a profound FMD impairment persisting at 9 weeks after procedure. However, our results are in agreement with previous studies done by Dawson et al[14] and Heiss et al[19] who found that endothelial and smooth muscle function recovers almost completely after 3 months of transradial catheterization.

In our study; radial artery diameter/radial sheath size <1 and catheter exchanges >2 times were the independent predictors for >50% decrease in FMD after trans-radial coronary angioplasty. These results are in total agreement to the results by Heiss et al.[19] In another study by Buturak et al, pre-procedural radial artery diameter to sheath size ratio was the independent predictor of NMD reduction.[13] One previous study showed that insertion of a 4-F sheath does not cause a decrease in FMD at 24 h, suggesting that the greater the size of the sheath the greater the inflicted injury to the RA.[11] Clinical implications of all these findings are that the number of catheters used should be kept to a minimum, and sheath size should be matched to the radial arterial diameter to protect vascular function and prevent potential arterial degeneration in the future.

The complete recovery of endothelial function (endothelial dependent as well as independent function) in the catheterized arm indicates that transradial catheterization should not be considered as an absolute contraindication to subsequent use of the radial artery as a bypass graft for CABG. However, some caution is required, as radial artery catheterization has been shown to produce intima medial thickening resulting in reduction in arterial lumen diameter[8] Despite good clinical outcomes, caution in using the radial artery as a graft is advocated by several groups due to its propensity to spasm, an increased likelihood of development of atherosclerosis, and damage induced by catheterization.[24,25] If possible, the RA should be avoided as a bypass graft for CABG for at least 3 months after transradial catheterization.

4.1. Limitations

There are few limitations to our study. Firstly, it was a relatively small study. Secondly, majority of patients were male. Thirdly, only 6F sheath was used in our study, so we could not evaluate the effect of sheath size. Further prospective studies with large number of patients are required to ascertain our results.

5. Conclusions

Transradial angioplasty results in reversible depression in endothelial dependent vasodilator function (FMD) as well as in endothelial independent vasodilator function (NMD) in the catheterized arm. This vascular dysfunction is not limited to the radial artery but also involves the upstream brachial artery. Radial artery diameter/radial sheath size <1 and catheter exchanges >2 are the independent predictors for reduction in FMD.

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None.
Abbreviations: FMD = flow mediated dilatation.
*For all *p* values < 0.05.

Abbreviations: NMD = Nitrate mediated dilatation.
*For all *p* values < 0.05.

Declaration of competing interest

None.

References

1. Valgimigli M, Frigoli E, Leonardi S, et al. Radial versus femoral access and bivalirudin versus unfractionated heparin in invasively managed patients with acute coronary syndrome (MATRIX): final 1-year results of a multicentre, randomised controlled trial. *Lancet.* 2018 Sep 8;392(10150):835—848.
2. Feldman DN, Swaminathan RV, Kaltenbach LA, et al. Adoption of radial access and comparison of outcomes to femoral access in percutaneous coronary intervention: an updated report from the National Cardiovascular Data Registry (2007-2012). *Circulation.* 2013;127:2295—2306.
3. Jolly SS, Yusuf S, Cairns J, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. *Lancet.* 2011;377: 1409—1420.
4. Romagnoli E, Biondi-Zoccai G, Sciahbasi A, et al. Radial versus femoral randomized investigation in ST-segment elevation acute coronary syndrome: the RIFLE-STEACS (Radial versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study. *J Am Coll Cardiol.* 2012;60: 2481—2489.
5. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J.* 2018;40(2):87—165, 2019 Jan 7.
6. Shimokawa H, Vanhoutte PM. Impaired endothelium-dependent relaxation to aggregating platelets and related vasoactive substances in porcine coronary arteries in hypercholesterolemia and atherosclerosis. *Circ Res.* 1989;64: 900—914.
7. Hariri RJ, Alonso DR, Hajjar DP, Coletti D, Weksler ME. Aging and arteriosclerosis. I. Development of myointimal hyperplasia after endothelial injury. *J Exp Med.* 1986;164:1171—1178.
8. Wakeyama T, Ogawa H, Iida H, et al. Intima-media thickening of the radial artery after transradial intervention. An intravascular ultrasound study. *J Am Coll Cardiol.* 2003;41:1109—1114.
9. Gaudino M, Leone A, Lupascu A, et al. Morphological and functional consequences of transradial coronary angiography on the radial artery: implications for its use as a bypass conduit. *Eur J Cardio Thorac Surg.* 2015 Sep;48(3): 370—374.
10. Okuyan H, Açikgoz SK, Tacoy G, Kocaman SA, Abaci A. Effect of transradial coronary angiography procedure on vascular diameter and vasodilator functions in the access site. *Angiology.* 2013;64(7):515—521.
11. Sanmartin M, Goicolea J, Ocaranza R, Cuevas D, Calvo F. Vasoreactivity of the radial artery after transradial catheterization. *J Invasive Cardiol.* 2004;16(11): 635—638.
12. Yan Z, Zhou Y, Zhao Y, Zhou Z, Yang S, Wang Z. Impact of transradial coronary procedures on radial artery function. *Angiology.* 2014;65(2):104—107.
13. Buturak A, Tekturk BM, Degirmencioglu A, et al. Transradial catheterization may decrease the radial artery luminal diameter and impair the vasodilatation response in the access site at late term: an observational study. *Heart Ves.* 2016 Apr;31(4):482—489.
14. Dawson EA, Rathore S, Cable NT, Wright DJ, Morris JL, Green DJ. Impact of catheter insertion using the radial approach on vasodilatation in humans. *Clin Sci (Lond).* 2010;118(10):633—640.
15. Burstein JM, Gidrewicz D, Hutchison SJ, Holmes K, Jolly S, Cantor WJ. Impact of radial artery cannulation for coronary angiography and angioplasty on radial artery function. *Am J Cardiol.* 2007;99(4):457—459.
16. Madssen E, Haere P, Wiseth R. Radial artery diameter and vasodilatory properties after transradial coronary angiography. *Ann Thorac Surg.* 2006;82(5): 1698—1702.
17. Pancholy S, Coppola J, Patel T, Roke-Thomas M. Prevention of radial artery occlusion-patent hemostasis evaluation trial (PROPHET study): a randomized comparison of traditional versus patency documented hemostasis after transradial catheterization. *Cathet Cardiovasc Interv.* 2008 Sep 1;72(3): 335—340.
18. Corretti MC, Anderson TJ, Benjamin EJ, 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(2): 257—265.
19. Heiss C, Balzer J, Hauffe 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(11):1067—1073.
20. Ichijo S, Yonetsu T, Murai T, et al. Impact of transradial catheterization on vascular function of the brachial artery assessed by flow-mediated dilatation. *Acta Cardiol Sin.* 2019 Mar;35(2):126—133.
21. Munoz-Mendoza J, Ghatak A, Miranda VP, et al. Time-course of vascular dysfunction of brachial artery after transradial access for coronary angiography. *Cathet Cardiovasc Interv.* 2016 Jan 1;87(1):101—106.

22. Sun D, Huang A, Smith CJ, et al. Enhanced release of prostaglandins contributes to flow-induced arteriolar dilation in eNOS knockout mice. *Circ Res*. 1999 Aug 6;85(3):288–293.

23. Pohl U, Holtz J, Busse R, Bassenge E. Crucial role of endothelium in the vasodilator response to increased flow in vivo. *Hypertension*. 1986;8(1):37–44.

24. Kobayashi J. Radial artery as a graft for coronary artery bypass grafting. *Circ J*. 2009;73(7):1178–1183.

25. Gardner TJ. Searching for the second-best coronary artery bypass graft: is it the radial artery? *Circulation*. 2007;115(6):678–680.