Biochemical and clinical evaluation of endothelial injury after distal or traditional transradial access in percutaneous interventions

Karol Momot[1], Maciej Zarębiński[2], Krzysztof Flis[2], Katarzyna Czarzasta[1], Liana Puchalska[1], Małgorzata Wojciechowska[1]

[1]Laboratory of Center for Preclinical Research, Department of Experimental and Clinical Physiology, Medical University of Warsaw, Warszawa, Poland
[2]Department of Invasive Cardiology, Lazarski University, John Paul II Independent Public Specialist Western Hospital, Grodzisk Mazowiecki, Poland

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Ruzsa et al.,
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Correspondence to:
Maciej Zarębiński, MD, PhD,
Department of Invasive Cardiology,
Lazarski University,
John Paul II Independent Public Specialist Western Hospital,
Daleka 11, 05–825 Grodzisk Mazowiecki, Poland,
phone: +48 22 755 92 90,
e-mail: maciej@zarebinski.pl

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ABSTRACT

Background: Distal transradial access (dTRA) has been proposed as an alternative to traditional transradial access (TRA) in cardiac catheterization.

Aims: The study aimed to compare these two transradial approaches: TRA and dTRA in terms of clinical and biochemical aspects.

Methods: Two hundred patients who qualified for the elective coronary procedure were included. The patients were assigned to one of the groups depending on their vascular access. The groups were compared in terms of perceived pain using the Visual Analogue Scale (VAS), time of gaining access, need for conversion, and local complications. Additionally, in forty patients circulating endothelial injury markers: endothelin 1 (ET-1), interleukin 8 (IL-8), and soluble vascular cell adhesion molecule-1 (sVCAM-1) were assessed.

Results: Successful cannulation was obtained in 84 (100%) in the TRA group and in 98 (84%) subjects in the dTRA (P <0.001). dTRA was associated with higher level of pain perceived at the time of gaining vascular approach than TRA; median VAS score (interquartile range [IQR]): 4 (2–5) vs. 2 (2–4) (P = 0.04). The mean time (standard deviation [SD]) needed to cannulate the artery in dTRA was longer than in TRA: 81 (8) seconds vs. 50 (4) seconds (P = 0.04). ET-1 concentration was (SD) 2.08 (0.19) pg/ml [dTRA] vs. 2.00 (0.29) [TRA] pg/ml (P = 0.83); sVCAM-1: 12.71 (3.97) ng/ml vs. 12.86 (4.29) ng/ml (P = 0.98); IL-8: 8.81 (0.42) ng/ml vs. 9.15 (0.52) ng/ml (P = 0.62). Th number of complications after procedures did not differ between these two approaches.

Conclusions: Cannulation of dTRA is associated with a lower success rate and higher pain perceived. dTRA is not inferior to TRA when safety issues and vascular injury are considered.

Key words: percutaneous interventions, coronary angiography, radial access

INTRODUCTION

A vast increase in the number of percutaneous diagnostic and therapeutic procedures performed within the last two decades has led to the need for arterial access associated with decreased complication rates and shorter postoperative care. The advantages of radial artery access over femoral have been well proven. The radial cannulation, which is predominantly used in coronary interventions, may be complicated by occlusion of the artery. The occlusion rate increases with repeating interventions. The distal transradial access (dTRA) (Figure 1) via the anatomical snuffbox decreases this complication rate even more, and it has been proposed as an alternative to

WHAT'S NEW?

This study provides a wider perspective on distal transradial access in percutaneous interventions. This report is the first one that compares transradial approaches in terms of endothelial injury. We list advantages and disadvantages of distal and traditional transradial access. We confirm that new distal transradial access should be widely used in invasive cardiology and radiology.

Figure 1. Distal transradial access

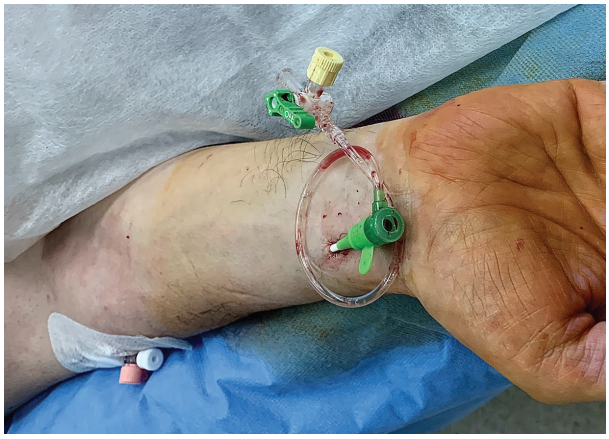

Figure 2. Traditional transradial access

traditional transradial access (TRA) (Figure 2) in percutaneous interventions. The anatomical snuffbox is located on the radial side of the wrist, it is bounded by the tendon of the extensor pollicis longus posteriorly and of the tendons of the extensor pollicis brevis and abductor pollicis longus anteriorly. The radial artery crosses the floor that is formed by the scaphoid and the trapezium bones [1].

First studies pointed out that dTRA was associated with an increased rate of cannulation failure, prolonged duration of cannulation, increased number of attempts and skin punctures compared to the TRA [2]. This was mainly due to the smaller diameter of the vessel, tortuosity of the radial artery in the area of the anatomical snuffbox, and operators' lack of experience. There are no data comparing the two accesses in terms of endothelial damage. During percutaneous intervention and hemostatic compression, mechanical stress on the cannulated vessels occurs. It is caused by the needle puncturing the artery wall, the sheath inserted in the lumen of the artery, and external pressure of the dressing. Studies show that after exposure to stress factors, the endothelium releases numerous substances like cytokines which can be assessed in blood plasma [3–9]. We believe that these substances are also released during percutaneous interventions.

In this study, concentrations of markers of endothelial injury were measured. This is a novel perspective as it is the first comparison of the analyzed percutaneous approaches based on biochemical assessment. The markers: endothelin 1 (ET-1), interleukin 8 (IL-8), and soluble vascular cell adhesion molecule-1 (sVCAM-1) were chosen based on relevant literature.

METHODS

Study patients

Two hundred adult patients, scheduled for elective coronary angiography or angioplasty, were recruited. Procedures were performed between November 2020 and April 2021. Participants signed written informed consent forms. The study was approved by the local Ethics Committee (no. KB/167/2020). Patients with estimated glomerular filtration rate (eGFR) <30 ml/min/1.73 m^2, dialyzed, with coronary artery bypass grafting (CABG), and/or diagnosed with active cancer were not included in this study. Based on research carried out by Koutouzis et al. [2] and our experience with the lack of distal pulse and the need for conversion from distal to traditional access, all qualified patients were allocated, by block randomization at a 3:2 ratio, into two groups of 120 and 80 patients receiving a dTRA and TRA approaches, respectively. Four subjects out of 120 initially assigned to the dTRA approach did not present a palpable pulse in an anatomical snuffbox before the procedure, and they were reassigned to the TRA group without any attempts to cannulate dTRA. Therefore, operators attempted to obtain 116 distal approaches and 84 traditional approaches. After a failed attempt to cannulate dTRA, these subjects were converted to TRA and were included in a third group named conversion (n = 18). Thus, the final dTRA group included 98 subjects. Demographic data of the patients are presented in Table 1. In 40 random patients (20 from the dTRA group and 20 from the TRA group) after the dressing removal, blood from the cephalic vein was collected and plasma concentrations of ET-1, IL-8, sVCAM-1 were determined using the enzyme-linked immunoassays (ELISA).

Table 1. Demographic data

Characteristics	TRA group (n = 84)	dTRA group (n = 98)	Conversion group (n = 18)	*P*-value
Age, years, mean (SD)	67 (10)	65 (10)	63.3 (9)	0.20
Male sex, n (%)	53 (63)	63 (64)	8 (44)	0.31
BMI, kg/m^2, mean (SD)	29.4 (5.7)	29.0 (5.2)	28.6 (6.4)	0.83
Obesity, n (%)	29 (35)	30 (31)	5 (28)	0.65
Current smoking, n (%)	40 (48)	35 (36)	6 (33)	0.21
Lipid disorders, n (%)	38 (45)	44 (45)	6 (33)	0.60
Diabetes or prediabetes, n (%)	30 (36)	27 (28)	4 (22)	0.35
Hypertension, n (%)	58 (69)	73 (74)	12 (66)	0.54
CKD, n (%)	4 (5)	9 (9)	1 (6)	0.36
Medications				
ASA, n (%)	40 (48)	62 (63)	10 (56)	0.13
ADP/P2Y inhibitors, n (%)	13 (15)	23 (23)	3 (17)	0.38
NOAC, n (%)	11 (13)	12 (12)	2 (11)	0.96
Statins, n (%)	38 (45)	44 (45)	6 (33)	0.60

Abbreviations: ADP, adenosine diphosphate; ASA, acetylsalicylic acid; BMI, body mass index; CKD, chronic kidney disease; dTRA, distal transradial access; NOAC, non-vitamin K antagonist oral anticoagulants; TRA, traditional transradial access

Procedure

The procedures of coronary interventions without ultrasound guidance were performed by European Association of Percutaneous Cardiovascular Interventions (EAPCI) certified operators, using radial access in more than 95% of routine procedures. The sheath size used for all the procedures was 6 F. Time needed to gain vascular access was assessed. The amount of injected contrast and the total radial dose were recorded. After the procedure, a pressure dressing was applied to the puncture site. The dressing was removed after 120 minutes. The puncture site was assessed for the presence of hematoma and pulse. After the removal of the dressing, 10 ml of blood from the cephalic vein was collected into tubes with EDTA-K2 anticoagulant and then centrifuged. Samples with obtained plasma were immediately frozen and stored at –20°C until the moment of biochemical assessment. Plasma concentrations of markers were analyzed using ELISA: IL-8 Human ELISA Kit (KHC0081; Thermo Fisher Scientific, Inc., Waltham, MA, US), Human sVCAM-1/CD106 ELISA Kit (MBS2505831; MyBioSource, San Diego, CA, US), and Endothelin-1 Quantikine ELISA Kit (DET100; R&D Systems, Inc., Minneapolis, MN, US). Each ELISA test was carried out in accordance with the instructions provided by the manufacturer.

Statistical analysis

Quantitative variables are presented as medians (interquartile range [IQR]) or means (standard deviation [SD]). The ANOVA test (normal distribution) and the Kruskal–Wallis H test (non-normal distribution) were performed in the comparison of numerical variables between the three groups. Appropriate *post-hoc* tests were then performed (Dunn and Tukey tests, respectively). Student t-test (normal distribution) and the Mann–Whitney U test (non-normal distribution) were used to perform inter-group comparisons. Equality of variances was assessed by Levene test. Categorical variables are expressed as numbers and percentages and compared using the χ^2 test. Statistical data were considered significant with a *P*-value <0.05. All statistical analyses were performed using Statistica 13 software.

RESULTS

The success rate of obtaining a vascular approach in the dTRA group was 84% and 100% in the TRA group (*P* <0.001). In eighteen dTRA subjects (16%) operators failed to gain vascular access. The approach was changed to TRA, and then access was successfully gained. These eighteen subjects were included in the third group named "conversion". Data on the procedure: the mean time required to gain the access, local complications, pain when gaining the vascular approach and during the maintenance of pressure dressing are presented in Table 2. The results of the biochemical evaluation are presented in Figure 3. Regardless of the approach, concentrations of endothelial markers were not correlated with smoking, diabetes, hypertension, kidney disease, or coronary disease. Subjects treated with statins had lower ET-1 concentration (SD) than subjects without statin therapy, irrespective of the access: 1.63 (0.24) pg/ml vs. 2.33 (0.21) pg/ml (*P* = 0.04). Subjects with obesity had higher levels of IL-8 than those without obesity, regardless of the approach (*P* = 0.04) (Figure 4).

DISCUSSION

Markers of endothelial injury

At the moment of publication, several studies have compared these two approaches. However, this research is the first one that provides a closer look at them in terms of endothelial injury. The aim was to evaluate selected markers of vascular injury, dysfunction, and inflammation between patients after distal transradial access and traditional transradial access. It is assumed that during percutaneous interventions endothelial injury, inflammation, and dysfunction are caused by vascular sheath and catheter insertion and hemostatic compression. These factors are closely linked to mechanical stretch, shear stress, and external pressure,

Table 2. Characteristics of procedures

Characteristics	TRA group (n = 84)	dTRA group (n = 98)	Conversion group (n = 18)	*P*-value
Time needed to gain vascular access, seconds, mean (SD)	50 (4)[1]	81 (8)	277 (51)[2, 3]	<0.001
Hematoma after procedure, n (%)	5 (6)	12 (12)	4 (22)	0.09
Radial artery occlusion after procedure, n (%)	2 (2)	3 (3)	1 (6)	0.78
VAS 1 score, median (IQR)	2 (2–4)	4 (2–5)	4 (2–5)	0.04
VAS 2 score, median (IQR)	2 (1–4)	2 (1–4)	2 (2–4)	0.57
Revascularization with stent implantation, n (%)	34 (40)	40 (41)	5 (28)	0.57
Radial dose during procedure, mGy, mean (SD)	958 (115)	888 (79)	630 (161)	0.37
Amount of contrast during procedure, ml, mean (SD)	110 (6.6)	117 (6.8)	101 (12.4)	0.50

[1]TRA vs. dTRA, *P* = 0.04. [2]dTRA vs. Conversion, *P* <0.001. [3]TRA vs. Conversion, *P* <0.001

Abbreviations: VAS, Visual Analogue Scale; VAS 1, pain at the time of gaining vascular approach; VAS 2, pain during the maintenance of pressure dressing; other — see Table 1

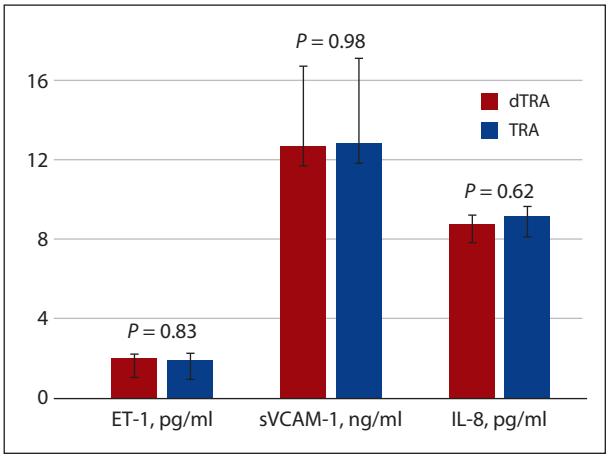

Figure 3. Biochemical evaluation of endothelial markers depending on the approach, 15 minutes after removal of hemostatic compression

Abbreviations: ET-1, endothelin 1; IL-8, interleukin 8; sVCAM-1, soluble vascular cell adhesion molecule-1; other — see Table 1

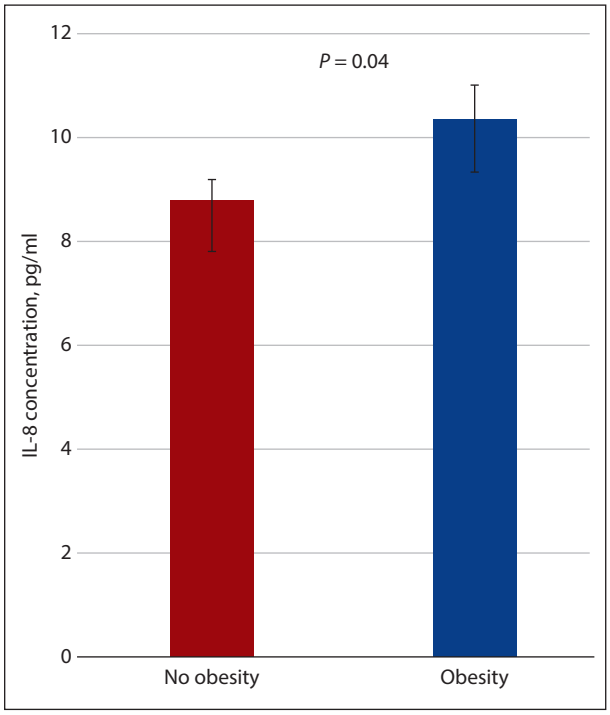

Figure 4. Interleukin-8 concentration regardless of the approach, 15 minutes after removal of hemostatic compression

Abbreviations: see Figure 3

which are factors stimulating release of endothelial injury markers in vitro. The choice of these markers was based on the literature found via PubMed, ScienceDirect, Scopus, or Google Scholar.

Endothelin 1

ET-1 is produced mainly by vascular endothelial cells (ECs), and it is considered the most common ET in humans. This particle is frequently assessed in diagnostics of endothelial dysfunction, injury, or inflammation. At the normal state, ET-1 is mainly secreted abluminally towards the vascular smooth muscles, and its levels in the blood are fairly low. However, in the case of endothelium stimulus, ET-1 is released into the blood from ECs [6, 10]. The mechanical strain of the vessel damages the vascular wall and stimulates secretion of ET-1 from ECs [11, 12]. Previous studies also indicate shear stress as a factor promoting ET-1 production [7, 8].

Soluble vascular cell adhesion molecule-1

sVCAM-1 is a circulating particle derived from damaged or activated ECs [3]. Damaging the endothelial glycocalyx of vessel walls leads to an increase of sVCAM-1 levels [13]. Shear stress is also the factor that stimulates sVCAM-1 from ECs [9]. Elevation of blood pressure activates the expression of adhesion molecules [14]. Prolonged mechanical wall stretch promotes VCAM-1 gene expression in ECs [15]. sVCAM-1 plays an important role in accelerating atherosclerosis by facilitating the attachment of inflammatory cells to the vascular endothelial wall and promoting their subsequent migration through the endothelium [16].

Interleukin 8

IL-8 is a proinflammatory chemokine produced by ECs. IL-8 is stored inside ECs, and ET-1 promotes releasing this chemokine *in vitro* [17]. Elevated levels of IL-8 have been found in the area of the injured endothelium [5]. The IL-8 concentration starts to increase 1 hour after the exposure to the stress factor, and it is caused by IL-8 gene expression [18]. External mechanical pressure on the ECs significantly raises IL-8 secretion from these cells *in vitro* [4]. IL-8 levels are increased as a result of many inflammatory conditions, so careful exclusion criteria for patients are required. Platelet-derived microparticles (PMPs), which are produced in the case of shear stress, induce IL-8 secretion by ECs [19]. IL-8 is a proinflammatory cytokine with atherogenic effects, it accelerates the movement of neutrophils and T lymphocytes under the endothelium and promotes monocyte adhesion to the vascular wall.

General

There were no statistically significant differences between the dTRA and TRA groups in the number of cases of hematoma, lack of the distal pulse after interventions, the mean amount of contrast used, and radial dose. The findings were similar to the results in other studies [2, 20]. Researchers point out that the cannulation time was longer in the dTRA group, which was also in line with our observations [20]. In our research, the level of pain at the time of gaining the vascular approach was significantly higher in the dTRA and conversion groups. The longer time of cannulation and more severe pain during the procedure can be probably explained by less experience of operators in using dTRA. Additionally, in some subjects, inexperienced operators had to make conversions when using dTRA. Probably anatomical characteristics of the radial artery in the snuffbox (tortuosity and small diameter) make the distal approach more complicated and require more experience from operators. In line with the results of other studies, operators should practice gaining a distal approach to obtain the same successful cannulation rate, level of pain, and time needed to gain access as in TRA [21, 22]. The advantage of dTRA postulated in other studies is shorter hemostatic compression after the procedure, but in the presented report it was identical in all patients as we wanted to provide the same conditions for biochemical and pain assessment [20, 23]. dTRA offers two more forearm approaches to evaluate, and this may reduce the need for femoral artery cannulation. If the radial artery occlusion has occurred during TRA, dTRA provides a possibility to recannulate the occluded radial artery [23]. dTRA offers the option to have the patient's left hand close to the right groin, which is more comfortable for the patient and the operator. dTRA is also beneficial for right-handed patients whose dominant upper limb is without immobilization during hemostatic compression [1]. The radial artery gives branches before entering the anatomical snuffbox; therefore, occlusion after dTRA is related to a smaller area of ischemia than after TRA. Since a standard sheath size of 6 F allows most coronary interventions, dTRA may probably serve as a good choice also for complicated high-risk procedures. The safety cannulation with a larger sheath has not been tested in our study, but with the use of thin-walled sheaths, it seems quite possible to apply advanced intravascular techniques, which require a larger lumen. Januszko et al. showed that TRA, as opposed to femoral access, is related to a higher risk of coronary artery perforation in patients treated with rotational atherectomy [24]. As this complication may also refer to using dTRA, future studies should be conducted.

There were no differences between dTRA and TRA in the plasma markers of endothelial injury. This means that in both groups the endothelial damage was similar and that in terms of biochemical assessment, dTRA is at least as safe as TRA. Regardless of the approach, elevated IL-8 levels in obese patients suggest that obesity may be connected with greater damage to the endothelium, but it cannot be excluded that IL-8 is constantly elevated in obese subjects, which would be in agreement with other studies [19]. Furthermore, patients treated with statins have significantly lower levels of ET-1 than patients without this treatment, which confirms that statin therapy reduces vascular inflammation [25].

The main limitations of this study were the lack of biochemical evaluation before percutaneous intervention and small sample size.

CONCLUSIONS

There were no differences between dTRA and TRA in the quotative markers of local endothelial injury. dTRA was more painful for the patient during the cannulation, but the difference should diminish as the operators gain experience. Consequently, the choice of dTRA is as good as that of TRA. Considering dTRA advantages listed in the discussion, it should be widely used in percutaneous interventions in invasive cardiology, neurology, and radiology.

Article information

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