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Distal vs Conventional Radial Access for Coronary Angiography and/or Intervention

A Meta-Analysis of Randomized Trials

Giuseppe Ferrante, MD, PhD,[a,b] Francesco Condello, MD,[a] Sunil V. Rao, MD,[c] Matteo Maurina, MD,[a,b] Sanjit Jolly, MD, MSc,[d] Giulio G. Stefanini, MD, PhD, MSc,[a,b] Bernhard Reimers, MD,[a,b] Gianluigi Condorelli, MD, PhD,[a,b] Thierry Lefèvre, MD,[e] Samir B. Pancholy, MD,[f,g] Olivier Bertrand, MD, PhD,[h] Marco Valgimigli, MD, PhD[i]

ABSTRACT

BACKGROUND Emerging evidence from randomized clinical trials (RCTs) comparing distal radial access (DRA) with conventional radial access (RA) is available.

OBJECTIVES The aim of this study was to provide a quantitative appraisal of the effects of DRA) vs conventional RA for coronary angiography with or without intervention.

METHODS The PubMed, Embase, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov databases were searched for RCT comparing DRA vs conventional RA for coronary angiography and/or intervention. Data were pooled by meta-analysis using a random-effects model. The primary endpoint was radial artery occlusion (RAO) at the longest available follow-up.

RESULTS Fourteen studies enrolling 6,208 participants were included. Compared with conventional RA, DRA was associated with a significant lower risk of RAO, either detected at latest follow-up (risk ratio [RR]: 0.36; 95% CI: 0.23-0.56; $P < 0.001$; number needed to treat [NNT] = 30) or in-hospital (RR: 0.32; 95% CI: 0.19-0.53; $P < 0.001$; NNT = 28), as well as EASY (Early Discharge After Transradial Stenting of Coronary Arteries) ≥II hematoma (RR: 0.51; 95% CI: 0.27-0.96; $P = 0.04$; NNT = 107). By contrast, DRA was associated with a higher risk of access site crossover (RR: 3.08; 95% CI: 1.88-5.06; $P < 0.001$; NNT = 12), a longer time for radial puncture (standardized mean difference [SMD]: 3.56; 95% CI: 0.96-6.16; $P < 0.001$), a longer time for sheath insertion (SMD: 0.37; 95% CI: 0.16-0.58; $P < 0.001$), and a higher number of puncture attempts (SMD: 0.59, 95% CI: 0.48-0.69; $P < 0.001$).

CONCLUSIONS Compared with conventional RA, DRA is associated with lower risks of RAO and EASY ≥II hematoma but requires longer time for radial artery cannulation and sheath insertion, more puncture attempts, and a higher access site crossover. (J Am Coll Cardiol Intv 2022;15:2297-2311) © 2022 the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

Compared with femoral access, the use of radial access (RA) is associated with lower mortality and major adverse cardiovascular events and minimizes major bleeding and vascular complications across the spectrum of patients with coronary artery disease undergoing coronary interventions.[1] These benefits seem to be preserved in the long term, as RA compared with femoral access

From the [a]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Italy; [b]Department of Cardiovascular Medicine, IRCCS-Humanitas Research Hospital, Rozzano, Italy; [c]NYU Langone Health System, New York, New York, USA; [d]Division of Cardiology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [e]Institut Cardiovasculaire Paris Sud, Hopital Jacques Cartier, Ramsay Santè, Massy, France; [f]Wright Center for Graduate Medical Education, Scranton, Pennsylvania, USA; [g]Apex Heart Institute, Ahmedabad, India; [h]Quebec Heart and Lung Institute, Quebec City, Quebec, Canada; and the [i]Cardiocentro Institute, Ente Ospedaliero Cantonale, Università della Svizzera Italiana, Lugano, Switzerland.
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ABBREVIATIONS AND ACRONYMS

DRA = distal radial access

NNTB = number needed to treat for an additional beneficial outcome

NNTH = number needed to treat for an additional harmful outcome

PCI = percutaneous coronary intervention

RA = radial access

RAO = radial artery occlusion

RCT = randomized clinical trial

RR = risk ratio

SMD = standardized mean difference

in the Minimizing Adverse Hemorrhagic Events by Transradial Access Site and Systemic Implementation of Angiox (MATRIX) study remained associated with improved net clinical benefit at 1 year.[2,3] The 2018 European Society of Cardiology/European Association of Cardio-Thoracic Surgery recommended RA as the preferred access site for any percutaneous coronary intervention (PCI) irrespective of clinical presentation, unless there are overriding procedural considerations.[4] RA has been endorsed as the default access site for coronary intervention in patients with acute coronary syndromes by the 2021 American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions Coronary Revascularization Guidelines.[5]

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Nevertheless, RA is associated with radial artery occlusion (RAO) in a variable proportion of patients, with mean pooled estimates at about 7.7% within the first 24 hours after the procedure.[6] Although RAO is not associated with clinically overt ischemic complications owing to the presence of numerous and large anastomotic vascular connections in the hand, and prior studies did not find a relation between RAO and the occurrence of hand motor functional impairment or instrumental signs of ischemia,[7-9] the occurrence of RAO limits future interventional cardiovascular procedures through the same access and reduces availability of potential useful conduits for coronary artery bypass grafting surgery and for arteriovenous fistula creation in patients requiring hemodialysis.[10]

Recently, the distal radial access (DRA) technique has been introduced as an alternative access to the conventional RA for coronary angiography and intervention.[11,12] DRA consists in a radial puncture distal to the superficial palmar arch from the anatomical snuffbox on the dorsal side of the hand and preserves anterograde flow in the forearm radial artery during hemostatic compression or in case of distal RAO, thus reducing the risk of retrograde thrombus formation with the potential of reducing the rate of forearm RAO.[12] Several randomized clinical trials (RCTs) comparing DRA with conventional RA for coronary interventions are quickly increasing the amount of evidence in this field.

The aim of this study was to provide a quantitative and comprehensive assessment of the effects of DRA vs conventional RA for coronary angiography and/or intervention.

METHODS

DATA SOURCES AND SEARCH STRATEGY. A meta-analysis of RCT was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 guidelines.[13] Ethical approval was not required, as this was a study-level meta-analysis of published data. The study protocol was registered on PROSPERO (the international prospective register of systematic reviews), and the number CRD42022302383 was assigned. Two reviewers (F.C., M.M.) independently identified the relevant studies by an electronic search of the MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov databases (from inception to March 2022). Additional information is reported in the Supplemental Appendix.

STUDY SELECTION. Two reviewers (F.C., M.M.) independently assessed trial eligibility on the basis of titles, abstracts, full-text reports. Discrepancies in the study selection were discussed and resolved with another reviewer (G.F.). Eligible trials were any randomized studies comparing DRA vs conventional RA for coronary angiography and/or intervention, reporting predefined clinical outcome measures.

DATA EXTRACTION AND QUALITY ASSESSMENT. Details of the extraction process are reported in the Supplemental Appendix. Two reviewers (F.C., M.M.) independently and systematically assessed the studies' methodological quality using the revised Cochrane risk-of-bias tool (RoB 2.0) assessing 5 domains of bias for each outcome: randomization process, deviation from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results.[14] A risk-for-bias summary reporting each risk-for-bias item for each included study was reported. Any disagreement was resolved with a third reviewer (G.F.).

DATA SYNTHESIS AND DATA ANALYSIS. Outcome measures. The primary endpoint of this study was

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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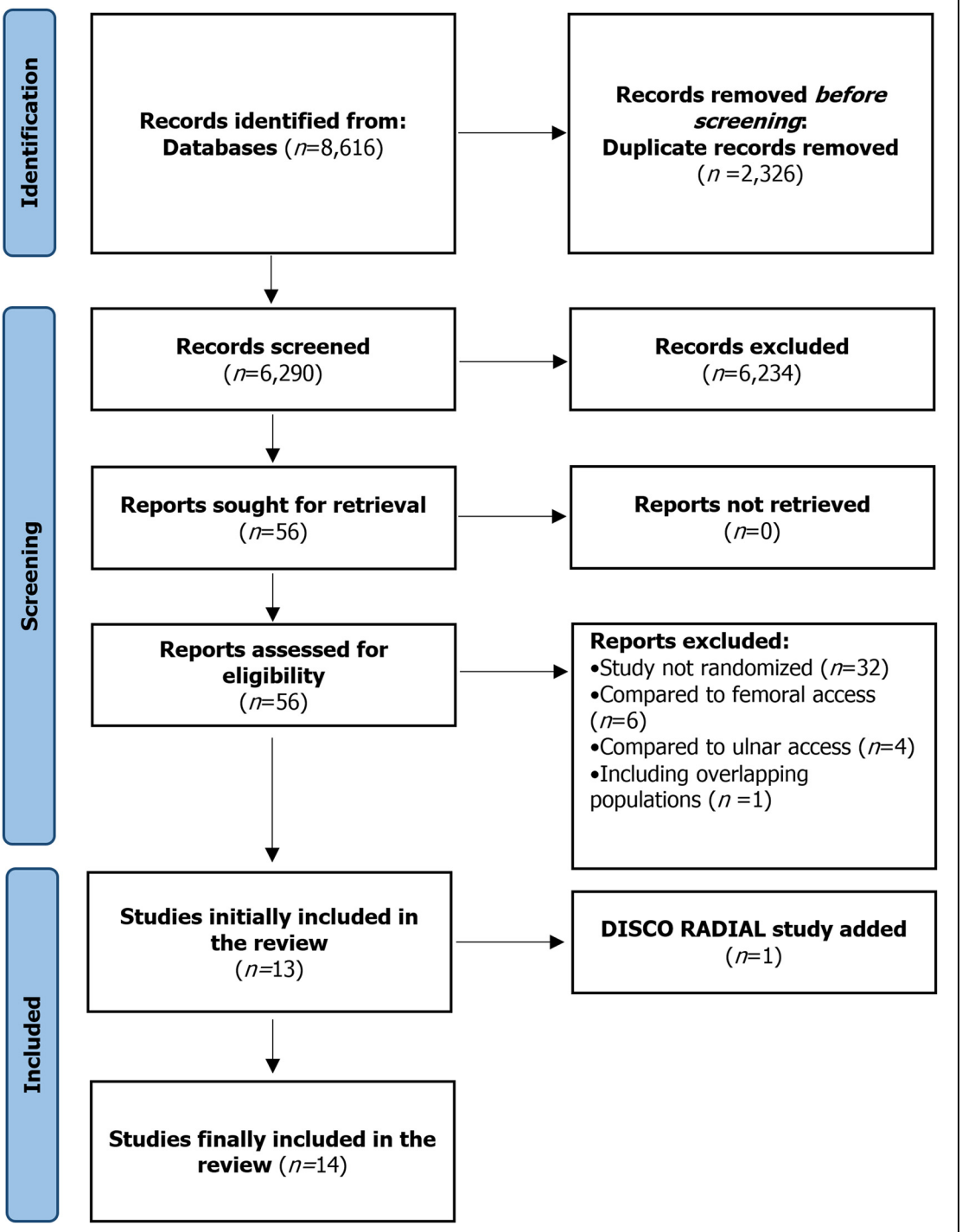
FIGURE 1 **Flow Diagram of the Search for Studies Included in the Meta-Analysis According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement**



DISCO RADIAL = Distal vs Conventional Radial Access.

TABLE 1 Main Clinical and Procedural Characteristics of the Included Studies

	Mokbel et al[21,a]	Koutouzis et al[22]	Vefalı and Sarıçam[33]	Eid-Lidt et al (DAPRAO Study)[28]	Sharma et al (DORA Study)[24]	Koledinskiy et al[25,a]	Lin et al[26]	Lu et al[23]	Özkan et al[27,a]	Flis et al[30,a]	Kozinski et al[29,a]	Lucreziotti et al[32,a]	Tsigkas et al (ANGIE Study)[31]	Aminian et al (DISCO RADIAL)[34]
Country, date	Romania, 2018	Greece, 2019	Turkey, 2019	Mexico, 2020	India, 2020	Russia, 2020	China, 2020	China, 2020	Turkey, 2020	Poland, 2021	Poland, 2021	Italy, 2021	Greece, 2022	Japan, 2022
Study design	1 center, RCT, open label	2 centers, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	3 centers, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	1 center, RCT, open label	Multicenter, RCT, open label
N	114	200	205	282	970	264	900	80	40	200	400	204	1,042	1,307
Primary outcome	RAO in forearm evaluated on discharge by ultrasonography	Any crossover to other access site	Not prespecified	Rate of RAO at 24 h by ultrasonography	Not prespecified	Not prespecified	The success rates of the catheterizations, with success defined as a successfully cannulated sheath	Puncture success rate, fluoroscopy time, and hemostasis time were determined	The success of both procedures and their effects on complications were investigated	Patient comfort, time of gaining access, need for conversion, and local complications	Incidence of RAO at 1 d and 60 d	Moderate-to-severe ASH (grade ≥II according to the EASY classification)	Rate of RAO at 60 d after randomization	The incidence of forearm RAO at hospital discharge
Inclusion criteria	NA	Patients with palpable distal and traditional radial artery undergoing transradial coronary angiography	Consecutive patients undergoing PCA and/or PCI	Patients older than 18 y of age who were candidates for PCA or PCI by the radial, conventional, or distal route; presence of a perceptible pulse from the radial artery in its proximal and distal segments	Patients with chronic stable angina who require coronary angiography	NA	Patients undergoing PCA or PCI	All patients who were willing to receive coronary angiography, but not PCI	NA	NA	NA	Consecutive patients referred for elective or urgent PCA and PCI and with palpable pulse both in the anatomical snuffbox and in the conventional radial site	Patients >18 y of age with an indication for PCA or PCI	Patients undergoing diagnostic coronary angiography or PCI, who were suitable for both DRA and conventional RA with the 6-F Glidesheath Slender (Terumo) as the standard access sheath

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TABLE 1 Continued

	Mokbel et al[21,a]	Koutouzis et al[22]	Vefalı and Sarıçam[33]	Eid-Lidt et al (DAPRAO Study)[28]	Sharma et al (DORA Study)[24]	Koledinskiy et al[25,a]	Lin et al[26]	Lu et al[23]	Özkan et al[27,a]	Flis et al[30,a]	Kozinski et al[29,a]	Lucreziotti et al[32,a]	Tsigkas et al (ANGIE Study)[31]	Aminian et al (DISCO RADIAL)[34]
Exclusion criteria	NA	Previous surgical cardiac revascularization, oral anticoagulant treatment, GFR <30 mL/min/1.73 m^2, previous cannulation of both radial arteries, planned PCI after angiography	Acute STEMI, Raynaud's disease, Parkinson's disease, upper limb vascular disorders, carpal tunnel syndrome, neural disorders of radial nerve innervations area, chronic tenosynovitis	STEMI at the time of primary angioplasty, cardiogenic shock or hemodynamic instability, patients in whom the main operator did not perceive the arterial pulse and patients with proximal RAO criteria by plethysmography, choice by the operator to perform the procedure via the femoral route	Patients having arteriovenous fistula for hemodialysis, post-CABG patients who used the radial artery as a graft, patients who had type III and type IV radial artery, patients not willing for the procedure	NA	Height >190 cm, absence of obvious pulsation of the radial artery, cardiogenic shock, >80 y of age	Women weighing <50 kg and patients who wanted to receive PCI at the same time if lesions were found after coronary angiography	NA	NA	NA	<18 y of age, pregnancy, STEMI or hemodynamic instability, choice of femoral access for operator's preference (ie, need for larger catheter, planned rotational atherectomy), estimated GFR calculated with CKD-EPI equation <30 mL/min/1.73 m^2	Patients presenting with STEMI or hemodynamic instability; nonpalpable right radial artery, prior CABG, anatomical restrictions (eg, fistula, orthopedic problems, or prior complicated right transradial intervention), and high probability for noncompliance with the study protocol (mainly distance from the study center or socioeconomic issues of the patients)	Medical conditions that may cause noncompliance with the study protocol and/or may confound the data interpretation, long-term hemodialysis, ST-segment elevation myocardial infarction, and PCI for chronic total occlusion
Distal radial artery puncture location	Not specified	Not specified	First intermetacarpal space	Anatomical snuffbox	First intermetacarpal space	Not specified	Anatomical snuffbox	Anatomical snuffbox	Not specified	Not specified	Anatomical snuffbox	Anatomical snuffbox	Anatomical snuffbox	Anatomical snuffbox or the dorsum of the hand
Puncture needle size and technique	NA	NA	NA	20G needle (cannula with through-and-through technique)	21G open needle Seldinger technique	NA	Intravenous catheter needle (1.02 mm)	21G open needle Seldinger technique	NA	NA	NA	20G micropuncture needle Seldinger technique	21G Seldinger needle	NA
Access sheath size	6 F	6-F Engage radial, 12 cm long (St Jude Medical)	Thena 5-F, 7 cm long (Tianck Medical Co, Ares Medical)	6-F (90.8%) Radifocus introducer II or GLIDESHEATH Slender (Terumo)	5-F	NA	6-F Radifocus introducer II (Terumo)	5-F or 6-F	NA	NA	NA	6-F (98%) 25-cm-long GLIDESHEATH or 7-F (2%) 16-cm-long GLIDESHEATH Slender (Terumo Interventional System)	Standard radial arterial sheath of 11 cm length: 5-F (63%), 6-F (37%), 7-F (<1%)	6-F GLIDESHEATH Slender (Terumo)

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TABLE 1 Continued

	Mokbel et al[21,a]	Koutouzis et al[22]	Vefalı and Sarıçam[33]	Eid-Lidt et al (DAPRAO Study)[28]	Sharma et al (DORA Study)[24]	Koledinskiy et al[25,a]	Lin et al[26]	Lu et al[23]	Özkan et al[27,a]	Flis et al[30,a]	Kozinski et al[29,a]	Lucreziotti et al[32,a]	Tsigkas et al (ANGIE Study)[31]	Aminian et al (DISCO RADIAL)[34]
Medications administered to prevent spasm or RAO	NA	50 IU/kg UFH and verapamil 5 mg	2,500 IU UFH and nitrate 200 μg	5,000 IU UFH, 2.5 mg verapamil, 200 μg nitroglycerin; in cases of PCI, an additional dose of UFH to reach a total dose of 100 IU/kg	5,000 IU UFH nitroglycerin 200 μg; a weight-adjusted dose of heparin was further added if PCI was needed	NA	UFH (50 UI/kg), nitroglycerin 0.5 mg	2,500 IU of UFH, 100 μg of nitrate and 1 mL (2.5 mg) of verapamil	NA	NA	NA	3,000-4,000 IU UFH in case of PCA and a weight-adjusted dose UFH in case of PCI, plus nitroglycerin 300 μg	Nitroglycerin 200 μg	5 mg verapamil and/or 100 to 200 μg nitroglycerin, an initial bolus of 5,000 IU unfractionated heparin
Guidewire size	NA	0.025″	0.018″	NA	0.021″-0.018″	NA	NA	0.018″	NA	NA	NA	0.025″		
Right arm	NA	152 (76)	33 (16.1)	263 (93.3)	NA	NA	NA	80 (100)	NA	NA	NA	159 (77.9)		1,053 (80.6)
Hemostasis system	A hemostasis device was verified at 1 h and then at 30-min intervals	Manual compression	Manual compression	TR band (Terumo Interventional System) The TR band was placed in site with a modified technique in the DRA group	Gauze rolled up tight to form a plug to place at the arterial entry site, then wrapped with a tight elastic bandage to tamponade t he artery	NA	Hemostatic band (Kangdelai Medical Devices) in RA group; manual compressive bandage with gauze in DRA group	Compressive dressing with a small gauze plug	NA	Pressure dressing	NA	TR band (Terumo Interventional System)	TR band (Terumo Interventional System) Plastic strip if TR band did not fit adequately the snuffbox area	NA
Timing and modality of RAO assessment	DUS before discharge	DUS after hemostasis was achieved	Not evaluated	DUS at 24 h after PCA or PCI	Manual palpation after 12 h; in patients whose radial artery pulse was absent, DUS was done to confirm RAO	During hospital stay	DUS before discharge	DUS during hospital stay	DUS at 1 d and 30 d after procedure	During hospital stay	DUS at 1 d and 60 d after procedure	Manual palpation by 1 operator or 2 operators, in case of weak arterial pulse, at discharge	DUS at a median follow-up of 46 d	DUS at hospital discharge
Hematoma definition	Not evaluated	EASY	Not evaluated	EASY	Not prespecified	Not specified	NA	NA	Not evaluated	Not specified	Not specified	EASY	mEASY	EASY

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TABLE 1 Continued

Clinical Variable	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA	DRA	RA
Age, y	NA	NA	63.8 ± 10.9	62.8 ± 11	60.89± 10.81	59.84± 8.48	63.1 ± 10.3	61.1 ± 11.1	55 ± 6	55 ± 7	63.3 ± 9.2	64.4 ± 8.4	55.28 ± 10.59	58.81 ± 9.42	54.3 ± 14.5	56.4 ± 13.7	NA	NA	65 ± 10	67 ± 10	67 ± x	66 ± x	71.8 ± 11.4	71.7 ± 10.8	65.7 ± 11.2	65.5 ± 12.3	68.0 ± 10.7	68.2 ± 11.1
Male	NA	NA	74 (74)	77 (77)	72 (70.6)	70 (68)	105 (75)	109 (76.7)	290 (60)	285 (59)	92 (69.7)	90 (68.2)	205 (45.56)	225 (50)	23 (57.5)	25 (62.5)	NA	NA	63 (64)	53 (63)	120 (60)	121 (60.5)	59 (59)	71 (68.3)	395 (76.3)	396 (75.6)	479 (73.7)	468 (71.2)
BMI, kg/m^2	NA	NA	28.6 ± 4.7	29.0 ± 5.3	27.8 ± x	27.6 ± x	NA	NA	NA	NA	NA	NA	24.06 ± 3.58	24.36 ± 2.64	NA	NA	NA	NA	29.0 ± 5.2	29.4 ± 5.7	NA	NA	27.5 ± 4.43	27.1 ± 4.6	28.2 ± 4.1	28.3 ± 4.2	27.7 ± 5.1	28.2 ± 5.1
Hypertension	NA	NA	73 (73)	63 (63)	56 (54.9)	55 (53.4)	84 (60)	88 (61.9)	NA	NA	110 (83.3)	108 (81.8)	112 (24.89)	113 (25.11)	NA	NA	NA	NA	73 (74)	58 (69)	NA	NA	83 (83)	78 (75)	324 (62.7)	290 (55.4)	496 (76.7)	520 (79.6)
Current smoking	NA	NA	35 (35)	28 (28)	28 (27.5)	26 (25.2)	29 (20.4)	24 (16.9)	NA	NA	92 (69.7)	97 (73.5)	124 (27.5)	101 (22.4)	NA	NA	NA	NA	35 (36)	40 (48)	NA	NA	50 (50)	56 (53.8)	168 (32.6)	169 (32.3)	126 (22.4)	121 (21.4)
Dyslipidemia	NA	NA	71 (71)	59 (59)	NA	NA	56 (39.4)	55 (38.7)	NA	NA	84 (63.6)	85 (64.4)	NA	NA	NA	NA	NA	NA	44 (45)	38 (45)	NA	NA	58 (58)	64 (61.5)	293 (56.7)	264 (50.5)	442 (69.2)	472 (72.4)
Diabetes mellitus	NA	NA	27 (27)	28 (28)	37 (36.2)	39 (37.8)	72 (51.4)	62 (43.7)	NA	NA	24 (18.2)	27 (20.5)	48 (10.67)	56 (12.44)	6 (15)	7 (17.5)	NA	NA	27 (28)	30 (36)	NA	NA	30 (30)	30 (28.8)	152 (29.4)	158 (30.2)	196 (30.2)	190 (28.9)
ACS	NA	NA	NA	NA	NA	NA	NA	NA	0 (0)	0 (0)	132 (100)	132 (100)	226 (50.23)	216 (48)	0 (0)	0 (0)	NA	NA	0 (0)	0 (0)	NA	NA	38 (38)	25 (24)	164 (31.6)	174 (33.3)	91 (7)	106 (8)
PCI	NA	NA	0 (0)	0 (0)	24 (23.5)	25 (24.3)	51 (36.5)	49 (34.5)	NA	NA	132 (100)	132 (100)	226 (50.23)	216 (48)	0 (0)	0 (0)	NA	NA	40 (41)	34 (40)	NA	NA	55 (55)	65 (62.5)	138 (26.6)	118 (22.5)	237 (36.5)	245 (37.3)

Values are n (%) or mean ± SD, unless otherwise indicated. [a]Study published as an abstract.

ACS = acute coronary syndrome; ANGIE = Anatomical Snuffbox for Coronary Angiography and Interventions; ASH = access-site hematoma; BMI = body mass index; CABG = coronary artery bypass grafting; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; DAPRAO = Distal Radial Artery Approach to Prevent Radial Artery Occlusion; DISCO RADIAL = Distal vs Conventional Radial Access; DORA = Dorsal radial artery access versus classical radial artery access; DRA = distal radial approach; DUS = Doppler ultrasonography; EASY = Early Discharge After Transradial Stenting of Coronary Arteries; GFR = glomerular filtration rate; IU = international units; mEASY = modified Early Discharge After Transradial Stenting of Coronary Arteries; NA = not available; PCA = percutaneous coronary angiography; PCI = percutaneous coronary intervention; RA = radial access; RAO = radial artery occlusion; RCT = randomized clinical trial; STEMI = ST-segment elevation myocardial infarction; UFH = unfractionated heparin.

the occurrence of forearm RAO at the longest available follow-up. As supportive secondary endpoint, in-hospital RAO was assessed. Other secondary endpoints were local hematoma defined as EASY (Early Discharge After Transradial Stenting of Coronary Arteries) or modified EASY ≥II hematoma, any local hematoma, radial spasm, time to successful radial puncture, number of radial puncture attempts, time to sheath insertion, contrast volume administration, fluoroscopy time, and access site crossover. Endpoints were attributed according to definition used in each study.

Statistical analysis. For dichotomous outcomes the risk ratios (RRs) with 95% CIs were calculated from the available data. Trial-specific RRs were combined with the DerSimonian and Laird random-effects model due to the presence of heterogeneity.[15] For continuous outcomes, the effect size was computed as the Hedges' g standardized mean difference (SMD), and trial-specific effect sizes were pooled with a random-effects model due to the presence of heterogeneity with the use of the Sidik-Jonkman method to estimate the between-study variance τ^2.[16,17] The number needed to treat for an additional beneficial outcome (NNTB) and the number needed to treat for an additional harmful outcome (NNTH) were calculated. The presence of heterogeneity among studies was evaluated with the Cochran Q chi-square test estimating the between-studies variance τ^2 and using the I^2 test to evaluate inconsistency.[18] The presence of publication bias for each endpoint was assessed by visual estimation with the use of contour-enhanced funnel plots.[19] When >10 studies were available, the publication bias was also investigated with the Harbord's modified test for dichotomous outcomes.[20] Additional statistical methods as well as prespecified meta-regression analyses and sensitivity analyses are reported in the Supplemental Appendix.

RESULTS

SEARCH RESULTS. **Figure 1** displays the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for study search and selection. Of the 8,616 citations screened, a total of 14 RCT including 6,208 patients were identified and included in the final analysis.[21-34] Nine studies were published as full papers,[22-24,26,28,31-34] while 5 studies were in the form of abstracts presented at main conference proceedings.[21,25,27,29,30]

STUDY CHARACTERISTICS AND BIAS ASSESSMENT. The main trial and patient characteristics of the included studies are reported in **Table 1** and in the Supplemental Appendix. The rate of RAO was reported in all but 1 study.[33] The site of distal radial puncture was specified as in the anatomical snuffbox in 6 studies,[23,26,28,29,31,32] in the first intermetacarpal space in 2 studies,[24,33] and at both locations in 1 study,[34] and was not reported in the remaining studies.[21,22,25,27,30] Coronary angiography alone was performed in 3 studies,[22,23,27] PCI was performed in a variable proportion of patients ranging from 24% to 100% across 8 studies, and no information was available in 3 studies.[24,29,30] Data regarding the clinical syndrome were reported in 5 studies,[25,26,31,32,34] with the proportion of acute coronary syndrome ranging from to 14% to 100%. Supplemental Figure 1 summarizes systematic bias assessment of the included studies. Overall, there was a high prevalence of "some concerns" for bias for most domains across most studies, and 5 out of 14 studies showed a high risk of bias,[24,25,30,32,33] while 2 studies were judged as low risk of bais.[28,24]

HETEROGENEITY, PUBLICATION BIAS, AND ASYMMETRY. Moderate heterogeneity was found for RAO outcomes and the majority of the remaining endpoints showed high heterogeneity, while EASY ≥II hematoma and puncture attempts showed low heterogeneity (Supplemental Table 1). Contour-enhanced funnel plots for all endpoints are reported in Supplemental Figures 2 to 13. Evidence for significant asymmetry was found for all endpoints, and small asymmetry was detected for any local hematoma and contrast volume (Supplemental Figures 5 and 11). No publication bias was detected with respect to the primary endpoint of RAO at the longest follow-up by the Harbord test ($P = 0.83$) (Supplemental Figure 14).

OUTCOMES. DRA use, compared with conventional RA use, was associated with a lower risk for RAO at latest follow-up (ranging from 1 to 60 days) (RR: 0.36; 95% CI: 0.23 to 0.56; $P < 0.001$; NNTB = 30), in-hospital RAO (RR: 0.32; 95% CI: 0.19 to 0.53; $P < 0.001$; NNTB = 28), and EASY ≥II hematoma (RR: 0.51; 95% CI: 0.27 to 0.96; $P = 0.04$; NNTB = 107) (**Table 2**, **Figures 2 to 4**, Supplemental Table 2).

The risks of any local hematoma (RR: 1.03; 95% CI: 0.79 to 1.34; $P = 0.84$), radial spasm (RR: 0.61; 95% CI: 0.21 to 1.77; $P = 0.36$), or hemostasis time (SMD: -2.32; 95% CI: -5.43 to 0.78; $P = 0.14$) did not significantly differ (**Tables 2 and 3**, Supplemental Figures 15 to 17).

DRA, compared with conventional RA, was associated with a significant higher time for radial artery

puncture (SMD: 3.56; 95% CI: 0.96 to 6.16; $P < 0.001$) and for sheath insertion (SMD: 0.37; 95% CI: 0.16 to 0.58; $P < 0.01$), a higher number of puncture attempts (SMD: 0.59, 95% CI: 0.48 to 0.69; $P < 0.001$), and a higher risk of access site crossover (RR: 3.08; 95% CI: 1.88 to 5.06; $P < 0.001$; NNTH = 12) (**Tables 2 and 3, Figure 5, Central Illustration,** Supplemental Table 2, Supplemental Figures 18 to 20). Fluoroscopy time and contrast volume did not differ between the 2 groups (**Table 3**, Supplemental Figures 21 and 22).

META-REGRESSION ANALYSES. Increasing age in the conventional RA group was associated with a reduced effect of DRA, compared with conventional RA, on the risk of RAO at the longest follow-up (Supplemental Figure 23, Supplemental Table 3). The other variables did not emerge as treatment effect modifiers (Supplemental Table 3).

SENSITIVITY ANALYSES. Similar results with respect to the comparison of DRA vs conventional RA on both RAO at the longest follow-up and in-hospital RAO were observed: 1) by including only studies published as full papers; 2) after excluding small studies; and 3) by leave-one out analysis (Supplemental Figures 24 and 25, Supplemental Table 4).

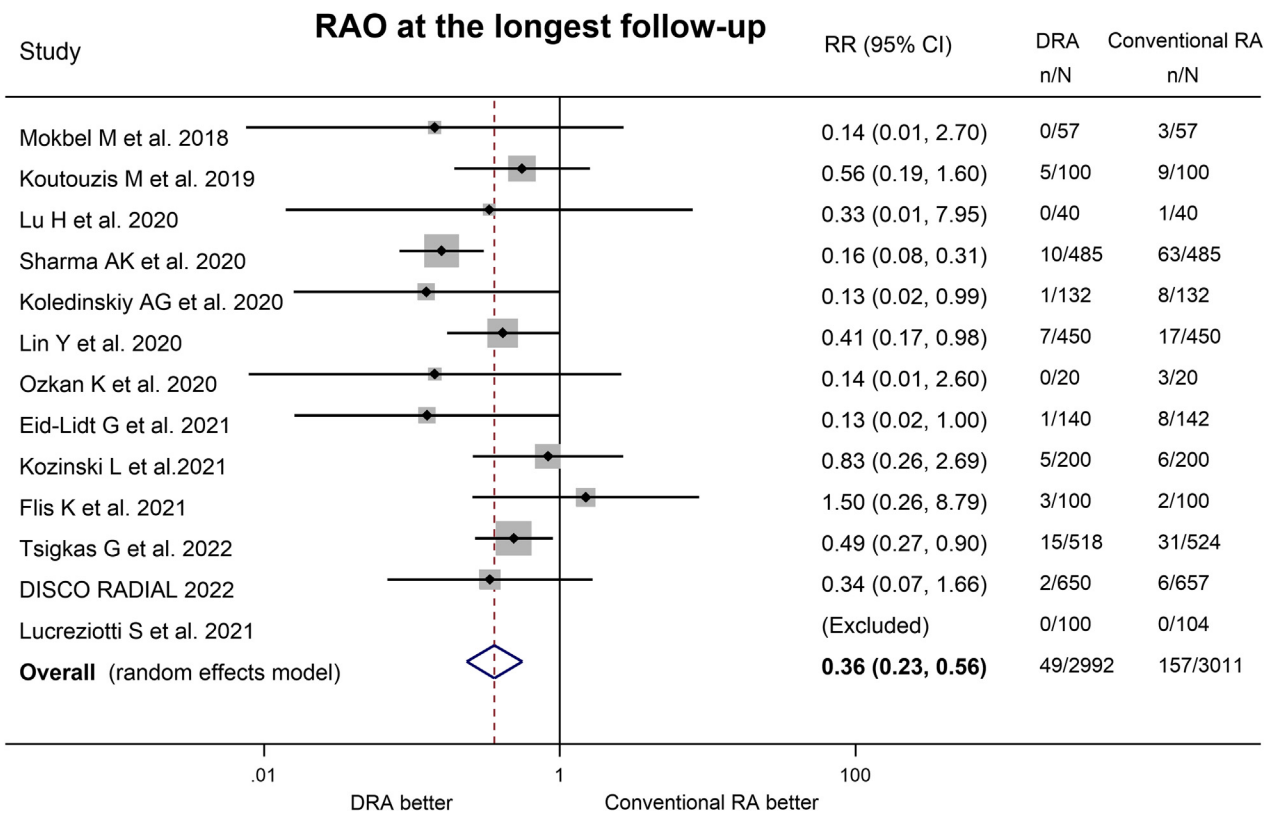
TABLE 2 Relative Treatment Effect Measures in the Overall Population: DRA vs Conventional RA

	Pooled Event Rate	RR	95% CI	*P* Value
RAO at the longest follow-up	1.6% vs 5.2%	0.36	0.23-0.56	<0.001
In-hospital RAO	1.4% vs 5.3%	0.32	0.19-0.53	<0.001
EASY ≥II hematoma	0.9% vs 1.9%	0.51	0.27-0.96	0.04
Any local hematoma	6.5% vs 6.4%	1.03	0.79-1.34	0.84
Radial artery spasm	2.6% vs 4.9%	0.61	0.21-1.77	0.36
Access site crossover	12.5% vs 3.8%	3.08	1.88-5.06	<0.001

DRA = distal radial access; EASY = Early Discharge After Transradial Stenting of Coronary Arteries; RA = radial access; RAO = radial artery occlusion; RR = risk ratio.

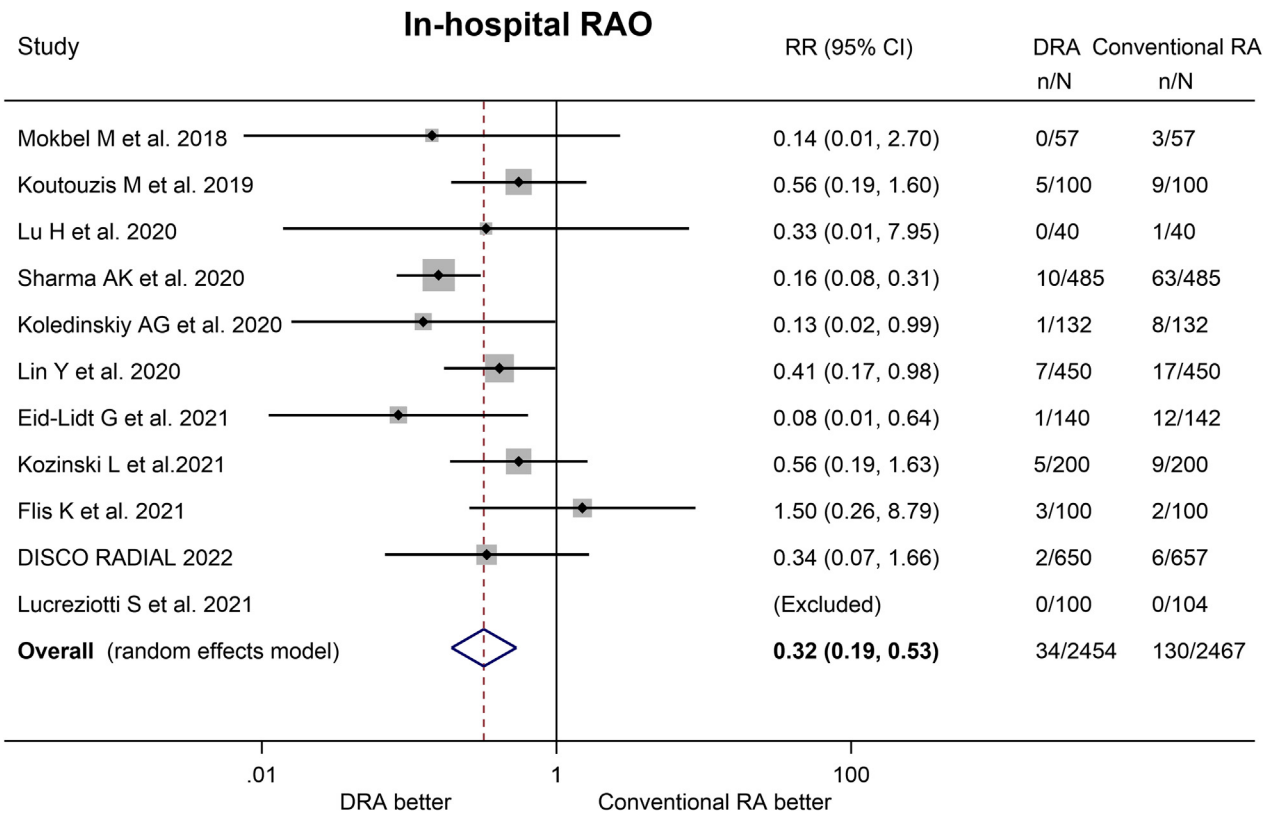
DISCUSSION. This meta-analysis including 6,208 patients from 14 RCTs provides a comprehensive evaluation of the effects of DRA vs conventional RA

FIGURE 2 Pooled Analysis of Studies Comparing DRA vs Conventional RA



Forest plot reporting trial-specific and summary risk ratios (RRs) with 95% CI for the endpoint of radial artery occlusion (RAO) at the longest follow-up. DISCO RADIAL = Distal vs Conventional Radial Access; DRA = distal radial access; RA = radial access.

FIGURE 3 **Pooled Analysis of Studies Comparing DRA vs Conventional RA**



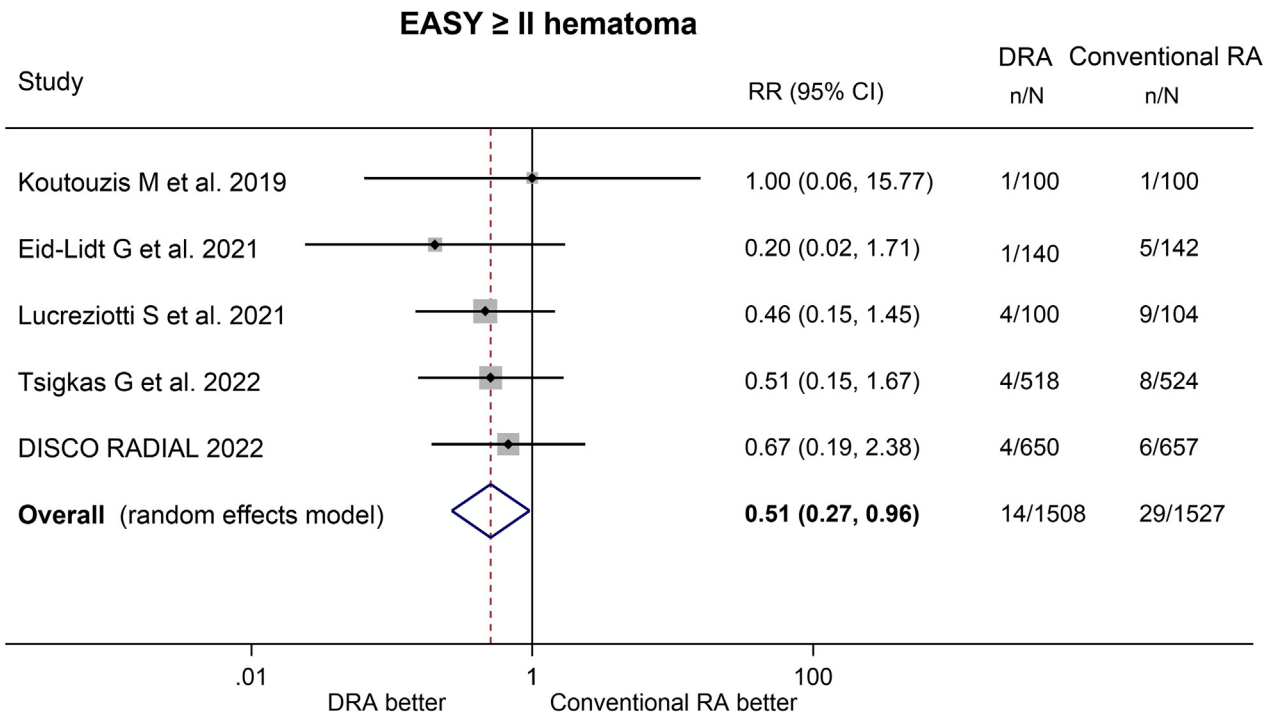
Forest plot reporting trial-specific and summary RRs with 95% CI for the endpoint of in-hospital RAO. Abbreviations as in **Figure 2**.

for coronary interventions. Our main study findings are as follows: 1) the use of DRA compared with conventional RA is associated with a 68% risk ratio reduction of in-hospital RAO and 64% risk ratio reduction of RAO at latest follow-up, with a relevant absolute treatment benefit as assessed by a NNTB of 28 and 30, respectively; 2) the use of DRA is associated with a 49% lower risk for EASY ≥II hematoma; 3) DRA, compared with conventional RA, is associated with an approximately 3-fold increase in the risk ratio of access site crossover with a NNTH of 12, and requires longer times for successful radial puncture and sheath insertion as well as more puncture attempts; and 4) contrast volume, fluoroscopy times, and hemostasis time after DRA are comparable to those of conventional RA.

Prespecified meta-regression analyses found that the beneficial effects of DRA, compared with conventional RA, on RAO are largely not affected by the prevalence of women, diabetics, smokers, and body mass index, while increasing age was associated with a lower treatment effect of DRA. Although the prevalence of acute coronary syndrome on admission and the rate of PCI following coronary angiography were not found to be treatment modifiers, the study populations across studies mainly consisted of chronic coronary syndromes and the rate of PCI was low. Therefore, these findings may not inform the access site selection in patients presenting with acute coronary syndrome or undergoing ad hoc PCI. Also, caution is needed in interpreting our results owing to the presence of high heterogeneity and bias in the comparison between DRA and conventional RA for the outcome measures.

The occurrence of RAO is a multifactorial phenomenon that is affected by modifiable and nonmodifiable as well as procedural and postprocedural risk factors.[10] On a pathophysiological standpoint, acute RAO has been related to the 3 factors of Virchow's triad including catheter-related intravascular vessel wall damage, a local hypercoagulable state, and a reduced flow induced by compressive hemostasis.[10,35] Of note, hemostasis time was shown to be an independent predictor of RAO, and evidence

FIGURE 4 Pooled Analysis of Studies Comparing DRA vs Conventional RA



Forest plot reporting trial-specific and summary RRs with 95% CI for the endpoint of EASY (Early Discharge After Transradial Stenting of Coronary Arteries) ≥II hematoma. Abbreviations as in Figure 2.

strongly suggests that shorter radial compression duration (≤120 minutes) is associated with reduced risk of RAO.[10,36] The implementation of patent hemostasis (eg, the persistence of antegrade blood flow through the radial artery during hemostatic compression) has been recommended to minimize the occurrence of RAO,[10] although prior studies have reported a large underutilization or failure to adopt this strategy in 20% to 50% of patients.[37,38]

Additional strategies for the prevention of RAO are the avoidance of sheath-to-artery mismatch with the use of smaller-sized sheaths and catheters or thin-walled radial sheaths, the adoption of sheathless catheters, the use of adequate procedural anticoagulation, and the use of prophylactic ulnar compression.[10] In this meta-analysis, there was heterogeneity in anticoagulation regimens and hemostasis protocols for RAO prevention among the included studies in the RA group, and mean hemostasis time was >120 minutes in 5 studies.[21,23,25,32,34] Also, manual compression was used for achieving hemostasis in some studies.[22,33] These factors may provide a potential explanation for the observed high pooled crude event rates of RAO at latest follow-up (5.2%) and in-hospital RAO (5.3%) in the conventional RA group, both of them being above the threshold of <5% identified as a quality measure to achieve in a recent international consensus document.[10] Of note, in the DISCO RADIAL (Distal vs Conventional Radial Access) study, in which systematic implementation of best practices for the prevention of RAO was performed,[10] the incidence of in-hospital RAO was 0.91% in the conventional RA group.[34]

DRA use has the theoretical advantage of avoiding flow interruption in the forearm radial artery, owing to the position of puncture site distal to the superficial anastomotic palmar arch.[12] Nevertheless, the overall pooled crude RAO rate in the DRA group in our study was at about 1.5%, indicating that a distal location of the radial puncture does not avoid the occurrence of RAO by itself.

Another finding of this meta-analysis is the lower risk of EASY ≥II hematoma associated with DRA use compared with conventional RA use. Prior studies have shown that EASY ≥II hematoma is typically related to intramuscular bleeding secondary to vascular injury, while EASY <II hematoma is related to radial puncture.[39,40] The overall incidence of EASY hematoma was about 10% in a recent study, and

TABLE 3 SMD in the Overall Population: DRA vs Conventional RA

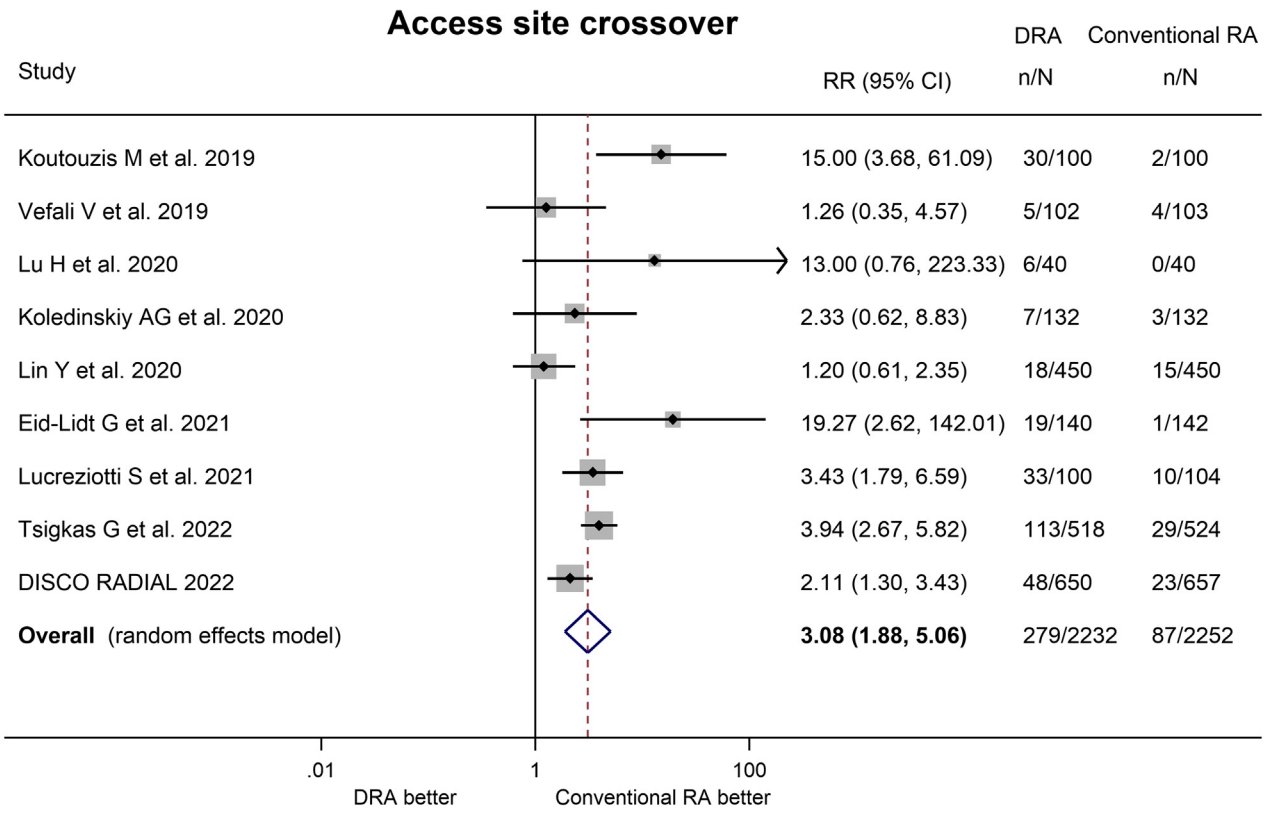
	SMD	95% CI	*P* Value
Radial artery puncture time	3.56	0.96 to 6.16	<0.001
Sheath insertion time	0.37	0.16 to 0.58	<0.01
Number of radial artery puncture attempts	0.59	0.48 to 0.69	<0.001
Hemostasis time	-2.32	-5.43 to 0.78	0.14
Fluoroscopy time	0.14	-0.04 to 0.32	0.13
Contrast volume	0.01	-0.09 to 0.11	0.85

DRA = distal radial access; RA = radial access; SMD = standardized mean difference.

several predictors have been identified such as female sex, multiple puncture attempts, longer hemostasis time, intensive antiplatelet therapy, and more complex procedures.[41] The lower risk for forearm hematoma with DRA may also relate to shorter traversal of the access wire into the forearm vasculature.

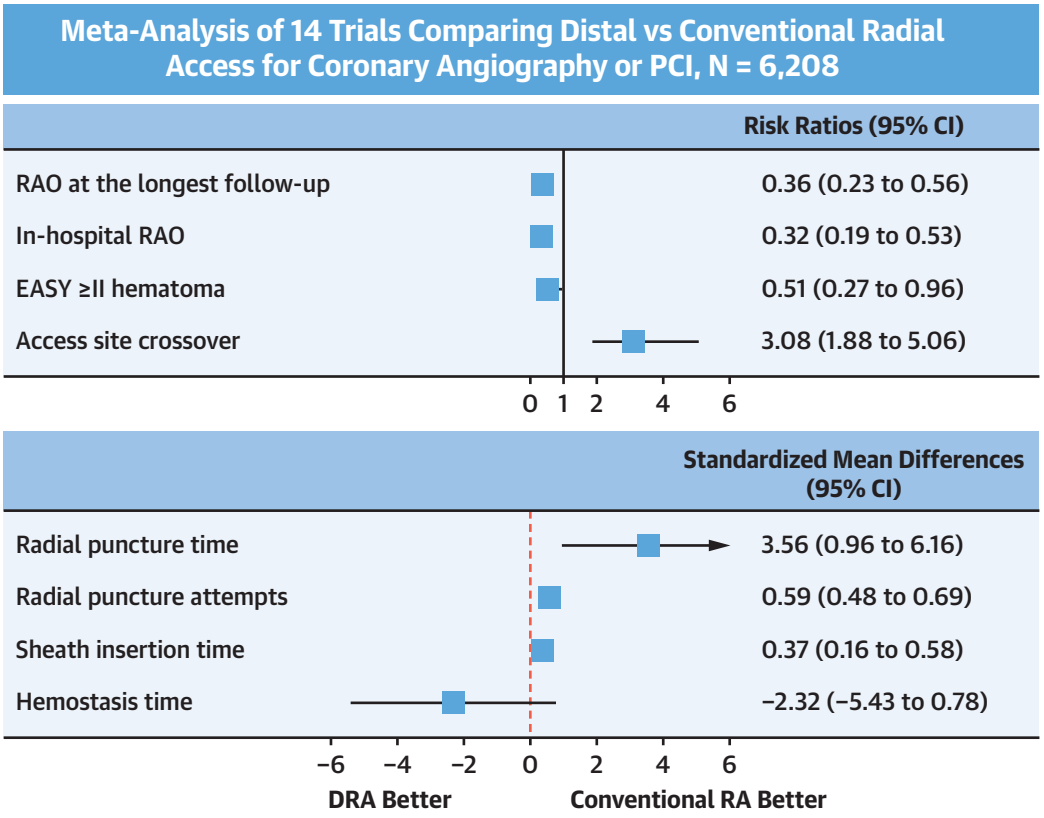
Beside these potential advantages of DRA use compared with conventional RA, this meta-analysis highlights the current limitations of DRA owing to higher access site crossover rate, longer time for successful radial puncture and sheath insertion as well as more puncture attempts, indicating that DRA use still lacks proficiency. The smaller diameter of the radial artery in its distal segment with angulation and tortuosity is associated with a higher failure of successful sheath insertion and therefore is likely to contribute to the final access site crossover.[10] A previous study has shown that female sex and systolic blood pressure <120 mm Hg were significant and independent predictors of the failed DRA.[42] Nevertheless, that study reported that puncture attempts, and DRA time decreased gradually with increasing operator's experience and found that a minimum of 200 cases of the DRA was required to maintain a consistently high success rate of >94.0%,[42] while a case volume of at least 50 PCIs or of 30 to 50 cases was deemed necessary to achieve proficiency with conventional RA in previous studies.[43,44] Nevertheless, these data underscore the importance of operator's learning curve for the use of DRA, which comprises the implementation of additional techniques for achieving successful radial cannulation and sheath insertion

FIGURE 5 Pooled Analysis of Studies Comparing DRA vs Conventional RA



Forest plot reporting trial-specific and summary RRs with 95% CI for the endpoint of access site crossover. Abbreviations as in Figure 2.

CENTRAL ILLUSTRATION **Forest Plot Reporting Summary Effects of Distal vs Conventional Radial Access**



Ferrante G, et al. J Am Coll Cardiol Intv. 2022;15(22):2297–2311.

DRA = distal radial access; EASY = Early Discharge After Transradial Stenting of Coronary Arteries; PCI = percutaneous coronary intervention; RA = radial access; RAO = radial artery occlusion.

such as the use of ultrasound guidance and smaller coronary guidewires, often with hydrophilic coating.[10]

Yet, the clinical implications of our findings and their generalizability remain to be ascertained in future analyses. In particular, the included studies did not assess hard clinical endpoints, and therefore whether DRA use may affect the risk of major adverse cardiovascular events cannot be ascertained. Also, whether the systematic use of DRA, compared with conventional RA, in the setting of acute coronary syndrome requiring PCI, in particular among patients with ST-segment elevation acute myocardial infarction, may lead a delayed revascularization and might be associated with worse outcome is not known. Therefore, the choice of DRA vs conventional RA should be evaluated on an individual basis, and DRA use should not be recommended as a routine approach. Subgroups of patients at high risk of RAO in whom radial loss may have long-term consequences, such as those requiring coronary artery bypass grafting surgery, arteriovenous fistula creation for hemodialysis, or undergoing multiple repeat coronary interventions, may be potential candidates for DRA, provided the proficiency of operators with DRA.

STUDY LIMITATIONS. The studies included in this meta-analysis differed with respect to enrolled patient population, trial design, endpoint definitions, and duration of follow-up. The primary and several secondary outcome measures were not reported in all included studies. Owing to the lack of individual-data participants, this aggregate data meta-analysis that has less power to detect differential treatment effects across individuals. Meta-regression analyses are more prone to ecological bias, probably caused by confounding across trials.[45] The lack of systematic implementation of best practices for the prevention of RAO across studies may have magnified the beneficial effect of DRA use on the risk of RAO. Finally, the included

studies are not "all-comer" trials reflecting everyday practice, as the enrolled patients were largely known to have both a radial and dorsal radial pulse.

CONCLUSIONS

This meta-analysis of all available RCT comparing DRA vs conventional RA among patients undergoing coronary angiography followed or not by intervention shows that DRA is associated with lower risks of forearm RAO and EASY ≥II hematoma but requires longer time for radial artery cannulation and sheath insertion, more puncture attempts, and a higher access site crossover.

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ADDRESS FOR CORRESPONDENCE: Dr Giuseppe Ferrante, Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20072 Pieve Emanuele, Milan, Italy. E-mail: giu.ferrante@hotmail.it.

PERSPECTIVES

WHAT IS KNOWN? The use of RA is considered the preferred access site for coronary interventions across the spectrum of patients with coronary artery disease, in particular among patients with acute coronary syndromes.

WHAT IS NEW? In patients undergoing coronary angiography followed or not by coronary intervention, mainly due to chronic coronary syndrome, the use of DRA, compared with conventional RA, reduces the occurrence of forearm radial occlusion and EASY ≥II hematoma but is associated with higher access site crossover, longer time for radial artery cannulation and sheath insertion, and more puncture attempts.

WHAT IS NEXT? Future studies investigating the effects of DRA use, compared with conventional RA use, on major adverse cardiovascular events, in particular among patients with acute coronary syndromes undergoing percutaneous coronary intervention are warranted.

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KEY WORDS coronary angiography, distal radial access, percutaneous coronary intervention, radial access, radial artery occlusion

APPENDIX For expanded Methods and References sections as well as a supplemental table and figures, please see the online version of this paper.