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Radial Artery and Ulnar Artery Occlusions Following Coronary Procedures and the Impact of Anticoagulation: *ARTEMIS* (Radial and Ulnar *ART*Ery Occlusion *M*eta-Analys*IS*) Systematic Review and Meta-Analysis

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***Background*—**Incidence of radial artery occclusions (RAO) and ulnar artery occclusions (UAO) in coronary procedures, factors predisposing to forearm arteries occlusion, and the benefit of anticoaggulation vary significantly in existing literature. We sought to determine the incidence of RAO/UAO and the impact of anticoagulation intensity.

***Methods and Results*—**Meta-analysis of 112 studies assessing RAO and/or UAO (N=46 631) were included. Overall, there was no difference between crude RAO and UAO rates (5.2%; 95% confidence interval [CI], 4.4–6.0 versus 4.0%; 95% CI, 2.8–5.8; *P*=0.171). The early occlusion rate (in-hospital or within 7 days after procedure) was higher than the late occlusion rate. The detection rate of occlusion was higher with vascular ultrasonography compared with clinical evaluation only. Low-dose heparin was associated with a significantly higher RAO rate compared with high-dose heparin (7.2%; 95% CI, 5.5–9.4 versus 4.3%; 95% CI, 3.5–5.3; Q=8.81; *P*=0.003). Early occlusions in low-dose heparin cohorts mounted at 8.0% (95% CI, 6.1–10.6). The RAO rate was higher after diagnostic angiographies compared with coronary interventions, presumably attributed to the higher intensity of anticoagulation in the latter group. Hemostatic techniques (patent versus nonpatent hemostasis), geography (US versus non-US cohorts) and sheath size did not impact on vessel patency.

***Conclusions*—**RAO and UAO occur with similar frequency and in the order of 7% to 8% when evaluated early by vascular ultrasonography following coronary procedures. More-intensive anticoagulation is protective. Late recanalization occurs in a substantial minority of patients. **(*J Am Heart Assoc*. 2017;6:e005430. DOI: 10.1161/JAHA.116.005430.)**

Key Words: coronary angiography • radial occlusion • transradial • transulnar • ulnar occlusion

Radial artery occlusion (RAO) remains the silent protagonist in transradial coronary procedures. Its percentage rate ranges from single- to 2-digit numbers and occurs within a broad spectrum of prophylactic anticoagulation.[1] When RAO happens, it prohibits the reuse of this artery for future transradial coronary procedures as well as the use of this artery as a graft for coronary artery bypass surgery. On the other hand, although RAO is almost always clinically silent in the acute setting, the long-term natural history of this condition is not very well characterized. Notably, although there is plenty of evidence regarding the incidence of forearm artery occlusion following cardiac catheterization, the populations studied and the sizes of the populations have been highly diverse and thus have provided highly variable estimates of RAO incidence. Furthermore, several studies have shown that anticoagulation prevents forearm artery occlusion, but the ideal intensity of prophylactic anticoagulation is rather ill-defined in the existing literature.[1–3] We therefore conducted this meta-analysis to systematically evaluate the incidence of RAO and ulnar artery occlusion (UAO) as well as the role of anticoagulation intensity on forearm artery occlusions following diagnostic and interventional coronary procedures, and to define potential clinical and procedural factors that may impact on this incidence.

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An accompanying Table S1 is available at http://jaha.ahajournals.org/content/6/8/e005430/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- Incident radial artery occlusion following coronary procedures range from single- to 2-digit numbers, occurs within a broad spectrum of prophylactic anticoagulation, and prohibits the subsequent use of the artery as an access site for future catheterization or as a potential graft.
- In this meta-analysis of 112 studies, we found that the rate of forearm artery occlusion following a cardiac catheterization (diagnostic coronary angiography or intervention) ranges between 6% and 8% on average when evaluated early after catheterization using vascular ultrasonography, whereas the occlusion rate is higher when anticoagulation intensity is low, when the patency status is assessed early, and when coronary angiography, rather than intervention, is performed.

What Are the Clinical Implications

- Postcatheterization unavailability of the radial artery raises several teleological, nephrological, and long-term natural history issues beyond its loss as a potential graft for bypass surgery.
- Therefore, reduction of forearm artery occlusion rates should become a priority target in interventional cardiology.
- This meta-analysis indicates that coronary angiography is not just a "simple" procedure, given that every tenth of these patients may be at risk for early vessel occlusion when on low-anticoagulation regimen.
- Adequate anticoagulation during coronary angiography, that is, ≥50 IU/kg of heparin and ultrasonographic patency assessment before discharge appear therefore mandatory.

Methods

We sought for relevant studies through electronic searches of MEDLINE, EMBASE database, and the Cochrane Central Register of Controlled Trials from 1989 through August 15, 2016, and we also searched the www.tctmd.com, www.clinicaltrials.gov, www.clinicaltrialresults.org, and www.cardiosource.com websites for preliminary reports within the past year. We matched the results derived after having used the following key words: for radial artery occlusion: "radial artery" OR "radial catheterization" OR "radial access" OR "radial spasm" OR "transradial" AND "radial occlusion" OR "radial thrombosis" (Table 1); for ulnar artery occlusion: "ulnar artery" OR "ulnar catheterization" OR "ulnar access" OR "ulnar spasm" OR "transulnar" AND "ulnar occlusion" OR "ulnar thrombosis" (Table 2). Reference lists of relevant studies was additionally scanned.

Study Selection

We included full-length publications in English, German, or French language reporting RAO or UAO rates after a coronary angiogram (CAG) or percutaneous coronary intervention (PCI). No restrictions regarding the detection methods of arterial (radial or ulnar) patency were applied. Therefore, studies reporting RAO or UAO based on clinical grounds (ie, palpation, clinical examination, and/or Allen's test as well as reverse Allen's test), Barbeau's test, or Doppler ultrasonography (duplex, color, or nonimaging) alone or in combination were included. We prioritized the first screening method for RAO/UAO detection (eg, clinical evaluation only when palpation was used to screen RAO/UAO), rather than selecting further downstream techiques utilized after the first abnormal test (eg, typically vascular ultrasonography if pulsation was absent). No restrictions regarding the mode and dose of anticoagulation were applied. Exclusion criteria were: (1) irretrievable data; (2) ongoing studies; (3) trials not reporting RAO or UAO rates; (4) data in abstract form; and (5) duplicate reports.

Table 1. Search Strategy for Radial Artery Occlusion

Search Terms
1. ("radial artery" OR "radial catheterization" OR "radial access" OR "radial spasm" OR "transradial")
2. ("radial occlusion" OR "radial thrombosis")
3. 1 AND 2

Data Extraction

The search of literature, selection of studies, extraction of data, and quality assessment were initiated independently by 2 investigators (G.H. and K.A.) by using a standardized approach. Disagreements were resolved by consensus. For each study, we recorded the arterial occlusion rates after transradial or transulnar procedure, as well as all variables which are reported in the section "Outcomes." Numerical aggregate data and categorical data as appearing in the publications were used for analysis.

Outcomes

The primary end points of this meta-analysis were the (1) general crude rate of RAO and UAO and (2) rate of RAO and

Table 2. Search Strategy for Ulnar Artery Occlusion

Search Terms
1. ("ulnar artery" OR "ulnar catheterization" OR "ulnar access" OR "ulnar spasm" OR "transulnar")
2. ("ulnar occlusion" OR "ulnar thrombosis")
3. 1 AND 2

UAO according to anticoagulation intensity. Frequency of forearm artery occlusions was estimated in studies reporting *early* (ie, in-hospital or within 7 days after CAG and PCI), *late* (ie, >7 days after the coronary procedure), and *total* occlusions (referring to all occlusions whether reported as early only or late only). The impact of anticoagulation intensity was assessed depending on whether patients received a low (ie, ≤5000 IU or up to 50 IU/kg body weight) versus a high (ie, >5000 IU or ≥70 IU/kg or activated clotting time >200 seconds) dose of unfractionated heparin (UFH). A patient group was allocated in the high-anticoagulation-dose group if a low dose of UFH was given but activated clotting time exceeded 200 seconds. Patients undergoing PCI had invariably received either ≥70 IU/kg of UFH or bivalirudin or both and were categorized into the high-anticoagulation group. We adopted the occlusion rates as mentioned in the original articles or according to the intention-to-treat principle when figures were additionally given in a per protocol analysis.

Subgroup analysis was performed to assess the potential effect of the following parameters on the primary outcome: (1) study design, that is, randomized versus nonrandomized studies regardless of whether RAO/UAO was the study primary end point; also studies reporting RAO/UAO as a primary end point versus studies reporting arterial occlusion as a nonprimary end point; (2) duplex or color Doppler ultrasonography as a mode of detection of RAO and UAO versus other detection methods; (3) studies performed in the United States versus outside the United States; (4) CAG versus PCI; (5) coronary procedures with ≤5- versus >5-Fr catheters; and (6) patent hemostasis versus all other hemostatic techniques after sheath removal. Coronary procedures performed with sheathless catheters were categorized according to their actual size relative to conventional sheath size (eg, a 6.5-Fr sheathless catheter was considered a ≤5-Fr catheter and a 7.5-Fr sheathless catheter a >5-Fr catheter).

Statistical Analysis

The rate of RAO and UAO of each study is reported as a percentage. We performed meta-analyses of studies estimating the rate of RAO to obtain the pooled estimate for the whole cohort of studies. Similar separate analysis was performed for UAO. The proportion of inconsistency across studies not explained by chance was quantified with the I^2 statistic. Heterogeneity between subgroups was calculated with Cochran's Q test.[4] Because of significant heterogeneity among studies, the random-effects model was used to obtain the pooled estimate. Finally, we performed stratified analysis to evaluate whether the pooled rates of RAO or UAO differ between subgroups (early versus late occlusion, high- versus low-dose heparin, use of Doppler to evaluate occlusion versus non-Doppler studies, CAG versus PCI studies, patent hemostasis versus all other hemostatic techniques after sheath removal, US versus non-US studies, use of ≤5- versus >5-Fr catheters, randomized versus nonrandomized studies, and studies assessing artery occlusion as a primary end point versus rest of studies). Univariable random-effects metaregression analysis was used to examine whether effect sizes were affected by these factors. Estimates of occlusion rates between subgroups were compared with a test of interaction.[5] In addition, age and duration of procedure at study level were included in univariable metaregression. All tests used in our analysis were 2-sided. Results were considered statistically significant at $P<0.05$. Rates of arterial occlusion and confidence intervals (CIs) were illustrated with forest plots.

Presence of publication bias was investigated graphically by funnel plots of precision, and its implications for our results were assessed by Duval and Tweedie's trim-and-fill method.[6] All analyses were performed with Comprehensive Meta Analysis software (Version 2; Biostat, Englewood, NJ).[7]

Results

Qualitative Summary

Our search identified 9949 potential eligible publications reporting RAO and 2041 publications reporting UAO, which were narrowed by preliminary review to 145 potentially relevant original articles. Of those, 28 articles were excluded because either no RAO/UAO rates were reported or they were reviews/editorials or meta-analyses not reporting original data on RAO/UAO rates, whereas 5 studies were excluded because they were duplicate reports (Figure 1). Finally, 112

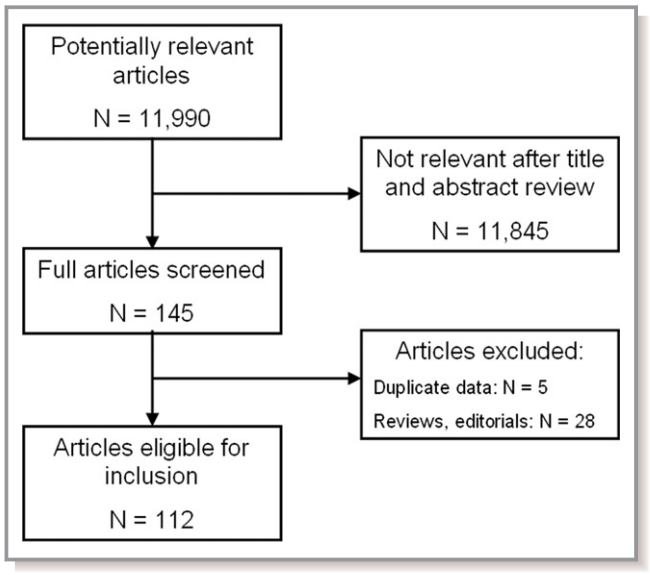

Figure 1. Electronic literature search. Summary of the literature search results.

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Table 3. Overview of Studies Assessing UAO Sorted by Date of Publication

Author, Year (Country)	Sample Size (N)	Age (y)	Women (%)	Study Design	Sheath Size	Anticoagulation Intensity	Hemostasis	UAO Rate (%) (Early/Late RA Patency Assessment)	Assessment of Arterial Occlusion	Comments and Authors' Conclusions
Terashima,[100] 2001 (Japan)	9	71	55.6	Observational	L	LD	Non-Patent	0.0/NA	Clinical	First report on TU catheterization; complications such as bleeding, loss of a UA pulse, ulnar nerve injury, and the formation of an aneurysm or fistula were *not observed* in any patient
Dashkoff,[101] 2002 (United States)	5	68	40	Observational	NA	NA	Non-Patent	0.0/0.0	Clinical	UA strongly palpable at 1-week and at 3-month F-U in all patients; authors' conclusion: "the TU approach to coronary procedures is feasible and may be preferable in selected cases"
Limbruno,[102] 2004 (Italy)	13	NA	NA	Observational	H	HD	Non-Patent	NA/0.0	Ultrasonography	TU primary PCI; authors' conclusion: "TU access may represent an additional option in patients undergoing primary angioplasty when the RA access site is not available"
Gourassas,[103] 2004 (Greece	3	61	33.3	Observational	H	HD	Non-Patent	0.0/NA	Clinical	TU PCI in 3 patients; authors' conclusion: "TU coronary angioplasty is feasible and may turn out to be the favorable method in certain cases where the radial artery may serve as a free graft for surgical revascularization"
Lanspa,[104] 2004 (United States)	1	52	100	Observational	L	LD	Non-Patent	0.0/NA	Clinical	TU CAG in the presence of RAO and normal inverse Allen's test in a patient with limited vascular access
Lanspa,[105] 2005 (United States) 12	12	68	NA	Observational	NA	LD	Non-Patent	0.0/NA	Clinical	TU CAG in 4 patients with pre-existing RAO (1 chronic and 4 acute RAOs)
Rath,[106] 2005 (India)	100	NA	NA	Observational	NA	NA	NA	0.0/NA	Clinical	This study was conducted to assess the safety and feasibility of a transulnar approach in performing coronary procedures
Mangin,[107] 2005 (Canada)	117	62	31.6	Observational	NA	HD	Non-Patent	0.0/NA	Clinical, ultrasonography	No ulnar pulse loss was noted
Aptecar,[108] 2005 (France)	17	60	24.9	Observational	L	NA	Non-Patent	NA/0.8	Ultrasonography	158 patients catheterized by the UA; 173 procedures performed, including 122 CAG and 51 PCI

Continued

Table 3. Continued

Author, Year (Country)	Sample Size (N)	Age (y)	Women (%)	Study Design	Sheath Size	Anticoagulation Intensity	Hemostasis	UAO Rate (%) (Early/Late RA Patency Assessment)	Assessment of Arterial Occlusion	Comments and Authors' Conclusions
Aptecar-UA,[28] 2005 (France)	216	63	24.5	RCT	H	HD	Non-Patent	NA/5.88	Ultrasonography	After sheath removal and local hemostasis, heparin infusion was continued at the discretion of the operators in those patients with ACSs (=55% of the TU group of patients); PCI patients n=103 (of the 216 patients in the UA group); access site artery occlusion more frequently after a second PCI; authors' conclusion: "the transulnar approach has the potential to spare injury to the RA in anticipation of its use as a coronary bypass conduit"
Knebel,[109] 2008 (United States)	28	60	32.1	Observational	NA	HD	Non-Patent	3.57/7.14	Clinical	A bolus of heparin (100 IU/kg) was given IV and additional doses (60 IU/kg) were repeated if the procedure lasted longer than 1 h; 5- and 6-Fr catheters were used for CAG or PCI;
Andrade,[110] 2008 (Brazil)	1	63	0	Observational	H	HD	Non-Patent	0.0/NA	Clinical	Primary TU PCI without ischemic hand complications despite past RAO; authors' conclusion: "the transulnar approach represents an alternative to the transradial approach in selected cases when performed by radial-trained operators, sharing a high success rate and extremely low incidence of access site complications"
Vassilev,[111] 2008 (Bulgaria)	131	69.1	36.6	Observational	H	NA	Non-Patent	0.0/NA	NA	PCI in 10 of 59 patients; spasm frequency: 13.6%; authors' conclusion: "the TU approach has higher access site failure rates in an unselected patient population"
Li-UA,[40] 2010 (China)	118	60	32.3	RCT	H	HD	Non-Patent	5.1/1.7	Ultrasonography	Asymptomatic UA stenosis 1 and 30 days after procedures: 11.0% and 12.3%
Hussein,[112] 2010 (Egypt)	1	71	0	Observational	H	HD	Non-Patent	NA/0.0	Ultrasonography	Recanalization of a CTO

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Table 3. Continued

Author, Year (Country)	Sample Size (N)	Age (y)	Women (%)	Study Design	Sheath Size	Anticoagulation Intensity	Hemostasis	UAO Rate (%) (Early/Late RA Patency Assessment)	Assessment of Arterial Occlusion	Comments and Authors' Conclusions
Agostoni,[113] 2011 (Italy)	1	67	0	Observational	H	HD	Non-Patent	0.0/NA	Clinical, oximetry	TU PCI in ipsilateral RAO
James,[114] 2012 (United States)	1	78	100	Observational	H	HD	Non-Patent	0.0/0.0	Barbeau's	Sheathless TU PCI
de Adrade,[60] 2012 (Brazil)	387	61.2	54.3	Observational	NA	NA	Non-Patent	0.73/NA	Clinical, Barbeau's	Allen's test not routinely performed
Kwan,[115] 2013 (United States)	17	77	23.5	Observational	L	HD	PH-modified	0.0/NA	Barbeau's	TU PCI with a 5-Fr Glide sheath in the presence of RAO In patients with RAO; authors' conclusion: "ipsilateral TU catheterization may not be an absolute contraindication. Our results suggest that extensive collaterals from the anterior interosseous artery may be the reason for protection against hand ischemia. . ."
Agostoni,[116] 2013 (Italy)	42	63	31	Observational	NA	NA	Non-Patent	11.9/NA	Clinical	Multicenter SWITCH registry: ipsilateral TU catheterization after TR failure; no hand ischemia after UAO; authors' conclusion: "in case of failed radial sheath insertion, switching directly to the homolateral UA for PCI is feasible and it appears to be safe, without cases of symptomatic hand ischemia"
Hahalis-UA,[117] 2013 (Greece)	462	64.3	21.6	RCT	NA	NA	PH-modified	NA/8.9	Ultrasonography	The AURA of ARTEMIS study the largest to-date comparison of a \default TU relative to TR comparison for coronary procedures in terms of feasibility and safety; need for crossover in the TU group inferior to TR access site with a difference of 26.3% (95% CI, 11.96–40.69; *P*=0.004); authors' conclusion: "as a result of higher crossover rates, a first-line TU strategy was proven inferior to the TR\ approach for coronary procedures. At present, the TU route should not be regarded as an acceptable alternative to the transradial access site"
Kedev,[118] 2014 (FYROM)	476	60	34.9	Observational	NA	NA	Non-Patent	NA/3.15	Ultrasonography	TU approach for CAG, PCI and carotid stenting; subgroup of 240 patients with ipsilateral RA unavailability

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Table 3. Continued

Author, Year (Country)	Sample Size (N)	Age (y)	Women (%)	Study Design	Sheath Size	Anticoagulation Intensity	Hemostasis	UAO Rate (%) (Early/Late RA Patency Assessment)	Assessment of Arterial Occlusion	Comments and Authors' Conclusions
Geng-UA,[73] 2014 (China)	271	64.2	31	RCT	NA	NA	Non-Patent	1.1/1.1	Ultrasonography	RA vs UA comparison for CAG and/or PCI; PCI in 58.7% of the patients; Allen's test and inverse Allen's test were not routinely performed; a motor abnormality of the hand was observed in 1 patient
Liu-UA,[75] 2014 (China)	317	58.6	30.9	RCT	H	HD	Non-Patent	NA/6.3	Clinical, oximetry, Ultrasonography	Prospective, randomized study of TU vs TR PCI in ACS patients; authors' conclusion: "the TU approach has results and access complications similar to the TR approach and is a safe and feasible alternative for ACS patients"
Gokhroo-UA,[99] 2015 (India)	410	58.6	?	Observational	NA	NA	Non-Patent	0.7/NA	Clinical	AJULAR study; comparison of the TU group with a retrospective cohort of patients undergoing TRA angiography; ad-hoc PCI in only 22 of 410 patients (ie, 5.2%) in the TU group
Roghani-Dehkordi,[119] 2015 (Iran)	97	57	44.3	Observational	NA	NA	Non-Patent	0.0/NA	Clinical	NA
Gokhroo-UA,[85] 2016 (India)	1270	67.12	36.4	RCT	NA	HD	Non-Patent	1.3/NA	Clinical	AJULAR trial; a RCT of the TR vs the TU approach for coronary procedures (Table S1)

ACS indicates acute coronary syndrome; CAG, coronary angiography; Fr, French size; H, high(er) sheath size (>5-Fr); HD, high(er) heparin dose/anticoagulation intensity; IU, international units; IV, intravenously; JL, Judkins left catheter; L, low(er) sheath size (≤5-Fr); LD, low(er) heparin dose/anticoagulation intensity; LMWH, low-molecular-weight heparin; NA, nonapplicable (not mentioned or mixed population regarding French size or anticoagulation intensity); PCI, percutaneous coronary intervention; PEP, primary end point of the study; PH, patent hemostasis; RA, radial artery; RAO(s), radial artery occlusion(s); RCT, randomized, control trial; SD, standard heparin dose/anticoagulation intensity; TR, transradial; TRA, transradial approach; UA, ulnar artery; UAO(s), ulnar artery occlusion(s); US, ultrasonography, Doppler ultrasound.

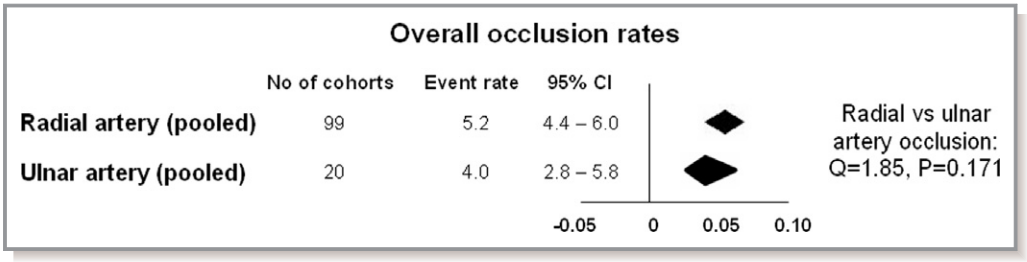

Figure 2. Overall rates of radial and ulnar occlusions. The diamonds and their width represent the pooled rates and the 95% CI (confidence interval), respectively.

original articles assessing RAO and/or UAO[8–119] were deemed eligible for our meta-analysis, of which 99 cohorts from 92 studies publishing RAO[8–99] and 25 cohorts reporting UAO were analyzed[28,40,73,75,85,100–119] (Tables S2 and 3).

In total, the included studies analyzed 46 631 subjects. All studies were published since 1989. Sample sizes ranged from 3[102,108,110–112] to 9609 individuals.[60] The quality of the included studies reporting RAO was assessed by using the Newcastle–Ottawa scale (Table S1). Overall, the majority of studies had a score of 6, whereas 5 studies had a score of 8.

Meta-Analysis

Overall arterial occlusion

The overall rate of RAO was 5.2% (95% CI, 4.4–6.0%; Q=812.5; I^2=87.9; 99 cohorts). The overall rate of UAO was 4.0% (95% CI, 2.8–5.8%; Q=50.2; I^2=62.2; 20 cohorts). There was no significant difference between the overall RAO and UAO rates (*P*=0.171; Figure 2). For these calculations, a mean of early and late occlusion was introduced in analysis when both were reported in a study.

Early and late arterial occlusion

When only early occlusion was considered, the rate of early RAO was nonsignificantly higher than the early UAO (5.6%; 95% CI, 4.7–6.5; 82 cohorts versus 3.4%; 95% CI, 2.0–5.7%, 15 cohorts; Q=3.08, *P*=0.079 between groups). There was no difference between late RAO and late UAO rates (5.1%; 95% CI, 4.2–6.2, 42 cohorts versus 4.8%; 95% CI, 2.9–7.8; 7 cohorts; Q=0.049; *P*=0.83). In the 27 studies reporting both early and late occlusion, the early combined occlusion rate (RAO or UAO) was significantly higher than the late combined occlusion rate (7.7%; 95% CI, 6.6–8.9 versus 4.8%; 95% CI, 3.9–5.8; *P*<0.001 for comparison between early and late occlusion; Figure 3). This difference was confirmed when the 24 studies reporting early and late RAO were analyzed, after the 2 studies reporting UAO were excluded.[40,109]

Effect of anticoagulation intensity

The overall rate of RAO (early, late, or combined) was significantly higher in the 24 studies using low-dose UFH compared with the 57 studies using high-dose UFH (7.2%; 95% CI, 5.5–9.4 versus 4.3%; 95% CI, 3.5–5.3; Q=8.81; *P*=0.003 between groups), with a mean of early and late RAO being introduced in analysis when both reported (Figure 4). Similarly, when only early RAO was considered, the rate of early RAO was significantly higher in the 21 cohorts using low-dose UFH (8.0%; 95% CI, 6.1–10.6) compared with the 45 cohorts using high-dose UFH (4.4%; 95% CI, 3.5–5.5; Q=10.69; *P*=0.001 between groups). In contrast, when late RAO was analyzed, the rate of late RAO was similar between the 12 cohorts of low-dose UFH (5.4%; 95% CI, 3.7–7.8) and the 21 cohorts of high-dose UFH (5.0%; 95% CI, 3.6–6.8; Q=0.11; *P*=0.745 between groups; Figure 4).

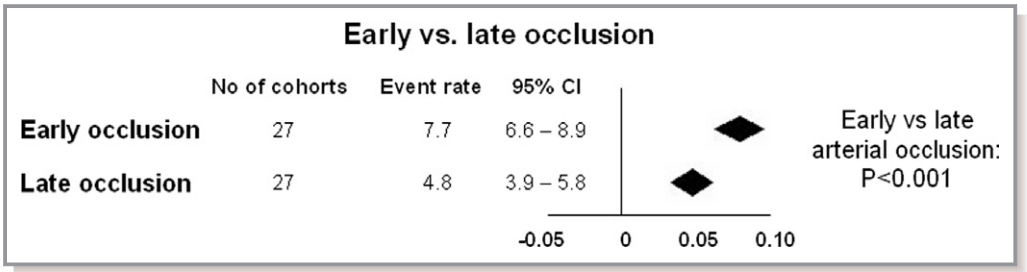

Figure 3. Rates of early vs late arterial occlusions (combined radial and ulnar occlusions) in studies reporting both early and late occlusions. Diamonds and their width as in Figure 1. CI indicates confidence interval.

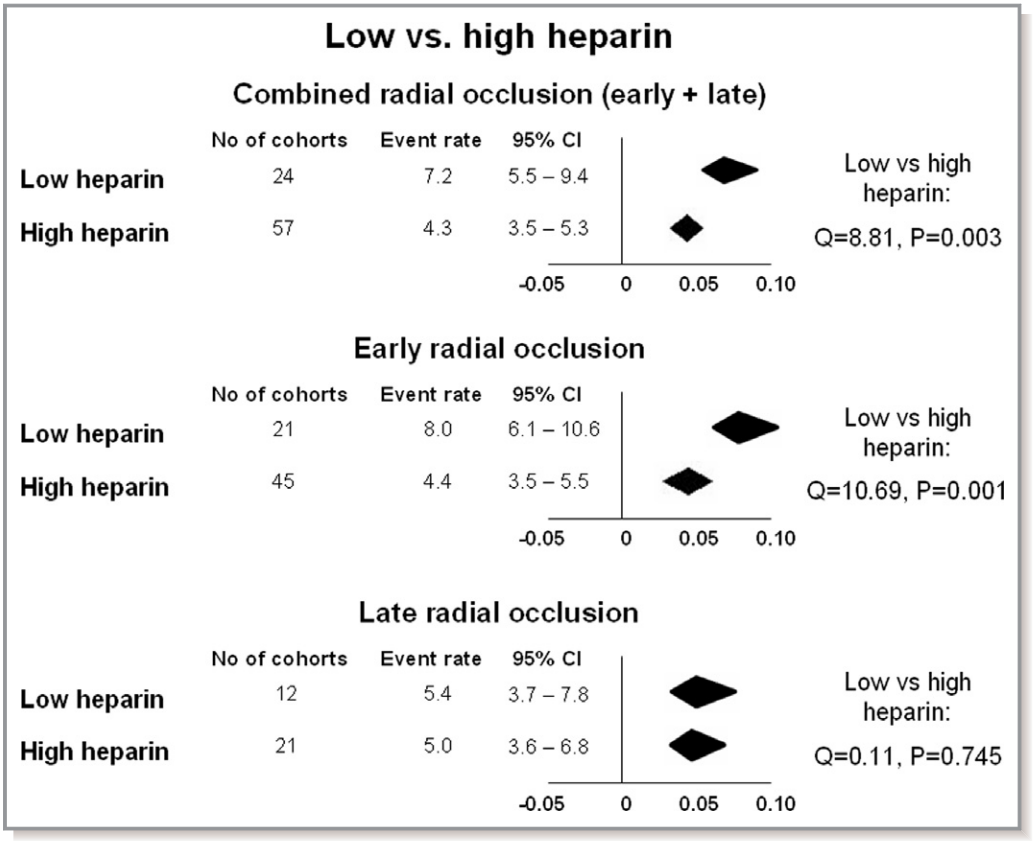

Figure 4. Effect of intensity of anticoaggulation on radial occlusion rate in unselected (randomized and observational) studies. Diamonds and their width as in Figure 1. CI indicates confidence interval.

Analysis of the 5 randomized studies specifically designed to address the impact of high versus low UFH dose on RAO showed that high UFH was accompanied by a significantly lower rate of RAO (3.7%; 95% CI, 1.8–7.7) compared with low UFH (9.6%; 95% CI, 4.9–17.9; Q=3.57; *P*=0.05 between subgroups with random-effects model; Figure 5).

Stratified Analysis According to Procedural Characteristics

The rate of combined RAO was significantly higher in the 50 cohorts that used Doppler for RAO diagnosis compared with the 31 cohorts using palpation of the radial artery (6.4%; 95% CI, 5.3–7.7 versus 3.8%; 95% CI, 2.9–4.9; Q=10.35; *P*=0.001; Figure 6). When only early RAO was considered, the rate of RAO was higher in the 38 cohorts that used Doppler compared with the 30 cohorts that used palpation only (6.7%; 95% CI, 5.4–8.3 versus 4.3%; 95% CI, 3.3–5.5; Q=6.77; *P*=0.009). On the other hand, there was no difference in late RAO between the 25 cohorts using Doppler and the 10 cohorts using palpation (5.8%; 95% CI, 4.5–7.4 versus 4.3%; 95 CI, 2.9–6.3, Q=1.67; *P*=0.196). Use of Barbeau's test was not associated with a difference in detection of the combined (early and late) RAO (5.7%; 95% CI, 4.0–8.1 in the 16 cohorts that used Barbeau's test versus 4.9%; 95% CI, 4.1–6.0 in the 64 cohorts that did not use Barbeau's test; Q=0.46; *P*=0.49). There was no significant difference in the overall rate of arterial occlusion between the 16 studies (14 RAO studies and 2 UAO study) using patent hemostasis compared with the 78 studies using occlusive hemostasis (5.3%; 95 CI, 3.7–7.5 versus 5.3%; 95% CI, 4.5–6.3, Q=0.0; *P*=0.99; Figure 6). The overall rate of RAO (early and late) was higher in the 27 studies done in patents undergoing CAG compared with the 40 PCI studies in which more-intense anticoagulation was used (5.9%; 95% CI, 4.5–7.7 versus 4.0; 95% CI, 3.0–5.2; Q=3.87; *P*=0.049; Figure 6). This difference was driven by the early RAO (6.8%; 95% CI, 5.1–9.1 in the 23 CAG studies versus 4.3%; 95% CI, 3.1–5.8 in the 32 PCI studies; Q=4.68; *P*=0.031). The size of sheath had no impact on the combined RAO and UAO occlusion frequency (5.8%; 95% CI, 4.6–7.3 in the 33 studies using sheaths ≤5 Fr versus 5.5%; 95% CI, 4.5–6.8 in the 43 studies using >5 Fr; Q=0.088; *P*=0.77; Figure 6).

Subgroup Analysis According to Study Design

In the 37 studies reporting RAO as a primary end point, the rate of combined RAO was significantly higher (7.1%; 95% CI,

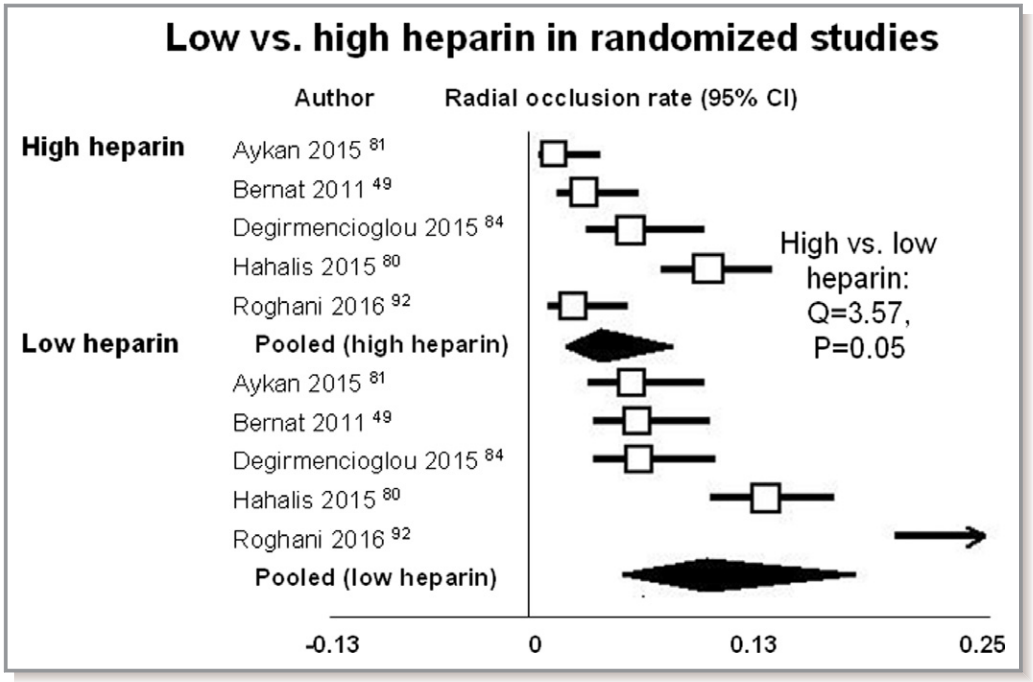

Figure 5. Effect of intensity of anticoaggulation on radial occlusion rate in randomized studies. Squares indicate the occlusion rate and lines indicate the respective 95% confidence interval (CI). The size of the squares corresponds to the number of subjects in each study. Diamonds and their width as in Figure 1.

5.8–8.8) compared with the 62 studies reporting RAO as a secondary end-point (4.2%; 95% CI, 3.5–5.1; Q=13.58; $P<0.001$; Figure 7). The rate of RAO was numerically higher, but statistically nonsignificant, in the 55 observational studies compared with the 43 randomized studies reporting rates of RAO (5.7%; 95% CI, 4.6–7.1 versus 4.5%; 95% CI, 3.6–5.7; Q=2.16; $P=0.142$; Figure 7). There was no significant difference in the overall rate of RAO between the 13 studies done in the United States (4.5%; 95% CI, 2.8–7.0) and the 86 non-US studies (5.3%; 95% CI, 4.5–6.2; Q=0.468; $P=0.494$; Figure 7).

Analysis of Continuous Variables

Univariable metaregression analysis showed that mean age at study level was not a predictor of arterial occlusion when both RAO/UAO and early/late occlusions were analyzed (Z=1.37; $P=0.17$ by meta-regression of 122 cohorts). In contrast, there was a weak positive relationship between early RAO and age (Z=2.55; $P=0.011$ in 79 cohorts). There was not an association between duration of procedure and early RAO (Z=−1.09; $P=0.27$).

Publication Bias

The funnel plots for the overall (early and late) RAO rate was slightly asymmetric to the left, indicating minor bias and possible unpublished or undiscovered studies with a high arterial occlusion rate (Figure 8). The trim-and fill method imputed 26 theoretically missing studies and recalculated our pooled risk estimate. The imputed RAO rate (6.9%; 95% CI, 5.8–8.1) was not substantially different from the initial estimate, suggesting the absence of significant publication bias.

Discussion

Main Findings

This meta-analysis in 46 631 patients found that the crude unadjusted rates of RAO and UAO rates were similar, relatively low and in the order of 4% to 6%. Incident arterial occlusion was variable, being highest in the order of 7% to 8% in studies with patients on less-intense anticoagulation; in early as compared with delayed assessment of vessel patency; in patients undergoing diagnostic angiography compared to angioplasty; in studies having the frequency of arterial occlusion as a primary end point; and in reports utilizing vascular ultrasonography to detect this kind of complication. Notably, the upper 95% CI for early RAO on low-heparin dose was 10.6% in the current meta-analysis, revealing that every tenth patient may be at risk for forearm artery occlusion if not appropriately anticoaggulated during and after a transradial coronary procedure. Recent publications confirm the difficult challenge encountered by the transradial interventionalists to maintain postprocedural forearm artery patency with ranging frequencies between 9.24%

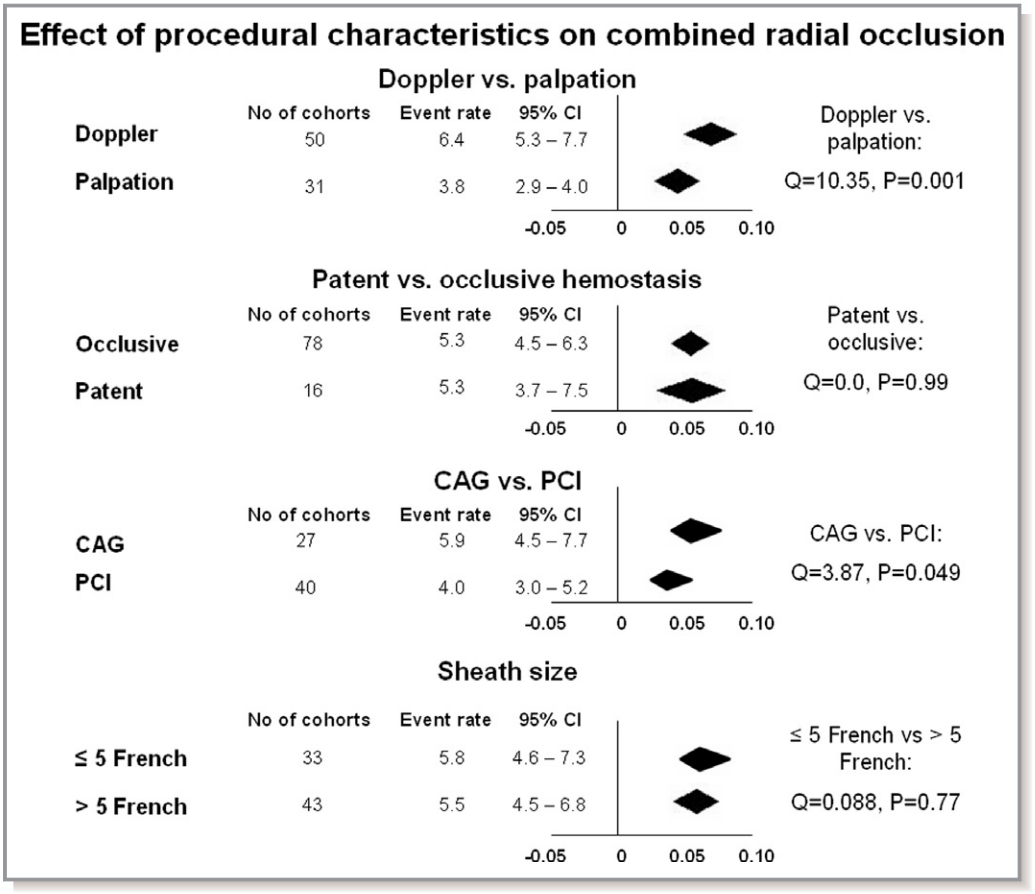

Figure 6. Effect of procedural characteristics on radial occlusion rates. Diamonds and their width as in Figure 1. CAG indicates coronary angiography; CI, confidence interval; PCI, percutaneous coronary intervention.

of ultrasonography-detected late RAOs using the patent hemostasis technique (56 of 606 patients)[89] and 25% of clinically detected RAOs with low-dose heparin.[92] Analysis of observational studies showed a benefit of higher heparin dose in terms of forearm artery patency, which was also confirmed after analyzing 5 small randomized, controlled trials[49,80,81,84,92] specifically designed to address this issue. We found no geographical disparity of RAO/UAO frequency. Catheter size and procedural duration had similarly no impact on arterial occlusion rates.

Anticoagulation

In observational studies, several independent risk factors for RAO have been identified; yet anticoagulation appeared only inconsistently to predict RAO.[47,51,81,91,92,117] In 1 report, a 1% reduction of RAO per 1-IU/kg heparin dose increase has been suggested.[117] Randomized, control trials and pooled 1-center data have indicated some benefit of "standard" (ie, 5000 IU) over low (ie, usually 2000–2500 IU) heparin dose, but have been inconclusive because of inadequate statistical power.[49,80,81,84,92] By considering both observational reports and randomized studies, this meta-analysis elucidates the advantage of higher anticoagulation intensity. The fact that larger versus smaller sheath sizes were not associated with higher forearm artery occlusions and that the longer-lasting PCI was associated with lower occlusion rates versus CAG may demonstrate a possible protective effect of a more-intensive anticoagulation regimen used in PCI over CAG. Whether antiplatelet therapy in PCI decreases further the risk of arterial occlusion remains hypothetical. In 1 study, no such favorable antiplatelet effect was evident.[80] Data from the study of Uhlemann et al[59] confirmed a higher than 2-fold RAO incidence with 6-Fr as opposed to 5-Fr catheters in CAG patients having received 2500 heparin units. An ongoing study (ClinicalTrials.gov Identifier: NCT02570243) comparing standard dose with high heparin dose may clarify the uncertainty with regard to heparin requirements in transradial CAG.

Early and Late Occlusion Rates

This meta-analysis confirms the prevailing belief of significantly lower late over early RAO and UAO rates. This finding may suggest late recanalization in a minority of patients as a

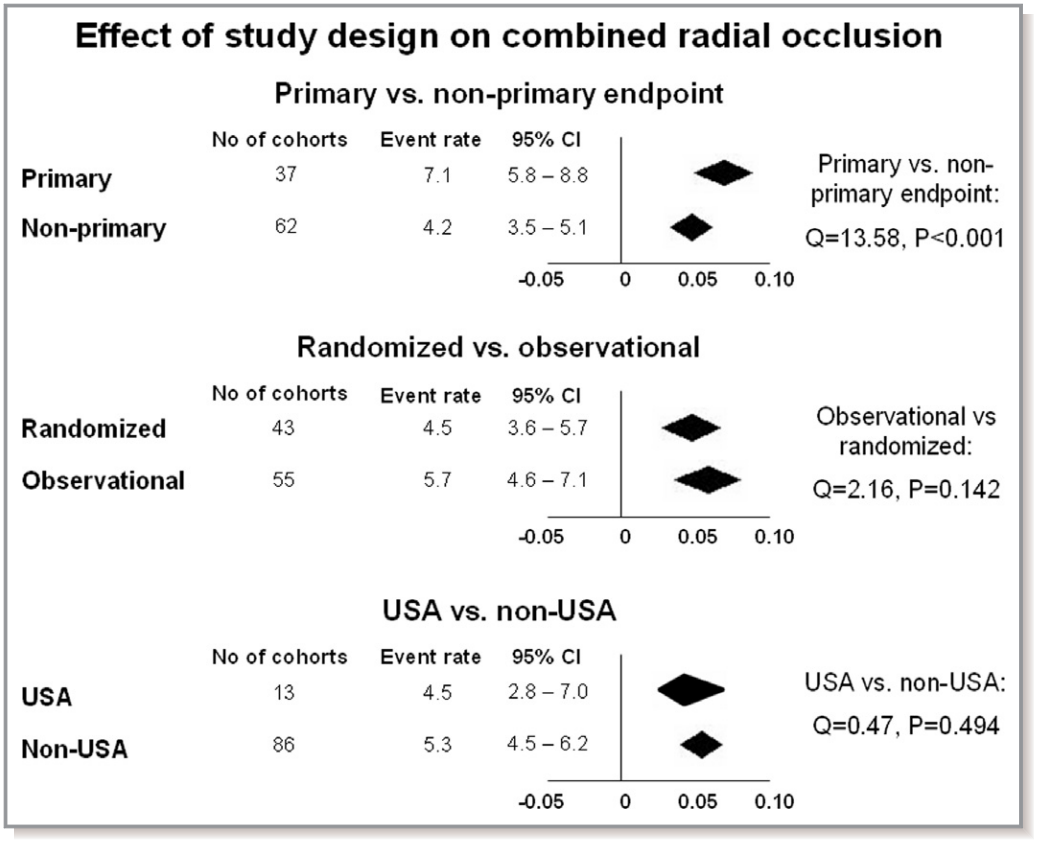

Figure 7. Effect of study design characteristics on radial occlusion rates. Diamonds and their width as in Figure 1. CI indicates confidence interval.

result of the disease natural history. Additionally, short-term anticoagulation with low-molecular-weight heparins may facilitate the delayed patency of the artery in some patients with early RAO.[27,46,52,59] This observational data provide further indirect evidence regarding the beneficial effect of anticoagulation on forearm vessel patency, but this has not been formally tested in a randomized, control trial. Interestingly, late RAOs not detected in the early phase have also been reported.[54,87]

Methods to Detect Arterial Patency

Ultrasonography demonstrated clear superiority over clinical evaluation with respect to RAO and UAO detection rates. Absence of flow on Doppler ultrasonography along with the simultaneously obtained anatomic information (eg, thrombus delineation)[18,19,21,46,89,91,96,98] appears as a straightforward detection technique of RAOs and UAOs. In this regard, the predictive accuracy of solely anatomic stenosis[20] or partial flow[46,92] remains to be established. Clinical methods (ie, arterial palpation) have been associated with both false-negative and false-positive findings attributed to low blood pressure, local edema and hematoma, subocclusive wall thrombus and trauma, remaining postprocedural tissue compression, as well as retrograde perfusion from the contralateral forearm artery. For example, although palpation appears to overestimate RAOs,[66,94,95] one fifth to one third of patients with ultrasonographically documented RAOs may demonstrate palpable radial artery.[59,94] Notably, the ulnar artery poses additional difficulties in determining patency status with palpation as a result of its deeper course compared with the radial artery.[117] Whether strategies for the accurate detection of RAOs and UAOs (such as the utilization of the Barbeau's test or ultrasonography once clinical evaluation indicates RAO/UAO) are sufficient remains hypothetical. Such strategies were reported in many of the studies in the current meta-analysis.* In this context, and while future systematic investigations on this topic are awaited, our meta-analysis reinforces the role of ultrasonography as a reliable and probably indispensable detection method.

Patent Hemostasis

Similar occlusion rates between patent hemostasis and all other applied hemostatic techniques, including simple compression bandage, should not be interpreted as a failure of

*References 8, 17, 24, 30, 33, 34, 43, 44, 47, 52, 58, 67, 90, 92, 95.

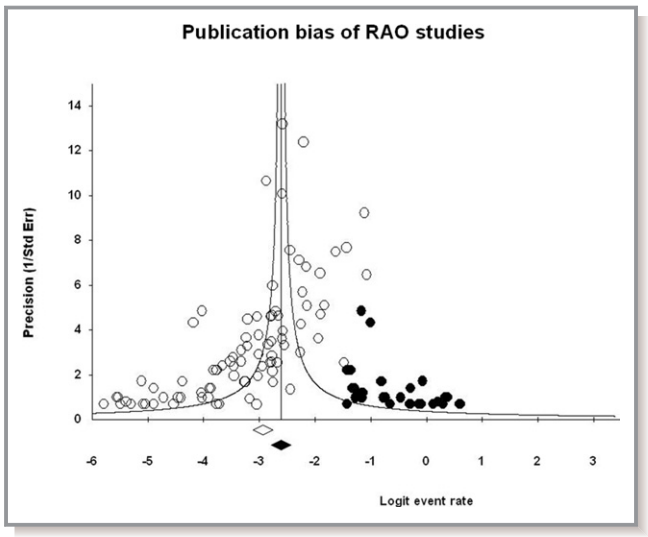

Figure 8. Publication bias and its potential impact. The funnel plots of precision plot a study's effect size against its precision, which is the inverse of standard error. The white circles represent individual original studies and the white diamond is the pooled mean difference and 95% CI for the meta-analysis. Large studies tend to appear toward the top and cluster near the mean effect. Small studies tend to appear toward the bottom and are dispersed across a range of values. A symmetric funnel plot (white circles symmetrically around the mean effect) indicates absence of publication bias. To check for publication bias, the trim-and-fill method imputes the—theoretically—missing studies (shown in black circles) and then recomputes the pooled effect (black diamond). Although the plots were slightly asymmetric, there was no significant difference between the recomputed effect and the respective effects derived from the original studies, suggesting absence of significant publication bias. CI indicates confidence interval; RAO, radial artery occlusion.

patent hemostasis. Whether meticulously carried out or not, patent or patent-like hemostasis was reported in only 16 studies,[†] most of which comprised predominantly older studies with diverse designs and end points. Although patent hemostasis has shown clear superiority in the pioneer work of Pancholy et al,[30] additional studies elucidating feasibility and other practical issues of this technique are needed. In a very recent work an impressive reduction of RAO has been documented after meticulous patent hemostasis protocol and additional compression of the contralateral UA,[120] thereby confirming a smaller study with similar design.[95]

Clinical Implications

Even the short-lasting CAG appears not to be just a "simple" procedure in terms of forearm artery occlusion. Interestingly, our analysis showed an average occlusion rate of ≈6% (with higher 95% CI at ≈8) after diagnostic angiography, which may result from less-intense-than-required periprocedural heparin administration, arterial spasm, longer procedures, multiple attempts for arterial access, etc.[80,94,117] Maintenance of radial artery and ulnar artery patency should become a target of highest priority in interventional cardiology. Ideally, interventionalists should have adequate experience on forearm procedures with low crossover rates, avoid and timely treat spasm,[104] administer at least 5000 heparin units for CAG,[3] apply hemostasis after sheath removal according to the "patent artery principle,"[1,30] and evaluate patients with ultrasonography in the short term with late re-evaluation when RAO or UAO was initially present.[1]

Limitations

The main limitation of the current meta-analysis is the lack of individual patients' data that would allow identifying independent predictors of forearm artery occlusions. An additional limitation is the inclusion of studies with substantial diversity of protocols and designs as well as the lack of rigorous, large-scale, randomized, control trial, thereby increasing the impact of the observed heterogeneity on the results. Finally, very few studies have reported time to achieve hemostasis depending on anticoagulation level; thus, we were unable to reach conclusive evidence on the trade-off of possible very long hemostasis time in patients on higher heparin dosage.

Conclusions

Incident RAO and UAO following coronary procedures is similar and relatively low, ranging between 5% and 8%, with occlusion rates being higher when the forearm arteries are evaluated early with ultrasonography. Higher anticoagulation levels are protective and probably neutralize the aggravating effects of larger sheath size and long-lasting coronary interventions. Ultrasonography appears as a first-line tool, but the simpler Barbeau's test may be equally useful in evaluating arterial patency. Studies elucidating the possible beneficial effect of angioplasty-equivalent heparin dosage for CAG and exploring the potential impact of procedural factors on arterial occlusion are currently warranted.

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Quality score of studies using the Newcastle - Ottawa scale (NOS)

Study	Representativeness of the Exposed Cohort	Selection of the Non-Exposed Cohort	Ascertainment of Exposure	Demonstration That Outcome of Interest Was Not Present at Start of Study	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Was Follow-Up Long Enough for Outcomes to Occur	Adequacy of Follow Up of Cohorts	NOS Score
Campeau (1) 1989 (Canada)	1	0	1	1	0	1	1	1	6
Otaki (2) 1992 (Japan)	0	0	1	1	0	0	1	0	3
Kiemeneij (3) 1994 (The Netherlands)	1	0	1	1	0	1	1	1	6
Lotan (4) 1995 (Israel)	1	0	1	1	0	1	1	1	6
Kiemeneij (5) 1995 (The Netherlands)	0	0	1	1	0	1	1	1	5
Spaulding (6) 1996 (France)	1	0	1	1	0	1	1	1	6
Kiemeneij (7) 1997 (The Netherlands)	1	0	1	1	0	0	1	0	4
Chatelain-CAG (8) 1997 (Switzerland)	1	0	1	1	0	1	1	1	6

Chatelain-PCI (8) 1997 (Switzerland)	1	0	1	1	0	1	1	1	6
Kiemeneij (9) 1997 (The Netherlands)	1	0	1	1	1	1	1	1	7
Stella (10) 1997 (The Netherlands)	1	0	1	1	0	1	1	1	6
Saito (11) 1999 (Japan)	1	0	1	1	0	1	1	1	6
Saito (12) 1999 (Japan	1	0	1	1	0	1	1	1	6
Nagai (13) 1999 (Japan)	1	0	1	1	0	1	1	1	6
Wu (14) 2000 (USA)	0	0	1	1	0	1	1	1	5
Pillay (15) 2000 (Malaysia)	1	0	1	1	0	1	1	1	6
Brito (16) 2001 (Brazil)	1	0	1	1	0	1	1	1	6
Dahm-5Fr (17) 2002 (Germany)	1	0	1	1	0	1	1	1	6
Dahm-6Fr (17) 2002 (Germany)	1	0	1	1	0	1	1	1	6
Bagger (18) 2005 (Denmark)	1	0	1	1	0	1	1	1	6

Kim (19) 2005 (Korea)	1	0	1	1	0	1	1	1	6
Venkatesh-CAG (20) 2006 (USA)	0	0	1	1	0	1	1	1	5
Venkatesh-PCI (20) 2006 (USA)	0	0	1	1	0	1	1	1	5
Aptecar-RA (21) 2006 (France)	1	0	1	1	0	1	1	1	6
Sanmartin (21) 2007 (Spain)	1	0	1	1	0	1	1	1	6
Pancholy-PH (23) 2008 (USA)	1	0	1	1	0	1	1	1	6
Pancholy-conventional (23) 2008 (USA)	1	0	1	1	0	1	1	1	6
Takeshita (24) 2008 (Japan)	0	0	1	1	0	1	1	1	5
Kindel-CAG (25) 2008 (Germany)	1	0	1	1	0	1	1	1	6
Kindel-PCI (25) 2008 (Germany)	0	0	1	1	0	1	1	1	5
Yan (26) 2008 (China)	1	0	1	1	0	1	1	1	6
Cubero (27) 2009 (Spain)	1	0	1	1	0	1	1	1	6
Pancholy (28) 2009 (USA)	1	0	1	1	0	1	1	1	6

Pancholy (29) 2009 (USA)	1	0	1	1	0	1	1	1	6
Brueck (30) 2009 (Germany)	1	0	1	1	0	1	1	1	6
Yan (31) 2010 (China)	1	0	1	1	0	1	1	1	6
Schiano (32) 2010 (France)	1	0	1	1	0	1	1	1	6
Li (33) 2010 (China)	1	0	1	1	0	1	1	1	6
Caussin (34) 2010 (France)	1	0	1	1	0	1	1	0	5
From (35) 2010 (USA)	0	0	1	1	0	1	1	1	6
Mamas (36) 2010 (UK)	1	0	1	1	0	1	1	1	6
Mizuno (37) 2010 (Japan)	0	0	1	1	0	1	1	1	5
Plante-CAG & heparin (38) 2010 (Canada)	1	0	1	1	0	1	1	1	6
Plante-PCI & bivalirudin (38) 2010 (Canada)	1	0	1	1	0	1	1	1	6
Zankl (39) 2010 (Germany)	1	0	1	1	0	1	1	1	6

Rathore (40) 2010 (UK)	1	0	1	1	0	1	1	1	6
Feray (41) 2011 (Turkey)	0	0	1	1	0	1	1	1	5
Bernat-LD (42) 2011 (Czech Republic)	1	1	1	1	1	1	1	1	8
Bernat-SD (42) 2011 (Czech Republic)	1	1	1	1	1	1	1	1	8
Egred (43) 2011 (UK)	1	0	1	1	0	1	1	1	6
Politi -1 (44) 2011 (Italy)	0	0	1	1	0	1	1	1	5
Politi -2 (44) 2011 (Italy)	0	0	1	1	0	1	1	1	5
Politi -3 (44) 2011 (Italy)	0	0	1	1	0	1	1	1	5
Singh (45) 2011 (USA)	1	0	1	1	0	1	1	1	6
Chiam (46) 2001 (China)	1	0	1	1	0	1	1	1	6
Youn (47) 2011 (Korea)	0	0	1	1	0	1	1	1	5
Park (48) 2012 (Korea)	1	0	1	1	0	1	1	1	6
Honda (49) 2012 (Japan)	1	0	1	1	0	1	1	1	6

Pancholy (50) 2012 (USA)	1	0	1	1	0	1	1	1	6
Pancholy (51) 2012 (USA)	1	0	1	1	0	1	1	1	6
Uhlemann (52) 2012 (Germany)	1	0	1	1	0	1	1	1	6
De Andrade (53) 2012 (Brazil)	1	0	1	1	0	1	1	1	6
Beyer (54) 2013 (USA)	0	0	1	1	0	1	1	1	5
Tewari (55) 2013 (India)	1	0	1	1	0	1	1	1	6
Tuncez (56) 2013 (india)	1	0	1	1	0	1	1	1	6
Chung (57) 2013 (India)	1	0	1	1	0	1	1	1	6
Kotowycz (58) 2014 (Canada)	1	0	1	1	0	1	1	1	6
Tumscitz (59) 2014 (Italy)	1	0	1	1	0	1	1	1	6
Yurtdas (60) 2014 (Turkey)	1	0	1	1	0	1	1	1	6
Amininian (61) 2014 (Belgium)	1	0	1	1	0	1	1	1	6
Marcovic (62) 2014 (Germany)	1	0	1	1	0	1	1	1	6

Hu (63) 2014 (China)	1	0	1	1	0	1	1	1	6
Pancholy (64) 2014 (USA)	1	0	1	1	0	1	1	1	6
Takeshita 4-Fr (65) 2014 (Japan)	0	0	1	1	0	1	1	1	5
Takeshita 6-Fr (65) 2014 (Japan)	0	0	1	1	0	1	1	1	5
Geng (66) 2014 (China)	1	0	1	1	0	1	1	1	6
Buturak (67) 2014 (Turkey)	1	0	1	1	0	1	1	1	6
Liu (68) 2014 (China)	1	0	1	1	0	1	1	1	6
Dharma (69) 2015 (Indonesia India)	1	0	1	1	0	1	1	1	6
Cong PD (70) 2015 (China)	1	0	1	1	0	1	1	1	6
Cong PC (70) 2015 (China)	1	0	1	1	0	1	1	1	6
Cong RC (70) 2015 (China)	1	0	1	1	0	1	1	1	6
Lisowka (71) 2015 (Poland)	1	0	1	1	0	1	1	1	6
Carg (72) 2015 (India)	1	0	1	1	0	1	1	1	6

Hahalis-LD (73) 2015 (Greece)	1	1	1	1	1	1	1	1	8
Hahalis-SD (73) 2015 (Greece)	1	1	1	1	1	1	1	1	8
Aykan-LD (74) 2015 (Turkey)	1	1	1	1	1	1	1	1	8
Aykan-SD (74) 2015 (Turkey)	1	1	1	1	1	1	1	1	8
Tian (75) 2015 (China)	1	0	1	1	0	1	1	1	6
Abdelaal (76) 2015 (Canada)	1	0	1	1	0	1	1	1	6
Degirmencioglu-LD (77) 2015 (Turkey)	1	1	1	1	1	1	1	1	8
Dedirmencioglu-SD (77) 2015 (Turkey)	1	1	1	1	1	1	1	1	8
Gokhroo RA (78) 2015 (India)	1	0	1	1	0	1	1	1	6
Van Leeuwen (79) 2015 (The Netherlands)	1	0	1	1	0	1	1	1	6
Peruga (80) 2015 (Poland)	1	0	1	1	0	1	1	1	6
Yoshimachi (81) 2016 (Japan)	1	0	1	1	0	1	1	1	6
Bi (82) 2016 (China)	1	0	1	1	0	1	1	1	6

Yoshimachi (83) 2016 (Japan)	0	0	1	1	0	1	1	1	5
Levin (84) 2016 (Israel)	0	0	1	1	0	1	1	1	5
Roghani-LD (85) 2016 (Iran)	1	1	1	1	1	1	1	1	8
Roghani-SD (85) 2016 (Iran)	1	1	1	1	1	1	1	1	8
Dautov (86) 2016 (Canada)	0	0	1	1	0	1	1	1	5
Costa (87) 2016 (The Netehrlands)	0	0	1	1	0	1	1	1	5
Koutouzis-UA compression & PA (88) 2016 (Greece)	1	0	1	1	0	1	1	1	6
Koutouzis-PA alone (88) 2016 (Greece)	1	0	1	1	0	1	1	1	6
Noble (89) 2016 (Canada)	1	0	1	1	0	1	1	1	6
Andrade (90) 2016 (Brazil)	1	0	1	1	0	1	1	1	6
Turan (91) 2016 (Turkey)	1	0	1	1	0	1	1	1	6
Gokhroo (92) 2016 (India)	1	0	1	1	0	1	1	1	6

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TABLE S2. Overview of studies assessing radial artery occlusion sorted by date of publication

Author, year (country)	Sample size N	Age (y)	Women (%)	Study design	Sheath size	Anticoagulation intensity	Hemostasis	RAO rate (%) (early/late RA patency assessment)	Method of assessment of arterial patency status	Comments and authors' conclusions
Campeau (8) 1989 (Canada)	100	NA	NA	Observational	L	HD	Non Patent	**6.0/1.0**	Clinical, Ultrasonography	Very early RAO rate: 24%; late assessment at 2-12 weeks; in 2 patients with diminished RA pulse and 1 with absent RA pulse the reverse Allen's test was "positive" (=normal);
Otaki (9) 1992 (Japan)	40	59	17.5	Observational	L	LD	Non Patent	**0/0**	NA	NA
Kiemeneij (10) 1994 (The Netherlands)	20	63	20	Observational	H	HD	Non Patent	**0/NA**	Clinical, Ultrasonography	In one patient some collagen (Vasoseal) was successfully applied subcutaneously near the puncture opening to stop prolonged bleeding
Lotan (11) 1995 (Israel)	100	66	21	Observational	H	HD	Non Patent	**3.0/1.0**	Clinical	A RA pulse was palpated in 91 of the patients before discharge, and in 6 others, adequate flow could be heard with Doppler. In 2 patients, radial flow was restored within several weeks; none of the patients suffered from ischemia of the hand.
Kiemeneij(12) 1995 (The Netherlands)	100	62	23	Observational	H	HD	Non Patent	**10.0/5.0**	Clinical	122 angioplasties in 100 patients; In 10 pts RA pulsations were absent at discharge. Of these 10 patients, late recanalization was evident in 5, and in 3 patients pulsations remained absent; no claudication was found.
Spaulding (13) 1996 (France)	415	58	14.9	Observational	L	LD	Non Patent	**26.3/26.3**	Ultrasonography	Claudication of the hand was tested by having patients open and close their hand 50 times; all patients with a RAO were asymptomatic at two months with the same echo-Doppler findings; incident RAO: 71% in the first 49 patients, 24% in the next 119 receiving 2,000-3,000 I.U. of heparin and 4.3% in the last 210 receiving 5,000 I.U. ($p < 0.05$); similar results of Group 2 with those of Uhlemann et al (59) published several years later with RAO rates of 24% vs. 25%; no late occlusions at two months were noted in the remaining patients; RAO predictors were no heparin administration in group 1, sex & RA diameter in group 2 (2,000-3,000 I.U. heparin) & none in group 3 (5,000 I.U. heparin)
Kiemeneij (14) 1997 (The Netherlands)	100	60	14	Observational	H	HD	Non Patent	**NA/0**	Clinical	Outpatient PCI; coumadin instead of ticlopidine premedication in 44 patients with preprocedural INR > 2.5 Mean age for the 150 pts: 60 yrs with 39 (out of 159) females No significant difference observed in the incidence of RA patency after compression (96% for patients who received 2,500 IU vs. 95% for those who received 5,000 IU heparin.
Chatelain-CAG (15) 1997 (Switzerland)	103	NA	NA	Observational	L	LD	Non Patent	**4.85/NA**	Clinical	No significant difference observed in the incidence of RA patency: 96% for patients who received 2,500 I,U, vs. 95% for those who received 5,000 I,U. heparin; neither heparin dosage nor the use of a 6-Fr sheath affected the rate of RA patency
Chatelain-PCI (15) 1997 (Switzerland)	56	NA	NA	Observational	H	HD	Non Patent	**3.57/NA**	Clinical	Same comment as above
Kiemeneij (16) 1997 (The Netherlands)	300	61	26.3	RCT	H	HD	Non Patent	**5.0/3.0**	Clinical	ACCESS trial, a randomized comparison of percutaneous transluminal coronary angioplasty by the radial, brachial and femoral approaches; heparin (5,000 I.U.) after sheath insertion and every hour during prolonged angioplasty procedures; no ACT measures;after sheath removal, heparin infusion continued overnight in selected cases

Stella (17) 1997 (The Netherlands)	563	59	24.7	Observational	H	HD	Non Patent	**5.3/2.8**	Clinical, Ultrasonography	Incidence and outcome of RAO following TR coronary angioplasty; presence of claudication tested by opening and closing the hand 50 times consecutively;short-term (<2 wk) tenderness of the forearm was especially mentioned by 12 patients (2.1%), but none of these patients had symptoms of RAO either by physical examination or US study (7/12 patients).
Saito (18) 1999 (Japan)	294	NA	NA	Observational	H	HD	Non Patent	**NA/2.8**	Ultrasonography	Influence of the RA diameter-to-sheath outer diameter ratio on RA flow after TR PCI in Japanese patients; TR PCI in 1791 lesions (1360 patients); 294 patients examined with ultrasonography
Saito (19) 1999 (Japan	250	NA	32	Observational	H	HD	Non Patent	**6.8/NA**	Ultrasonography	Feasibility study of using GCs > 7 Fr in TR PCI; none of the patients developed RAO (grade 0); incidence of severe flow reduction (grade 1): 6.8% ; RA diameter/sheath ratio predicted RAO
Nagai (20) 1999 (Japan)	162	64	36,4	Observational	NA	LD	Non Patent	**9.0/3.7**	Ultrasonography	Early after the procedure, segmental stenosis was noted in 22% and no flow by color Doppler in 9% (pulse was unpalpable in only 2% of the patients);late after the procedure, segmental stenosis was noted in 2, diffuse stenosis in 22%, and no flow in 5% of the patients; late recanalization was observed in 60% of RAOs; RAO predictors: diabetes mellitus, RA diameter & RA diameter/sheath ratio; authors' conclusion: *"US of the RA useful in selecting both an access route and an appropriate size of the sheath to determine early and late vascular complications"*
Wu (21) 2000 (USA)	42	65	11,9	Observational	H	HD	Non Patent	**NA/14,7**	Ultrasonography	Feasibility of 6-Fr and 8-Fr TR PCI and post-procedural arm function with forearm and intrinsic hand function tests in 24 catheterized out of 42 patients; 8-Fr and RAO did not affect hand strength or endurance;
Pillay (22) 2000 (Malaysia)	50	54	5.8	Observational	H	HD	Non Patent	**6.0/NA**	Clinical	PCI patients
Brito (23) 2001 (Brazil)	103	57	12.6	Observational	H	HD	Non Patent	**2.06/NA**	Clinical	PCI patients
Dahm-5Fr (24) 2002 (Germany)	87	60	41,4	RCT	L	HD	Non Patent	**1.15/NA**	Clinical, Ultrasonography	A tendency of higher procedural success rates and lower vascular access complications was documented after 5-Fr in comparison to 6-Fr PCI
Dahm-6Fr (24) 2002 (Germany)	84	61	40,4	RCT	H	HD	Non Patent	**5.95/NA**	Clinical, Ultrasonography	Same comment as above
Bagger (25) 2005 (Denmark)	221	63	29.9	Observational	L	HD	Non Patent	**4.7/NA**	Barbeau's	Total duration of TR CAG shorter over TF CAG
Kim (26) 2005 (Korea)	220	62	33.2	Observational	H	HD	Non Patent	**2.7/NA**	Clinical	Retrospective analysis in primary PCI
Venkatesh-CAG (27) 2006 (USA)	51	63	45,1	Observational	L	HD	Non Patent	**1.9/0.0**	Barbeau's	Nonrandomized comparison; aim of the study: first, divided dosing with heparin should provide the same protection against postprocedure RAO during CAG as the standard 5,000 I.U. single dose; second, the safety profile of bivalirudin during PCI should not be altered if it is given after an initial reduced heparin dose; outcome analysis on LD heparin vs. bivalirudin in PCI patients regarding incident bleeding and RAO; one case of RAO resolved with 2 weeks of LMWH; six (15%) of patients in Group 1B were receiving warfarin prior to the procedure, as opposed to none in Group 2B; authors' conclusion: „*single bolus of heparin can be preferred in case of diagnostic CAG whereas Bival can be contemplated in case of ad hoc PCI"*

Venkatesh-PCI (27) 2006 (USA)	66	66	40.9	Observational	H	HD	Non Patent	**0.0/NA**	Barbeau's	Same comment as above
Aptecar-RA (28) 2006 (France)	215	63	27	RCT	H	HD	Non Patent	**NA/4.65**	Ultrasonography	The PCVI-CUBA Study; US in 86 out of the 216 patients undergoing PCI; three of nine (33.3%) RAOs occurred after a second PCI.
Sanmartin (29) 2007 (Spain)	275	63	21.1	Observational	H	HD	Non Patent	**10.55/NA**	Barbeau's	Interruption of blood flow during compression and RAO after TR catheterization; 6 Fr catheters only; 70-100 I.U. heparin per kilo body weight; the pulse oximeter signal in the index finger during ipsilateral UA compression was used for the assessment of RA flow (oximeter sign and plethysmography curve).Interruption of blood flow during compression and RAO after TR catheterization;
Pancholy-PH (30) 2008 (USA)	219	65,9	NA	RCT	L	LD	Patent	**12.33/7.31**	Barbeau's	PROPHET study (PH over conventional hemostasis technique); PH was a RAO predictor; the PH technique as described by the authors: the sheath was pulled out 4–5 cm and a plastic band ‘‘hemoband’’ was placed around the forearm at the site of entry; the needle cap and gauze composite was placed over the site of entry; a pulse oximeter sensor was placed over the index finger, the hemoband was tightened, and the sheath was removed; ipsilateral UA was occluded and the hemoband was loosened till plethysmographic signal returned (confirming RA patency) or bleeding occurred; if bleeding occurred at the pressure required to maintain patency, manual compression was used in n=8 or 3.6%; RA patency was checked at least once every hour. authors' conclusions: "*PH is highly effective in reducing RAO after radial access and guided compression should be performed to maintain RA at the time of hemostasis*"
Pancholy-conventional (30) 2008 (USA)	217	63.5	NA	RCT	L	LD	Non Patent	**5.05/1.83**	Barbeau's	Low body weight was RAO predictive
Takeshita (31) 2008 (Japan)	19	NA	NA	Observational	L	HD	Non Patent	**0.0/NA**	Clinical, Ultrasonography	PCI using a 4-Fr coronary accessor allowing the catheter to be inserted into a 4-Fr introducer sheath; the inner diameter of which can accommodate most currently available coronary stents; RAO defined as absence of RA pulse confirmed by a negative reversed Allen’s test or by visible obstruction with 2-D US or the absence of a positive Doppler signal, alone or in combination
Kindel-CAG (32) 2008 (Germany)	158	NA	NA	RCT	NA	LD	Non Patent	**NA/9.49**	Ultrasonography	Authors' conclusion:*"Hydrophilic-coated sheaths for TR access will reduce patient discomfort but do not involve fewer cases of occlusion than traditional non-coated sheath*
Kindel-PCI (32) 2008 (Germany)	42	NA	NA	RCT	H	HD	Non Patent	**NA/0.0**	Ultrasonography	Same comment as above.
Yan (33) 2008 (China)	57	70	24.7	Observational		LD	Non Patent	**1.8/1.8**	Clinical, Ultrasonography	Primary PCI in the elderly; 57 patients had TR while 46 patients had the TF approach; RA diameter & duration of hemostasis predicted RAO; authors' conclusion: *"TR approach as compared with TF primary PCI safe and feasible for elderly patients with AMI"*
Cubero (34) 2009 (Spain)	351	65	32,8	RCT	H	LD	Non Patent	**6.55/NA**	Barbeau's, Ultrasonography	RACOMAP trial; TR band guided by the mean artery pressure -Group A- vs. conventional hemostasis - Group B; RA flow was defined as absent if oximeter and plethysmography readings were negative during UA compression (inverse Allen test) and confirmed with bidirectional Doppler; pressure exerted on the RA in group A was lower in comparison with group B
Pancholy (35) 2009 (USA)	500			Observational	L	HD	Non Patent	**7.8/5.2**	Barbeau's	Authors' conclusion: *"A significant reduction in RAO was noted with hemostasis using the TR Band compared to the HemoBand";*
Pancholy (36) 2009 (USA)	500	64	38.6	RCT	L	LD	Non Patent	**5.8/3.6**	Barbeau's	A non-significant RAO rate reduction in the SD heparin group; authors' conclusion: *"I.A. and I.V. heparin administration provide comparable efficacy in preventing RAO, favoring a probable systemically mediated mechanism of action, rather than a local effect.*
Brueck (37) 2009 (Germany)	512	63	43	RCT	NA	NA	Non Patent	**0.59/NA**	Clinical	A delay of 15 s before the return of color to the blanched hand was considered an αbnormal Allen’s test

Yan (38) 2010 (China)	638	60,6	22	Observational	NA	NA	Non Patent	**5.96/NA**	Ultrasonography	This study aimed to investigate the anatomy of the forearm arteries with US and to evaluate the effect of the anatomy of the right RA on the outcomes of TR coronary procedures; sex, height, weight and arm circumference were the independent factors determining a diameter of the RRA ≥2 mm; small RA diameter and RA anatomical abnormalities could result in longer procedure time, more incidence of procedure failure and RAO
Schiano (39) 2010 (France)	162	63.5	20,4	RCT	L	HD	Non Patent	**0.0/NA**	Ultrasonography	The AWARE study: adjusted-weight anticoagulation for TR elective coronarography; 5,000 IU heparin or 50 IU/kg with an upper limit of 5,000 IU; ACT values lower in the adjusted anticoagulation group (231.4 min, vs. 265.6 min, p=0.04).
Li (40) 2010 (China)	122	61	34.4	RCT	NA	NA	Non Patent	**6.6/4.9**	Ultrasonography	The mean diameter of the UA and RA at the wrist was similar; compared to the RA, the UA was larger in 44.9% of patient; artery intimal thickness occurred in 62.7% vs. 68.0% of patients one day after TU or TR PCI, and in 18.6% vs. 13.9% of patients 30 days after TU or TR PCI
Caussin (41) 2010 (France)	351	66	33	RCT	NA	LD	Non Patent	**3.5/NA**	Ultrasonography	Reduction in spasm with a long hydrophylic TR sheath; No difference was found regarding procedure failure respectively; 1.2% vs. 0.6%, local complication 0.6% vs. 1.2%, and RA occlusion 3.5% vs. 3.5%.
From (42) 2010 (USA)	10	69	10	Observational	H	LD	Non Patent	**0.0/NA**	Clinical	Sheathless TR Intervention using standard guide catheters; a 5-Fr diagnostic catheter inserted into and through a 7-Fr GC and over a 0.035 inch standard J-tip wire for easier percutaneous insertion of the GC into the RA
Mamas (43) 2010 (UK)	100	59.4	25	Observational	L	HD	Non Patent	**NA/2.0**	Clinical, Ultrasonography	The aim of this study was to investigate the feasibility of using a 6.5-Fr sheathless GC (which has an outer diameter of less than 5-Fr) as a default system in TR PCI
Mizuno (44) 2010 (Japan)	18	NA	NA	Observational	L	HD	Non Patent	**0.0/NA**	Clinical, Barbeau's, Ultrasonography	PCI using a virtual 3 Fr GC; 36 lesions in 27 patients of whom in 18 patients via the TR approach
Plante-CAG & heparin (45) 2010 (Canada)	200	59	26	RCT	H	HD	Non Patent	**NA/7.0**	Ultra-sonography, Barbeau's	RAO definition: absent Doppler flow and absence of waveform on combined plethysmography/pulse oximetry; RAO predicted by body weight & short (!) procedural duration (HR: 7.52, 95% CI 1.57–36.0, p=0.011); type of anticoagulant therapy was not a RAO predictor
Plante-PCI & bivalirudin (45) 2010 (Canada)	200	60	22	RCT	H	HD	Non Patent	**NA/3.5**	Ultrasonography Barbeau's	Same comment as above.
Zankl (46) 2010 (Germany)	488	NA	NA	Observational	NA	NA	Non Patent	**8.8/4.3**	Ultrasonography	After 4 weeks, 26 (86.7%) of the symptomatic patients showed a partial or complete recanalization of the RA after treatment with LMWH, compared with 4 (19.1%) of the asymptomatic patients without anticoagulation
Rathore (47) 2010 (UK)	790	63	26,1	RCT	H	HD	Non Patent	**9.24/6.83**	Clinical	TR PCI for chronic total occlusions; maller wrist, spasm & no heparin administration during the procedure were RAO predictors .
Feray (48) 2011 (Turkey)	39	55.6	30.8	Observational	H	HD	Non Patent	**4.0/4.0**	Clinical, Ultra-sonography	This study was to assess the efficacy of 60 mg enoxaparin for prevention of RAO after TR CAG &/or PCI.
Bernat-LD (49) 2011 (Czech Republic)	222	62	35.6	RCT	L	LD	Patent	**5.9/NA**	Ultrasonography	LD vs. SD heparin for RAO prevention; acute RAO after TR catheterization could be recanalized by early 1-hour homolateral UA compression; Non-significant RAO rate reduction in the SD heparin group

Bernat-SD (49) 2011 (Czech Republic)	243	62	32.1	RCT	L	SD	Patent	**2.9/NA**	Ultrasonography	Same comment as above
Egred (50) 2011 (UK)	77	67	18.1	Observational	H	HD	Non Patent	**0.0/NA**	Clinical	Feasibility and safety of 7-Fr radial approach for complex PCI
Politi -1 (51) 2011 (Italy)	50	54	26	RCT	H	HD	Non Patent	**0.0/NA**	Barbeau	This study evaluated the occurrence of 24-hour RAO and the rate of bleeding of a novel hemostatic device for radial closure after PCI, in adjunct to short-time compression. hemostasis time: 15 minutes for groups 1 and 2; 2 hours for group 3; the entry site was then revised and in case of failure, the compression was conventionally restored, maintained for additional 2 hours and observed thereafter until bleeding stopped. when ACT value was < 200 s none of the patients developed bleeding in group 1, while all patients with a ACT value > 399 developed it. The cutoff ACT value for the risk of bleeding was 287 s with a sensitivity of 80% and specificity of 75%; hemostasis time:15 minutes for groups 1 and 2; 2 hours for group 3
Politi -2 (51) 2011 (Italy)	20	61	30	RCT	H	HD	Non Patent	**5.0/NA**	Barbeau	Same comment as above.
Politi -3 (51) 2011 (Italy)	50	60	28	RCT	H	HD	Non Patent	**5.0/NA**	Barbeau	Same comment as above.
Singh (52) 2011 (USA)	155	63	32,2	Observational	H	HD	Non Patent	**0.65/0.0**	Clinical, Ultrasonography	Retrospective analysis of patients who underwent TR PCI with the use of bivalirudin; one case of documented RAO that resolved with 2 weeks of LMWH
Chiam (53) 2001 (China)	288	57	15,6	RCT	L	HD	Non Patent	**0.74/NA**	Clinical	288 procedures in 269 patients
Youn (54) 2011 (Korea)	25	66	64	RCT	L	HD	Non Patent	**0.0/8.0**	Clinical	Sheathless sheath PCI (GC diameter less than 6 Fr over conventional GC); RAO, early 0%; late 8%
Park (55) 2012 (Korea)	120	60.5	57.5	RCT	NA	HD	Non Patent	**0.0/0.0**	Ultrasonography	Trimethazidine vs. control to assess flow-mediated dilatation of the RA
Honda (56) 2012 (Japan)	500	70.7	35.8	Observational	L & H	LD	Non Patent	**10.4/NA**	Ultrasonography	This study was designed to determine the incidence and risk factors for access site-related complications such as RAO and bleeding complications; multiple logistic analysis using age, sheath size, BMI, heparin, antithrombotic therapy and PCI showed that sheath size (p = 0.027) and BMI (p = 0.0015) were independent risk factors for bleeding complications; sheath size (p = 0.027) and the lack of statin treatment (p = 0.045) but not heparin, were independent risk factors for RA0
Pancholy (57) 2012 (USA)	400	63.5	37.5	RCT	L	LD	Patent	**7.25/4.75**	Barbeau's	PHARAOH Study: a priori vs. provisional heparin administration; PH was obtained in 67% in the a priori group and 74% in the provisional group (in total 71%); patent RA during hemostasis & diabetes mellitus but not heparin predicted RAO; the concept of PH (authors' conclusion:: *"Maintaining and monitoring RA patency during hemostatic compression..."*
Pancholy (58) 2012 (USA)	412	64	28,9	RCT	L	LD	Patent	**8.0/4.1**	Barbeau's, Ultrasonography	Authors' conclusion: *"Seldinger technique is a faster and more predictable RA access technique compared with modified Seldinger technique with no increase in bleeding or RAO"*
Uhlemann (59) 2012 (Germany)	455	65	37,8	Observational	H	HD	Non Patent	**25.0/NA**	Ultrasonography	Leipzig registry; 2,500 I.U. heparin for CAG, 100 I.U./kg heparin for PCI; 5-Fr sheaths reduced the rate of RAO by 55%; among patients with a RAO, the RA pulse was still palpable in 19.5% of them; 79% of 6-Fr procedures were 2,500 I.U. heparin-CAG; among patients with RAO, 59% were treated with LMWH; the recanalization rates were significantly higher in patients receiving LMWH compared with conventional therapy (55.6% vs. 13.5%, p < 0.001) after a mean of 14 days; RAO predictors: female sex, larger sheath size, peripheral arterial disease & younger age

De Andrade (60) 2012 (Brazil)	9609	61.4	40.1	Observational	NA	NA	NA	**0.9/NA**	Clinical, Barbeau's	NA
Beyer (61) 2013 (USA)	83	61.2	.20.5	RCT	H	HD	Patent	**1.2/NA**	Ultra-sonography	PRE-DILATE trial: It sought to determine whether pre-procedural administration of topical nitroglycerin and lidocaine increases RA size˝ PEP: change in RA size; Spasm occurred in 25% of the patients; Nitroglycerin + lidocaine increased RA size
Tewari (62) 2013 (India)	2246	57	14	OBS	H	HD	Non Patent	**5.34/NA**	Clinical	Retrospective analysis; heparin dose not reported for CAG
Tuncez (63) 2013 (india)	106	58	56.6	Observational	L	HD	Non Patent	**9.4/NA**	Ultrasonography	Study aimed to assess the incidence and predictors of RAO; univariate RAO predictors: female gender & low body weight
Chung (64) 2013 (India)	1872			Observational	H	LD	Non Patent	**0.65/0.16**	Ultra-sonography	PRIMAFACIE-TRI trial; search for the utility using US to of imaging of both arms to facilitate TR and TU CAG and PCI; F-U on RAO & UAO available in the last consecutive 613 patients with one RAO at 4 weeks three RAO and one UAO detected immediately post-CAG were treated with additional I.V. heparin and 20-min compression of the other artery which successfully re-canalized them
Kotowycz (65) 2014 (Canada)	130	65	23.1	Observational	H	LD	Non Patent	**3.4/3.4**	Barbeau's, Ultrasonography	Good RA Size Prediction (GRASP) Study; this study aimed to identify bedside predictors of RA diameter; For assessment of the reverse Allen's and reverse plethysmography times, patients were instructed to clench their fist while the examiner compressed their radial and ulnar arteries; reverse Allen's time was the time (in seconds) for maximal palmar blush to return after release of the RA; reverse plethysmography time was the time (in seconds) for a normal pulsatile tracing to appear on a pulse oximeter that was placed on the ipsilateral thumb, after release of the RA; all acute RAO were persistent at 1 month. patients with RAO had smaller arteries than those without RAO, although the difference was not statistically significant; in each case of RAO, the internal diameter of the RA was smaller than the outer diameter of the sheath.
Tumscitz (66) 2014 (Italy)	175	67.4	16	Observational	H	HD	Non Patent	**NA/7.27**	Ultrasonography	Study aiming to evaluate the feasibility, safety and rate of late RAO after 7-Fr TR complex PCI procedures; Allen's test and plethysmography before catheterization not performed; no RAO predictors found; authors' conclusion: *"7-F RA access site procedures are feasible and safe"*
Yurtdas (67) 2014 (Turkey)	427	52,8	34,2	Observational	H	HD	Non Patent	**6.28/NA**	Ultrasonography	Retrospective analysis; RAO definition: absence of palpable RA pulsation verified by a negative Allen test, and/or visible obstruction on US and/or the absence of a Doppler flow signal at or distal to the access site
Amininian (68) 2014 (Belgium)	114	63	35,1	Observational	H	HD	Patent	**NA/0.88**	Ultrasonography	Glidesheash Slender radial sheath; hydrophillic sheath which combines an inner diameter of a 6-Fr GC with an outer diameter approximately to current 5-Fr sheaths; failure to achieve patent hemostasis in hemostasis in 1.7%; CAG & PCI RAO not reported separately; authors' conclusion: *"routine use of the Glidesheath Slender for TR CAG and PCI is safe and feasible with a high rate of procedural success and a low rate of RAO".*
Marcovic (69) 2014 (Germany)	369	67.7	15.2	Observational	H	HD	Patent	**3.79/NA**	Ultrasonography	Baseline and procedural parameters did not differ statistically between patients with RAO and patients without RAO
Hu (70) 2014 (China)	1362	61,5	41,4	RCT	L	HD	Non Patent	**1.76/NA**	Clinical	Left RA: a feasible alternative for CAG with shorter procedural and fluoroscopy time, as well as less hydrophilic wire use over the right RA
Pancholy (71) 2014 (USA)	250	72	73.6	Observational	L	LD	Patent	**9.6/5.2**	Barbeau's	3:1 matched comparison of warfarin with INR 2-4 vs. heparin; higher incidence of early and late RAO in warfarin compared with SD heparin patients; PH was achieved with comparable rates in 77% in group 1 patients and 74% in group 2 patients
Takeshita 4-Fr (72) 2014 (Japan)	80	68	21.3	RCT	L	HD	Non Patent	**0.0/NA**	Clinical	NAUSICA trial; RAO definition included the absence of RA pulse confirmed by a reverse Allen test; a comparison of complication rates in PCI with 4-Fr vs. 6-Fr GC showed a rate of 6% in the 6-Fr group (3 RAOs and 2 bleedings, 1 RA perforation and 1 massive hematoma; p=0.02)

Takeshita 6-Fr (72) 2014 (Japan)	80	68	20	RCT	H	HD	Non Patent	**3.75/NA**	Clinical	Same comment as above.
Geng (73) 2014 (China)	264	65.4	35.2	RCT	H	HD	Non Patent	**3.03/NA**	Doppler Ultrasonography	TR vs. TU comparison for CAG & PCI in unselected patients; US of the forearm artery was performed before the procedure as well as 2 and 30 days after the procedure; no RA vs. UA diameter difference; similar RAO with UAO rates; a motor abnormality of the hand was observed in one patient in the TU group
Buturak (74) 2014 (Turkey)	409	58	35.2	Observational	H	LD	Non Patent	**NA/16.4**	Ultrasonography	PEP: very late (i.e., at 6-12 months) RAO; very high RAO incidence (16.4%); absence of hypertension & post-procedural access site pain were RAO predictive
Liu (75) 2014 (China)	319	59,2	32.6	RCT	H	HD	Non Patent	**NA/4.7**	Ultrasonography	TR vs. TU CAG & PCI in ACS patients; similar RAO & UAO rates; more frequent RA spasm rates over UA
Dharma (76) 2015 (Indonesia India)	1706	59	31,6	RCT	H	HD	Patent	**9.95/NA**	Ultrasonography	Nitroglycerin I.A. vs. placebo before sheath removal; Heparin dose (I.U.) 5,000 (2,500–17,000) overall; 5,000 (2,500–17,000) for nitro group; 5,000 (5,000–15,000) for placebo group; RAO predictors: duration of hemostasis >4 h & absence of nitroglycerin use
Cong PD (77) 2015 (China)	550	62	27	RCT	H	LD	Non Patent	**15.6/12.0**	Ultrasonography	Comparison of 3 hemostatic devices; the incidence of early (24 hours after the procedure) RAO significantly higher in the pressure dressing group than in the pneumatic compression dressing and rotary compression pad groups; RAO was predicted by diabetes mellitus, larger RA diameter, pressure device compression & RA patency during compression
Cong PC (77) 2015 (China)	550	62.6	28.7	RCT	H	LD	Non Patent	**5.82/2.7**	Ultrasonography	Same comment as above.
Cong RC (77) 2015 (China)	550	61.2	25,1	RCT	H	LD	Non Patent	**4.55/2.1**	Ultraonography	Same comment as above.
Lisowka (78) 2015 (Poland)	220	64	24.1	Observational	H	HD	Non Patent	**15.0/12.7**	Doppler Ultrasonography	TR PCI in ACS patients; PCI duration predictive of RAO; authors conclusion: *"no implications to routine US periprocedural RA evaluation"*
Carg (79) 2015 (India)	198	38	29.3	Observational	H	HD	Patent	**15.2/11.0**	Ultrasonography	Pre-PCI use of ultrasonography; meticulous PH protocol; RA patency checked at least once every 15 minutes; RA diameter ≤2.5 mm & preprocedural peak systolic US velocity of the RA were RAO predioctors;
Hahalis-LD (80) 2015 (Greece)	378	65	25.9	RCT	L	LD	Non Patent	**12.96/NA**	Ultrasonography	LD vs. SD heparin for 5-Fr CAG; largest-to-date comparison of LD vs.SD heparin in TR CAG; crossover to TF CAG was an exclusion criterion of the study; nonsignificant trend for lower RAO rates in the SD heparin group; RAO predictors: spasm, 0lder age & female gender
Hahalis-SD (80) 2015 (Greece)	367	65	24,3	RCT	L	LD	Non Patent	**9.9/NA**	Ultrasonography	Same comment as above.
Aykan-LD (81) 2015 (Turkey)	217	59	27.2	RCT	H	LD	Patent	**NA/5.5**	Ultrasonography	LD vs. SD heparin for CAG; first study to show that CAG patients in the SD heparin group had lower RAO rates compared to LD group; female gender, sheath removal time, administration of LD heparin and absence of hypertension were independent RAO predictors; even with a PH protocol, SD heparin associated with lower RAO rates as compared with LD heparin

Aykan-SD (81) 2015 (Turkey)	242	61	25.2	RCT	H	LD	Patent	**NA/1.2**	Ultrasonography	Same comment as above.
Tian (82) 2015 (China)	2658	61,5	27.1	Observational	H	LD	Non Patent	**7.04/NA**	Ultrasonography	Continuing compression of ipsilateral UA was an effective approach to maintain RA patency; continuous manual ipsilateral UA compression was applied at 1 h after the RA bandage removal; the duration of UA compression depended on the restoration of RA pulsation after releasing the UA; all subjects in Group W (=weak RA pulse) had a negative reversed Allen's test, defined as the hand returned to normal color >30 s; after releasing the RA, when and after compression of both UA and RA; RAO predictors were sheath retention time, post-PCI bandage time, & invasive systolic blood pressure
Abdelaal (83) 2015 (Canada)	119	63	26,1	Observational	L	HD	Non Patent	**13.0/NA**	Doppler Ultrasonography	Sheathless 5-Fr PCI; a 4-Fr diagnostic catheter as a dilator appeared traumatic for the RA; younger age was a univariate RAO predictor
Degirmencioglu-LD (84) 2015 (Turkey)	202	60,2	39,6	RCT	H	LD	Patent	**5.9/NA**	Barbeau's	LD vs. SD heparin for CAG; SD heparin: the only independent predictor of bleeding; nonsignificant trend for smaller hematomas in LD heparin group
Dedirmencioglu-SD (84) 2015 (Turkey)	202	59,7	33,2	RCT	H	LD	Patent	**5.4/NA**	Barbeau's	Same comment as above.
Gokhroo-RA (85) 2016 (India)	1262	63.13	39.1	RCT	NA	HD	Non Patent	**1.5/NA**	Clinical	AJULAR trial; a RCT of the TR vs. the TU approach for coronary procedures; exclusion criteria: inability to palpate one or both forearm vessels (RA or UA of either side); PEP: a composite of major adverse cardiac events (death, myocardial infarction, stroke, or urgent target-vessel revascularization), major vascular events during hospital stay or crossover rates; crossover rate of the right RA access: 3.8%; inability to palpate both arteries:2.5%; twelve patients in the UA group had transient ulnar nerve parasthesia with no residual manifestation at the time of discharge
Van Leeuwen (86) 2015 (The Netherlands)	286	64	27.6	Observational	H	HD	Non Patent	**NA/6.4**	Barbeau	This study analyzed the change of upper limb function after PCI; upper limb function was not affected after TR PCI; a lack of patent dual palmar arch circulation was present in 8.0% of patients when assessed with the Allen's test and 6.2% when assessed with the Barbeau's test; inadequate postprocedural patency of the RA was present in 6.4% of the patients, as assessed with the reverse Barbeau's test
Peruga (87) 2015 (Poland)	109	59,2	29.4	Observational	NA	NA	Non Patent	**6.4/6.4**	Early, Late	The diameter of the RA by US evaluation was larger compared to that of the UA.
Yoshimachi (88) 2016 (Japan)	260	70,8	30	Observational	L	HD	Non Patent	**Early**	Clinical	The V3 Registry; a prospective multicenter study using a virtual 3-Fr PCI system; the virtual 3-Fr system (V3) is an extremely small-diameter PCI system, equivalent to a sheathless 5-Fr GC
Bi (89) 2016 (China)	606	63,5	37	Observational	H	NA	Patent	**Late**	Ultrasonography	Influence of puncture site on RAO; sheath-to-artery ratio & puncture site relative to RA styloid process predicted RAO; high incidence of RAO (=9.24% or 56 out of 606 patients) despite PH protocol
Yoshimachi (90) 2016 (Japan)	21	61,5	14.3	Observational	L	LD	Non Patent	**0.4/NA**	Clinical, Ultra-sonography	Glidesheath Slender (GSS) is compatible with a 5-Fr GC and designed solely for TR access; all the 5-Fr GCs used in Japan are compatible with the 5-Fr GSS; the latter has a thinner wall, which reduces the outer diameter by 1 Fr, while the diameter of the inner lumen is unchanged; the length of the 5-Fr GSS is 16 cm.
Levin (91) 2016 (Israel)	43	65	2,3	Observational	H	HD	Non Patent	**NA/19.0**	Ultra-sonography	Long-term RA patency following TR coronary catheterization via a 7-Fr sheath; in a bivariate model using receiver operator characteristic (ROC) curves, the combination of lower weight and shorter ACT offered best prediction of RAO (area under the ROC curve was 0.813); authors' conclusion: "*femoral vascular access should be considered when there is need for insertion of large-bore sheaths in patients with low body weight"*
Roghani-LD (92) 2016 (Iran)	220	62.9	44.1	RCT	L	LD	Non Patent	**25.0/NA**	Clinical, Ultrasonography	Prospective, double-blind RCT of LD vs. SD heparin in CAG; no increase of hematomas in the SD heparin group; RAO predictors were LD heparin, low body weight, female gender, absence of hypertension, smoking, diabetes mellitus, number of catheters used and fluoroscopy time

Roghani-SD (92) 2016 (Iran)	221	62,5	47.1	RCT	L	SD	Non Patent	**2.3/NA**	Clinical, Ultrasonography	Same comment as above.
Dautov(93) 2016 (Canada)	56	NA	NA	Observational	H	HD	NA	**NA/5.36**	Ultrasonography	Transradial 8-Fr sheathless technique in patients undergoing CTO recanalization; comparison of long-term outcomes of RA in bilateral TR PCI: 8-Fr sheathless technique on one side and a regular 6-Fr sheath on the other side;
Costa (94) 2016 (The Netehrlands)	90	64.6	27,8	Observational	NA	HD	PH-like	**3.4/3.9**	Ultra-sonography	Rotterdam Radial Access Study; US evaluation performed before radial cannulation, 3 hours post-procedure when the compressive device was removed, and at 4 to 6 weeks; the total wall thickness of the RA at the puncture site tripled 3 hours after cannulation, and further increased by 28% at 30 days; two (out of three) patients with RAO at 30 days also had loss of radial pulsation; RAO predictors were the number of puncture attempts; yet, no correlation between the number of puncture attempts and the RA anatomic disturbances of the RA at F-U; authors' conclusion: *"after catheterization, RA puncture site is associated with increased intima and total wall thickness and with modest decrease of inner lumen diameter. Acute injuries of the vessel wall were ubiquitous, but contrary to repeated puncture attempts, did not seem to affect postprocedural radial occlusion or loss of pulsation"*
Koutouzis-UA compression & PA (95) 2016 (Greece)	119	63.5	30,3	Observational	NA		PH-like	**0.0/NA**	Clinical, Ultrasonography	ULTRA study to prevent RAO; a comparison of consecutive patients undergoing UA compression vs. a previous cohort of patients with conventional PH; initially, the device was screwed tightly and promptly partially unscrewed for minimum hemostatic pressure (conventional patent hemostasis method), without performing Barbeau's test; at the same time, 1-hour ipsilateral UA compression with another closure device was used to increase peak velocity blood flow into the RA; when the UA was palpable, the physician compressed the artery until no palpation was felt distal to the closure device; if the ulnar pulse was too weak, , the device was deployed over the expected anatomically ulnar territory; no pulse oxymetry; no US performed in case of UA compression
Koutouzis-PA alone (95) 2016 (Greece)	121	64.4	24	Observational	NA	NA	PH-modified	**5.0/NA**	Clinical, Ultrasonography	Same comment as above.
Noble (96) 2016 (Canada)	233	69,2	52.4	RCT	NA	HD	Non Patent	**2.33/NA**	Ultrasonography	Sheathless 6,5-Fr or 7,5-Fr GCs vs. conventional GCs for TR PCI (6.5-Fr vs. 6-Fr for women and 7.5-Fr vs. 7-Fr for complex PCI in men); the sheathless GC has a hydrophilic coating and a tapered central dilator, which, together, facilitate catheterizing small-calibre radial arteries (<2.5 mm), as well as crossing of radial or brachial tortuosities
Andrade (97) 2016 (Brazil)	120	62,5	30	RCT	H	HD	Patent	**NA/5.8**	Barbeau's	Comparison of a vascular closure device vs. the radial approach to reduce access site complications in non-ST-segment elevation acute coronary syndrome patients; PH achieved in 85% of the patients; authors' conclusion: *"Angio-Seal seems noninferior in the incidence of access site complications at 30 days when compared with the radial approach"*
Turan (98) 2016 (Turkey)	206	60.3	36.9	RCT	L	LD	Non Patent	**8.74/NA**	Ultrasonography	JL-3.5 single catheter vs. two-catheter approach with JL-3.5 and right Judkins-4.0 catheters; 19% of the patients received PCI;
Gokhroo (99) 2015 (India)	200	55	NA	Observational	NA	NA	Non Patent	**0.4/NA**	Clinical	Retrospective comparison of TR CAG with prospectively enrolled patients for TU CAG & PCI

ACS= acute coronary syndrome; ACT=activated clotting time; CAG= coronary angiography; FU=follow-up; Fr=French size; GC= guiding catheter; H=high(er) sheath size (> 5-Fr);); HD= high(er) heparin dose/anticoagulation intensity; HR (95% CI)=hazard ratio (95% confidence intervals); I.A.=intra-arterially; I.U.=international units; I.V.=intravenously; JL=Judkins left catheter; L=low(er) sheath size (≤ 5-Fr); LD= low(er) heparin dose/anticoagulation intensity; LMWH=low molecular weight heparin; NA=non-applicable (not mentioned or mixed population regarding French size or anticoagulation intensity); PCI= percutaneous coronary intervention; PEP=primary end-point of the study; PH=patent hemostasis; RA=radial artery; RAO(s)=radial artery occlusion(s); RCT=randomized control trial; SD=standard heparin dose/anticoagulation intensity; TF=transfemoral; TR=transradial; UAO(s)=ulnar artery occlusion(s); US=ultrasonography, Doppler ultrasound

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