ORIGINAL RESEARCH

Radial Artery Occlusion After Transradial Interventions: A Systematic Review and Meta-Analysis

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***Background*—**Radial artery occlusion (RAO) may occur posttransradial intervention and limits the radial artery as a future access site, thus precluding its use as an arterial conduit. In this study, we investigate the incidence and factors influencing the RAO in the current literature.

***Methods and Results*—**We searched MEDLINE and EMBASE for studies of RAO in transradial access. Relevant studies were identified and data were extracted. Data were synthesized by meta-analysis, quantitative pooling, graphical representation, or by narrative synthesis. A total of 66 studies with 31 345 participants were included in the analysis. Incident RAO ranged between <1% and 33% and varied with timing of assessment of radial artery patency (incidence of RAO within 24 hours was 7.7%, which decreased to 5.5% at >1 week follow-up). The most efficacious measure in reducing RAO was higher dose of heparin, because lower doses of heparin were associated with increased RAO (risk ratio 0.36, 95% CI 0.17–0.76), whereas shorter compression times also reduced RAO (risk ratio 0.28, 95% CI 0.05–1.50). Several factors were found to be associated with RAO including age, sex, sheath size, and diameter of radial artery, but these factors were not consistent across all studies.

***Conclusions*—**RAO is a common complication of transradial access. Maintenance of radial patency should be an integral part of all procedures undertaken through the radial approach. High-dose heparin along with shorter compression times and patent hemostasis is recommended in reducing RAO. **(*J Am Heart Assoc*. 2016;5:e002686 doi: 10.1161/JAHA.115.002686)**

Key Words: radial artery occlusion • transradial catheterization or access • vascular complications

Transradial access (TRA) has grown to become the default access site in the United Kingdom, [1–4] Europe, and Asia[5] and is rapidly growing in the United States.[6–8] Compared with transfemoral access, TRA has been shown to reduce mortality and adverse cardiac events even in high-risk patient groups,[3,9] reduces major bleeding and access site–related vascular complications[10] and patient discomfort, and allows early mobilization and reduced procedure-related costs.[11,12] However, TRA is not without challenges and complications. TRA is technically more difficult with a longer learning curve and is associated with radial artery spasm and radial artery occlusion (RAO) particularly in females and elderly patients.[13,14]

RAO is a quiescent complication of TRA that rarely leads to critical hand ischemia requiring intervention because of the dual vascular supply of the hand from the palmar arch. RAO is often overlooked, and in fact more than 50% of operators do not even assess radial artery patency before discharge.[5] Once the radial artery is occluded, its future use as an access site for percutaneous coronary intervention (PCI), as a conduit for coronary bypass grafting, or fistula formation in hemodialysis patients is precluded. The reported incidence of RAO varies widely, from 0.8% to as high as 38% in the published data.[15–19] Studies have reported that baseline patient characteristics such as body mass index and diabetes may influence RAO.[20] A number of procedural variables such as sheath size,[21] use of anticoagulants,[17,22] and patent hemostasis[17] have also been shown to reduce the incidence of RAO.

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Many studies have evaluated the incidence and risk factors for RAO, with several studies assessing interventions to reduce its likelihood. However, there has yet to be a systematic review that collectively synthesizes the evidence. We therefore conducted a systematic review with both pooled- and meta-analyses to investigate the incidence and factors influencing RAO in the TRA setting.

Methods

We searched MEDLINE and EMBASE in February 2015 using the broad search terms: ("radial occlusion" OR "radial artery occlusion") AND ("transradial" OR "radial catheterization" OR "radial artery catheterization" OR "radial catheterisation" OR "radial artery catheterisation"). The search results were reviewed by 2 independent investigators (C.S.K., M.R.) for studies that met the inclusion criteria and relevant reviews. Additional studies were retrieved by checking the bibliographies of included studies and relevant reviews.

We included primary studies that evaluated RAO. Studies were considered for detailed screening for inclusion if their abstract potentially met 1 of 3 criteria:

1. Primary studies with participants and evaluation of radial occlusion.
2. Any study that discusses RAO avoidance strategy.
3. Any study that evaluates pharmacology, access site management, sheath and catheter types, radial artery diameter, and risk of radial occlusion.

We excluded studies that did not have results on RAO, but there was no restriction on the basis of types of interventions evaluated, language of study, or single-arm studies. We also excluded expert opinion and editorial reviews. We included conference abstracts or presentations in the hope of minimizing publication bias.

Data were extracted from each study into preformatted tables generated in Microsoft Word. The data collected were on the year, country, number of participants, age of participants, percentage of male participants, participant inclusion criteria, and type of interventions, follow-up assessment, results, and limitations. With regard to limitations, we documented whether the study was retrospective in nature or was only available in conference abstract form as well as if it was single arm or there was a large loss to follow-up.

On the basis of the availability of data, we synthesized the results using meta-analysis with quantitative pooling, graphically, or by narrative synthesis. Random effects meta-analysis was performed by the Mantel-Haenszel method for dichotomous data using RevMan 5.3 (Nordic Cochrane Centre, København, Denmark) in order to estimate pooled risk ratios. Statistical heterogeneity was assessed using I^2 statistic, with values of 30% to 60%, representing a moderate level of heterogeneity.[23] The method of pooling has been previously described.[24] In the final analysis, we excluded studies by the same research group over the same time period where there was the potential that the same participants were studied more than once. Where there were similar study participants, we chose the study with the largest sample size or highest adverse

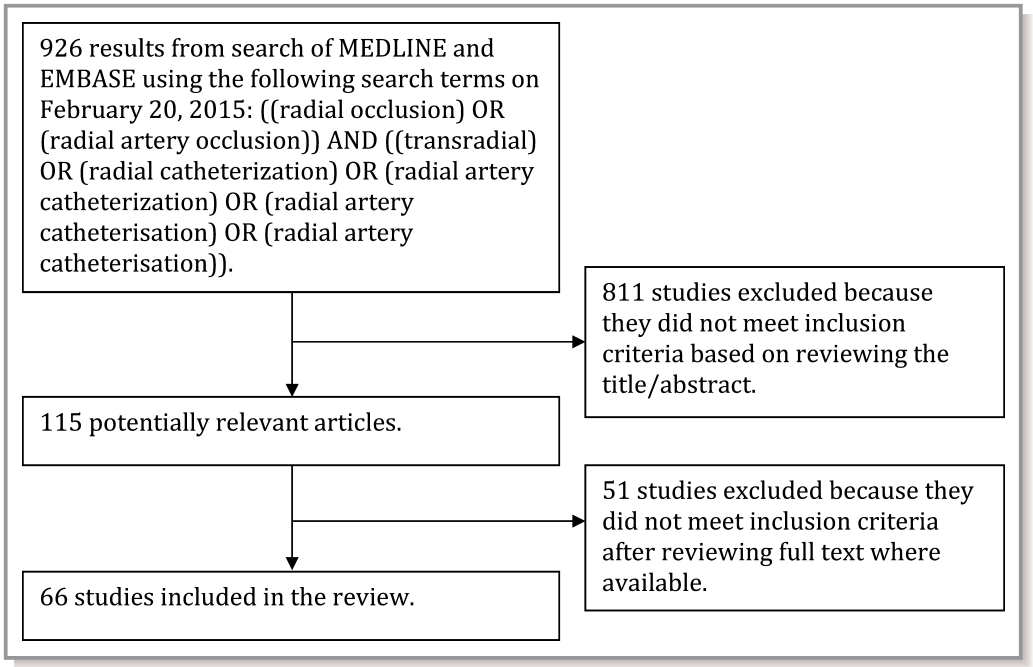

Figure 1. Flow diagram of study selection.

Table 1. Study Design and Participant Characteristics

Study ID	Design; Country; Year	No. of Participants	Age	% Male	Participants Inclusion Criteria and Setting
Abboud 2013[25]	Retrospective cohort study; USA; NA	400	NA	NA	Patients undergoing radial artery catheterization who received vasodilator cocktail before and both before and after catheterization
Ahmed 2012[26]	Matched cohort study; USA; NA	336	72 y	65%	Patients undergoing radial artery catheterization where group I had INR >2.0 and were on warfarin while group II was not on warfarin
Aminian 2014[27]	Prospective cohort study; Belgium; May to June 2013	113	63 y	65%	Patients undergoing radial artery catheterization with Glidesheath Slender radial sheath
Ang 2013[28]	Retrospective cohort study; Singapore; Nov 2008 to Jun 2013	832	NA	NA	Patients undergoing transradial coronary intervention sheathless 6.5-Fr hydrophilic-coated guiding catheter compared to the standard 5-Fr guiding catheter
Aykan 2014[29]	Randomized study; Turkey; NA	459	60 y	77%	Patients undergoing radial artery catheterization who were randomized to 2500 or 5000 IU heparin
Bernat 2011[30]	Randomized study; Czech Republic; NA	465	61 y	63%	Patients undergoing radial artery catheterization who were randomized to 2000 or 5000 IU heparin and ulnar artery compression
Buturak 2014[31]	Prospective cohort study; Turkey; NA	409	59 y	NA	Patients underwent transradial coronary procedure
Caussin 2010[32]	Randomized study; France; Jan to Jun 2006	351	66 y	67%	Patients undergoing transradial angiography who were randomized to long hydrophilic coated or a short sheath
Chiam 2011[33]	Retrospective cohort study; Singapore; Nov 2008 to Sept 2010	269 patients, 292 procedures	57 y	85%	Patients undergoing transradial coronary intervention who received sheathless 6.5- and 5-Fr catheters
Chou 2014[34]	Randomized study; China; NA	100	NA	NA	Patients underwent first-time transradial catheterization and were randomized to QuikClot or prolonged compression
Cubero 2009[18]	Randomized study; Spain; Dec 2007 to Apr 2008	351	65 y	67%	Patients underwent transradial coronary angiography and were randomized to pneumatic compression guided by mean arterial pressure or standard procedure
Chugh 2013[19]	Prospective cohort, India, 2006–2011	613	57 y	63%	Patients undergoing diagnostic or interventional cardiac catheterization
Dangoisse 2012[35]	Randomized study; Belgium; Jan 2009 to Jun 2011	2107	NA	NA	Transradial angiography using TR Band closure device
Dahm 2002[36]	Randomized study; Germany; Mar 2000 to Oct 2001	171	61 y	59%	Patients with coronary lesions suitable for at least 5-Fr transradial angiography randomized to 5- or 6-Fr PCI
Dharma 2015[83]	Randomized study; International; NA	1706	59 y	68%	Patients undergoing transradial catheterization
Edris 2014[37]	Retrospective cohort study; USA; NA	115	NA	NA	Patients underwent transradial catheterization with TR band with standard protocol or rapid deflation
Feray 2010[38]	Prospective cohort study; Turkey; NA	39	55.6 y	69%	Patients underwent transradial catheterization with enoxaparin therapy
Gadkar 2011[39]	Prospective cohort study; India; NA	400	NA	NA	Patients underwent transradial angiography with 4-Fr sheathless catheter
Garg 2015[20]	Prospective cohort study; India; Jan 2012 to Jun 2012	198	58 y	81%	Patients who underwent PCI

Continued

Table 1. Continued

Study ID	Design; Country; Year	No. of Participants	Age	% Male	Participants Inclusion Criteria and Setting
Hadi 2010[40]	Cohort study; UK; NA	161	NA	77%	Patients who underwent PCI who received 6.5- or 7.5-Fr sheathless catheter
Hahalis 2013[41]	Randomized study; Greece; Jun 2010 to Jan 2013	603	NA	74.5%	Patients with transradial catheterization were randomized to 2500 or 5000 IU
Honda 2012[42]	Prospective cohort study; Japan; NA	500	70.7 y	64%	Patients underwent transradial catheterization
Kindel 2008[43]	Randomized study; Germany; NA	200	NA	NA	Patients underwent transradial catheterization who were randomized to coated/5-Fr, control/5-Fr, coated/6-Fr, and control 6-Fr
Kinoshita 2011[44]	Prospective cohort study; Japan; Aug 2009 to Aug 2010	325	NA	NA	Patients who underwent PCI with 6.5-Fr sheathless guides and 6.5-Fr guides
Kwan 2012[45]	Prospective cohort study; USA; Dec 2010 to Feb 2011	116	66 y	74	Patients underwent transradial intervention with 7-Fr sheathless guiding catheter
Lala 2014[46]	Retrospective cohort study; USA; Jan 2011 to Dec 2011	106	71 y	NA	Patients underwent transradial PCI with 5-, 6-, and 7-Fr catheter
Lee 2014[47]	Prospective cohort study; Taiwan; Jan 2010 to Jun 2012	133	66 y	75%	Patients underwent transradial intervention
Levin 2014[48]	Prospective cohort study; Israel; NA	43	NA	NA	Patients underwent transradial intervention with 7-Fr sheath
Lisowska 2015[49]	Prospective cohort study; Poland; 2010–2012	220	64 y	76%	Patients with acute coronary syndrome who underwent coronary angiography and angioplasty via radial access
de Sá 2013[50]	Randomized study; Brazil; Nov 2010 to Jul 2011	228	60 y	58%	Patients underwent transradial catheterization and were randomized to brand new introducers or reprocessed introducers
Markovic 2015[51]	Prospective cohort study; Germany; NA	369	68 y	85%	Patients underwent transradial catheterization with 5- or 6-Fr sheath
Mamas 2010[52]	Prospective single-arm study; UK; Jul 2008 to Nov 2008	100	60 y	75%	Patient underwent PCI via transradial angiography with 6.5-Fr sheaths guide catheter
Matsumoto 2011[53]	Retrospective cohort study; Japan; Jun to Sept 2010	100	NA	NA	Patient underwent PCI via transradial angiography using 7.5-Fr sheathless guide catheter
Mizuno 2010[54]	Retrospective cohort study; Japan; Dec 2008 to Sept 2009	27	73 y	59%	Patient underwent PCI using virtual 3-Fr guiding catheter
Moarof 2014[55]	Prospective observational study; Switzerland; Jan 2010 to Oct 2013	395	66 y	88%	Patients underwent transradial coronary angiography or PCI
Monsegu 2012[56]	Prospective cohort study; International; NA	574	NA	NA	Patients underwent cardiac catheterization with 5- or 6-Fr introducer sheath and catheter
Nakamura 2011[57]	Cohort study; Japan; Jun 2005 to Dec 2009	892	NA	NA	Patients underwent transradial intervention of 6.5-Fr sheathless guide catheter
Nagai 1999[58]	Retrospective cohort study; Japan; Sept 1996 to Dec 1997	162	64 y	64%	Patients undergoing transradial coronary angiography and angioplasty

Continued

Table 1. Continued

Study ID	Design; Country; Year	No. of Participants	Age	% Male	Participants Inclusion Criteria and Setting
Ozdemir 2013[59]	Randomized study; Turkey; Apr to Oct 2012	103	NA	NA	Patients underwent coronary angiography with transradial approach and were randomized to enoxaparin or no enoxaparin therapy
Pancholy 2008[17]	Randomized study; USA; NA	463	65 y	50%	Patients underwent transradial catheterization who were randomized to conventional pressure application or pressure application confirming radial artery patency using Barbeau's test in the PROPHET study
Pancholy 2009[22]	Randomized study; USA; Nov 2007 to Dec 2008	500	64 y	61%	Patients underwent transradial diagnostic coronary angiography and were randomized to intravenous or intra-arterial heparin
Pancholy 2009[60]	Randomized study; USA; Nov 2007 to Dec 2008	500	NA	NA	Patients underwent transradial catheterization who were randomized to HemoBand or inflatable TR band
Pancholy 2011[61]	Retrospective cohort study; USA; NA	400	64 y	63%	Patients underwent transradial catheterization who had 2 or 6 h of hemostatic compression
Pancholy 2012[62]	Randomized study; USA; NA	412	64 y	71%	Patients underwent transradial catheterization and were randomized to Seldinger and modified Seldinger technique
Pancholy 2012[63]	Randomized study; USA; NA	400	64 y	63%	Patients underwent transradial catheterization and were randomized to heparin or no heparin in the PHAROAH study
Pancholy 2014[64]	Case–control study; USA; Jan 2009 to Dec 2011	336	72 y	65%	Patients underwent transradial catheterization who had therapeutic warfarin matched to controls
Plante 2010[65]	Cohort study; Canada; NA	400	60 y	76%	Patients underwent transradial catheterization and received heparin or bivalirudin
Politi 2011[66]	Randomized study, Italy; Nov 2009 to Jan 2010	120	62 y	73%	Patients underwent transradial catheterization and were randomized to QuikClot, short compression, or conventional compression
Rathore 2010[67]	Randomized study; UK; Nov 2006 to Jan 2008	794	63 y	74%	Patients underwent transradial catheterization and were randomized to TR band or Radistop compression
Rathore 2010[68]	Randomized study; UK; Nov 2006 to Jan 2008	790	63 y	74%	Patients underwent transradial catheterization and were randomized to long, short, coated, and uncoated sheaths
Ruhnau 2013[69]	Cohort study; Germany; NA	415	66 y	66%	Transradial intervention using 6-Fr sheath
Sanmartin 2007[16]	Prospective cohort study; Spain; NA	275	64 y	79%	Patients underwent transradial catheterization
Schiano 2010[70]	Randomized study; France; Sept 2007 to Mar 2008	162	63 y	65%	Patients underwent radial catheterization
Shantha 2014[71]	Prospective cohort study; USA; Jan 2009 to Dec 2013	1251	65 y	63%	Patients underwent 6-Fr PCI
Spaulding 1996[72]	Prospective cohort study; France; Mar 1994 to Jun 1995	415	58 y	85%	Patients underwent transradial catheterization and assessed for procedural success and vascular complications
Sreevatsa 2014[73]	Cohort study; India; NA	176	56 y	85%	Patients underwent transradial PCI who either had patent hemostasis or conventional hemostasis
Stella 1997[15]	Prospective cohort study; Netherlands; Aug 1992 to Oct 1995	563	60 y	76%	Patients with transradial PCI
Takeshita 2014[74]	Randomized study; International; NA	160	68 y	79%	Patients undergoing transradial catheterization who were randomized to 4- or 6-Fr guiding catheter

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Table 1. Continued

Study ID	Design; Country; Year	No. of Participants	Age	% Male	Participants Inclusion Criteria and Setting
Tuncez 2013[75]	Prospective cohort study; Turkey; Aug 2011 to Mar 2012	106	58 y	43%	Patients underwent transradial coronary angiography and PCI
Tonomura 2014[76]	Prospective cohort study; Japan; Jul 2010 to Dec 2012	132	70 y	71%	Patient undergoing elective PCI via transradial approach using virtual 3-Fr sheathless guide system
Uhlemann 2011a[77]	Prospective cohort study; Germany; Nov 2010 to Jan 2011	33	72 y	67%	Patients with transradial cardiac catheterization who had oral anticoagulation
Uhlemann 2011b[78]	Prospective cohort study; Germany; Nov 2009 to Aug 2010	455	65 y	62%	Patients with transradial cardiac catheterization who had 5- and 6-Fr sheath
Wong 2012[79]	Randomized study; Singapore; NA	217	58 y	NA	Patients undergoing PCI via 6-Fr transradial approach
Wu 2000[80]	Randomized study; USA; NA	40	NA	NA	Transradial coronary intervention
Zhou 2007[81]	Cohort study; China; Aug 2002 to Feb 2006	7125	64 y	71%	Patients with transradial PCI
Zankl 2010[82]	Cohort study; Germany; 2007 and Apr 2009	488	64 y	65%	Patients undergoing transradial catheterization

INR indicates international normalized ratio; NA, not available, PCI, percutaneous coronary intervention.

outcome event rate. We also performed sensitivity analysis to detect the incidence of RAO according to the starting year of the study, the completion year of the study, and type of procedure performed (ie, diagnostic coronary angiography versus PCI). We pooled the timings of the study according to whether the studies were performed prior to 2007, 2007–2008, 2009–2010, and 2011 onwards.

Results

A total of 66 studies met the inclusion criteria.[15–20,22,25–83] The process of study selection is shown in Figure 1. The details of the study design and participants are described in Table 1. The included studies consisted of 9 retrospective cohort studies, 24 prospective cohort studies, 24 randomized studies, 2 matched/case–control studies, and 7 cohort studies. There were a total of 31 345 participants with a mean age of 64 years and 70% male reported by 48 studies. The study size varied from 27 participants[54] to the largest cohort of 7125.[81]

The use of interventions, follow-up time, results, and study limitations are shown in Table 2. Evaluation of RAO took place as soon as 2 to 3 hours after the procedure and as late as 507 days after the procedure. Twenty-five of the studies were only available in abstract or presentation form. Thirty-three studies reported RAO outcomes by using ultrasound assessment (Table 3).

The incidence of RAO reported by the included studies ranged from <1% to 33%, and we observed differences based on the timing of RAO evaluation (Figure 2). Of the studies that evaluated RAO within 24 hours, 24 studies with 10 938 participants reported a RAO incidence of 7.7% (SD=4.23%, 95% CI ±0.08) (Figure 3A). Among 8 studies that assessed for RAO between 24 hours and 1 week, the combined results with 1377 participants was a RAO incidence of 9.5% (SD=3.69%, 95% CI ±0.19) (Figure 3B). For RAO evaluated >1 week follow-up, the combined results of 33 studies and 10 821 participants suggests that the RAO incidence was 5.56% (SD=5.19, 95% CI ±0.1) (Figure 3C). In our sensitivity analysis to detect the temporal incidence of RAO over time, we found a rising trend in incidence of RAO over time (P=0.02, for initiation year of study) (Table 4). Additionally, we also found that the incidence of RAO during the diagnostic coronary angiogram setting was much higher at 8.8% compared to the 4.5% in PCI settings (P<0.001).

We found 14 trials that evaluated similar interventions that could be statistically pooled using meta-analysis* (Figure 4). The only measure that significantly decreased RAO incidence was a higher dose of heparin (risk ratio 0.36; 95% CI 0.17–0.76).[30,31,42,73] None of these studies reported increased bleeding risk with higher dose (5000 IU) of heparin. Another intervention shown to reduce RAO was the duration of

*References 28–30, 34, 36, 40, 41, 43, 44, 46, 66, 72, 78, 80.

Table 2. Results of Studies and Quality Assessment

Study ID	Use of Any Interventions	RAO Outcomes and Timing of Evaluation	Results	Study Limitations
Abboud 2013[25]	Administration of vasodilator cocktail with 2.5 mg verapamil and 200 μg nitroglycerin before and both before and after catheterization	Incidence of RAO. Follow-up in clinic but unclear timing	Incidence of RAO in both groups: 17/400. RAO with cocktail before and after: 1/200. RAO with cocktail before: 16/200	Abstract only, retrospective and lack of randomization
Ahmed 2012[26]	Warfarin vs no warfarin groups	Incidence of RAO with plethysmography at 24 hours and 30 days	Incidence early RAO in both groups: 41/336. Early RAO with warfarin: 16/86 (18.6%). Early RAO without warfarin: 25/260 (9.6%). Incidence chronic RAO in both groups: 26/336. Chronic RAO with warfarin: 12/86 (13.9%). Chronic RAO without warfarin: 14/260 (5.4%)	Abstract only, and lack of randomization
Aminian 2014[27]	All patients had Glidesheath Slender radial sheath (OD-5-Fr)	Incidence of RAO at 1 month follow-up	Incidence of RAO: 1/113	None
Ang 2013[28]	6.5-Fr hydrophilic-coated sheathless guiding catheter (OD=4 Fr) compared to the standard 5-Fr guiding catheter	RAO in each group (no timing specified)	Incidence of RAO in both groups: 2/832. RAO with 5-Fr group: 1/146. RAO with 6.5-Fr group: 1/686	Abstract only, retrospective and lack of randomization
Aykan 2014[29]	2500 IU vs to 5000 IU heparin	Radial artery patency evaluated 1 month after angiography with Doppler US	Incidence of RAO in both groups: 15/459. RAO with 2500 IU heparin: 12/217. RAO with 5000 IU heparin: 3/242	Presentation slides only
Bernat 2011[30]	2000 IU vs 5000 IU heparin. Ulnar artery compression	RAO with duplex US after 3 to 4 hours	Incidence of early RAO in both groups: 20/465. Early RAO with 2000 IU heparin: 13/222 (5.9%). Early RAO with 5000 IU heparin: 7/243 (2.9%). Incidence of final RAO in both groups: 11/465. Final RAO with 2000 IU heparin: 9/222 (4.1%) Final RAO with 5000 IU heparin: 2/243 (0.8%)	None
Buturak 2014[31]	No intervention	Doppler US at 6 to 15 months	Late-term RAO incidence: 67/342 (19.5%). RAO with age: 55.9 y vs 59.1 y. RAO with hypertension: 9.8% vs 23.0%	Abstract only
Caussin 2010[32]	Long hydrophilic-coated vs a short sheath	RAO a day after procedure with US Doppler	RAO incidence: 10/351. RAO with long sheath: 5/177 (2.8%). RAO with short sheath: 5/174 (2.8%)	Not primary outcome of trial
Chiam 2011[33]	6.5-Fr sheathless vs 5-Fr guiding catheters	RAO in hospital	RAO incidence: 2/292. RAO with sheathless group: 1/146 (0.7%) RAO with 5-Fr group: 1/146 (0.7%)	Retrospective, unclear outcome ascertainment
Chou 2014[34]	Short compression with QuikClot (15 minutes) and a conventional prolonged compression (2 hours)	Early RAO <24 hours and Late RAO 1 to 2 months with color Doppler	Early RAO incidence: 1/100. Early RAO short compression: 0/50 (0%). Early RAO conventional compression: 5/50 (10%). Late RAO incidence: 3/100. Late RAO short compression: 0/50 (0%). Late RAO conventional compression: 3/50 (6%)	Abstract only

Continued

Table 2. Continued

Study ID	Use of Any Interventions	RAO Outcomes and Timing of Evaluation	Results	Study Limitations
Cubero 2009[18]	Compression guided by mean arterial pressure or standard compression by pneumatic air device	24 to 72 hours using inverse Allen's test and bidirectional Doppler	Incidence of RAO: 23/351. RAO in mean arterial pressure group: 2/176. RAO in standard compression group: 21/175	Single-blinded study
Chugh 2013[19]	Assessment of radial artery diameter using ultrasound	Early RAO after the procedure using ultrasound Doppler. Late RAO at 4 weeks	Early RAO incidence: 3/613 Late RAO incidence: 1/613	Single cohort study with limited follow-up in last 10 months only
Dangoisse 2012[35]	Low (13 cm^3) volume of air vs Ultra low (10 cm^3) volume of air in TR Band	RAO assessment at 24 hours using pulse oximetry	RAO at 24 hours: 169/2107 (8%)	Abstract study only
Dahm 2002[36]	5 Fr vs 6 Fr	Radial artery assessment using duplex at unclear timing	Incidence of RAO: 6/171. 5-Fr arm: 1/87 (1.1%) 6-Fr arm: 5/84 (5.9%) Four of the 5 6-Fr patients had artery:catheter ratio <1	Unclear timing of RAO
Dharma 2015[83]	Intra-arterial administration of nitroglycerin (500 μg) vs placebo postprocedure	RAO assessment at 24 hours using ultrasound duplex	Incidence of RAO: 170/1706 (9.9%) RAO incidence in nitroglycerin arm: 70/853 (8.2%) RAO incidence in placebo arm: 100/853 (11.7%)	None
Edris 2014[37]	Standard technique vs rapid deflation technique	RAO at 24 hours using a reverse-Barbeau test	Incidence of RAO: 11/115. RAO in standard group: 9/56 (16%). RAO in rapid deflation group: 2/59 (3.4%)	Abstract only, retrospective, nonrandomized
Feray 2010[38]	All patients received 60 mg enoxaparin through the radial sheath	RAO at discharge and 5.5 days follow-up with Doppler exam	Incidence of RAO: 2/40 (5%)	Single-arm study
Gadkar 2011[39]	4-Fr sheathless	RAO at unclear timing of evaluation	Incidence of RAO 8/400 (2%)	Nonrandomized
Garg 2015[20]	None	US Doppler 1 day before, 1 day after, and 3 months after the procedure	Incidence of RAO: 30/198 (15.2%)	None
Hadi 2010[40]	6.5-Fr vs 7.5-Fr sheathless catheter	RAO at 1 month	Incidence of RAO: 6/161. RAO in 6.5-Fr sheathless: 5/131 (3.8%). RAO in 7.5-Fr sheathless: 1/30 (3.3%)	Abstract only, significant loss to follow-up 35%
Hahalis 2013[41]	2500 IU vs 5000 IU of heparin	Median follow-up of 8 days with Doppler US	Incidence of RAO: 61/603. RAO in 2500 IU arm: 36/302 (12.0%) RAO in 5000 IU arm: 25/301 (8.3%)	Abstract only. Significant loss to follow-up 52%
Honda 2012[42]	None	US at 24 hours	Incidence of RAO: 52/500	None
Kindel 2008[43]	Hydrophilic-coated vs noncoated sheaths and 5-Fr vs 6-Fr catheters	RAO at 1 month with US Doppler	Incidence of total RAO: 15/200. Incidence of early occlusion: 12/200. Coated/5 Fr: 3/50. Control/5 Fr: 4/50. Coated/6 Fr: 4/50. Control/6 Fr: 1/50. Incidence of late occlusion: 3/200. Coated/5 Fr: 1/50. Control/5 Fr: 0/50. Coated/6 Fr: 1/50. Control/6 Fr: 1/50	None

Continued

Table 2. Continued

Study ID	Use of Any Interventions	RAO Outcomes and Timing of Evaluation	Results	Study Limitations
Kinoshita 2011[44]	6.5-Fr sheathless guides vs 6-Fr guides	RAO at 3 months	Incidence of RAO: 6/333. RAO in 6.5-Fr sheathless guide group: 0/211 (0%) RAO in 6-Fr guide group 6/122 (5%)	Abstract only
Kwan 2012[45]	7-Fr sheathless guiding catheter	7 days and 30 days RAO plethysmography assessment	Incidence of RAO: 9/116. RAO 7 days 6/116 (5%) RAO 30 days: 3/116 (2.5%)	None
Lala 2014[46]	5-, 6-, and 7-Fr guiding catheter	RAO at 1 day and 30 days	Incidence of RAO: 12/106. RAO with 5 Fr: 1/44 (2%) RAO with 6 Fr: 4/28 (14%) RAO with 7 Fr: 7/34 (20%)	Abstract only, retrospective, nonrandomized study
Lee 2014[47]	Sheathless standard guiding catheters for complex coronary interventions and carotid artery stenting	RAO at 1 year	Incidence of RAO: 6/133. RAO for coronary intervention: 3/105 (2.86%). RAO for carotid artery intervention: 3/28 (10.71%)	None
Levin 2014[48]	7-Fr sheath catheter	507 days by US and Barbeau test	Incidence of RAO: 8/43 (19%)	Abstract only
Lisowska 2015[49]	None	US at 48 to 72 hours and 6 to 12 months	Periprocedural RAO: 33/220 (15%). Long-term RAO: 28/220 (13%)	None
de Sá 2013[50]	Brand new introducers vs reprocessed introducers	RAO was evaluated at 24 hours (early) and 30 days (late) with the reverse Barbeau test	Incidence of early RAO: 24/228. Incidence of late RAO: 17/186. RAO in new introducers: early 10/100 (10%), late 6/80 (7.5%). RAO in reprocessed introducers: early 14/128 (10.9%), late 11/106 (10.4%)	Loss to follow-up 18.4%
Markovic 2015[51]	None	Doppler US at 24 hours	Incidence of RAO: 14/369. RAO with 5 Fr: 1/45 (2%). RAO with 6 Fr: 13/324 (4%)	None
Mamas 2010[52]	TRA PCI using 6.5-Fr sheathless guide catheter	RAO at 60 days using Doppler US	RAO at 60 days: 2/100 (2%)	Single-arm study
Matsumoto 2011[53]	PCI via TRA using 7.5-Fr sheathless guide catheter	RAO assessment at unclear timing and method	Incidence of RAO: 0%	Abstract study with limited information. Single-arm study
Mizuno 2010[54]	PCI using 3-Fr virtual sheathless guiding catheter	RAO assessment at unclear timing using Allen's test and US Doppler	Incidence of RAO in TRA group: 0/18 (0%)	Single-arm study with unclear timing of assessment of RAO
Moarof 2014[55]	None	Color duplex US up to 34 months	Incidence of long-term RAO: 7/385	Abstract only
Monsegu 2012[56]	None	Color Doppler with and without ulnar compression at 24 hours	Incidence of RAO 22/574 (3.8%)	Abstract only
Nakamura 2011[57]	6.5-Fr sheathless guide catheter	6 to 9 months RAO with Doppler	Incidence of RAO: 6/892 (0.67%)	Abstract only, loss to follow-up 23%

Continued

Table 2. Continued

Study ID	Use of Any Interventions	RAO Outcomes and Timing of Evaluation	Results	Study Limitations
Nagai 1999[58]	US assessment of radial artery postprocedure	Radial artery assessment at early (1–8 days) and late (37–182 days)	Early undetectable flow confirmed on US 15/162 (9%). Late RAO=6/162 (3.7%)	Retrospective single-arm study
Ozdemir 2013[59]	Subcutaneous enoxaparin (60 mg/day) after 4 hours of sheath removing and each after 3 days vs no enoxaparin	RAO at 7 days using US Doppler and pulse oximetry	Incidence of RAO: 14/103. RAO in enoxaparin group: 1/51 (2%). RAO in control group: 13/52 (25%)	Abstract only
Pancholy 2008[17]	Conventional pressure application for hemostasis vs pressure application confirming radial artery patency using Barbeau's test	24 hours and 30 days using plethysmography	Incidence of RAO at 24 hours: 38/436. Incidence of RAO at 30 days: 20/436. RAO in conventional group at 24 hours: 27/219 (12%). RAO in conventional group at 30 days: 16/219 (7%). RAO in Barbeau's test group at 24 hours: 11/217 (5%). RAO in Barbeau's test group at 30 days: 4/217 (2%)	None
Pancholy 2009[22]	Intravenous vs intra-arterial heparin	RAO with plethysmography at 24 hours and 30 days	Incidence of early RAO: 29/500. Incidence of chronic RAO: 18/500. Early RAO in intravenous group: 14/250 (5.6%). Chronic RAO in intravenous group: 8/250 (3.2%). Early RAO in intra-arterial group: 15/250 (6%). Chronic RAO in intra-arterial group: 10/250 (4%)	None
Pancholy 2009[60]	HemoBand vs TR Band for hemostasis	RAO at 24 hours and 30 days with Barbeau's test	Incidence of RAO at 24 hours: 39/500. Incidence of RAO at 30 days: 26/500. RAO at 24 hours with Hemoband: 28/250 (11.2%). RAO at 30 days with Hemoband: 18/250 (7.2%). RAO at 24 hours with TR Band: 11/250 (4.4%). RAO at 30 days with TR Band: 8/250 (3.2%)	None
Pancholy 2011[61]	Duration of compression 2 hours vs 6 hours	RAO at 24 hours and 30 days	Incidence of early RAO: 35/400. Incidence of chronic RAO: 24/400. Early RAO in 6-hour group: 24/200 (12%). Chronic RAO in 6-hour group: 17/200 (8.5%). Early RAO in 2-hour group: 11/200 (5.5%). Chronic RAO in 2 hours group: 7/200 (3.5%)	Retrospective cohort study
Pancholy 2012[62]	Seldinger technique vs modified Seldinger technique	RAO at 24 hours and 30 days	Incidence of early RAO: 33/412. Early RAO with Seldinger: 17/210 (8%). Early RAO with modified Seldinger: 16/202 (7.9%). Incidence of late RAO: 17/412. Late RAO with Seldinger: 9/210 (4.3%). Late RAO with modified Seldinger: 8/202 (3.9%)	None

Continued

Table 2. Continued

Study ID	Use of Any Interventions	RAO Outcomes and Timing of Evaluation	Results	Study Limitations
Pancholy 2012[63]	A priori heparin vs provisional heparin	Plethysmograph for RAO at 24 hours and 30 days	Incidence of early RAO: 29/400. Incidence of late RAO: 19/400. Early RAO in a Priori: 15/200 (7.5%). Early RAO in provisional: 14/200 (7%). Late RAO in a Priori: 9/200 (4.5%). Late RAO in provisional: 10/200 (5%)	None
Pancholy 2014[64]	Warfarin vs intra-arterial heparin	Plethysmograph for RAO at 24 hours and 30 days	Incidence of early RAO: 40/336. Incidence of late RAO: 25/336. Early RAO in warfarin group: 16/86 (18.6%). Early RAO in heparin group: 24/250 (9.6%). Late RAO in warfarin group: 12/86 (13.9%). Late RAO in heparin group: 13/250 (5.2%)	Retrospective study
Plante 2010[65]	Heparin vs bivalirudin	RAO at 4 to 8 weeks echography-Doppler and reverse Allen's test with pulse oximetry	Incidence of RAO 21/400 (5.3%). RAO with heparin 14/200 (7.0%). RAO with bivalirudin 7/200 (3.5%)	Nonrandomized study
Politi 2011[66]	Short compression with the QuikClot, short compression or conventional prolonged compression	Radial artery patency was assessed using the Barbeau's test 12 at 24 hours	Incidence of RAO: 6/120. RAO with QuikClot: 0/50 (0%). RAO with short compression: 1/20 (5%). RAO with prolonged compression: 5/50 (10%)	None.
Rathore 2010[67]	Radistop device vs TR band hemostasis	RAO at discharge and follow-up after 4 to 6 months with plethysmography and oximetry	Incidence of RAO at discharge: 73/790 (9.2%). Incidence of RAO at follow-up: 43/790 (5.4%). RAO at discharge with Radistop: 38/395 (9.6%). RAO at discharge with TR band: 35/395 (8.9%). RAO at follow-up with Radistop: 25/395 (6.3%). RAO at follow-up with TR band: 18/395 (4.6%)	None
Rathore 2010[68]	Long vs short sheet and hydrophilic coated vs noncoated sheet	RAO at discharge and follow-up	Incidence of RAO at discharge: 73/790 (9.2%) Incidence of RAO at follow-up: 43/625 (6.9%) RAO with long sheet: discharge 31/396, follow-up 27/325. RAO with short sheet: discharge 42/394, follow-up 16/302. RAO with coated: discharge 35/397, follow-up 24/316. RAO with uncoated: discharge 28/393, follow-up 19/311	None
Ruhnau 2013[69]	TRA using 6-Fr sheath	RAO at 4 to 68 weeks using US duplex	Incidence of RAO: 15/418 (3.6%) Females are at higher risk of RAO (n=10 vs n=5)	Abstract study only
Sanmartin 2007[16]	None	RAO at 7 days with pulse oximeter and plethysmograph	Absent pulsation: 12/279 (4.3%). Absent radial flow: 29/279 (10.4%)	None

Continued

Table 2. Continued

Study ID	Use of Any Interventions	RAO Outcomes and Timing of Evaluation	Results	Study Limitations
Schiano 2010[70]	5000 IU heparin vs weight-adjusted (50 units/kg) heparin	RAO assessment at 24 hours using US Doppler	Incidence of RAO: 0/162 (0%). Incidence of RAO in control group 0/79 (0%) Incidence of RAO with weight-adjusted heparin group 0/83 (0%). Radial compression time was higher in the standard protocol group (235.5 minutes vs 204.5 minutes, $P<10^{-5}$)	None
Shantha 2014[71]	Introducer sheath or without introducer sheath	Radial artery patency was assessed using reverse Barbeau's test and RAO was confirmed by US	Lower RAO with introducer sheath: Propensity-matched odds of RAO predischarge: OR 0.20 (0.13–0.32). Propensity-matched odds of RAO at 24 hours: OR 0.13 (0.07–0.25). Propensity-matched odds of RAO at 30 days: OR 0.18 (0.10–0.40)	Abstract only. Unclear variables in propensity matching
Spaulding 1996[72]	No heparin, heparin 2000 to 3000 units and heparin 5000 units	RAO assessment postprocedure and at 2-month follow-up using echo-Doppler measurements	Incidence of RAO: 73/415. No-heparin group: 35/49 (71%). Heparin 2000 to 3000 units: 29/119 (24%). Heparin 5000 units: 9/210 (4.3%)	Nonrandomized study. 59% of participants were excluded
Sreevatsa 2014[73]	Patent hemostasis vs occluded hemostasis	Barbeau's test and Doppler at 24 hours	Incidence of RAO: 23/176 (13.1%). RAO with patent hemostasis: 6/87. RAO with occluded hemostasis: 17/89	Abstract only
Stella 1997[15]	None	RAO assessment at discharge and 1 month via palpation and Allen's test	Incidence of early RAO: 30/563 (5.3%) Incidence of late RAO (30 days): 16/563 (2.8%)	None
Takeshita 2014[74]	4-Fr vs 6-Fr guiding catheter	RAO on reverse Allen's test	Incidence of RAO: 3/160. RAO in 4-Fr group: 0/80. RAO in 6-Fr group: 3/80	None
Tuncez 2013[75]	None	RAO at 24 hours with US Doppler	Incidence of RAO: 10/106. Predictor of RAO: low weight (P=0.01)	None
Tonomura 2014[76]	3-Fr sheathless guide system	2 to 3 days postprocedure using reverse Allen's test	Incidence of RAO: 0/111 (0%)	Single cohort; follow-up not done on all patients
Uhlemann 2011a[77]	All patients had oral anticoagulation	RAO at discharge on Duplex US	Incidence of RAO: 11/33 (33%)	None
Uhlemann 2011b[78]	5-Fr sheath and 6-Fr sheath	RAO at discharge on Duplex US	Incidence of RAO: 113/455. RAO with 5-Fr sheath: 21/152 (13.8%). RAO with 6-Fr sheath: 92/303 (30.4%)	Nonrandomized study
Wong 2012[79]	Intravenous enoxaparin vs intra-arterial UFH	RAO assessment at 6 weeks	Incidence of RAO 10/217. Incidence of RAO in enoxaparin group: 5/106 (4.71%). Incidence of RAO in control group: 5/111 (4.50%)	Abstract study
Wu 2000[80]	8- and 6-Fr sheath	RAO assessment at 1 year	Incidence of RAO in 8 Fr arm: 2/18 (11%). Incidence of RAO in 6-Fr arm: 3/16 (19%)	Small study; limited follow-up in 8-Fr arm

Continued

Table 2. Continued

Study ID	Use of Any Interventions	RAO Outcomes and Timing of Evaluation	Results	Study Limitations
Zhou 2007[81]	None	RAO unclear timing of evaluation	Incidence of RAO: 68/7215 (1%)	Single-arm study
Zankl 2010[82]	RAO post transradial angiography treated with LMWH for 4 weeks	RAO assessed at 24 hours	Incidence of RAO at 24 hours: 51/488 (10.5%). RAO at 4 weeks in patients treated with LMWH: 4/30 (13.3%). RAO at 4 weeks in patients not treated with LMWH: 17/21 (81%)	None

LMWH indicates low molecular weight heparin; OR, odds ratio; UFH, unfractionated heparin; PCI, percutaneous coronary intervention; RAO, radial artery occlusion; TRA, transradial access; US, ultrasound.

compression, with a 15-minute compression associated with reduced risk of RAO compared to a 2-hour compression (risk ratio 0.28; 95% CI 0.05–1.50);[34,66] however, Politi et al reported increased bleeding rates in patients subjected to shorter compression time.

We evaluated the incidence of RAO by size of catheter among 19 studies* (Figure 5). We found a higher incidence of RAO with the increase in the size (outer diameter) of the catheter; however, the trend was not consistent among all studies, particularly studies evaluating 8-Fr size catheters, which consisted of a single study limited to 1 center. The incidence of RAO was 11% among 1297 participants in studies evaluating 6-Fr catheter, dropping markedly to 2% in 2662 participants in studies using 5-Fr catheter.

Several studies evaluated significant predictors of RAO* (Table 5). Age was reported to be a significant predictor of RAO in 3 studies,[47,77,78] while sex was significant in 6 studies.[29,49,69,73,77,78] Body weight was reported as a significant predictor in 3 studies.[17,65,75] In terms of procedural variables, use of a smaller introducer sheath has been shown to be predictive of lower RAO[71] and use of larger diameter of sheath[42,78,81] and duration of compression[61,81] was associated with higher occlusion rates. Other predictors included baseline radial artery diameter,[19,84,85] peripheral artery disease,[79] statin use,[42] procedural success,[47] serum creatinine,[49] and heparin use.[66]

Two studies evaluated the effectiveness of the TR band compared to other TRA hemostatic devices in reducing radial occlusion.[60,67] Pancholy et al conducted a study of 500 patients and reported a statistically significant reduction in RAO with use of the TR band compared to HemoBand (4.4% versus 11.2%).[60] Rathore et al compared Radistop and TR band in 790 patients and found a nonsignificant reduction in RAO with TR band compared to Radistop (5.6% versus 8.0%, P=0.273).[67]

Several studies reported the influence of medications on RAO. Abboud et al reported an abstract where they showed that administration of a radial artery vasodilator cocktail before and after the procedure significantly reduced RAO compared to just before the procedure (0.5% versus 8%).[25] Ahmed et al conducted a study of participants with warfarin and reported higher incidences of RAO in the warfarin group compared to matched controls who received intraprocedural heparin.[26] Pancholy et al conducted a second study that compared administration of heparin after sheath insertion to no application of heparin unless postprocedure there was no radial patency and concluded that provisional use of heparin appears to be feasible and safe when patent hemostasis is maintained.[63] Plante et al compared bivalirudin and heparin and found no significant difference in RAO (3.5% bilvalirudin, 7.0% heparin), so they concluded that heparin should be preferred because its of low cost.[65]

Discussion

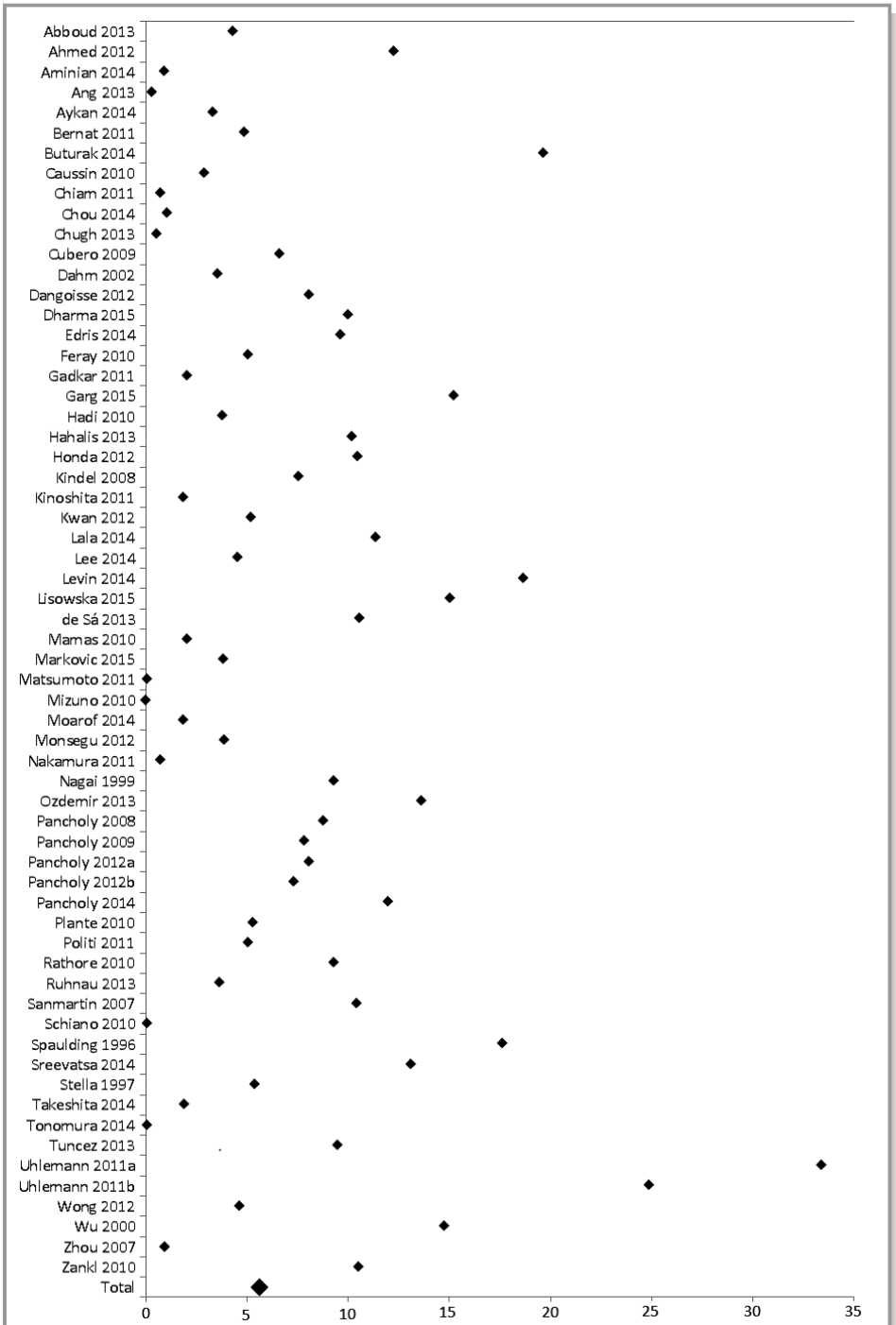
TRA has become the default access site for cardiac catheterization in many countries, and strategies to preserve the patency of the radial artery for future use are becoming an

Table 3. Exclusion of Studies Without Ultrasonic Assessment of RAO

Group	No. of Studies	RAO Events	Total	Mean%	SD%	95% CI Margin
RAO at 1 day	12	360	5349	6.73	5.06	0.14
RAO at 2 to 6 days	7	126	1261	9.99	3.55	0.2
RAO at 7+ days	17	365	5721	6.22	6.47	0.17
Total	33	883	11 193	7.89	7.79	0.14

RAO indicates radial artery occlusion.

*References 27, 28, 36, 39, 40, 43–46, 48, 52–54, 57, 69, 74, 76, 78, 80.
*References 17, 18, 20, 29, 31, 34, 42, 47–49, 55, 56, 62, 63, 65, 66, 69, 73, 75, 77, 78, 81.

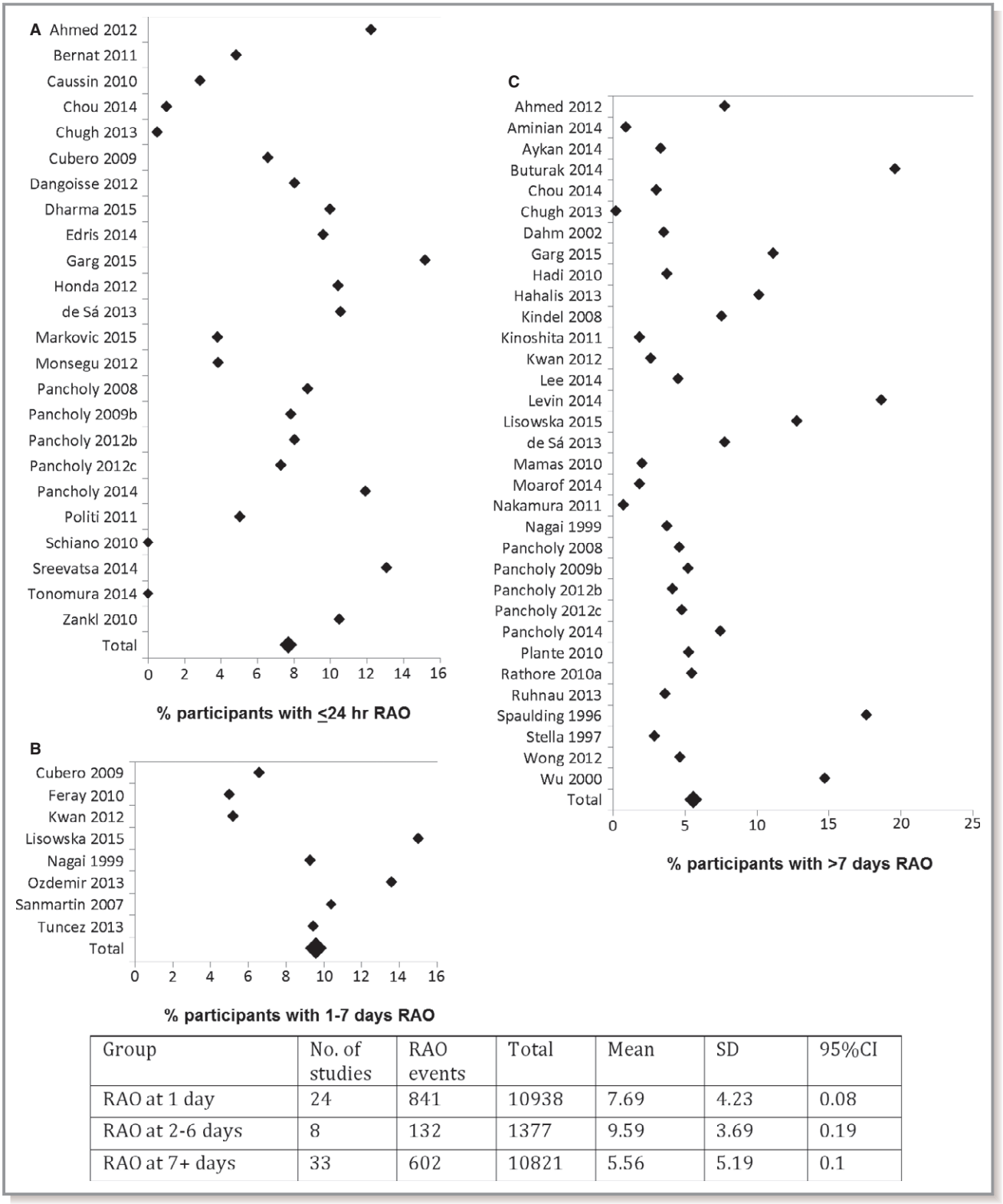


Group	No. of studies	RAO events	Total	Mean	SD	95%CI
Total	62*	1619	28747	5.63	6.50	0.08

*4 studies were not included because of duplicate analysis of the same cohort.

Figure 2. Incidence of radial artery occlusion (RAO) at shortest follow-up time for each study.

integral part of the catheterization procedure. Our analysis represents the first systematic review of such radial protection strategies, synthesizing evidence from over 66 studies and 31 345 participants, to assess the incidence of and risk factors for RAO as well as to examine the efficacy of the measures used to prevent it.



Group	No. of studies	RAO events	Total	Mean	SD	95%CI
RAO at 1 day	24	841	10938	7.69	4.23	0.08
RAO at 2-6 days	8	132	1377	9.59	3.69	0.19
RAO at 7+ days	33	602	10821	5.56	5.19	0.1

Figure 3. Incidence of radial artery occlusion (RAO) by follow-up time. (A) Percentage of particpants with ≤24 hr RAO; (B) percentage of particpants with 1-7 days RAO; (C) percentage of participants with >7 days RAO.

Our analysis suggests that RAO is common, with incident rates of 7.7% for early RAO within 24 hours, declining to 5.5% at 1 month. Clinically, absence of radial pulse is often described as occluded artery; however, this can underestimate the true incidence of RAO. For example, in one study RAO incidence defined by absence of pulse was found to be 4.4%, whereas

Table 4. Sensitivity Analysis According to the Timing of the Studies and Setting of Procedure

Analysis by Timing of Studies	Studies	Events/Total	% RAO
Starting year of study			
<2006	9	284/11 172	2.5
2007–2008	8	119/2743	4.3
2009–2010	14	482/5280	9.1
2011+	5	67/626	10.7 (P=0.02)
Completion year of study			
<2006	6	202/8877	2.3
2007–2008	5	137/1903	7.2
2009–2010	8	184/2698	6.8
2011+	17	429/6343	6.8 (P=0.38)
Group	Studies	Events/Total	%RAO
Analysis by setting of procedure			
Percutaneous coronary intervention (PCI)	21	206/4533	4.5 (P<0.001)
Coronary angiograms (CA)	13	364/4147	8.8 (P<0.001)
PCI+CA	18	451/6631	6.8

RAO indicates radial artery occlusion.

absence of radial artery flow was found to be at 10.5%.[16] It is therefore recommended to use a more objective method of assessment of RAO using radial flow as assessed by ultrasound.[86] In support of this, when studying the method of assessment of RAO, we observed that the incidence of RAO increased from 5.6% to 7.8% when ultrasound is used for detection of RAO. Many baseline patient characteristics such as sex, age, body mass index, and procedural variables such as artery-to-sheath ratio, heparin use, and duration of compression have been reported to be associated with RAO, but there appears to be a lot of heterogeneity in the literature. The incidence of RAO varies according to the timing of assessment of radial artery patency postprocedure. Acute RAO rates are higher acutely and decline with time. In the PROPHET study, the acute incidence of RAO (12%) was almost halved by the passage of 28 days (7%).[17] In accordance with these observations, our analysis also suggests a decreased incidence of RAO over a period of 28 days from 7.7% to 5.8%. This decline in the incidence of RAO with time can be explained by the spontaneous recanalization of the radial artery. Recanalization occurs as the results of activation of primary fibrinolysis. The damaged endothelium facilitates this by releasing tissue plasminogen activator and urokinase, thus allowing fibrinolysis to occur.

TRA also negatively affects the structure and function of the radial artery, culminating in nonocclusive injury.[13] Endothelial and vascular smooth muscle integrity play a central role in preserving the function of the arterial wall. Damaged and dysfunctional endothelium has been strongly attributed to development of vascular disease and atherosclerosis.[87] More recently, changes in flow-mediated dilatation has been used as a surrogate of endothelial dysfunction.[88] Flow-mediated dilatation is an in vivo bioassay of NO-mediated endothelial function in which vascular endothelium releases NO as a vasodilatory response according to the changes in the vascular blood flow. Yan et al recently demonstrated that average flow-mediated dilatation post 5-Fr TRA reduced significantly from 11.5% to 4.1% immediately after the procedure and dropped even further to 0.7% at 3 months.[89] This suggests that endothelial damage may actually persist longer than perceived. Additionally, TRA also results in structural damage to the radial artery. Yonetsu et al studied the structural changes in radial artery from acute vascular trauma and found that 67% of radial arteries had intimal tears and 36% had medial dissections immediately after transradial PCI.[90] The combination of these structural and functional changes in arterial wall lead to significant arterial remodeling, which may have important clinical implications. For instance, Sakai et al[91] studied patients undergoing repeated transradial interventions in the same arm and found that the rate of successful radial access decreases with successive procedures.

Acute artery occlusion is thought to be a thrombotic phenomenon on a background of chronic occlusive changes. Sheath insertion and instrumentation during TRA causes endothelial damage, exposing the thrombogenic connective tissue. In addition, blood stasis while achieving hemostasis provides the nidus for thrombus formation. Therefore, reducing endothelial damage by minimizing compression time and using small introducer sheath size along with patent hemostasis may help in reducing the occlusion rates. Saito et al[21] studied the relationship between arterial blood flow and sheath size outer diameter and found that incidence of blood flow reduction is significantly low when radial artery inner diameter/cannulated sheath outer diameter is ≥1.0 (artery/sheath diameter ratio >1). In this study, although the incidence of severe flow reduction was low without any ischemic sequel, the incidence of RAO was not reported.

We found that compression time of 15 minutes reduces RAO incidences significantly.[34,66] Although the results were very promising and statistically significant, both of these studies were underpowered, with <200 patients in total in both arms (Figure 3). Furthermore, Politi et al reported increased bleeding in patients subjected to shorter compression time in patent hemostasis settings. More recently, duration of compression (>4 hours versus <4 hours) was studied in a large randomized study by Dharma et al. They found that duration of compression alone was a strong predictor of RAO (odds ratio 3.11; 95% CI 1.62–5.82), supporting the hypothesis of minimizing radial injury by reducing compression time.[83]

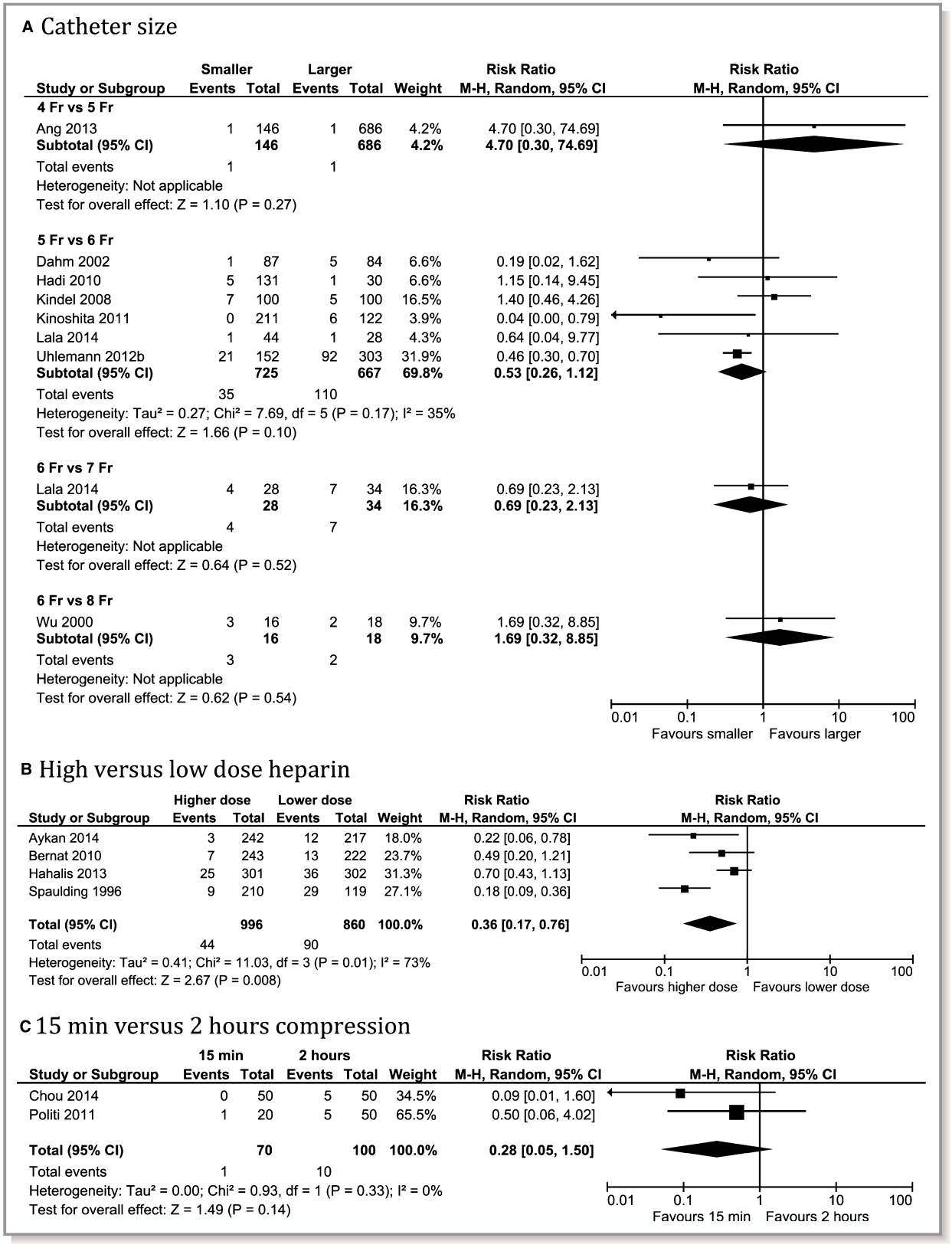
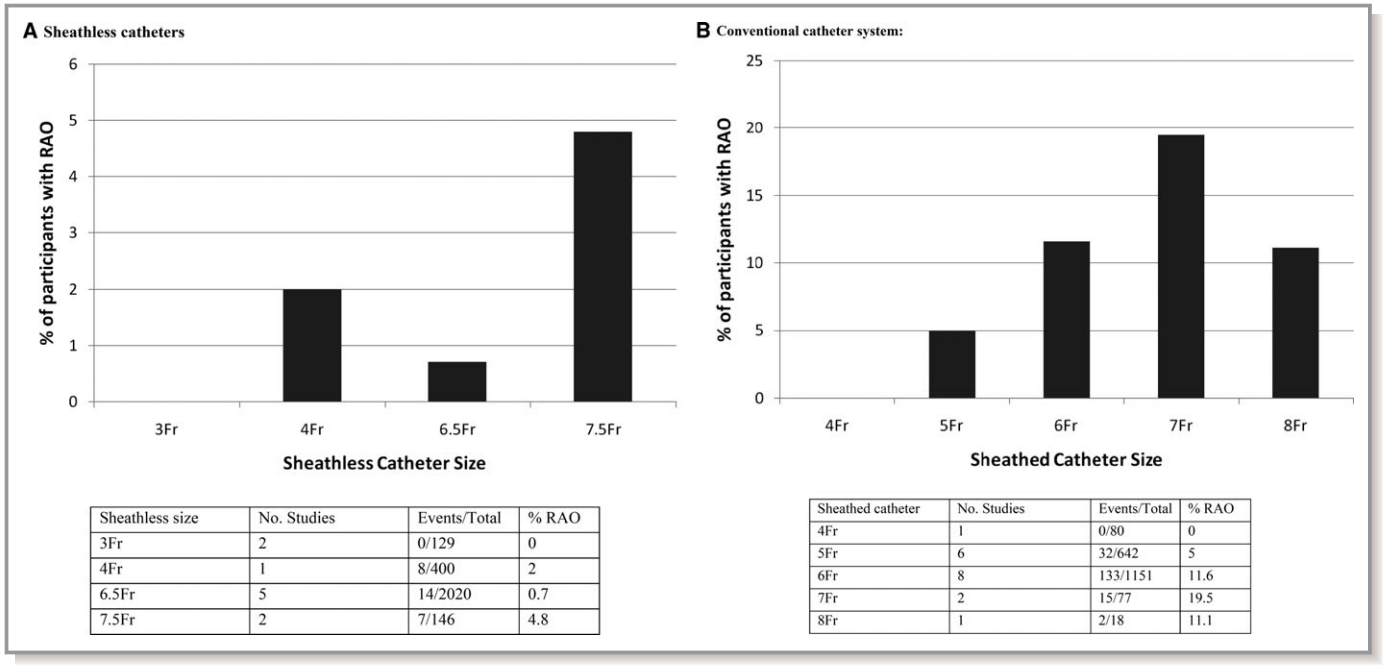


Figure 4. Meta-analysis of radial artery occlusion (RAO) by different interventions. The comparison of catheter size is shown in (A), High versus low dose heparin in (B), Duration of compression in (C). M-H indicates Mantel-Haenszel.



Sheathless size	No. Studies	Events/Total	% RAO
3Fr	2	0/129	0
4Fr	1	8/400	2
6.5Fr	5	14/2020	0.7
7.5Fr	2	7/146	4.8

Sheathed catheter	No. Studies	Events/Total	% RAO
4Fr	1	0/80	0
5Fr	6	32/642	5
6Fr	8	133/1151	11.6
7Fr	2	15/77	19.5
8Fr	1	2/18	11.1

Figure 5. Pooled incidence of radial artery occlusion (RAO) by catheter size. A, Sheathless catheters. B, Conventional catheter system.

Use of low molecular weight heparin (LMWH) is another routine practice to prevent thrombus formation and occlusive injury to the vessel by the mechanism as discussed above. In very early studies investigating the role of anticoagulants, Lefevre et al showed that the administration of heparin into the radial artery significantly reduced RAO.[92] Our results show that incidence of RAO increases by reducing the dose of intra-arterial heparin (Figure 5B). We found that a heparin dose of 5000 IU was very effective in preserving the patency of radial artery when compared with lower doses of 2000 to 3000 IU (risk ratio 0.36 95% CI 0.17–0.76). No increased risk of bleeding was reported in the higher heparin arm. We also observed a lower rate of RAO in the PCI setting (4.5%) compared to the diagnostic coronary angiogram setting (8.8%), which may relate to routine use of dual antiplatelet therapy and anticoagulants such as heparin or bivalirudin during the PCI procedure.

Other anticoagulants such bivalirudin and warfarin have also been studied as potential alternatives but did not show any significant benefit over LMWH;[64,65] therefore, LMWH remains a preferred anticoagulant due to lower costs. Our finding resonates with the recommendation made by the Society for Cardiovascular Angiography and Interventions transradial working group, which advocates the use of 5000 IU heparin in all patients undergoing TRA.

Since the inception of TRA, there have been numerous advances in catheter and sheath designs to facilitate the procedure and minimize the insult to the artery. We studied radial sheath length and coating and found no influence on RAO outcome. In a randomized trial of 790 compared long (23 cm) versus short (13 cm) sheaths and hydrophilic-coated or uncoated introducer sheaths, the authors found that neither sheath length nor coating affects RAO.[68] However, it has been suggested that using a small-diameter guide catheter may reduce the injury to radial artery and result in fewer occlusion rates.[52] This led to various innovations in the catheter design to minimize the outer diameter, including the development of sheathless guide catheters. Typically a 6-Fr sheathless guide catheter has an outer diameter that is smaller than that of a 5-Fr introducer sheath. We performed a pooled analysis to study the effect of various sizes (3, 4, 5, 6, 7, and 8 Fr) on incidence of RAO (Figure 4). We observed that RAO rates increase with increasing size of guide catheter systems used. Although the size of the catheter seems to correlate with incidence of RAO in these studies, the overall results failed to show a statistically significant benefit between smaller and larger catheter sizes (Figure 5A). This may be because of under-representation of the smaller-size catheter in these studies (Figure 4). Furthermore, a fair number of studies were single cohort studies undertaken without true randomization and may be subject to selection biases. In addition, there was no information available on the size (diameter) of radial artery in these studies, which may also explain the inconsistencies of relation of RAO to catheter size. Radial artery diameter and sheath-to-artery size ratio have been associated with better RAO outcomes.[21,85] Nevertheless, the individual studies have shown promising results in reducing radial injury, supporting the hypothesis that small catheter size causes less radial artery trauma. Larger randomized studies with preprocedure ultrasonic assessment of radial artery diameter and sheath-to-artery ratio are required to show direct influence of catheter size on RAO.

Table 5. Predictors of Radial Artery Occlusion (RAO)

Study ID	Results
Aykan 2014[29]	Predictors of RAO: male (P=0.008), age (P=0.950), body mass index (P=0.838), hypertension (P=0.035), dyslipidemia (P=0.034), diabetes (P=0.963), smoking (P=0.252), glucose (P=0.941), HDL (P=0.094), LDL (P=0.309), triglycerides (P=0.237), creatinine (P=0.747), GFR (P=0.179), fluoroscopy time (P=0.893), procedure time (P=0.659), sheath removal time (P=0.001), heparin group (P=0.010)
Buturak 2014[31]	Predictor of RAO: sheath-to-artery ratio >1 (P<0.001)
Chou 2014[34]	Predictor of RAO: duration of occlusive compression OR 12.7, P=0.001
Cubero 2009[18]	Univariate predictors of RAO: ex- or active smoker P=0.04, absence of antiaggregant P=0.04 Multivariate predictors of RAO: presence of RA flow after procedures HR 0.06 (0.01–0.2), total hematoma HR 3.7 (1.2–11.0), standard pneumatic compression HR 18.8 (3.8–92.2)
Dharma 2015[83]	Multivariate predictors of RAO: Duration of hemostasis >4 hours OR 3.11 (1.66–5.82), intra-arterial nitroglycerin use OR 0.62 (0.44–0.87).
Garg 2015[20]	Predictors of RAO: female sex OR 0.75 (0.19–2.93), diabetes OR 0.74 (0.22–2.51), BMI 0.91 (0.83–1.56), radial artery size ≤2.5 mm OR 40.54 (9.91–165.81), radial artery peak systolic velocity OR 0.94 (0.90–1.00), radial artery diameter-to-sheath ratio <1 OR 0.89 (0.16–5.06)
Honda 2012[42]	Significant predictors of occlusion: outer diameter of sheath OR 5.24 (1.21–22.8), statin medications OR 0.501 (0.255–0.985)
Lee 2014[47]	Significant predictors of RAO: age (P=0.032), procedure success (P=0.032)
Levin 2014[48]	Predictors of RAO: reduced body weight (P=0.031)
Lisowska 2015[49]	Significant predictors of RAO: men (P=0.025), creatinine (P=0.04)
Moarof 2014[55]	Predictors of RAO: sheath size OR 0.67 (0.13–3.50), compression time OR 0.87 (0.45–1.67), sex OR 0.59 (0.70–5.00), heparin dose OR 0.98 (0.85–1.11), procedure time OR 0.99 (0.97–1.01)
Monsegu 2012[56]	Significant predictors of RAO: no-use of profile sheath (P<0.001), no pulse after TR Band withdrawal (P<0.001), procedure performed by young radialist physician (P=0.022)
Pancholy 2008[17]	Significant predictors of RAO: weight (P<0.05), patency (P≤0.05)
Pancholy 2011[61]	Significant predictor of RAO: duration of compression (P=0.037)
Pancholy 2012[62]	Predictors of RAO: patent radial artery during hemostasis OR 0.03 (0.004–0.28), diabetes OR 11 (3–38), heparin OR 0.45 (0.13–1.54).
Plante 2010[65]	Independent predictors of RAO: bivalirudin OR 0.45 (0.11–2.06), body weight OR 2.78 (1.08–8.00), procedure ≤20 minutes OR 7.52 (1.57–36.0)
Politi 2011[66]	Significant predictors of RAO: heparin OR 0.70 (0.49–0.99)
Ruhnau 2013[69]	Predictors of RAO: women (66.7% in RAO vs 40.3% comparison, P=0.03), diabetes (40% vs 26%), renal insufficiency (20% vs 11%), coronary intervention (13% vs 26%). Hypertension, dyslipidemia, present or past smoking, body height, age, and BMI did not have significant influence
Shantha 2014[71]	Lower RAO with introducer sheath: Propensity-matched odds of RAO predischarge: OR 0.20 (0.13–0.32). Propensity-matched odds of RAO at 24 hours: OR 0.13 (0.07–0.25). Propensity-matched odds of RAO at 30 days: OR 0.18 (0.10–0.40)
Sreevatsa 2014[73]	Predictors of RAO: diabetes, female, prior radial intervention, radial artery diameter, type of hemostasis, sheath-to-artery diameter ratio
Tuncez 2013[75]	Predictor of RAO: low weight (P=0.01)
Uhlemann 2011a[77]	Predictors of RAO: female sex OR 2.36 (1.50–3.73), 6-Fr sheath OR 2.68 (1.56–4.59), peripheral arterial occlusive disease OR 2.04 (1.02–4.22), age OR 0.96 (0.94–0.98)
Uhlemann 2011b[78]	Significant risk factors for RAO: 6-Fr sheath OR 2.742 (1.574–4.776), age (10 y) OR 0.663 (0.523–0.842), female OR 2.591 (1.575–4.264), peripheral arterial disease OR 2.936 (1.300–6.632)
Zhou 2007[81]	Predictors of RAO: male OR 1.692 (0.837–3.156), smoking OR 1.157 (0.685–1.736), diabetes OR 0.633 (0.352–1.107), previous transradial intervention OR 0.728 (0.403–1.076), 7-Fr catheter OR 5.063 (2.010–12.634), compression time >90 minutes OR 2.319 (1.218–4.657), precoated hydrophilic catheter OR 1.781 (1.355–2.369)

BMI indicates body mass index; GFR, glomerular filtration rate; HDL, high-density lipoprotein; HR, hazard ratio; LDL, low-density lipoprotein; OR, odds ratio; RA, radial artery.

Patient's baseline characteristics and procedural variables have been an area of interest to the researchers to predict occurrence of RAO (Table 4). Age, sex, and body mass index have been investigated to predict RAO at the patient level while sheath-to-artery diameter, duration of compression,[34,66] and anticoagulation[29,30] have been studied as possible predictors of RAO. In our analysis, no factors were found to have consistent predictability of RAO among all the studies; however, age, sex, and body weight were most commonly reported predictors of RAO but there was no consistent direction of effect. For instance, 9 studies evaluated sex and 6 found that it was significant in predicting the RAO outcomes. Similarly, age was found to be a positive predictor in 3 of the 5 studies reporting on RAO. A more streamlined reporting of these variables in future trials may help in understanding the influences on RAO.

We also analyzed the effect of various pharmacological interventions in reducing RAO. In one study, administration of vasodilator cocktail in addition of to IV heparin before and after the procedure seems to have reduced the incidence of RAO.[25] Ahmed et al[26] also compared warfarin with LMWH to reduce RAO and concluded that warfarin was inferior to LMWH. In another prospective study, Zankl and colleagues[82] studied the efficacy of LMWH in treating the RAO postprocedure and found that LMWH significantly improved the recanalization rates of radial artery. These studies suggest that use of additional anticoagulation postprocedure may improve RAO outcome, but these studies were conducted without true randomization. Larger randomized studies are required to study the true effect of these medications in reducing RAO. Finally, Bernat et al[30] used a nonpharmacological novel intervention of compressing the ulnar artery postprocedure to increase the flow in radial artery once occluded. They found significantly lower rates of RAO post–ulnar artery compression and concluded that by doing so, flow through the radial artery increases, helping to reopen the artery postocclusion.

Our study has several limitations. Many of the studies were included were single-arm studies for which we were only able to evaluate the incidence of RAO. We included conference abstracts to reduce publication bias, but quality assessment from these studies was poor because reporting of methods was brief. While we found sufficient studies with similar interventions for statistical pooling, many of the included studies were underpowered.

Conclusions

To our knowledge, this is first systematic review and meta-analysis to date studying the incidence of RAO and factors influencing RAO. We found the incidence of RAO overall was 7.7% up to 24 hours and 5.8% at up to 30 days, which is comparable with currently published literature. There was variation in the timing of assessment of RAO in many studies, and RAO rates decreased with time. Shorter compression time in a patent hemostasis setting and higher dose of heparin independently appear to reduce RAO. The relation of RAO to radial artery diameter needs to be evaluated in larger studies. Smaller sheath sizes have shown promising effects on reducing RAO in individual studies, but these results needs to replicated in larger randomized trials to show the true effect of sheath size. Furthermore, adequately powered trials are needed to confirm whether other interventions may reduce RAO. We studied the predictors and pharmacological treatments used to reduce RAO but found no consistency in the literature with better RAO outcomes.

Disclosures

None.

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