Evaluation of Peripheral Vascular Function After Distal Radial Artery Access for Invasive Percutaneous Coronary Procedures

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Abstract

Objective: The aim of this study is to investigate the difference in impact between distal transradial access (dTRA) and classical transradial access (TRA) on vascular function using flow-mediated vasodilation (FMD) following coronary diagnostic and therapeutic catheterizations.

Methods: The analysis involves a non-randomized inclusion of patients undergoing either diagnostic or elective percutaneous coronary intervention, using a dTRA access or a conventional standard TRA. Two hours after the procedure ended, the endothelium-dependent flow-mediated dilation of the brachial artery was measured by ultrasound.

Results: A total number of 50 patients were included. There was no statistically significant difference between the two groups (7.20% vs 6.99%, $p < 0.09$ for non-inferiority). Additionally, there were higher baseline values observed for BA diameters in the conventional approach group.

Regarding the other secondary endpoints, there were no major access site complications, radial occlusion, in-hospital major bleeding or severe arterial spasm recorded in both groups.

Conclusion: Compared to conventional TRA, accessing distal radial artery for diagnostic and therapeutic coronary interventions has the same impact on short-term vascular endothelial function and was safely performed without any major vascular complications.

Keywords

flow-mediated vasodilation, vascular dysfunction, distal radial artery, complex coronary interventions, railway sheathless

Abbreviations

FMD: flow-mediated vasodilation
BA: brachial artery
RA: radial artery
dTRA: distal transradial access
MACEs: major adverse cardiovascular events
PCI: percutaneous coronary intervention
RS: Railway™ system
RTT: RailTracking technique
TRA: transradial access
TFA: transfemoral access

Introduction

Transradial access (TRA) is becoming the access of choice for most coronary procedures due to reductions in vascular complications and major bleeding events [1,2]. In elective and acute settings, the TRA is strongly recommended by the European Guidelines [3].

However, there are some limitations of TRA, which include the presence of radial artery spasm (RAS) in up to 34% of cases [4] and a transient impairment of the endothelial function [5].

The endothelial dysfunction in patients undergoing transradial catheterization is related to local mechanical injury at the radial arterial access site, a locoregional release of inflammatory mediators induced by hand ischemia, and the systemic inflammatory response [5,6]. The arterial puncture and the mechanical effect of vascular sheath and catheters was related to histological changes in the radial artery: intimal hyperplasia, medial inflammation, and tissue necrosis.

A different vascular access – by distal radial artery (dRA) – has been used successfully, and results have been published recently in several articles [7,8].

The rationale to promote this technique is based on anatomic and physiological principles. Preservation of flow in the forearm radial artery without hand ischemia during the procedure and a significant decrease of RA occlusions are the most meaningful reasons to consider dTRA catheterization. Additional advantages are safer hemostasis with a decrease in bleeding complications and higher comfort for the patient [7].

Our group has previously published different techniques of distal radial access using a new technique called RailTracking (RTT): this is the use of the 6Fr and 7Fr Railway Sheathless (RS) access system (Cordis Corporation) [9]. The *razor effect*, which causes vessel wall trauma after catheters cross, seems, from a practical point of view, to be less pronounced after using the RTT [10].

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In our study we hypothesized that the main advantages of dRA over conventional proximal radial artery (absence of hand ischemia, preserved patency of the proximal radial artery) could have less negative impact on the endothelial function in comparison with conventional TRA percutaneous coronary interventions.

Methods

1. Design

The study was performed in a single Belgian center between June 2021 and October 2021. The analysis involves a non-randomized inclusion of patients undergoing either diagnostic or elective percutaneous coronary intervention, using a dTRA or a conventional standard TRA.

2. Trial Population

A total of 50 consecutive patients were included, each scheduled for either a diagnostic or percutaneous therapeutic coronary procedure. Two hours after the procedure ended, the endothelium-dependent flow-mediated dilation of brachial artery was measured by ultrasound.

Patients were excluded from the study if they had undergone previous radial cannulation in the past 12 months. Other exclusion criteria were: acute inflammation (C-reactive protein > 0.5 mg/dl), active malignancies, heart rhythm other than sinus rhythm, and heart failure of New York Heart Association functional class III to IV.

3. Conventional TRA

After assessment of the radial artery pulse, local anesthesia was applied by a subcutaneous injection of 0.5 ml lidocaine 2%.

Radial artery puncture and access were performed using the Radifocus 5Fr or 6Fr introducer sheet kit (Terumo, Tokyo, Japan), as per standard practice.

4. Distal TRA

Access to the dRA was made in the portion running through anatomical snuffbox located medially in the dorsal side of the wrist (fovea radialis). This area was identified by the edges of the tendon of the extensor pollicis longus posteriorly and the tendons of the extensor pollicis brevis and abductor pollicis longus anteriorly.

Firstly, the snuffbox was checked for the presence of distal radial pulse and, with the arm pronated, the area was disinfected. Then a 0.5 ml lidocaine 2% solution was injected subcutaneously together with 1mg of isosorbide dinitrate. The puncture was done with a 21-gauge bare needle from lateral to medial with an angle of ~ 35°. Care was taken to only puncture the anterior vessel wall, thus avoiding possible patient discomfort caused by contact of the needle with the periosteum of the trapezium and scaphoid bones.

After sheath insertion, all patients received intravenous administration of unfractionated heparin 5,000 U (in case of diagnostic procedures) and 100 U/kg (in case of planned percutaneous coronary interventions, at the start of the procedure, followed by ACT-related adjustments).

Verapamil 2 mg was administered intra-arterially in all patients at the moment of sheath insertion.

A prophylactic anxiolytic standard treatment with midazolam 1–2 mg was administered for all patients.

Diagnostic and/or PCI procedures were performed according to standard local practices.

Contrast products used were the same for all the cases. Additionally, for active smokers there was a minimal period of at least 12 h of smoking cessation required in order be included in the study.

5. Determination of vascular function with ultrasound

FMD was measured according to the guidelines [11]. As it is required for coronary procedures, measurements were performed while patients were fasting for at least eight hours.

Two hours after the TRA procedure, following a 10-minute equilibrium period, brachial artery diameter was measured at baseline and during post-reactive hyperemia, using a 12-MHz linear-array peripheral vascular probe (St. Jude Medical ultrasound system). All images were recorded using ECG-gating and were analyzed offline using manual measurements. Baseline heart rate and blood pressure were recorded. BA diameter was measured using intima-to-intima edges [11].

The transient ischemia was induced by inflating a forearm blood pressure cuff to 50mmHg above patient's resting systolic blood pressure for 5 minutes. Upon cuff release, images of long axis BA were recorded at 4, 8, 12, 16, 36, 56, 76, 96 seconds in cycles of 4 seconds.

BA baseline diameter was evaluated using 3 recordings of 10-second cycles. Maximum diameter from each cycle was noted and final diameter was calculated using an average of the three measurements [11].

BA diameter after cuff deflation was measured at each of the 8 cycles recorded. The largest diameter was noted from all the values recorded and it was used as the final value for FMD calculation [11]. Percent change in flow-mediated dilation (%FMD) was defined as the difference between maximal brachial artery (BA) diameter and the baseline BA diameter divided by BA baseline diameter x 100 [11].

All measurements were performed offline by a different, single operator who was blinded to the patients› information. No identification of a patient's access site was possible.

The validity of the measurements was assessed using a surrogate analysis by estimating intra-observer variability with Pearson *r* correlation coefficient.

All patients signed informed consents for participating in the study.

6. Statistical Analysis

Continuous variables are expressed as mean +/- standard deviation. Categorical variables are presented as absolute and relative values. Hypothesis testing for intergroup comparison was performed using independent samples for the Student t-test. Statistical analysis was performed using NCSS 2021 Statistical Software (2021 version, NCSS LLC, Utah USA). All the measurements were performed by

a single operator. Intra-observer reliability was measured using Pearson *r* correlation coefficient.

7. Study endpoints

The primary endpoint consists of intergroup comparison for the endothelial dysfunction measured by FMD at 2 hours after the procedures.

The secondary endpoints included the rate of access-site vascular complications. Also, for the secondary endpoint, a Visual Analog Scale (VAS) was used to assess discomfort/pain during the procedure localized anywhere distally to the elbow region. Results of the VAS scale were recorded at the end of the procedure.

Results

1. Baseline Clinical Characteristics (Table 1)

Between June 2021 and October 2021, a total of 50 consecutive patients were included in this study (1:1 ratio). The clinical characteristics of the study population are summarized in Table 1. There were no significant differences between the two groups.

2. Procedural characteristics (Table 2)

Twenty-three (46%) of the patients included underwent PCI procedures. dTRA was more frequently used in PCI cases (13 [26%] vs 10 [20%] $p < 0.087$). Additionally, longer total procedure times (26.7 +/-11.6 minutes vs 24.5 +/-19.9 minutes) were noted in dTRA, but without statistical significance. For 3 (6%) of the patients a 7Fr guide catheter was required, all of them from the dTRA group, and the sheathless system by RTT was used in all the cases.

Despite a trend for higher FMD values in the distal group, there was no statistically significant difference between the two groups (7.20% vs 6.99%, $p < 0.09$ for non-inferiority). Additionally, there were higher baseline values observed for BA diameters in the conventional approach group. Considering the formula used for FMD calculation, this aspect might partially contribute to the final neutral results observed in the present analysis.

Intra-observer average correlation as estimated with Pearson *r* was 0.83, suggesting a non-significant contribution of any subjective influences during vessel border measurements.

There were no acute access site–related complications. Also, no major vascular complications were noticed 24 hours after the interventions.

Clinically significant (visible and palpable local tumescence, accompanied by ecchymosis) hematoma was observed in 1 (2%) patient of the distal group patients and 2 (4%) in the conventional radial group ($p < 0.09$).

Procedural pain score (VAS scale, 1-10): The patients with dTRA complained of pain more frequently than the patients with TRA (3.1 ± 2.1 vs 2.8 ± 2.2, $p < 0.006$). Other secondary endpoints are listed in Table 3.

Regarding the other secondary endpoints, there were no events recorded in either group (major access site complications, radial occlusion, in-hospital major bleeding, severe arterial spasm).

Table 1 - Baseline Characteristics

Baseline Characteristics	Proximal Radial Artery Access	Distal Radial Artery Access
Number of Patients	25 (50%)	25 (50%)
Age (years)	64,74 ± 10,3	65,14 ± 8,3
Males	13 (26%)	15 (30%)
BMI (kg/m2)	28,7 ± 5,5	29,3 ± 4,8
Diabetes	6 (12%)	5 (10%)
Hypercholesterolemia	24 (48%)	19 (38%)
Triglycerides (mg/dl)	227 ± 112	217 ± 98
Total cholesterol (mg/dl)	190 ± 52	183 ± 45
HDL cholesterol (mg/dl)	56 ± 29	54 ± 25
LDL cholesterol (mg/dl)	135 ± 29	141 ± 22
Hematocrit (%)	44 ± 3	47 ± 4
Hypertension	16 (32%)	20 (40%)
Chronic kidney disease (CrCl < 60 ml/min/m2)	2 (4%)	3 (6%)
Acute coronary syndrome	4 (8%)	7 (14%)
Congestive heart failure	3 (6%)	1 (2%)
Tobacco abuse	6 (12%)	2 (4%)
Previous Stroke	1 (2%)	1 (2%)
Peripheral Arterial Disease	1 (2%)	1 (2%)
Prior PCI	12 (24%)	13 (26%)
Prior CABG	2 (4%)	1 (2%)
EF < 50 %	3 (6%)	1 (2%)
Medications		
Aspirine (%)	15 (30%)	22 (44%)
Clopidogrel (%)	9 (18%)	7 (14%)
Beta Blockers (%)	14 (28%)	11 (22%)
Nitrates (%)	8 (16%)	5 (10%)
Statins (%)	21 (42%)	17 (34%)
ACE inhibitors (%)	8 (16%)	12 (24%)
Calcium-channel blockers (%)	8 (16%)	3 (6%)
SBP, mmHg	134,4 ± 19,6	144,4 ± 18,6
DBP, mmHg	77,3 ± 11,7	76,4 ± 10,7
HR, bpm	75,0 ± 13,9	74,1 ± 12,9

Table 2 - Procedural and angiographic characteristics

	Proximal Radial Access	Distal Radial Access
Nr of patients	25 (50%)	25 (50%)
PCI	10 (20%)	13 (26%)
Diagnostic Catheterization	15 (30%)	12 (24%)
Procedural time, (min)	24,5 ± 19,9	26,7 ± 11,6 min
Contrast amount, (ml)	180 ± 89	177 ± 68
Left side access	2 (4%)	1 (2%)
Introducers and Catheters		
5Fr Introducer (n)	Per group 16 (32%)	18 (36%)
6Fr Introducer (n)	16 (32%)	0 (0%)
5Fr Catheter (n)	11 (22%)	10 (20%)
Therapeutic guide catheters used, (n)		
6Fr Catheter (n)	12 (24%)	14 (28%)
7Fr Catheter (n)	0 (0%)	3 (6%)
Sheathless procedures (n)	0 (0%)	13 (26%)
Railway Dilator used (n)	1 (2%)	12 (24%)
6Fr Railway Dilator (n)	1 (2%)	9 (18%)
7Fr Railway Dilator (n)	0 (0%)	3 (6%)

Table 3 - Clinical Outcomes at 30 days

Clinical Outcomes at 24 hours	Proximal Radial Access	Distal Radial Access
Radial occlusion	0 (0%)	0 (0%)
Major access site complication	0 (0%)	0 (0%)
Haematoma ≥ 2 cm	2 (4%)	1 (2%)
In-hospital major bleeding	0 (0%)	0 (0%)
Procedural pain score	2,8 ± 2,9	3,1 ± 2,1
Cross over to other access site	0 (0%)	0 (0%)
Severe radial artery spasm	0 (0%)	0 (0%)

Discussions

In the present study the endothelial function was assessed by FMD in patients undergoing proximal or distal transradial catheterization.

Apart from local mechanical injury at the entry site, impairments in endothelial function have been noted after TRA [5]. FMD has been proposed as a functional bioassay for endothelial function assessment [16]. Several studies have shown that endothelial function measured by brachial artery FMD is significantly decreased after conventional TRA [17, 18].

In the present analysis, we did not observe any significant differences between dTRA and conventional TRA with regard to the endothelial function as assessed by FMD. Although there is a small trend towards less endothelial dysfunction following dTRA (higher FMD values) there is no statistical significance which can be inferred from this.

This could be related to the characteristics of the TRA procedures, which were diagnostic angiograms in 54% of patients and short exams of 24.5 ± 19.9 minutes. The operators used, in the majority of cases, 5Fr and 6Fr catheters and there were no difficult technical scenarios encountered (for example, severe radial spasm). This aspect could also partly explain the absence of any proximal radial occlusion recorded during the study.

A different population study, with more complex procedures that require longer procedures and larger guide catheters, could maybe benefit in terms of endothelial function evaluation, at least in the short term, from a dTRA compared to conventional approach. But this hypothesis needs a clinical validation.

Post-procedural sequelae after TRA are a result of vascular or neurological distress and can range from cold intolerance or occasional hand discomfort [12–14] to complete radial occlusion [15].

As already reported, fewer local adverse events are observed during the dTRA approach.

To our knowledge, this is the first comparison between conventional and dTRA using an assessment of the vascular endothelial function.

Limitations of the study are firstly related to the fact that baseline, preprocedural FMD was not assessed, so that the effects of TRA per se cannot be fully estimated in this study. The FMD measurements were all performed shortly after the procedure. An ongoing effect of the administered vasoactive substances is expected, and might have influenced the results. This state of increased arterial reactivity could explain the higher FMD values recorded in both groups compared to what has been previously reported [17, 18]. Nevertheless, using similar conditions for both groups might have had an autocorrecting effect on the final results. The quantity of contrast and potential differences between the quantities of vasoactive medications were not recorded in this analysis. Other limitations include the small number of patients included, and the open non-randomized study design. Lastly, the operators were experienced in both distal and conventional TRA, possibly making the results not widely applicable.

Conclusions

Compared to conventional TRA, accessing the distal radial artery for diagnostic and therapeutic coronary interventions has the same impact on short-term vascular endothelial function, and was safely performed without any major vascular complications.

Conflict of interest

none declared.

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