Radial artery occlusion after transradial interventions: a systematic review and meta-analysis

Short running title: Radial artery occlusion in transradial interventions

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Abstract

Objectives: To investigate the incidence and factors influencing radial artery occlusion (RAO) post trans-radial access (TRA) for cardiac catheterization.

Background: RAO may occur post trans-radial intervention and limits the radial artery as a future access site and precludes its use as an arterial conduit. In this study, we investigate the incidence and factors influencing the RAO in the current literature.

Methods & Results: We searched MEDLINE and EMBASE for studies of RAO in TRA. Relevant studies were identified and data was extracted. Data was 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% to 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 greater than 1 week follow up). The most efficacious measure in reducing RAO was higher dose of heparin as lower doses of heparin were associated with increased RAO (RR 0.36, 95%CI 0.17-0.76) whilst shorter compression times also reduced RAO (RR 0.28, 95%CI 0.05-1.50). Several factors were found to be associated with RAO including age, gender, sheath size and diameter of radial artery but these factors were not consistent across all studies.

Conclusions: RAO is a common complication of TRA. 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 radial artery occlusion.

Keywords: Radial artery occlusion, transradial catheterization or access, vascular complications

Introduction

Trans radial access (TRA) has grown to become the default access site in the UK (1-4) Europe and Asia (5) and is rapidly growing in the USA. (6-8) Compared with transfemoral access (TFA), TRA has been shown to reduce mortality and adverse cardiac events even in high-risk patient groups, (3,9) reduced major bleeding and access site related vascular complications (10) and patient discomfort, 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 quiescent complication of TRA that rarely leads to critical hand ischemia requiring intervention owing to the dual vascular supply of hand from palmar arch. RAO is often overlooked and in fact more than 50% of operators do not even assess radial artery patency before discharge. (15) Once occluded, future use radial artery as an access site for 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. (16-20) Studies have reported that baseline patient characteristics such as body mass index and diabetes may influence RAO. (21) A number of procedural variables such as sheath size, (22) use of anticoagulants, (18,23) and patent hemostasis (18) have also been shown to reduce the incidence of RAO.

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 a both pooled- and meta-analyses to investigate the incidence and factors influencing radial artery occlusion in the TRA setting.

Methods

We searched MEDLINE and EMBASE on February 2015 using the broad search terms: ("radial occlusion" OR "radial artery occlusion") AND ("transradial" OR "radial catheterization" OR "radial artery catheterization" OR "radial artery catheterization" OR "radial artery catheterization"). The search results were reviewed by two independent investigators (CSK, MR) 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 radial artery occlusion. Studies were considered for detailed screening for inclusion if their abstract potentially met one of three criteria:

1. Primary studies with participants and evaluation of radial occlusion.
2. Any study which 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 radial artery occlusion 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 regards 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.

Base on the availability of data we either synthesized the results using meta-analysis, quantitative pooling; graphically or by narrative synthesis. Meta-analysis was performed by means of the random effects using RevMan 5.3 (Nordic Cochrane Centre, København, Denmark) in order to estimate pooled risk ratios (RRs). Statistical heterogeneity was assessed using I^2 statistic, with values of 30-60% representing a moderate level of heterogeneity. (24) The method of pooling has been previously described. (25) 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 outcome event rate. We also performed sensitivity analysis to detect the incidence of RAO according to the starting year of study, the completion year of the study and type of procedure performed i,e. diagnostic coronary angiography versus percutaneous coronary intervention. 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. (18,20,25-88) 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, 23 prospective cohort studies, 23 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 (56) to the largest cohort of 7,125. (86)

The use of interventions, follow up time, results and study limitations are shown in Table 2. Evaluation of RAO took place as short as 2-3 hours after procedure and as long as 507 days after procedure. 25 of the studies were only available in abstract or presentation form. 33 studies reported RAO outcomes by using ultrasound assessment. (Figure 2 supplementary table 1)

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 3). The studies which 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 2A). Among 8 studies that assessed for RAO between 24 hours to 1 week, the combined results with 1,377 participants was a RAO incidence of 9.5% (SD =±3.69%, 95%CI ±0.19%)(Figure 2B). 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 2C). 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). (See Supplementary table 2). Additionally we also found that incidence of RAO during diagnostic

coronary angiogram setting was much higher at 8.8% compared to the 4.5% in percutaneous coronary intervention (PCI) settings ~~-~~ ($p<0.001$)~~.-~~

We found 14 trials which evaluated similar interventions that could be statistically pooled using meta-analysis (Figure 5).(29-31,35,37,42,43,45,46,48,69,76,83,85) The only measure that significantly decreased RAO incidence was a higher dose of heparin RR 0.36 (95%CI 0.17-0.76).(31,32,44,77) None of these studies reported increased bleeding risk with higher dose (5000IU) of heparin. Another intervention shown to reduce RAO was the duration of compression; with a 15 min compression associated with reduced risk of RAO compared to a 2-hour compression (RR 0.28 95% CI 0.05-1.50),(35,69) 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. (28, 29, 37, 40,42,45-48,50,54-56,59,72,79,81,83,85) (Figure 4) We found a higher incidence of RAO with the increase in the size (outer diameter) of the catheter however the trend was not consistent amongst all studies particularly studies evaluating 8Fr size catheters, that consisted of a single study limited to 1 center. The incidence of RAO was 11% amongst 1297 participants in studies evaluating 6Fr catheter dropping markedly to 2% in 2662 participants in studies using 5Fr catheter.

Several studies evaluated significant predictors of RAO.(18,19,30,32,35,41,44,49-51,57,58,65,66,68,69,72,77,80,82,83,86) Age was reported to a significant predictor of RAO in 3 studies (49,82,83) while gender was significant in 6 studies.(30,51,72,77,82,83) Body weight was reported as a significant predictor in 3 studies.(18,68,80) In terms of procedural variables, use of smaller introducer sheath has been shown to be predictive of lower RAO (75) and use of larger diameter of sheath (44,83,86) and duration of compression (64,86) was associated with higher occlusion rates. Other predictors included baseline radial artery

diameter (20,97-98), peripheral artery disease, (84) statin use, (44) procedural success, (49) serum creatinine, (51) and heparin use.(69)

Two studies evaluated the effectiveness of TR band compared to other TRA hemostatic devices in reducing radial occlusion.(63,70) Pancholy et al conducted a study of 500 patients and reported a statistically significant reduction in RAO with use of TR band compared to HemoBand (4.4% vs 11.2%). (63) Rathore et al compared Radistop and TR band in 790 patients and found a non-significant reduction in RAO with TR band compared to Radistop (5.6% vs 8.0%, p=0.273). (70)

Several studies reported the influence of medications on RAO. Abboud et al reported an abstract where they showed that administration of radial artery vasodilator cocktail administration before and after procedure significantly reduced RAO compared to just before procedure (0.5% vs 8%). (26) 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 intra-procedural heparin. (27) Pancholy et al conducted a second study which compared administration of heparin after sheath insertion to no application of heparin unless post-procedure there was no radial patency and concluded that provisional use of heparin appears to be feasible and safe when patent hemostasis is maintained. (66) 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. (68)

Discussion

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

Our analysis suggests that RAO is common, with incident rates for early RAO within 24 hours 7.7% 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 were found to be 4.4% whereas absence of radial artery flow was found to be at 10.5%. (17) It is therefore recommended to use more objective method of assessment of RAO using radial flow using ultrasound. (96) 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 gender, Age, BMI 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 post procedure. Acute RAO rates are higher acutely and decline with time. In PROPHET study the acute incidence of RAO (12%) was almost halved by the passage of 28 days (7%). (18) 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 radial artery occlusion with time can be explained by the spontaneous recanalization of radial artery. Recanalization occurs as the results of activation of primary fibrinolysis. The

damaged endothelium facilitates this by releasing the tissue plasminogen activator and urokinase, thus allowing fibrinolysis to occur.

TRA also negatively affects the structure and function of radial artery culminating in non-occlusive 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. (89) More recently changes in flow-mediated dilatation (FMD) has been used as a surrogate of endothelial dysfunction. (90) Flow mediated dilatation is (FMD) 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 FMD post 5Fr TRA reduced significantly from 11.5% to 4.1% immediately after the procedure and dropped even further to 0.7% at 3 months. (91) 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. (92) 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 (93) 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 trans-radial access causes endothelial damage exposing the thromobogenic connective tissue. In addition, blood stasis whilst 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 reducing the occlusion rates. Saito et al (94) 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 equal to or greater than 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. (35,69) Although the results were very promising and statistically significant, both these studies were underpowered with less then 200 patients in total in both arms. (See Figure 3). Furthermore, Politi et al reported increase bleeding in patients subjected to shorter compression time in patent hemostasis settings. More recently, Duration of compression (>4hours versus <4 hours) was studied in a large randomized study by Dhrama et al. The found that duration of compression alone was strong predictor of RAO (OR 3.11 95% CI 1.62-5.82) supporting the hypothesis of minimizing radial injury by reducing compression time. (88)

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 anti-coagulants, Lefevre et al showed that the administration of heparin into the radial artery significantly reduced RAO. (95) Our results show that incidence of RAO increases by reducing the dose of intra-arterial heparin. (Figure 5B) We found that heparin dose of 5000IU was very effective in preserving the patency of radial artery when compared with lower doses of 2000-3000IU (RR 0.36 95%CI 0.17-0.76). No increased risk of bleeding was reported in higher heparin arm. We also observed a lower rate of RAO in PCI setting (4.5%) compared to diagnostic coronary angiogram setting

(8.8%), which may relate to routine use of dual antiplatelet therapy and anti coagulants such as heparin or bivalirudin during the PCI procedure.

Other anti-coagulants such Bivalirudin and warfarin have also been studied as potential alternatives but did not show any significant benefit over LMWH, (67,68) therefore LMWH remains a preferred anti-coagulant due to lower costs. Our finding resonates with the recommendation made by SCAI trans radial working group who advocates the use of 5000IU 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 (23cm) versus short (13cm) sheaths and hydrophilic-coated or uncoated introducer sheaths, the authors found that neither sheath length nor coating affects RAO. (71) However, it has been suggested that using small diameter guide catheter may reduce the injury to radial artery and resulting in less occlusion rates. (54) This led to various innovations in the catheter design to minimize the outer diameter including the development of sheathless guide catheters. Typically a 6Fr sheathless guide catheter has an outer diameter that is smaller than that of a 5Fr introducer sheath. We performed a pooled analysis to study the effect of various sizes (3Fr, 4Fr, 5Fr, 6Fr, 7Fr, 8Fr) on incidence of RAO (Figure 4). We observe that radial artery occlusion rates increase with increasing size of guide catheter systems used. Although, the size of catheter seems to correlate with incidence of RAO in these studies, the overall results failed to show statistically significant benefit between smaller and larger catheter sizes (figure 5A). This may be because of under representation of 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 (22,98). 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 pre-procedure ultrasonic assessment of radial artery diameter and sheath to artery ratio are required to show direct influence of catheter size on radial artery occlusion.

Patient's baseline characteristics and procedural variables have been an area of interest to the researchers to predict occurrence of RAO (Table 3). Age, gender and BMI have been investigated to predict RAO at patient level whilst sheath to artery diameter, duration of compression (35,69) and anticoagulation (30,31) have been studied as possible predictors of RAO. In our analysis, no factors were found to have consistent predictability of RAO amongst all the studies; however, age, gender and body weight was most commonly reported predictors of RAO but there was no consistent direction of effect. For instance, 9 studies evaluated gender and 6 found that it was significant in predicting the RAO outcomes. Similarly age was found to be a positive predictor on 3 out of the 5 studies reporting on RAO. A more streamlined reporting of these variables in the future trials may help to understand 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 IV heparin before and after the procedure seems to have reduced the incidence of RAO. (26) Ahmed et al (27) also compared warfarin with LMWH to reduce RAO and concluded that warfarin was inferior to LMWH. In another prospective study, Zankl and colleagues (87) studied the efficacy of LMWH in treating the RAO post procedure and found that LMWH significantly improved the recanalization rates of radial artery. These studies suggest that use of additional

anticoagulation post procedure 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 radial artery occlusion. Finally, Bernat et al (31) used a non-pharmacological novel intervention of compressing the ulnar artery post procedure to increase the flow in radial artery once occluded. They found significant lower rates of RAO post ulnar artery compression and concluded that by doing so flow thorough radial artery increases helping to reopen the artery post occlusion.

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

Conclusion

To our knowledge, this is first systematic review and meta-analysis to date studying the incidence of radial artery occlusion and factors influencing RAO. We found 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 patent hemostasis setting and higher dose of heparin independently appears to reduce RAO. 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 if 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.

Figure 1: Flow diagram of study selection

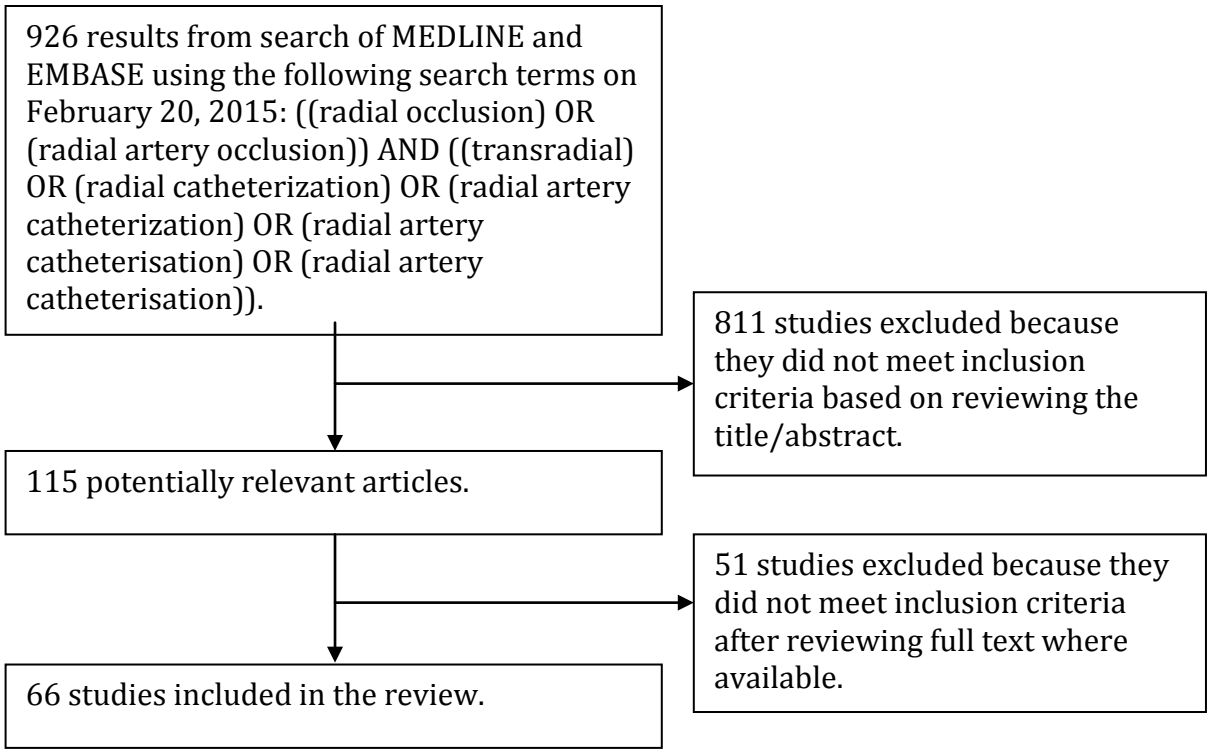
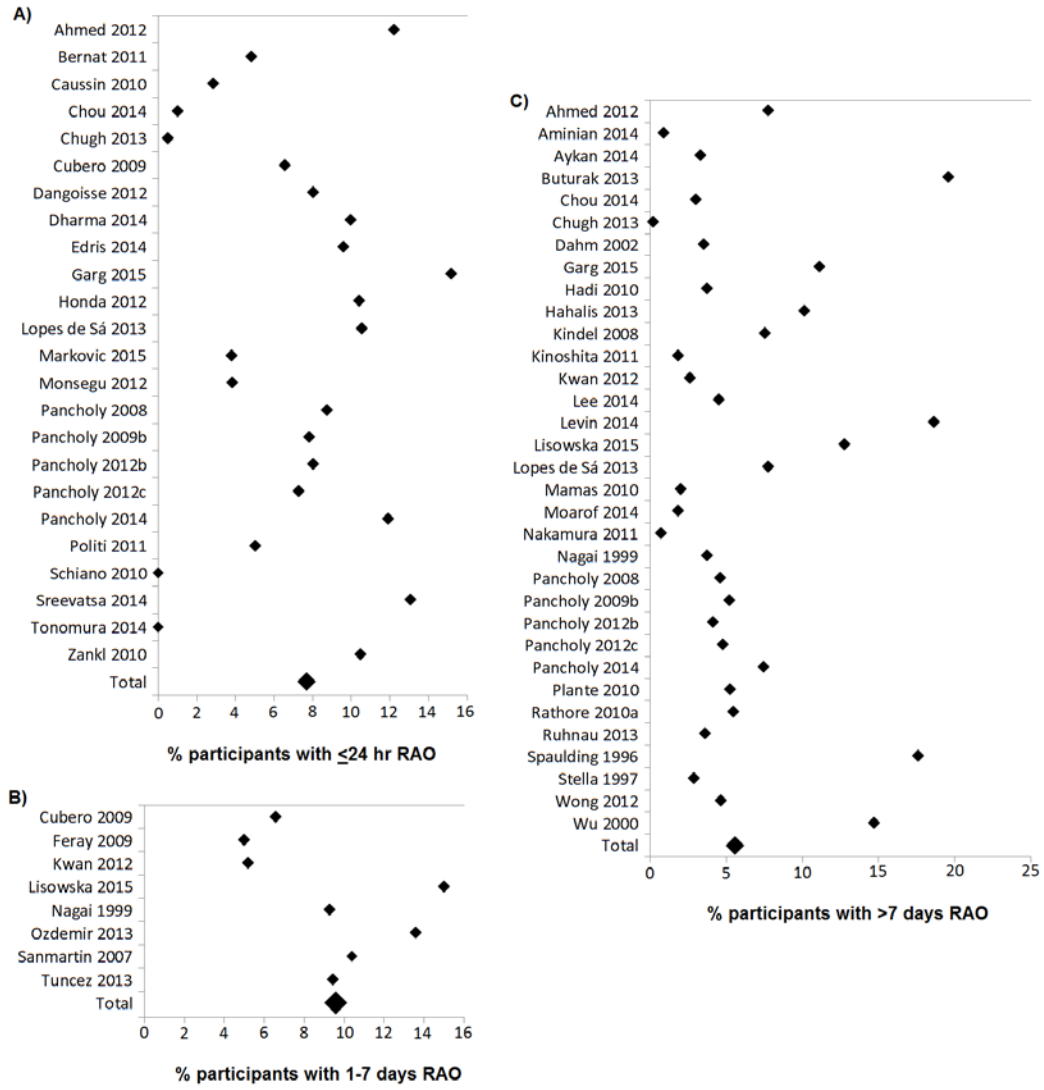


Figure 2: Incidence of RAO by follow up time

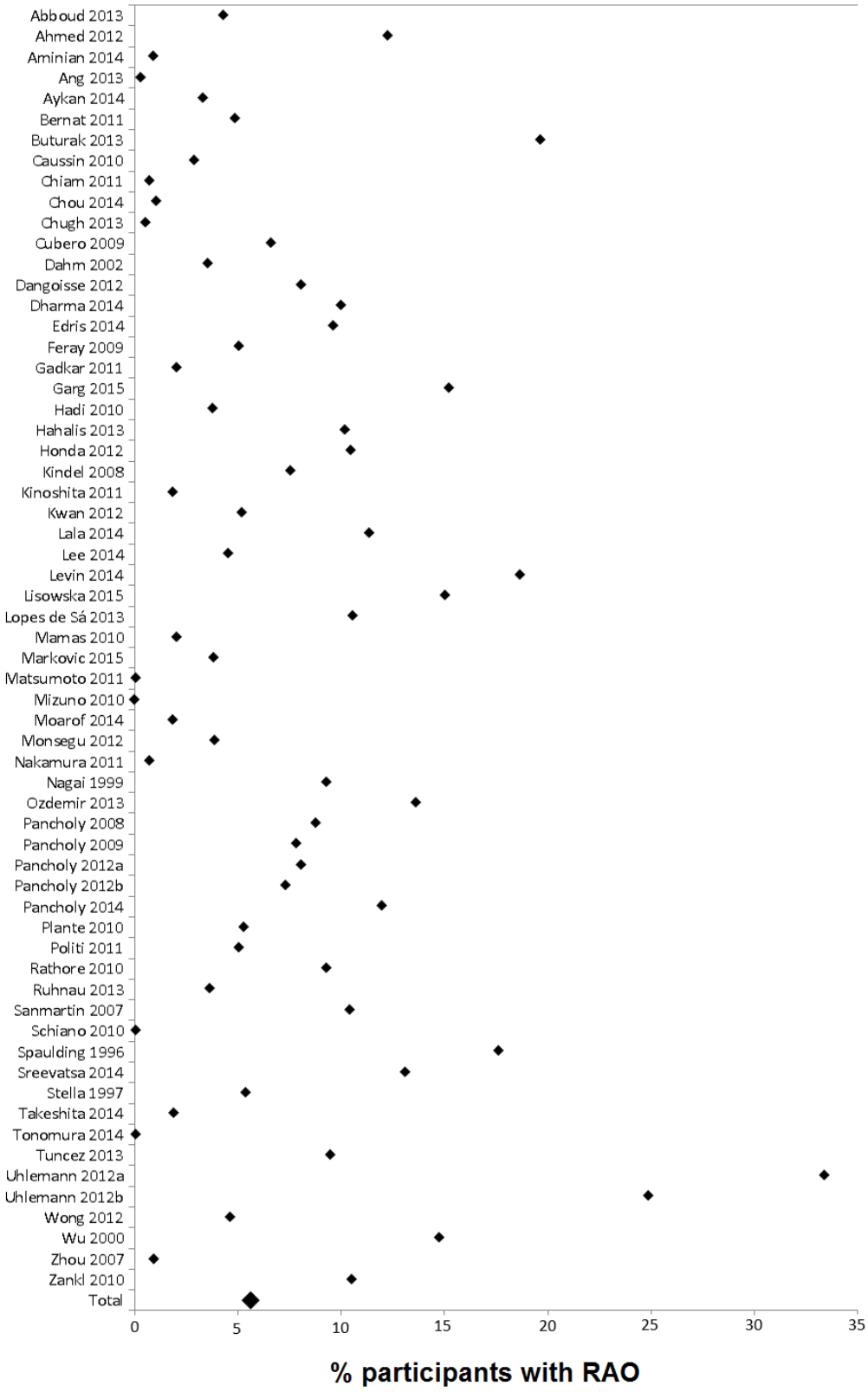


Group	No. of studies	RAO events	Total	Mean%	SD%	95%CI Margin
RAO at 1 day	24	841	10938	7.69	4.23	0.08
RAO at 2-6 days	8	132	1377	9.59	3.69	0.19
RAO at 7+ days	33	602	10821	5.56	5.19	0.1

Figure 2: supplementary table 1
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 2-6 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	11193	7.89	7.79	0.14

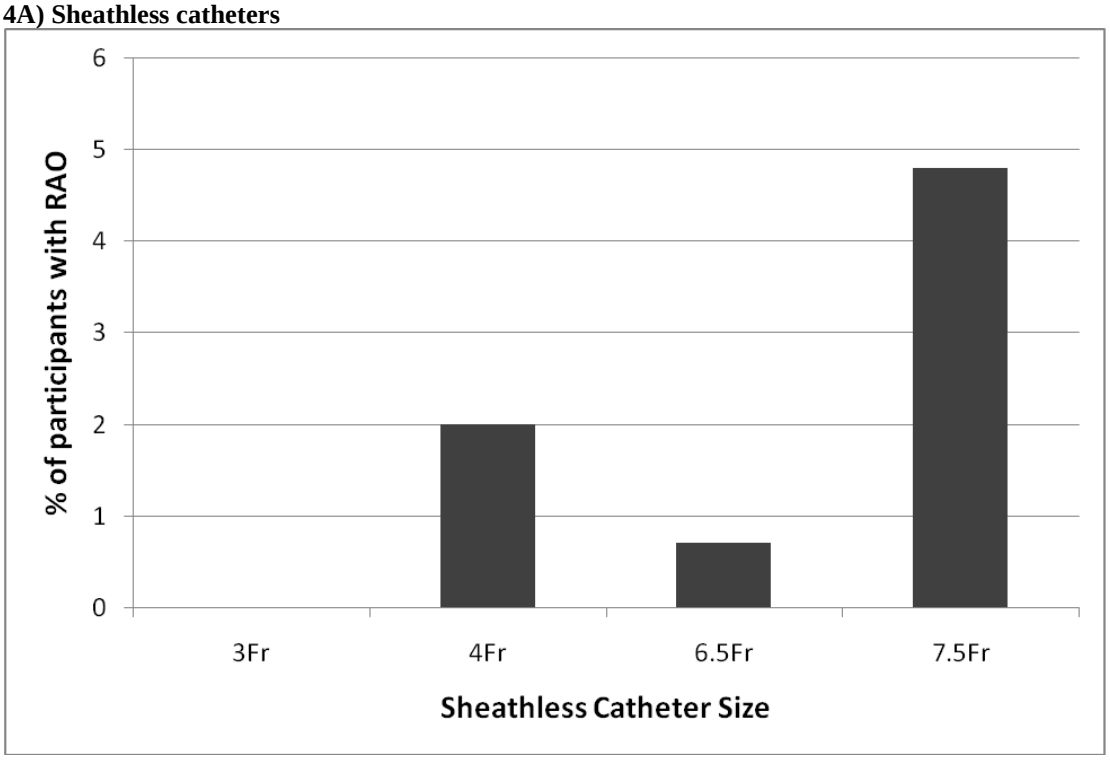
Figure 3: Incidence of RAO at shortest follow up time for each study



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

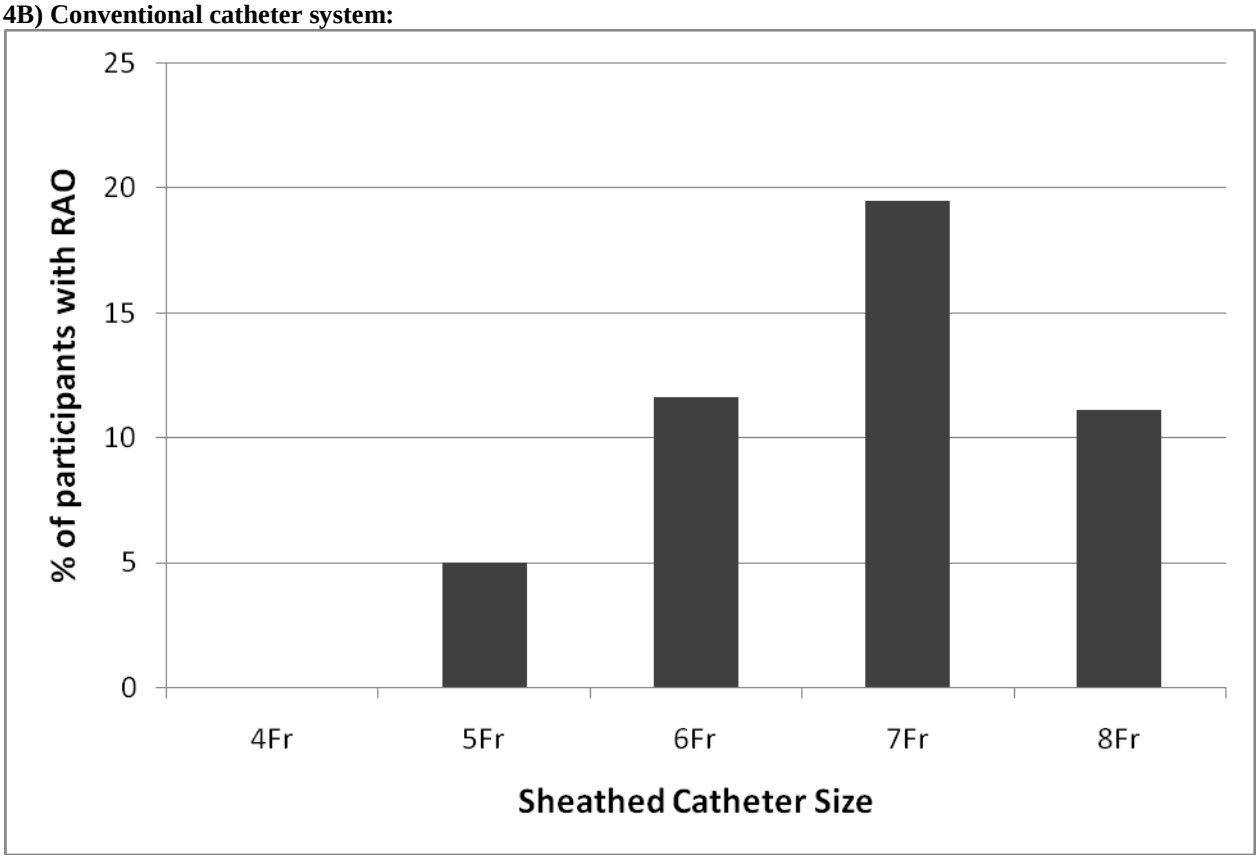
*4 studies were not included because of duplicate analysis of the same cohort.

Figure 4: Pooled Incidence of RAO by catheter size
4A) Sheathless catheters



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

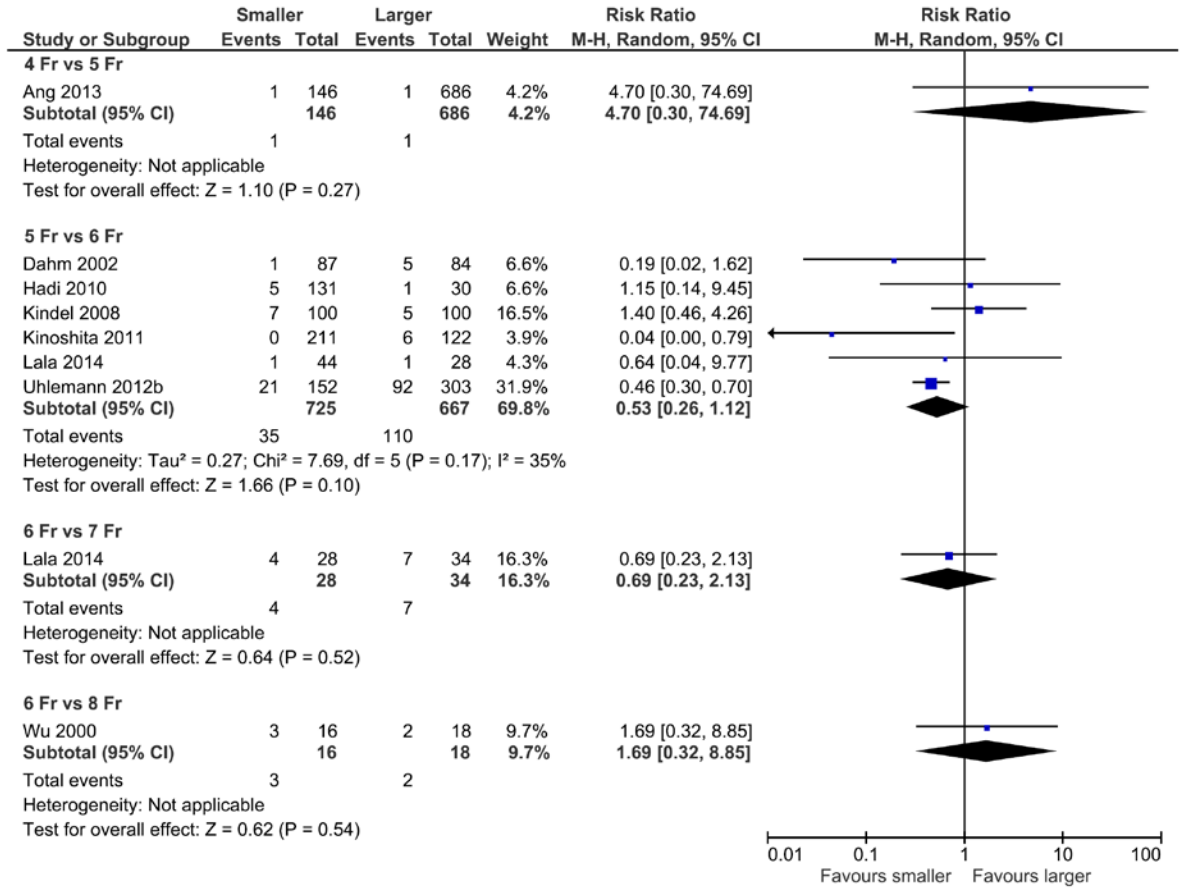
Figure 4: Pooled Incidence of RAO by catheter size
4B) Conventional catheter system:



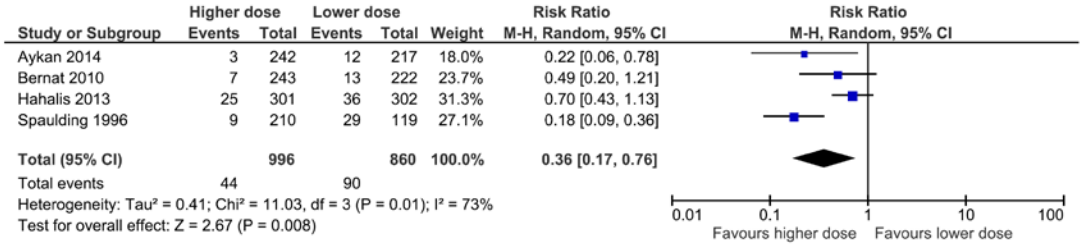
Sheathed catheter	No. Studies	Events/Total	% RAO
4Fr	1	0/80	0
5Fr	6	32/642	5
6Fr	8	133/1151	11.6
7Fr	2	15/77	19.5
8Fr	1	2/18	11.1

Figure 5: Meta-analysis of RAO by different interventions

A) Catheter size



B) High versus low dose heparin



C) 15 min versus 2 hours compression

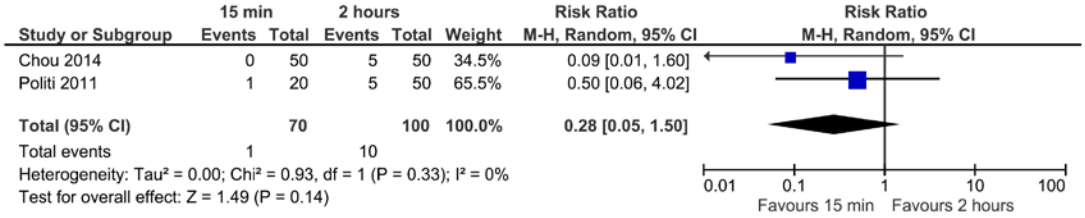


Table 1: Study design and participant characteristics

Study ID	Design; Country; Year	No. of participants	Age	% male	Participants inclusion criteria and setting
Abboud 2013	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	Matched cohort study; USA; NA.	336.	72 years.	65%.	Patients undergoing radial artery catheterization where group I had INR >2.0 and were on warfarin while group II were not on warfarin.
Aminian 2014	Prospective cohort study; Belgium; May to Jun 2013.	113.	63 years.	65%.	Patients undergoing radial artery catheterization with Glidesheath Slender radial sheath.
Ang 2013	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	Randomized study; Turkey; NA.	459.	60 years.	77%.	Patients undergoing radial artery catheterization who were randomized to 2,500 IU or 5,000 IU heparin.
Bernat 2011	Randomized study; Czech Republic; NA.	465.	61 years.	63%.	Patients undergoing radial artery catheterization who were randomized to 2,000 IU or 5,000 IU heparin and ulnar artery compression.
Buturak 2013	Prospective cohort study; Turkey; NA.	409.	59 years.	NA.	Patients underwent transradial coronary procedure.
Caussin 2010	Randomized study; France; Jan to Jun 2006.	351.	66 years.	67%.	Patients undergoing transradial angiography who were randomized to long hydrophilic coated or a short sheath.
Chiam 2011	Retrospective cohort study; Singapore; Nov 2008 to Sept 2010.	269 patients, 292 procedures.	57 years.	85%	Patients undergoing transradial coronary intervention who received sheathless 6.5 Fr and 5Fr catheters.
Chou 2014	Randomized study; China; NA.	100.	NA.	NA.	Patients underwent first time transradial catheterization and were randomized to QuikClot or prolonged compression.
Chugh 2013	Prospective cohort, India, 2006 to 2011	613.	57 years	63%	Patients undergoing diagnostic or interventional cardiac catheterization.
Cubero 2009	Randomized study; Spain; Dec 2007 to Apr 2008.	351.	65 years.	67%.	Patients underwent transradial coronary angiography and were randomized to pneumatic compression guided by mean arterial pressure or standard procedure.
Dahm 2002	Randomized study; Germany; Mar 2000 to Oct 2001.	171.	61 years.	59%.	Patients with coronary lesions suitable for at least 5 Fr transradial angiography randomized to 5 Fr or 6 Fr PCI.
Dangoisse 2012	Randomized study; Belgium; Jan 2009 to Jun 2011.	2,107.	NA.	NA.	Transradial angiography using TR Band closure device.
Dharma 2014	Randomized study; International; NA	1,706.	59 years.	68%	Patients undergoing transradial catheterization.
Edris 2014	Retrospective cohort study; USA; NA.	115.	NA.	NA.	Patients underwent transradial catheterization with TR band with standard protocol or rapid deflation.

Feray 2009	Prospective cohort study; Turkey; NA.	39.	55.6 years.	69%.	Patients underwent transradial catheterization with enoxaparin therapy.
Gadkar 2011	Prospective cohort study; India; NA.	400.	NA.	NA.	Patients underwent transradial angiography with 4 Fr sheathless catheter.
Garg 2015	Prospective cohort study; India; Jan 2012 to Jun 2012.	198.	58 years.	81%.	Patients who underwent PCI.
Hadi 2010	Cohort study; UK; NA.	161.	NA.	77%.	Patients who underwent PCI who received 6.5 Fr or 7.5 Fr sheathless catheter.
Hahalis 2013	Randomized study; Greece; Jun 2010 to Jan 2013.	603.	NA.	74.5%.	Patients with transradial catheterization were randomized to 2,500 or 5,000 IU.
Honda 2012	Prospective cohort study; Japan; NA.	500.	70.7 years.	64%.	Patients underwent transradial catheterization.
Kindel 2008	Randomized study; Germany; NA.	200.	NA.	NA.	Patients underwent transradial catheterization who were randomized to coated/5F, control/5F, coated/6F and control 6F.
Kinoshita 2011	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	Prospective cohort study; USA; Dec 2010 to Feb 2011.	116.	66 years.	74.	Patients underwent transradial intervention with 7 Fr sheathless guiding catheter.
Lala 2014	Retrospective cohort study; USA; Jan 2011 to Dec 2011.	106.	71 years.	NA.	Patients underwent transradial PCI with 5, 6 and 7 Fr catheter.
Lee 2014	Prospective cohort study; Taiwan; Jan 2010 to Jun 2012.	133.	66 years.	75%	Patients underwent transradial intervention.
Levin 2014	Prospective cohort study; Israel; NA.	43.	NA.	NA.	Patients underwent transradial intervention with 7 Fr sheath.
Lisowska 2015	Prospective cohort study; Poland; 2010 to 2012.	220.	64 years.	76%.	Patients with acute coronary syndrome who underwent coronary angiography and angioplasty via radial access.
Lopes de Sá 2013	Randomized study; Brazil; Nov 2010 to Jul 2011.	228.	60 years.	58%.	Patients underwent transradial catheterization and were randomized to brand new introducers or reprocessed introducers.
Mamas 2010	Prospective single arm study; UK; Jul 2008 Nov 2008.	100.	60 years.	75%.	Patient underwent PCI via transradial angiography with 6.5 Fr sheathes guide catheter.
Markovic 2015	Prospective cohort study; Germany; NA.	369.	68 years.	85%	Patients underwent transradial catheterization with 5 Fr or 6 Fr sheath.
Matsumoto 2011	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	Retrospective cohort study; Japan; Dec 2008 to Sept 2009.	27.	73 years.	59%.	Patient underwent PCI using virtual 3 Fr guiding catheter.
Moarof 2014	Prospective observational study; Switzerland; Jan 2010 to Oct 2013.	395.	66 years.	88%	Patients underwent transradial coronary angiography or PCI.
Monsegu 2012	Prospective cohort study;	574 .	NA.	NA.	Patients underwent cardiac catheterization with 5 Fr or 6 Fr

	International; NA.				introducer sheath and catheter.
Nakamura 2011	Cohort study; Japan; Jun 2005 to Dec 2009.	892.	NA.	NA.	Patients underwent transradial intervention of 6.5 Fr sheathless guide catheter.
Nagai 1999	Retrospective cohort study; Japan; Sept 1996 to Dec 1997.	162.	64 years.	64%.	Patients undergoing transradial coronary angiography and angioplasty.
Ozdemir 2013	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	Randomized study; USA; NA.	463.	65 years.	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 2009a	Randomized study; USA; Nov 2007 to Dec 2008.	500.	64 years.	61%.	Patients underwent transradial diagnostic coronary angiography and were randomized to intravenous or intra-arterial heparin.
Pancholy 2009b	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 2012a	Retrospective cohort study; USA; NA.	400.	64 years.	63%.	Patients underwent transradial catheterization who had 2 or 6 hours of hemostatic compression.
Pancholy 2012b	Randomized study; USA; NA.	412.	64 years.	71%.	Patients underwent transradial catheterization and were randomized to Seldinger and modified Seldinger technique.
Pancholy 2012c	Randomized study; USA; NA.	400.	64 years.	63%.	Patients underwent transradial catheterization and were randomized to heparin or no heparin in the PHAROAH study.
Pancholy 2014	Case-control study; USA; Jan 2009 to Dec 2011.	336.	72 years.	65%.	Patients underwent transradial catheterization who had therapeutic warfarin matched to controls.
Plante 2010	Cohort study; Canada; NA.	400.	60 years.	76%	Patients underwent transradial catheterization and received heparin or bivalirudin.
Politi 2011	Randomized study, Italy; Nov 2009 to Jan 2010.	120.	62 years.	73%.	Patients underwent transradial catheterization and were randomized to QuikClot, short compression or conventional compression.
Rathore 2010a	Randomized study; UK; Nov 2006 to Jan 2008.	794.	63 years.	74%.	Patients underwent transradial catheterization and were randomized to TR band or Radistop compression.
Rathore 2010b	Randomized study; UK; Nov 2006 to Jan 2008.	790.	63 years.	74%.	Patients underwent transradial catheterization and were randomized to long, short, coated and uncoated sheaths.
Ruhnau 2013	Cohort study; Germany; NA.	415.	66 years.	66%.	Transradial intervention using 6 Fr sheath.
Sanmartin 2007	Prospective cohort study; Spain; NA.	275.	64 years.	79%.	Patients underwent transradial catheterization.
Schiano 2010	Randomized study; France; Sept 2007 to Mar 2008.	162.	63 years.	65%.	Patients underwent radial catheterization.
Shantha 2014	Prospective cohort study; USA; Jan 2009 to Dec 2013.	1,251.	65 years.	63%.	Patients underwent 6 Fr PCI.
Spaulding 1996	Prospective cohort study; France;	415.	58 years.	85%.	Patients underwent transradial catheterization and assessed for

	Mar 1994 to Jun 1995.				procedural success and vascular complications.
Sreevatsa 2014	Cohort study; India; NA.	176.	56 years.	85%.	Patients underwent transradial PCI who either had patent hemostasis or conventional hemostasis.
Stella 1997	Prospective cohort study; Netherlands; Aug 1992 to Oct 1995.	563.	60 years.	76%.	Patients with transradial PCI
Takeshita 2014	Randomized study; International; NA.	160.	68 years.	79%.	Patients undergoing transradial catheterization who were randomized to 4 Fr or 6 Fr guiding catheter.
Tonomura 2014	Prospective cohort study; Japan; Jul 2010 to Dec 2012.	132.	70 years.	71%.	Patient undergoing elective PCI via transradial approach using virtual 3Fr sheathless guide system.
Tuncez 2013	Prospective cohort study; Turkey; Aug 2011 to Mar 2012.	106.	58 years.	43%.	Patients underwent tranradial coronary angiography and PCI.
Uhlemann 2012a	Prospective cohort study; Germany; Nov 2010 to Jan 2011.	33.	72 years.	67%.	Patients with transradial cardiac catheterization who had oral anticoagulation.
Uhlemann 2012b	Prospective cohort study; Germany; Nov 2009 to Aug 2010.	455.	65 years.	62%.	Patients with transradial cardiac catheterization who had 5 Fr and 6 Fr sheath.
Wong 2012	Randomized study; Singapore; NA.	217.	58 years.	NA.	Patients undergoing PCI via 6 Fr trans radial approach.
Wu 2000	Randomized study; USA; NA.	40.	NA.	NA.	Trans radial coronary intervention.
Zhou 2007	Cohort study; China; Aug 2002 to Feb 2006.	7,125.	64 years.	71%	Patients with transradial PCI.
Zankl 2010	Cohort study; Germany; 2007 and Apr 2009 .	488.	64 years.	65%.	Patients undergoing trans radial catheterization.

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	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	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 (5.2%).	Abstract only, and lack of randomization.
Aminian 2014	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	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 5Fr group: 1/146. RAO with 6.5Fr group: 1/686.	Abstract only, retrospective and lack of randomization.
Aykan 2014	2,500 IU versus to 5,000 IU heparin.	Radial artery patency evaluated 1 month after angiography with Doppler US.	Incidence of RAO in both groups: 15/459. RAO with 2,500 IU heparin: 12/217. RAO with 5,000 IU heparin: 3/242.	Presentation slides only.
Bernat 2011	2,000 IU versus 5,000 IU heparin. Ulnar artery compression	RAO with duplex US after 3-4 hours.	Incidence of early RAO in both groups: 20/465. Early RAO with 2,000 IU heparin: 13/222 (5.9%). Early RAO with 5,000 IU heparin: 7/243 (2.9%). Incidence of final RAO in both groups: 11/465. Final RAO with 2,000 IU heparin: 9/222 (4.1%) Final RAO with 5,000 IU heparin: 2/243 (0.8%)	None.
Buturak 2013	No intervention.	Doppler US at 6-15 months.	Late term RAO incidence: 67/342 (16.4%). RAO with age: 55.9 years vs 59.1 years. RAO with hypertension: 9.8% vs 23.0%.	Abstract only.
Caussin 2010	Long hydrophilic-coated versus a short sheath.	RAO a day after procedure with US Doppler.	RAO incidence: 10/351. RAO with long sheath: 5/177 (3.5%). RAO with short sheath: 5/174 (3.5%).	Not primary outcome of trial.
Chiam 2011	6.5Fr sheathless versus 5Fr guiding catheters.	RAO in hospital.	RAO incidence: 2/292. RAO with sheathless group: 1/146 (0.7%)	Retrospective, unclear outcome ascertainment.

			RAO with 5Fr group: 1/146 (0.7%)	
Chou 2014	Short compression with QuikClot (15 minutes) and a conventional prolonged compression (2 hours)	Early RAO <24hrs and Late RAO 1-2 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.
Chugh 2013	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.
Cubero 2009	Compression guided by mean arterial pressure or standard compression by pneumatic air device.	24-72 hrs using inverse Allen 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.
Dahm 2002	5Fr versus 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 five 6Fr Patient had artery: catheter ratio <1.	Unclear timing of RAO.
Dangoisse 2012	Low (13cc) volume of air versus Ultra low (10cc) volume of air in TR Band.	RAO assessment at 24hours using pulse oximetry.	RAO at 24 hours: 169/2107 (8%).	Abstract study only.
Dharma 2014	Intra-arterial administration of nitroglycerin (500mcg) versus placebo post procedure.	RAO assessment at 24 hours using ultrasound duplex	Incidence of RAO: 170/1706 (9.9%) RAO incidence in nitroglycerin arm: 70/853(8.3%) RAO incidence in placebo arm: 100/853(11.7%)	None.
Edris 2014	Standard technique versus rapid deflation technique.	RAO at 24 hrs 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, non-randomized.
Feray 2009	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 (4%).	Single arm study.
Gadkar 2011	4 Fr sheathless.	RAO at unclear timing of evaluation.	Incidence of RAO 8/400 (2%).	Non-randomized.
Garg 2015	None.	US Doppler 1 day before, 1 day after, and 3 months after the	Incidence of RAO: 30/198 (15.2%).	None.

		procedure.		
Hadi 2010	6.5 Fr versus 7.5 Fr sheathless catheter.	RAO at one 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	2,500 versus 5,000 IU of heparin.	Median follow-up of 8 days with Doppler US.	Incidence of RAO: 61/603. RAO in 2,500 IU arm: 36/302 (12.0%) RAO in 5,000 IU arm: 25/301 (8.4%)	Abstract only. Significant loss to follow up 52%.
Honda 2012	None.	US at 24 hrs.	Incidence of RAO: 52/500.	None.
Kindel 2008	Hydrophilic-coated versus non-coated sheaths and 5F versus 6F catheters.	RAO at one month with US Doppler.	Incidence of total RAO: 15/200. Incidence of early occlusion: 12/200. Coated/5F: 3/50. Control/5F: 4/50. Coated/6F: 4/50. Control/6F: 1/50. Incidence of late occlusion: 3/200. Coated/5F: 1/50. Control/5F: 0/50. Coated/6F: 1/50. Control/6F: 1/50.	None.
Kinoshita 2011	6.5 Fr sheathless guides versus 6F guides.	RAO at 3 months.	Incidence of RAO: 6/333. RAO in 6.5 Fr sheathless guide group: 0/211 (0%) RAO in 6F guide group 6/122 (5%).	Abstract only.
Kwan 2012	7F 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	5Fr, 6Fr and 7Fr guiding catheter.	RAO at 1 day and 30 days.	Incidence of RAO: 12/106. RAO with 5Fr: 1/44 (2%) RAO with 6Fr: 4/28 (14%) RAO with 7Fr: 7/34 (20%)	Abstract only, retrospective, non-randomized study.
Lee 2014	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	7 Fr sheath catheter.	507 days by US and Barbeau test.	Incidence of RAO: 8/43 (19%).	Abstract only.
Lisowska 2015	None.	US at 48-72 hrs and 6-12 months.	Periprocedural RAO: 33/220 (15%). Long term RAO: 28/220 (13%).	None.
Lopes de Sá 2013	Brand new introducers versus reprocessed introducers.	RAO was evaluated at 24 hrs (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%).	Loss to follow up 18.4%.

			RAO in reprocessed introducers: early 14/128 (10.9%), late 11/106 (10.4%).	
Mamas 2010	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.
Markovic 2015	None.	Doppler US at 24 hrs.	Incidence of RAO: 14/369. RAO with 5Fr: 1/45 (2%). RAO with 6Fr: 13/324 (4%).	None.
Matsumoto 2011	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	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	None.	Color duplex US up to 34 months.	Incidence of long term RAO: 7/385.	Abstract only.
Monsegu 2012	None.	Color Doppler with and without ulnar compression at 24 hrs.	Incidence of RAO 22/574 (3.8%).	Abstract only.
Nakamura 2011	6.5 French sheathless guide catheter.	6-9 months RAO with Doppler.	Incidence of RAO: 6/892 (0.67%).	Abstract only, loss to follow up 23%.
Nagai 1999	US assessment of radial artery post procedure.	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%).	Retrospective single arm study.
Ozdemir 2013	Subcutaneous enoxaparin (60 mg/day) after 4 hours of sheath removing and each after 3 days versus 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	Conventional pressure application for hemostasis versus pressure application confirming radial artery patency using Barbeau's test.	24 hrs and 30 days using plethysmography.	Incidence of RAO at 24 hrs: 38/436. Incidence of RAO at 30 days: 20/436. RAO in conventional group at 24 hrs: 27/219 (12%). RAO in conventional group at 30 days:16/219 (7%). RAO in Barbeau's test group at 24 hrs: 11/217 (5%). RAO in Barbeau's test group at 30 days: 4/217 (2%).	None.
Pancholy 2009a	Intravenous versus 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%).	None.

			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%).	
Pancholy 2009b	HemoBand versus TR Band for haemostasis.	RAO at 24 hrs and 30 days with Barbeau's test.	Incidence of RAO at 24 hrs: 39/500. Incidence of RAO at 30 days: 26/500. RAO at 24 hrs with Hemoband: 28/250 (11.2%). RAO at 30 days with Hemoband: 18/250 (7.2%). RAO at 24 hrs with TR Band: 11/250 (4.4%). RAO at 30 days with TR Band: 8/250 (3.2%).	None.
Pancholy 2012a	Duration of compression 2 hrs versus 6 hrs.	RAO at 24 hrs and 30 days.	Incidence of early RAO: 35/400. Incidence of chronic RAO: 24/400. Early RAO in 6 hrs group: 24/200 (12%). Chronic RAO in 6 hrs group: 17/200 (8.5%). Early RAO in 2 hrs group: 11/200 (5.5%). Chronic RAO in 2 hrs group: 7/200 (3.5%).	Retrospective cohort study.
Pancholy 2012b	Seldinger technique versus modified Seldinger technique.	RAO at 24 hrs 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.
Pancholy 2012c	A Priori heparin versus provisional heparin.	Plethysmograph for RAO at 24 hrs 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	Warfarin versus intra-arterial heparin.	Plethysmograph for RAO at 24 hrs 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	Heparin versus bivaluridin.	RAO at 4-8 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%).	Non randomized study
Politi 2011	Short compression with the	Radial artery patency	Incidence of RAO: 6/120.	None.

	QuikClot, short compression or conventional prolonged compression.	was assessed using the Barbeau's test 12 at 24 hrs.	RAO with QuikClot: 0/50 (0%). RAO with short compression: 1/20 (5%). RAO with prolonged compression: 5/50 (10%).	
Rathore 2010a	Radistop device versus TR band hemostasis.	RAO at discharge and follow up after 4-6 months with plethysmography and oximetry	Incidence of RAO at discharge: 73/790 (9.2%). Incidence of RAO at follow up: 43/790 (6.8%). 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 (8%). RAO at follow up with TR band: 18/395 (5.6%).	None.
Rathore 2010b	Long versus short sheet and hydrophilic coated versus non coated sheet.	RAO at discharge and follow up.	Incidence of RAO at discharge: 73/790 (9.5%) 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	TRA using 6Fr sheath.	RAO at 4-68 weeks using US duplex.	Incidence of RAO: 15/418 (3.6%) Female are at higher risk of RAO (n=10 vs n=5)	Abstract study only.
Sanmartin 2007	None.	RAO at 7 days with pulse oximeter and plethysmograph.	Absent pulsation: 12/279 (4.4%). Absent radial flow: 29/279 (10.5%).	None.
Schiano 2010	5000IU heparin versus weight adjusted (50units/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 min, vs. 204.5 min, $p<10\text{-}5$).	None.
Shantha 2014	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 pre-discharge: OR 0.20 (0.13-0.32). Propensity matched odds of RAO at 24 hrs: OR 0.13 (0.07-0.25).	Abstract only. Unclear variables in propensity matching.

			Propensity matched odds of RAO at 30 days: OR 0.18 (0.10-0.40).	
Spaulding 1996	No heparin, heparin 2000-3000 units and heparin 5000 units.	RAO assessment post-procedure and at 2 month follow-up using echo-Doppler measurements	Incidence of RAO: 73/415. No heparin group: 35/49 (71%). Heparin 2,000-3,000 units: 29/119 (24%). Heparin 5000 units: 9/210 (4.3%).	Non randomized study. 59% of participants were excluded.
Sreevatsa 2014	Patent hemostasis versus occluded hemostasis.	Barbeau's test and Doppler at 24 hrs.	Incidence of RAO: 23/176 (13.1%). RAO with patent hemostasis: 6/87. RAO with occluded hemostasis: 17/89.	Abstract only.
Stella 1997	None.	RAO assessment at discharge and one month via palpation and Allen's test	Incidence of early RAO: 30/563 (5.3%) Incidence of late RAO (30days): 16/563 (2.8%)	None
Takeshita 2014	4Fr versus 6Fr guiding catheter.	RAO on reverse Allen test.	Incidence of RAO: 3/160. RAO in 4Fr group: 0/80. RAO in 6Fr group: 3/80.	None.
Tonomura 2014	3 Fr sheath less guide system	2-3 days post procedure using reverse Allen's test	Incidence of RAO: 0/111 (0%).	Single cohort; follow up not done on all patients.
Tuncez 2013	None.	RAO at 24 hours with US Doppler.	Incidence of RAO: 10/106. Predictor of RAO: low weight (p=0.01).	None.
Uhlemann 2012a	All patients had oral anticoagulation.	RAO at discharge on Duplex US.	Incidence of RAO: 11/33 (33%).	None.
Uhlemann 2012b	5F sheath and 6F sheath.	RAO at discharge on Duplex US.	Incidence of RAO: 113/455. RAO with 5F sheath: 21/152 (13.7%). RAO with 6F sheath: 92/303 (30.5%).	Non-randomized study.
Wong 2012	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	8 Fr and 6 Fr sheath.	RAO assessment at one year.	Incidence of RAO in 8Fr arm: 2/18 (11%). Incidence of RAO in 6Fr arm: 3/16 (19%).	Small study; limited follow up in 8Fr arm.
Zhou 2007	None.	RAO unclear timing of evaluation.	Incidence of RAO: 68/7215 (1%).	Single arm study.
Zankl 2010	RAO post transradial angiography treated with LMWH for four weeks.	RAO assessed at 24 hours.	Incidence of RAO at 24 hours: 51/488 (10.5%). RAO at 4 week in patients treated with LMWH: 4/30 (13.3%).	None.

			RAO at 4 weeks in patients not treated with LMWH: 17/21 (81%).	

Supplementary table 2: Sensitivity analysis according to the timing of the studies and setting of procedure

a) Analysis by timing of studies

Starting year of study	**Studies**	**Events/Total**	**% RAO**
<2006	9	284/11,172	2.5
2007-2008	8	119/2,743	4.3
2009-2010	14	482/5,280	9.1
2011+	5	67/626	10.7 (p=0.02)
Completion year of study	**Studies**	**Events/Total**	**% RAO**
<2006	6	202/8,877	2.3
2007-2008	5	137/1,903	7.2
2009-2010	8	184/2,698	6.8
2011+	17	429/6,343	6.8 (p=0.38)

b) Analysis by setting of procedure:

Group	**Studies**	**Events/Total**	**%RAO**
Percutaneous coronary intervention (PCI)	21	206/4533	4.5
Coronary angiograms (CA)	13	364/4147	8.8
PCI + CA	18	451/6631	6.8

Table 3: Predictors of radial artery occlusion

Study ID	Results
Aykan 2014	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 2013	Predictor of RAO: sheath-to-artery ratio >1 (p<0.001).
Chou 2014	Predictor of RAO: duration of occlusive compression OR 12.7, p=0.001.
Cubero 2009	Univariate predictors of RAO: ex-or active smoker p=0.04 , absence antiaggregant p=0.04 Multivariate predictors of RAO: presence of RA flow after procedures HR 0.06 (0.01-0.2), total haematoma HR 3.7 (1.2-11.0), standard pneumatic compression HR 18.8 (3.8-92.2).
Dharma 2014	Multivariate predictors of RAO: Duration of hemostasis >4hours OR 3.11(1.66-5.82), Intra-arterial nitroglycerin use OR 0.62(0.44-0.87).
Garg 2015	Predictors of RAO: female gender 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 ≤2.5mm 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	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	Significant predictors of RAO: age (p=0.032), procedure success (p=0.032).
Levin 2014	Predictors of RAO: reduced body weight (p=0.031).
Lisowska 2015	Significant predictors of RAO: men (p=0.025), creatinine (p=0.04).
Moarof 2014	Predictors of RAO: sheath size OR 0.67 (0.13-3.50), compression time OR 0.87 (0.45-1.67), gender 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	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	Significant predictors of RAO: weight (p=<0.05), patency (p≤0.05).
Pancholy 2012a	Significant predictor of RAO: duration of compression (p=0.037)
Pancholy 2012b	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	Independent predictors of RAO: bivalirudin OR 0.45 (0.11-2.06), body weight OR 2.78 (1.08-8.00), procedure ≤20 min OR 7.52 (1.57-36.0).
Politi 2011	Significant predictors of RAO: heparin OR 0.70 (0.49-0.99).
Ruhnau 2013	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 body mass index did not have significant influence.
Shantha 2014	Lower RAO with introducer sheath: Propensity matched odds of RAO pre-discharge: OR 0.20 (0.13-0.32). Propensity matched odds of RAO at 24 hrs: OR 0.13 (0.07-0.25). Propensity matched odds of RAO at 30 days: OR 0.18 (0.10-0.40).
Sreevatsa 2014	Predictors of RAO: diabetes, female, prior radial intervention, radial artery diameter, type of haemostasis, sheath-to-artery diameter ratio.
Tuncez 2013	Predictor of RAO: low weight (p=0.01).
Uhlemann 2012a	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 2012b	Significant risk factors for RAO: 6F sheath OR 2.742 (1.574-4.776), age (10 yrs) 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	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), 7F catheter OR 5.063 (2.010-12.634), compression time >90 min OR 2.319 (1.218-4.657), pre-coated hydrophillic catheter OR 1.781 (1.355-2.369).

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