Distal Radiation Access as an Alternative to Conventional Radial Access for Coronary Angiography and Percutaneous Coronary Interventions (According to TENDERA Trial)

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Abstract: The aim of this study was to assess the immediate and medium-term (3 months) results of the safety and efficacy of distal radial access (DRA) in coronary interventions compared with conventional transradial radial access (TRA). TRA is the recommended access for coronary procedures because of increased safety: fewer local complications, large and small bleeding. Recently, DRA has emerged as a promising alternative access to minimize radial artery occlusion (RAO) risk, as well as other complications. A large-scale, international, randomized trial comparing medium-term

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results with TRA and DRA is lacking. An analysis of 776 patients of the prospective randomized TENDERA trial was carried out: the distal artery access group (DRA) - 391, the transradial access group (TRA) - 385. Statistically more often the crossover access was in the DRA group (5.1% and 0.8%, $P < 0.001$). The primary endpoint was early or late thrombosis/occlusion of the radial artery (RA). Secondary endpoints: (1) composite complications from access vessels; (2) access parameters. Statistically significant differences were obtained for the primary endpoint: DRA 2.7% (n = 10), TRA 6.8% (n = 26), $P = 0.008$. Occlusion of the distal radial artery (DRAt), with patent RA: DRA 1.3% (n = 5), TRA 0 (0), $P = 0.023$. At the secondary composite endpoint, statistically significant differences were obtained for the following groups of complications: BARC type I bleeding (DRA: 3.8% (n = 14), TRA: 21.7% (n = 83), $P < 0.001$); hematoma larger than 5 cm on day 1 (DRA: 10% [n = 37], TRA: 25.9% [n = 98], $P < 0.001$); hematoma larger than 5 cm on day 7 (DRA: 12.4% [n = 45], TRA: 34.6% [n = 132], $P < 0.001$). Of the access parameters, the following statistically significantly differed: puncture time DRA 19.0 (8.0; 50), TRA 13.5 (5.0; 29), $P < 0.001$; insertion of introducer DRA 42.0 (26.0; 84.0), TRA 35.0 (23.0; 55.0), $P < 0.001$, access artery hemostasis duration (min.) DRA 180.0 (120.0; 480.0), TRA 155.0 (115.0; 195.0), $P < 0.001$. The duration of the procedure and fluoroscopy, radiation dose, RA spasm in both groups had no statistically significant differences. In the TENDERA trail, DRA demonstrated efficacy and safety in interventional coronary interventions compared with TRA in the medium-term follow-up period: a statistically significant lower incidence of RA occlusion and local complications. (Curr Probl Cardiol 2023;48:101546.)

Introduction

For many decades, the femoral artery has been the access of choice for the interventional cardiologist.[1] With the increase in the number of coronary angiography (CAG), and subsequently percutaneous

coronary interventions (PCI), the number of access-related complications began to increase, including those fatal due to massive bleeding.[2-4]

The 1990s were marked by a new era - the era of the beginning and development of transradial access (TRA) in endovascular surgery, primarily due to Lucien Campeau[5] and Ferdinand Kiemeneij.[6] TRA in many countries quickly began to gain popularity due to greater comfort for patients, rapid activation and reduction of hospital stay, reduction in the number of complications, especially bleeding, which became important due to the active use of antiplatelet and anticoagulant therapy.[7,8] However, some interventional cardiologists in the developed countries of Europe and North America remained conservative, so it took more than 2 decades to form a reliable evidence base for the efficacy and safety of TRD so that it could be used as the preferred access for any PCI, regardless of the clinical picture, according to the ESC / EACTS recommendations on myocardial revascularization.[9]

In addition, the radial artery (RA), due to its small diameter and variable anatomy, is also not without certain complications, such as spasm, dissection, and perforation, which can lead to a change in access and prolongation of the procedure.[10] However, the most common complication with the use of TRD remains early and late RA occlusion (RAO), the frequency of which varies in different studies from 5% to 30%.[11] In the absolute majority of RAO, it is asymptomatic, but RA itself is problematic to reuse for any endovascular interventions in the future, and it is also completely impossible in the formation of an arteriovenous fistula in a dialysis patient or as a conduit for coronary bypass graft.[12]

About 10 years ago, independently of each other, 3 Russian interventional surgeons (Babunashvili A., Kaledin A., Korotkikh A.) began to actively use access through an anatomical snuffbox in endovascular interventions, having conducted the first retrospective studies that revealed certain advantages (reduction in the number of local complications) of the new approach.[13-16] In 2017, there was a surge in popularity of DRA around the world, with scientific articles on case series, retrospective studies, meta-analyses, and a small number of prospective studies comparing DRA in the field of anatomical snuffbox and conventional TRA. Subsequently, puncture in DRA was modernized and began to be performed even more distally - in the first interdigital space of the dorsal surface of the hand.

Currently, DRA is actively used not only in diagnostic studies and PCI in stable patients, but also in the treatment of acute coronary syndrome (ACS) with ST segment elevation,[17] oncopathology,[18] neurointerventional,[19,20] and peripheral procedures.[21]

Nevertheless, all the conducted retrospective studies have 1 big drawback - the duration of the observation does not exceed several days after the procedure. The last largest DISCO RADIAL study was published in June 2022, and the follow-up period does not exceed 30 days.[22] The study itself has a number of limitations, due to which, in our opinion, it did not show a statistically significant difference in the primary endpoint - RAO in the DRA and TRA groups.

The aim of this work is to evaluate the immediate and medium-term (3 months) results of safety and efficacy of DRA in coronary interventions compared with conventional TRA according to the TENDERA study.

Materials and Methods

Study Design and Oversight

TENDERA (Traditional ENtry point and Distal puncturE of Radial Artery) trial (NCT04211584) is a prospective, multicenter, open-label RCT designed to evaluate the benefits of DRA versus TRA in terms of the incidence of forearm RAO up to 1 year after the procedure. The recruitment period for the study is from December 2017 to October 2021. In 2021, interim data from the TENDERA trial were published, which showed a statistically significant lower number of local complications of DRA.[23] In this article, a mid-term analysis (3 months) of patients included in the study was carried out.

Investigated accesses require certain qualification skills and work experience from the surgeon. Criteria for the selection of surgeons for the study: (1) regularly performs a wide range of interventions for TRA in the coronary arteries, including the treatment of ACS; (2) except for the TRA, he owns all other accesses at a high level (ulnar, femoral, etc.); (3) performed at least 100 DRA procedures.

The main hypothesis of the entire study is that TRA is superior to DRA in terms of incidence of forearm RAO at follow-up up to 1 year. For the TRA group, the incidence of RAO at 1 year was assumed 5%, derived as an average value based on a large number of studies over the past 10 years. For the DRA group, the incidence of RAO was assumed 1.5%. There are currently no studies with a follow-up period of more than 1 month for DRA, and in the available ones - RAO is about 1%. However, we believe that for periods up to 1 year, the number of RAO will increase, so the percentage of RAO has been increased. For a statistical power of 80%, a 2-sided error of the first kind Alpha of 0.05%, and a censoring of 5%, 422 patients per group are needed. Thus, the total sample size was 850 patients. In this article, we analyzed 776 patients in the primary

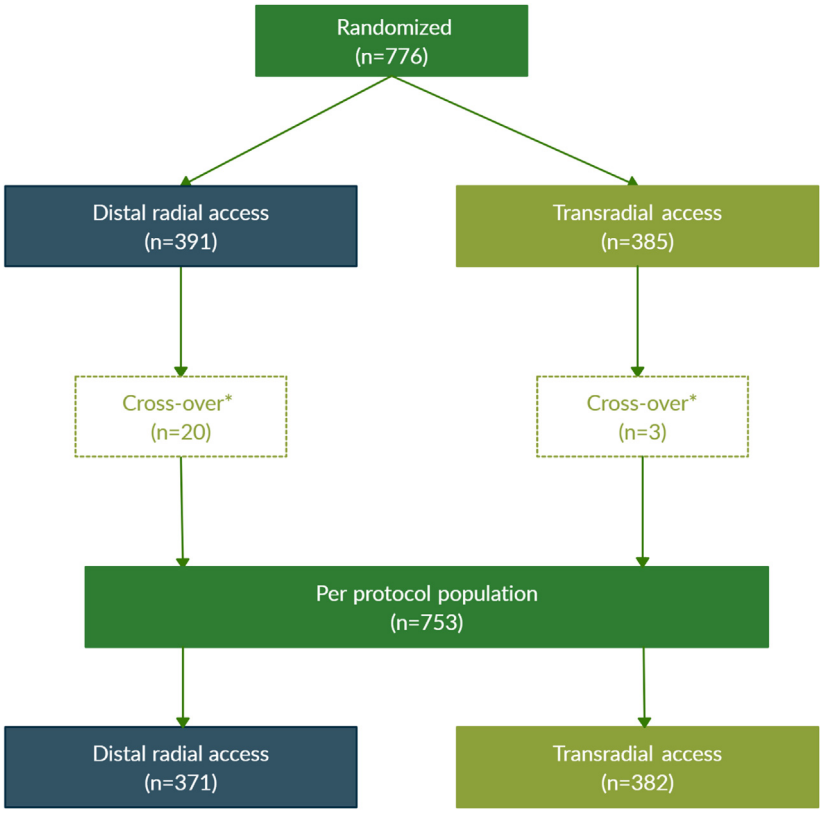

FIG. 1. Study flowchart.
Note: *crossover was defined as initial failure to obtain vascular access, after which access was obtained from the contralateral arm or from another artery. (Color version of figure is available online.)

sample (taking into account the results obtained, the actual power of the study was 90.2%) (Fig. 1).

Trial Population and Randomization

The study included patients who underwent CAG or PCI using a hydrophilic introducer 5F or 6F (surgeons used the following types of introducers Radifocus Introducer II Coat, Terumo; Prelude Ease, Merit Medical; Brilliant, Lepu Medical Technology) through DRA and TRA. Inclusion criteria: patient age from 18 to 90 years without hereditary coagulopathy; previously unused RA with a diameter at the puncture site $\geq$1.5 mm; the presence of antegrade passable at least 2 main arteries of the forearm. Exclusion criteria: severe somatic condition or severe

comorbidity, which may lead to noncompliance with the study protocol and/or distort the interpretation of data; inability to perform RA puncture for any reason; uncompensated coagulopathy; ST-segment elevation myocardial infarction; the only passable RA; the patient's height is more than 195 cm. Patients were followed until hospital discharge.

Eligible patients were randomly assigned in a 1:1 ratio to DRA vs TRA. Concealed allocation of study treatment was performed using a web-based interactive randomization system. Randomization was achieved with a computer-generated random sequence with a random block size stratified at site level.

The ethics committee at each trial center approved the protocol, and the study was conducted according to the Declaration of Helsinki. All patients provided written informed consent.

Trial Procedures

Before the puncture, all patients were assessed under ultrasound control of the RA of the forearm and hand, while which access to use - right or left, was decided directly by the operator. Intravenous access for the administration of medications was recommended in the contralateral arm. The puncture was recommended to be performed only with a puncture of the anterior wall of the artery, if not possible, according to the classical Seldinger technique.

DRA was performed not in the area of the anatomical snuffbox, but in the more distal part, in the first interdigital space of the dorsal surface of the hand; under local anesthesia, a puncture was performed with an entry angle of 15˚-30˚ to the skin in the direction of maximum pulsation. All operators tried to perform the puncture as atraumatically as possible for the periosteum of the carpal bones, the injury of which causes increased pain and can lead to RA spasm. The classical RA puncture was performed according to the standard technique at a point 2 cm above the styloid process.

After installing a hydrophilic introducer during CAG, 5000 IU of unfractionated heparin was necessarily injected intra-arterially, during PCI - from 7500 IU and above until the Activated Coagulation Time (ACT) of 250-300 seconds was reached. In long-term procedures, such as recanalization of chronic coronary occlusion or complex bifurcation stenting, ACT was determined every hour and, if necessary, additional unfractionated heparin was administered intravenously.

The administration of 200 mg nitroglycerin and/or 5 mg verapamil to prevent spasm was at the discretion of the operator, and more often occurred already at the initial signs of RA spasm.

The puncture was considered successful when the sheath was inserted into the target artery. If it was not possible to successfully catheterize a randomized access site due to any reason, then all attempts to obtain vascular access at a different point on this or the contralateral limb were considered a change of access.

During the procedure, the following angiographic studies were performed related to the access artery, according to the protocol: after the insertion of the introducer - the access artery (RA and forearm arteries), in case of severe tortuosity or anomaly in the anatomical course of the brachiocephalic branches, the final diagnostic angiography of the access artery before removal of the introducer.

The introducer was removed from the RA immediately after the procedure was completed. Since at the beginning of the study in the Russian Federation there were no specialized branded devices for hemostasis during DRAt puncture, a pressure gauze bandage was used for 2 hours for CAG or for 4 hours for PCI. After that, the bandage was removed and an aseptic sticker was applied. In case of continued bleeding after removing the bandage, the latter was applied again for another 2 hours until complete hemostasis. In the case of TRA, patent hemostasis was used (patented devices from Terumo, Merit Medical or Lepu Medical Technology). The hemostatic device was applied without pressure change for 2 hours after CAG and for 4 hours of PCI. Subsequently, air was released (reducing the pressure in the pad) gradually using the attached special syringe (Terumo, Lepu Medical Technology) or by gradually unscrewing the wheel (Merit Medical).

The trial assessed directly periprocedural and long-term outcomes: history data, risk factors, local status with mandatory Doppler ultrasound, drug therapy, access artery catheterization parameters, angiography and PCI data, complications, patient comfort scale and dynamometry. All patients included in the study with successful catheterization of the target artery had to be observed on the day of discharge, on the 7th day after the puncture and after 3 months. Cholesterol, creatinine, arterial hypertension, ACS, diabetes mellitus, and smoking were chosen as risk factors that can affect the patency of the target artery.

The trial used the following scale for assessing pain or discomfort at the RA puncture site for the patient: 0 - no pain and/or discomfort; (1) episodic pain (immediately after completion) and passed within 60 minutes; (2) there is pain (feeling of discomfort), but it is tolerable and

does not require special measures; (3) pain (feeling of discomfort) is present, but disappears after a single application of an anesthetic; (4) pain (feeling of discomfort) is present and requires repeated use of an anesthetic drug; (5) pain disturbing the patient's comfort, despite analgesic therapy.

The force of compression of the hand and fingers by the patient was checked before the procedure and subsequently at all stages of control, it was estimated in kg. The following dynamometers were used in the study: Jamar Hydraulic Hand Evaluation Kit and KYTO EH101.

Trial Endpoints

The primary endpoint was immediate (in-hospital) or late RA thrombosis/occlusion, as assessed by an independent expert investigator not involved in the procedures and indifferent to the study results. An artery was considered occluded if no blood flow was detected in the target vessel by duplex ultrasound or by angiography during re-intervention through a different vascular access. If any repeated endovascular procedure within 3 months for 1 reason or another in any medical institution was performed through the access under study, then on the date of the access, it was recognized as passable and reached the primary endpoint.

Secondary endpoints: (1) composite of access artery complications: hematoma > 5 cm, bleeding according to Bleeding Academic Research Consortium (BARC) criteria (excluding CABG related bleeding), RA dissection, dissection of another upper limb artery, RA perforation, thrombosis of the pulmonary artery, loss of sensitivity at the puncture site, the formation of arteriovenous fistulas and false aneurysms, infection of the access site; (2) access parameters: change of access, duration of the stages of the procedure, fluoroscopy and hemostasis, radiation dose, total procedure time, presence/absence of spasm, pain at the access site, dynamometry.

Statistical Analysis

Statistical data analysis was carried out using the Microsoft Office 2019 spreadsheet software package, IBM SPSS Statistics v.27, jamovi 2.0. The nature of the distribution of quantitative data was assessed using the Shapiro-Wilk test, as well as indicators of asymmetry and kurtosis. In the case of a normal distribution, quantitative data are presented as arithmetic means (M) and standard deviations (SD), 95% confidence interval (95% CI). If the distribution of the trait

differs from normal, quantitative data are presented using the median (Me) and interquartile range (Q1-Q3). Relative indicators (shares, %) with indication of absolute values were used to represent qualitative features. Comparison of 2 independent groups on a quantitative basis with a normal distribution was carried out using Student's t-test (Student's t-test). Comparison of 2 independent groups for 1 or more traits that have at least one of the groups a distribution other than normal, or if the type of distributions was not analyzed, was carried out by testing the statistical hypothesis of equality of the average ranks using the Mann-Whitney U test. The odds ratio (OR) with 95% confidence interval (95% CI) calculated using binary logistic regression was used to determine the effect size when comparing relative rates. A P value < 0.05 was considered to indicate statistical significance.

Results

From December 2017 to May 2021, 776 patients were randomized in the study (Fig 1). Taking into account the excluded patients due to access change, the group with DRA was 371 people (hereinafter - group I), the group with TRA - 382 people (hereinafter - group II). Access change was statistically more frequent in-group I (5.1% and 0.8%, $P < 0.001$).

All data of this study are entered in the patented database "Results of distal and conventional radial access during PCI and CAG."[24]

The baseline patient characteristics are presented in Table 1, the groups are well balanced. The overall mean age of the patients was 62.8 years, 65.9% male, 86.7% hypertensive, and 27.1 diabetic. A total of 85.8% of patients took aspirin, and 42.1% received anticoagulants in tablet or injectable form.

Procedural characteristics are presented in Table 2, where there are statistically significant differences that do not affect the endpoint, but are only related to the choice of the operator - the right side of the access (67.1% and 59.7%, $P = 0.034$), or anatomical variants: calcification brachiocephalic trunk (5.7% and 1.3%, $P = 0.001$), which was not assessed with access through the left hand, lesion to the trunk of the left coronary artery (5.7% and 1.3%, $P = 0.001$). It is worth noting very significant statistical differences in the number of puncture attempts, puncture time and installing the introducer, while not affecting the overall procedure duration, fluoroscopy time and radiation dose, as well as a shorter duration of compression of the DRAt puncture site (180 and 155 minutes, $P < 0.001$)

TABLE 1. Baseline patient characteristics

Indicator	Group I (n = 371)	Group II (n = 382)	*P*	V
Age, years	63.0 (56.0-70.0)	63.0 (56.0-69.0)	0.873	
Male, n (%)	242 (65.2)	254 (66.5)	0.715	
IBM, kg/m^2	29.0 (25.8-32.0)	28.6 (26.0-32.0)	0.738	
Arm circumference, cm	19.0 (17.5-21.0)	19.0 (17.5-21.0)	0.530	
Height, cm	171.0 (164.0-176.0)	171.0 (164.0-178.0)	0.529	
Risk factors				
Unstable angina, n (%)	55 (14.8)	57 (14.9)	0.970	0.001
Arterial hypertension, n (%)	322 (86.8)	331 (86.6)	0.954	0.002
Diabetes, n (%)	102 (27.5)	102 (26.7)	0.807	0.009
Smoking, n (%)	110 (29.6)	119 (31.2)	0.654	0.016
Cholesterol, mmol/l	4,8 (3.9-5.8)	4.7 (3.8-5.6)	0.300	
Creatinine, μmol/l	87.2 (76.7-100.0)	87.0 (75.0-99.0)	0.783	
Blood-thinning drugs				
Aspirin, n (%)	319 (86.0)	327 (85.6)	0.881	0.005
Clopidogrel, n (%)	168 (45.3)	175 (45.8)	0.884	0.005
Ticagrelor, n (%)	52 (14.0)	63 (16.5)	0.345	0.034
Unfractionated heparins, n (%)	61 (16.4)	62 (16.2)	0.937	0.003
Low molecular weight heparins, n (%)	38 (10.5)	62 (16.2)	0.021	0.084
Warfarin, n (%)	11 (3.0)	13 (3.4)	0.732	0.012
INR	1.1 (1.2-1.5)	1.2 (1.3-1.8)	0.331	
Oral anticoagulants, n (%)	34 (9.2)	36 (9.4)	0.902	0.004

Note: IBM, index body mass; INR, international normalized ratio.

and more frequent injection of antispasmodics in group I (43.7% and 34.3%, $P = 0.008$).

The groups in terms of hand strength and grip strength of the thumb and forefinger before the procedure and at the control points after it did not have statistically significant differences. These parameters were assessed in 55% of group I and 56% of group II. The results are presented as histograms in Figure 2A and 2B.

Primary outcome. Statistically significant differences were obtained for the primary endpoint, RAO occurred in 10 patients in group I and 26 in group II (2.7% and 6.8%, $P = 0.008$) (Table 3). At the same time, there is no statistically significant difference in the day of detection of RAO, 48.5 (2.0-90.0) and 7.0 (2.0-90.0), $P = 0.520$. DRAt occlusion in patent RA also had statistically significant differences between the groups (1.3% and 0%, $P = 0.023$).

Secondary outcomes. Secondary outcomes showed statistically significant differences in favor of DRA for such complications as hematoma > 5 cm at the puncture site on day 1 (10.0% and 25.9%, $P < 0.001$), hematoma > 5 cm at puncture site on day 7 (12.4% and 34.6%, $P < 0.001$), bleeding type BARC 1 (3.8% and 21.7%, $P < 0.001$); all indicators with an average statistical relationship according to Cramer's test. In addition, RA dissection is very close to a statistically significant difference (1.6% vs 3.9%, $P = 0.054$). A complete analysis of the outcomes is presented in Table 3.

TABLE 2. Procedural characteristics

Indicator	Group I (n = 371)	Group II (n = 382)	*P*	V
Right access side, n (%)	249 (67.1%)	228 (59.7%)	0.034	0.077
Positive Allen test, n (%)	354 (95.4)	367 (96.1)	0.699	0.031
Coronary angiography, n (%)	207 (55.8)	193 (50.5)	0.147	0.053
PCI, n (%)	164 (44.2)	189 (49.5)	0.147	0.053
Radial artery diameter, mm	2.2 (2.0-2.5)	2.3 (2.0-2.5)	0.518	
Distal radial artery diameter, mm	2.5 (2.3-2.8)	2.5 (2.3-2.9)	0.213	
Number of puncture attempts	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.022	
Puncture time, sec.	19.0 (8.0-50.0)	13.5 (5.0-29.0)	<0.001	
Installing the introducer, sec.	42.0. (26.0 – 84.0)	35.0 (23.0 – 55.0)	<0.001	
First catheterization of the coronary artery ostium, sec.	190.0 (135.0-300.0)	184.5 (135.0-300.0)	0.677	
Introducer diameter, F	6.0 (6.0-6.0)	6.0 (6.0-6.0)	0.708	
Catheter diameter, F	5.0 (5.0-6.0)	5.0 (5.0-6.0)	0.851	
Change of catheters, n (%)	125 (33.7)	145 (38.0)	0.222	0.044
Procedure duration, min.	20.0 (9.0-35.0)	20.0 (7.0-35.0)	0.395	
Radiation dose, mGy	922.3 (487.3-1729.2)	1005.0 (554.6-1893.0)	0.178	
Fluoroscopy time, min.	5.4 (3.0-10.2)	6.0 (2.8-10.8)	0.682	
Patent hemostasis, n (%)	—	376 (98.4)		
Pressure gauze bandage, n (%)	371 (100.0)	6 (1.6)	<0.001	0.984
Total compression time, min.	180.0 (120.0 -480.0)	155.0 (125.0- 195.0)	<0.001	
Score of subjective feelings, (0-5)	0.0 (0.0-2.0)	0.0 (0.0-2.0)	0.065	
Radial artery spasm, n (%)	87 (23.5)	87 (22.8)	0.826	0.008
Injected drugs				
Heparin, IU	5000.0 (5000.0-10000.0)	5000.0 (7500.0-10000.0)	0.164	
Spasmolytic, n (%)	162 (43.7)	131 (34.3)	0.008	0.084
IIb/IIIa receptor blockers, n (%)	3 (0.8)	4 (1.0)	0.733	0.012
Type of coronary artery lesion				
Left coronary artery trunk, n (%)	22 (5.9)	11 (2.9)	0.041	0.07
Single-vessel lesion, n (%)	87 (23.5)	94 (24.6)	0.710	0.014
Multi-vessel lesion, n (%)	106 (28.6)	118 (30.9)	0.487	0.025
Chronic coronary artery occlusion, n (%)	46 (12.4)	34 (8.9)	0.119	0.057
Bifurcation lesion, n (%)	75 (20.2)	85 (22.3)	0.495	0.025
Anatomy of the brachiocephalic arteries				
Calcification of the brachiocephalic trunk, n (%)	21 (5,7)	5 (1,3)	0,001	0,119
Radial artery tortuosity, n (%)	23 (6,2)	21 (5,5)	0,681	0,015
High discharge of the radial artery, n (%)	13 (3.5)	24 (6.3)	0.078	0.064
Brachiocephalic trunk tortuosity, n (%)	35 (9.4)	38 (9.9)	0.812	0.078

Note: PCI, percutaneous coronary intervention.

Discussion

The TENDERA trial was the first prospective, multicenter RCT comparing DRA and TRA in patients undergoing percutaneous coronary procedures with follow-up periods of more than 1 month, as well as in conditions as close as possible to daily work (different types and diameters of sheaths, diagnostic, and therapeutic interventions, a small number of criteria exceptions). The main aim of the trial was to show the superiority of DRA over TRA through a smaller number of RAO in the early, middle and long-term follow-up, which was detected on duplex ultrasound scanning or angiography. For this, an optimal study protocol was developed with the correct sample size, in contrast to the DISCO RADIAL study, where the result was a low incidence of RAO in both

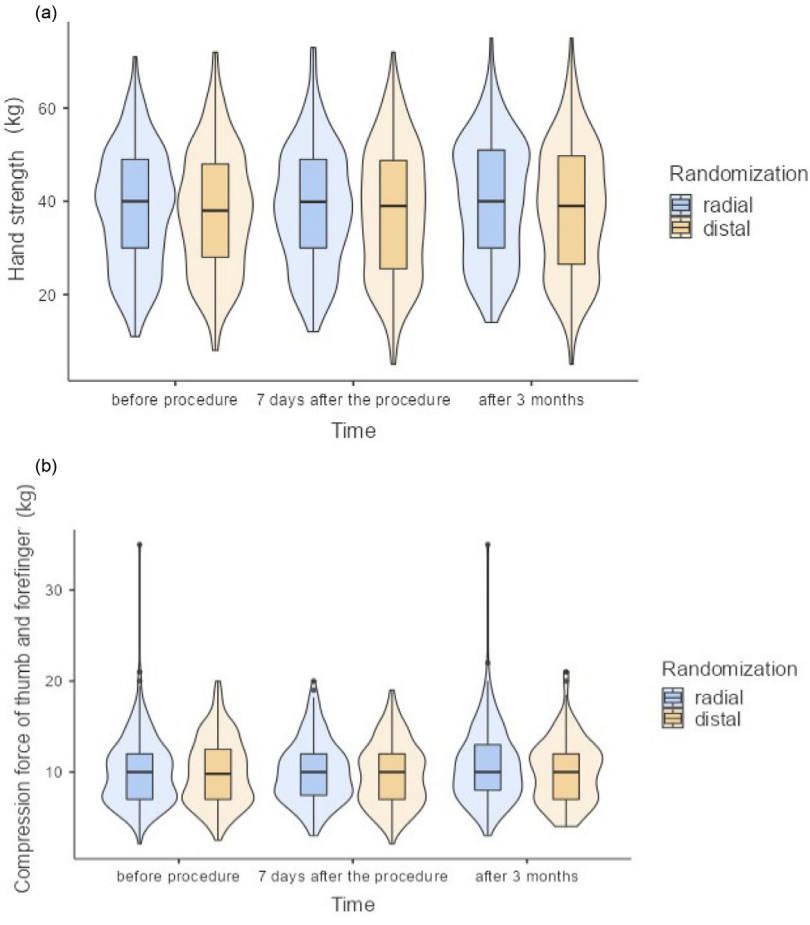

FIG. 2A. Hand strength histogram over time.
2B. Histogram of thumb and forefinger compression over time. (Color version of figure is available online.)

groups, and due to the inherent small type II error, no statistically significant differences were obtained between groups.[22]

The results obtained on the frequency of RAO in the study groups in the medium-term correlate with the data of Eid-Lidt G et all., where RA patency was checked at 24 hours and 1 month.[25] Noteworthy is the fact that the frequency of RAO may increase with time after the intervention. Thus, Gasparini GL et al. found that the amount of RAO increases after 1 month compared with the first day after the procedure, which may be associated with vessel remodeling.[26] Perhaps a similar process occurs throughout the year after the intervention. In one of the studies, the

TABLE 3. Primary and secondary outcomes

Показатель / Indicator	Group I (n = 371)	Group II (n = 382)	*P*	V
Forearm RAO, n (%)	10 (2.7)	26 (6.8)	0.008	
Distal radial artery occlusion, n (%)	5 (1.3)	0 (0)	0.023	0.083
Radial artery dissection, n (%)	6 (1.6)	15 (3.9)	0.054	0.07
Radial artery thrombosis, n (%)	0 (0.0)	1 (0.3)	0.324	0.036
Radial artery perforation, n (%)	3 (0.8)	5 (1.3)	0.503	0.024
Dissection of other upper limb arteries, n (%)	5 (1.3)	4 (1.0)	0.704	0.014
Loss of sensitivity, n (%)	2 (0.5)	1 (0.3)	0.546	0.022
Hematoma > 5 cm at the puncture site on day 1, n (%)	37 (10.0)	98 (25.9)	<0.001	0.204
Hematoma > 5 cm at the puncture site on day 7, n (%)	45 (12.4)	132 (34.6)	<0.001	0.264
Bleeding, BARC type 1, n (%)	14 (3.8)	83 (21.7)	<0.001	0.268
Arteriovenous fistula, n (%)	0	0		
False aneurysm, n (%)	0	2 (0,5)	0.499	0.051
Infection at the puncture site, n (%)	0	0	-	

Note: BARC, Bleeding Academic Research Consortium; RAO, radial artery occlusion.

authors in a multivariate regression analysis revealed an association of RAO with several factors: female gender, age, manual compression and diameter of the radial artery, and in the DISCO RADIL trial they suggested that their low incidence of RAO was associated with the use of modern thin introducers, adequate anticoagulant periprocedural therapy, nonocclusive and short-term hemostasis.[22,27] These relationships will also be explored in detail in the TENDERA trial. Interestingly, in TENDERA, the pressure dressing time in the DRA group was statistically longer than in the TRA group, but this was not reflected in the primary endpoint, but may have been reflected in some complications of the secondary endpoint.

An important mid-term outcome of the TENDERA trial is the presence of DRAt occlusions with patent RA in the DRA group, which preserves the possibility of RA reuse for endovascular procedures or other purposes in the future. In addition, if the DRAt were closed together with RA in these patients, then the number of RAO in group I would be 15, and then there would be no statistical difference in the primary endpoint (4.0% and 6.8%, $P = 0.094$). For the first time, such a benefit of access through the DRAt for maintaining the patency of the RA and the patient as a whole is mentioned.

Distinctive features of this study are the multivariate comparison of 2 approaches to search for criteria that may affect the primary endpoint, as well as the inclusion of only experienced surgeons in the study with respect to not only classical approaches, but also DRA.

Secondary endpoints and procedural characteristics are important for a better understanding of DRA. Change of access in the DRA group was 5.1%, which is more than 6 times higher than in the TRA group (0.8%).

This difference is much higher than in other similar studies and meta-analyses. In the DISCO RADIAL trial, which was most similar in design, the difference was 2-fold in favor of DRA.[22] However, if we compare specific figures, then the frequency of access changes in DISCO RADIAL in the DRA group is 7.3%, and in the TRA group, it is 3.5%,[22] which may indicate less experience of surgeons in relation to RA and DRAt. In the DAPROA trial, the frequency of changing access when trying to puncture the DRAt was 13.3%, and in ANGIE - 22.3%.[25,28]

Attention is drawn to a much greater number of RA spasms than in previous studies, while antispasmodics were used by surgeons at their discretion, which could affect this indicator, as well as a different approach to determining RA spasm - not only clinically, but also according to angiography, which was performed for all patients according to the protocol at the beginning and end of the procedure.[18,22,25,28-30]

Despite the statistically significant longer puncture time and sheath insertion in the DRA group, no differences were obtained in terms of the total duration of the operation and fluoroscopy or radiation dose, as in DISCO RADIAL, in contrast to ANGIE.[22,28]

For the first time, one of the criteria for comparing the studied approaches was the strength of the hand and the force of compression of the thumb and forefinger. There were no statistically significant differences in the groups, which can be explained by the study of this criterion in only half of the patients and the imperfection of the developed dynamometry protocol, but in the future, this approach can be improved and studied in more detail.

According to the secondary end point, serious local complications such as false aneurysm, arteriovenous fistula, infection did not occur at all or were isolated, which correlates with literature data.[12] However, significant differences were obtained in type I BARC bleeding and hematomas > 5 cm at the initial follow-up in favor of DRA, which may be due to the statistically shorter duration of hemostasis in-group II. Similar data have not been obtained in other studies.[12,18,22,25,28]

The obtained mid-term results of the TENDERA trial already provide unique data on the use of DRA in coronary practice by experienced transradial endovascular surgeons. The main limitations are related to the smaller diameter of the DRAt, which is reflected in the beginning of the procedure and requires a certain learning curve (about 50 procedures[16]), but is in no way related to the PCI or CAG itself. Moreover, the same anatomical and physiological features of DRAt, on the contrary, contribute to reliable, fast and safe hemostasis at the end of the intervention, while reducing the amount of RAO.

Study Limitations

For the first time, the results of a multicenter, prospective, randomized study comparing DRA and TRA with a follow-up period of 3 months (according to the TENDERA trial) are presented. However, there are certain limitations that may be taken into account and eliminated by other researchers. The lack of a registered device for DRAt hemostasis in the Russian Federation at the beginning of the study led to the development of a hemostasis protocol using a bandage. The use of patented hemostasis in DRA can further reduce the number of hematomas and bleeding at various follow-up periods. Given the time dependence of primary PCI in ST-segment elevation myocardial infarction, this cohort of patients was excluded from the present study. The use of antispasmodic drugs at the discretion of the operator led to statistically significant differences in the groups, while the development of RA spasm in the groups did not differ statistically.

Conclusion

In the TENDERA trial, DRA showed efficacy and safety in coronary interventions compared with YRA in the medium-term follow-up period: a statistically significant lower incidence of RAO and local complications. TRA currently remains the gold standard in interventional cardiology, but DRA may already be a viable alternative, especially in younger patients.

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