



Original Article

Meta-analysis comparing radial versus femoral approach in patients 75 years and older undergoing percutaneous coronary procedures



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ABSTRACT

Introduction: Elderly patients (≥ 75 years) undergoing coronary angioplasty are increasing. Meta-analyses have shown the benefits of radial access which might reduce hospital stay by decreasing access site complications with associated secondary benefits, however, the population over the age of 75 years were not a large part of the cohort and may behave differently due to increased atherosclerotic burden and age-related vascular changes. In addition, complications unique to this age group such as delirium and deconditioning might occur which could have a bearing on the outcome.

Methods: We searched Pubmed, SCOPUS, Medline, Dynamed, Cochrane. The search terms used were femoral and radial, femoral versus radial, radial or femoral access site, radial or femoral comparison. There were no restrictions.

Results: There was a significant decrease (85%) in the incidence of access site complications in the radial group. The time to achieve ambulation was lower by 14.25 h (8.86–19.56 h). However, the incidence of crossover (in effect failure to perform catheterization by radial access) from radial to femoral was significantly higher. Radial access was associated with longer procedural times (2.75 min) and increased contrast dose however, there was no statistical difference in the fluoroscopy time between the two.

Conclusions: Radial access has similar benefits in elderly patients as those under the age of 75 and may be beneficial in patients at risk of delirium or deconditioning. However, crossover rates, contrast dose and procedure time were higher. It is conceivable that as experience is gained, these rates will diminish.

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1. Introduction

Across the world the population over the age of 75 years is growing at a faster rate than those over 60.¹ With better access to interventional cardiac procedures, the number of elderly (≥ 75 years) undergoing coronary angioplasty has increased and it reflects the changing demographic profile.

Historically, femoral artery has been the preferred vascular access site for cardiac catheterization over radial access. However, radial access is gaining extensive popularity² due to the benefits of earlier ambulation, fewer access site complications and decreased rates of bleeding.³ These advantages in turn reduce mortality, hospital stay and improve the quality of life.^{4,5}

The elderly are a unique group with increased atherosclerotic burden due to longstanding metabolic diseases which is bound to

influence the access site complications rates. Age related vascular and cerebral changes might increase the propensity for deconditioning and delirium unique to this age group. With these factors in mind we decided to conduct an outcome meta-analysis of studies that have either studied Patients ≥ 75 years exclusively or had this subgroup in their studies.

2. Methods

We searched Pubmed, SCOPUS, Medline, Dynamed, and Cochrane. The search terms used were femoral and radial, femoral versus radial, radial or femoral access site, radial or femoral comparison. There were no restrictions. The details of the search are illustrated in [Tables 1 and 2](#).

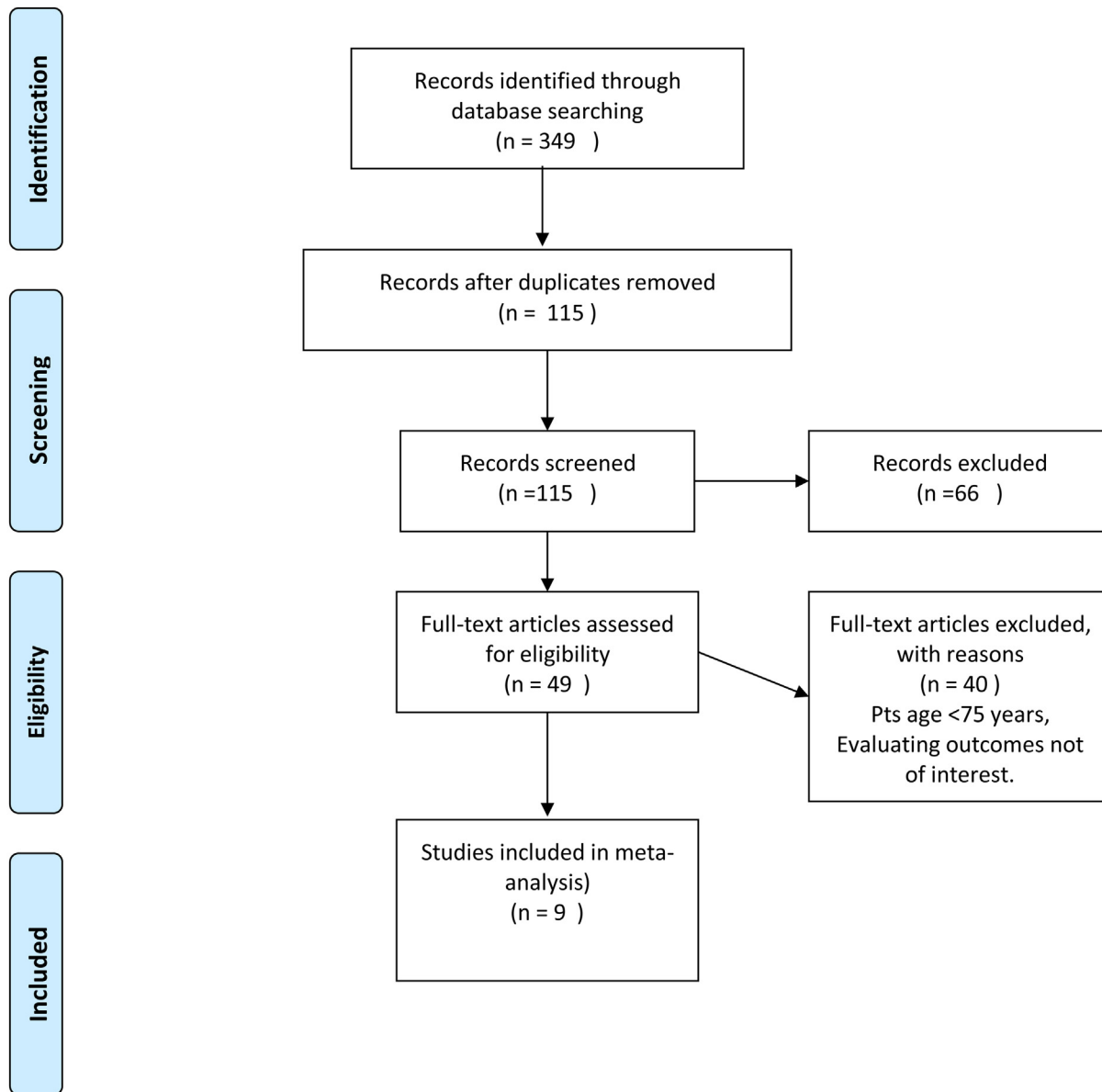
2.1. Data extraction

Data was independently abstracted into a standardized form from all the studies included.^{6–14} The following data were

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Table 1
PRISMA flow diagram.



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

collected: study design, year of publication, country of the population studied and the primary reported outcome.

Additional data related to cannulation site crossover, periprocedural myocardial infarction, local access site complications, major bleeding, time to ambulation, time, length of stay, procedure time and contrast dose was also extracted. Mortality related to

procedure in either group was obtained. If the data was expressed in terms of median and interquartile range, authors were contacted for the mean and SD values. However, if authors did not reply, as a last resort we estimated the mean using the validated formula: $\text{mean} = (2m + a + b)/4$, where m is the median and a and b are the 25th and 75th centiles respectively.¹⁵ The standard deviation (SD)

Table 2
Studies included in meta-analysis.

	Name of study	Year of publication	Country	Type of study	Sample size	Mean age (R)	Mean age (F)	Male (R)	Male (F)	Number (R)	Number (F)	Major bleeding (R)
Hu et al. ⁹	Comparison between radial and femoral approach for percutaneous coronary intervention in patients aged 80 years or older	2012	Beijing, China	Retrospective	268	82.68 ± 2.63	82.75 ± 3.31	76	96	112	156	0
Jaffe et al. ⁸	Comparison of radial versus femoral approach for percutaneous coronary interventions in octogenarians	2007	Canada	Prospective, non-randomized, operators discretion	228	82 ± 2	83 ± 4	65	70	97	131	4
Louvard et al. ⁷	Comparison of transradial and transfemoral approaches for coronary angiography and angioplasty in octogenarians (the OCTOPLUS study)	2004	France	Prospective, randomized, multicentered intention to treat	360	82.6 ± 2.7	83 ± 3.1	106	94	180	175	1
Achenbach et al. ¹⁰	Transradial versus transfemoral approach for coronary angiography and intervention in patients above 75 years of age	2008	Germany	Randomized prospective trial	307	78 ± 3	78 ± 3	70	68	152	155	0
Klinke et al. ⁶	Comparison of treatment outcomes in patients >80 years undergoing transradial versus transfemoral coronary intervention	2004	Canada	Prospective non-randomized propensity matched study	225	83.3 ± 2.5	83.4 ± 2.5	75	56	125	128	NA
You et al. ¹³	Comparison of short and long term outcome after percutaneous transluminal interventional therapy in octogenarians with coronary artery disease from radial or femoral approach	2013	Hong Kong	Retrospective	488	82 (80–83)	82 (80–84)	184	173	235	253	3
Gao et al. ¹²	Comparison of radial versus femoral approach for percutaneous coronary interventions in octogenarians with acute coronary syndrome	2014	China	Retrospective	279	79 ± 11.2	78.5 ± 10.5	72	83	125	154	2
Secco et al. ¹¹	Transradial versus transfemoral approach for primary percutaneous coronary interventions in elderly patients	2013	Italy	Prospective non-randomized, no exclusion criteria	283	81.6 ± 4	83.3 ± 4	101	45	177	106	NA
Koutouzis et al. ¹⁴	Radial vs. femoral approach for primary percutaneous coronary intervention in octogenarians	2010	Sweden	Retrospective	341	84 ± 2.7	84 ± 2.9	15	171	40	301	0

	Major bleeding (F)	Pseudoaneurysm (R)	Pseudoaneurysm (F)	Ambulation time (R), h	Ambulation time (F), h	Post-procedural complications (R) – all	Post-procedural complications (F) – all	In hospital mortality (F)	In hospital mortality (R)	Periprocedural MI (R)	Periprocedural MI (F)	Stroke (R)
Hu et al. ⁹	2	0	3	5 ± 2 h	20 ± 4 h	37	8	0	0	12	15	NA
Jaffe et al. ⁸	19	NA	NA	5 ± 3	11 ± 6	31	91	0	0	21	31	1
Louvard et al. ⁷	3	1	2	NA	NA	7	49	6	8	NA	NA	0
Achenbach et al. ¹⁰	3	0	8	0 mobilized immediately after procedure	12 h – per protocol, bed rest for 12 h	2	16	0	0	0	0	0
Klinke et al. ⁶	NA	NA	NA	NA	NA	30.072	39.125	14	3	NA	NA	NA
You et al. ¹³	12	0 (0.0)	8 (5.2)	3.6 (2.8–4.2)	24.4 (24.0–25.1)	61	131	NA	NA	NA	NA	1 (0.8)
Gao et al. ¹²	2	0	8	4.2 ± 0.9	19.3 ± 4.1	11	40	NA	NA	1	1	1
Secco et al. ¹¹	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Koutouzis et al. ¹⁴	5	0	NA	1 h	12–24 h	0	17	18	2	NA	NA	0

	Stroke (F)	Access site crossover (R)	Access site crossover (F)	Cannulation time (R), min	Cannulation time (F), min	Dose of contrast (R)	Dose of contrast (F)	Access site complications (F)	Access site complications (R)	LOS (F), days	LOS (R), days	Procedural time (R)	Procedural time (F)
Hu et al. ⁹	NA	11	6	3.0 ± 2.8	2.0 ± 1.9	227 ± 48	205 ± 39	32	8	6.4 ± 3.3	5.3 ± 2.2	NA	NA
Jaffe et al. ⁸	0	11	5	3.1 ± 2.9	2.0 ± 2.0	224 ± 46	182 ± 20	40	6	1.8 ± 2.39	1.6 ± 3.39	NA	NA
Louvard et al. ⁷	1	20	17	NA	NA	NA	NA	35	1	NA	NA	18.5 ± 10.5	15.9 ± 9.5
Achenbach et al. ¹⁰	1	13	1	NA	NA	88 ± 33	79 ± 28	16	0	NA	NA	18.1 ± 10	15.0 ± 8
	NA	NA	NA	NA	NA	NA	NA	NA	NA	3.1	1.7	54.8	58.1

Klinke et al. ⁶													
You et al. ¹³	1 (0.6)	NA	NA	NA	NA	155 (120–190)	150 (100–200)	NA	NA	6.7 ± 2.5	6.4 ± 2.3	40 (25–64.3)	37.5 (25–60)
Gao et al. ¹²	1	13	6	NA	NA	204.1 ± 32.4	210.3 ± 29.5	26	6	6.7 ± 2.3	6.4 ± 2.3	NA	NA
Secco et al. ¹¹	NA	NA	NA	NA	NA	NA	NA	14	5	NA	NA	NA	NA
Koutouzis et al. ¹⁴	0	9	4	NA	NA	164 ± 55	193 ± 97	17	0	NA	NA	47.9 ± 35.3	50.3 ± 29.5
	Hematoma (R)	Hematoma (F)	Door to balloon time (R), min	Door to balloon time (F)	Needle to balloon time (R)	Needle to balloon time (F)	Radiation fluoroscopy time (R)	Fluoroscopy time	Fluoroscopy time (SD)	Radiation fluoroscopy time (F)	Fluoroscopy time	Fluoroscopy time (SD)	
Hu et al. ⁹	5	17	NA	NA	NA	NA	23 ± 15	23	15	19 ± 12	19	12	
Jaffe et al. ⁸	15	1	NA	NA	NA	NA	19 ± 16	19	16	16 ± 12	16	12	
Louvard et al. ⁷	1	33	NA	NA	NA	NA	4.5 ± 3.7	4.5	3.7	6.0 ± 4.4	6	4.4	
Achenbach et al. ¹⁰	0	1	NA	NA	NA	NA	5.6 ± 5.9	5.6	5.9	4.7 ± 3.9	4.7	3.9	
Klinke et al. ⁶	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	N/A	N/A	
You et al. ¹³	3 (2.4)	14 (9.1)	NA	NA	NA	NA	NA	NA	NA	NA	N/A	N/A	
Gao et al. ¹²	NA	NA	NA	NA	NA	NA	19.7 ± 3.4	19.7	3.4	20.1 ± 3.2	20.1	3.2	
Secco et al. ¹¹	3	9	103.1 ± 58.4	110.3 ± 62.4	NA	NA	NA	NA	NA	NA	N/A	N/A	
Koutouzis et al. ¹⁴	0	7	NA	NA	21.8 ± 11.7	22.9 ± 12.2	827 ± 528	827	528	928 ± 728	928	728	

R – radial, F – femoral.

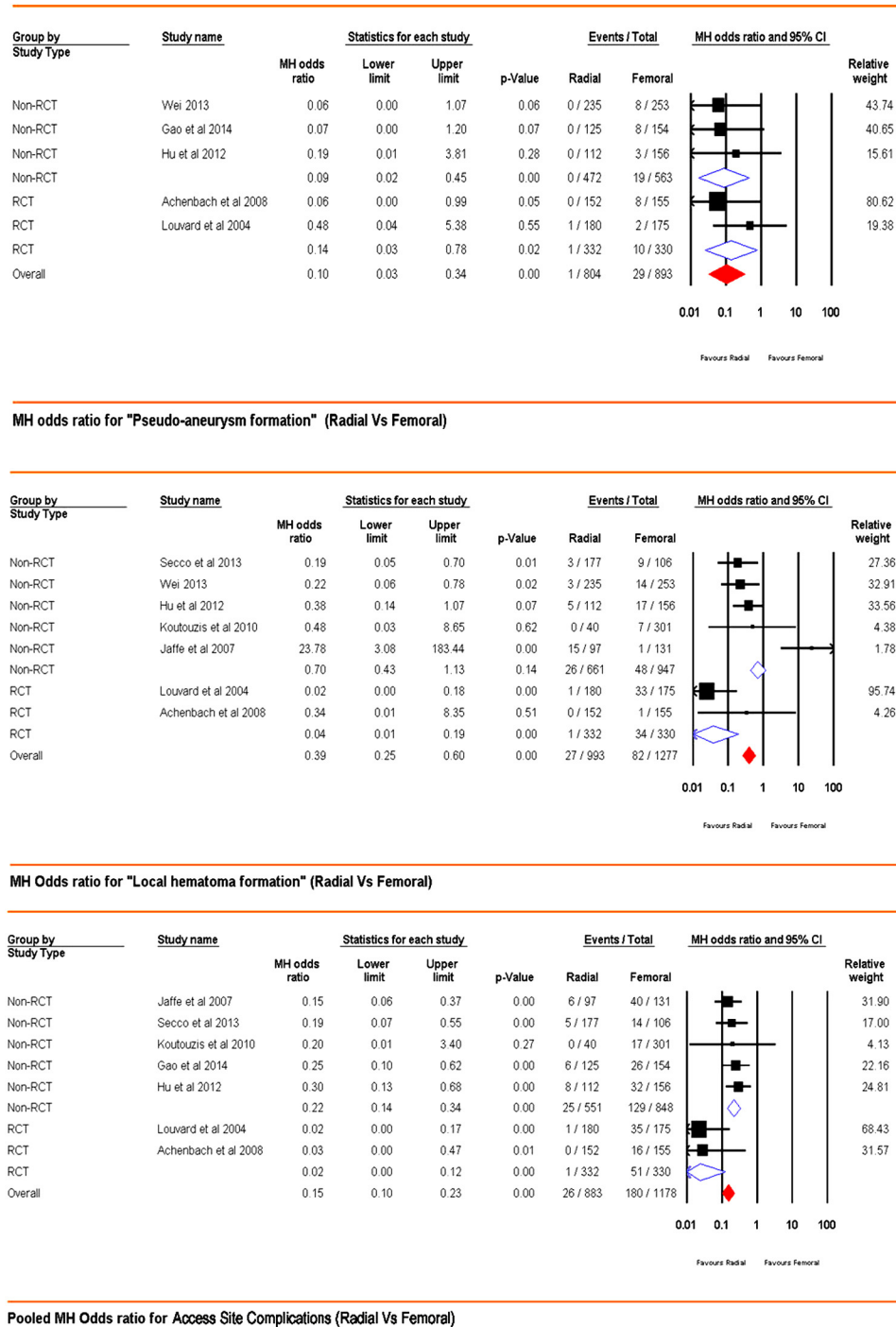


Fig. 1. Forest plot showing pooled mean differences for (from top to bottom) pseudoaneurysm formation, local hematoma formation and access site complications. Randomized and nonrandomized controlled trials are shown separately with the summary represented by the empty diamonds in the graphs. Solid diamonds at the bottom of comparisons denote the final net effect.

was estimated by the formula given by the Cochrane collaboration: $IQR = 1.35SD$.

2.2. Statistical analysis

Statistical analysis of the pooled data was performed using Comprehensive Meta-Analysis-Version 2 (Biostat Inc., USA). Statistical analysis was performed initially using fixed effect modeling and eventually, with random-effect methods (after

assessment of heterogeneity with fixed modeling), therefore, all values reported in the current analysis were from random effect modeling. The extent of heterogeneity in between the trials was quantified using the I2 statistic. Values of $I2 < 40%$ were considered unimportant, 30–60% were considered to represent moderate heterogeneity, 50–90% represented high heterogeneity and values $>75%$ represented considerable heterogeneity. The results were expressed as mean difference with 95% CI. $P < 0.05$ was considered statistically significant and the Mantel-Haenszel risk ratio

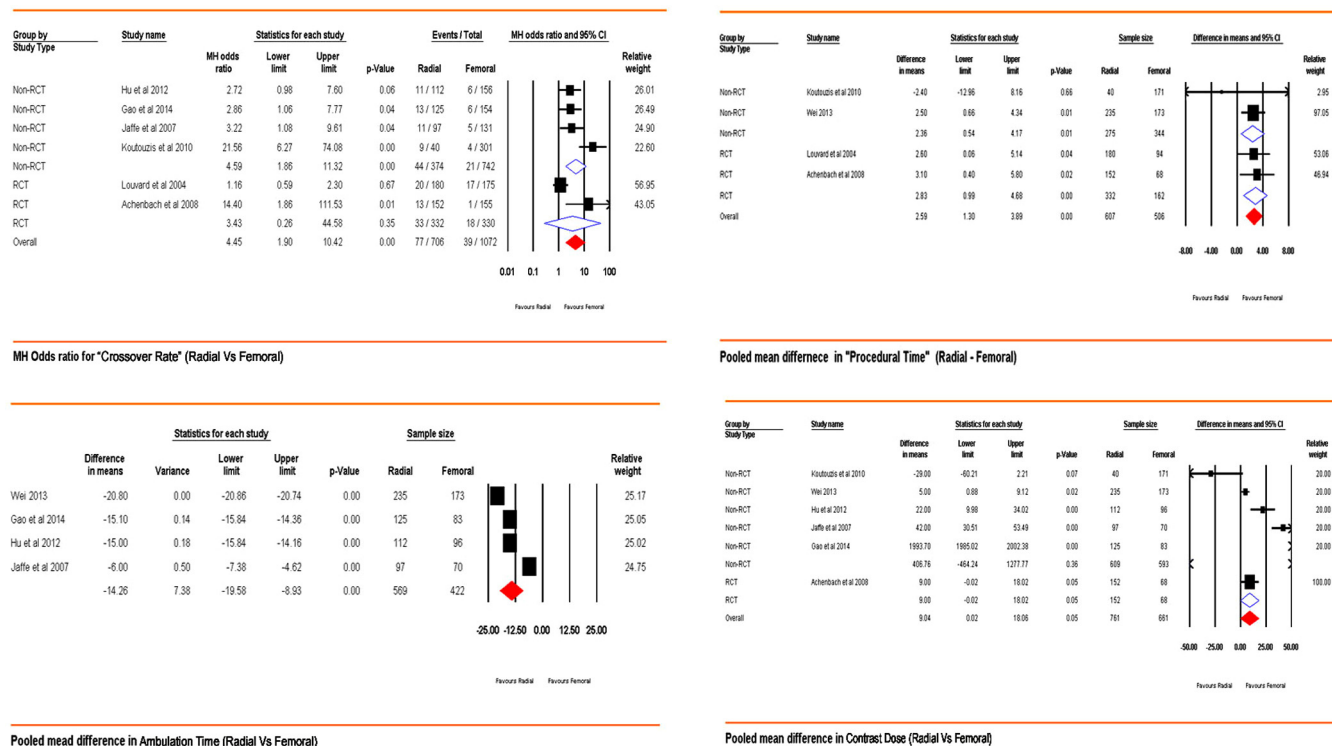


Fig. 2. Forest plot showing pooled mean differences for (in clockwise direction) crossover rate, procedural time, ambulation time and contrast dose. Randomized and nonrandomized controlled trials are shown separately with the summary represented by the empty diamonds in the graphs. Solid diamonds at the bottom of comparisons denote the final net effect.

calculated. Potential publication bias was further evaluated by funnel plot.

3. Results

A total of 349 studies were obtained during our search. Out of the 349 studies 105 studies compared the femoral access site and radial access site during cardiac catheterization in various scenarios. Studies which did not include patients ≥ 75 years were excluded. Nine studies were identified with the desired endpoints which were included in our meta-analysis. Two of the trials were available in mandarin language and relevant information was extracted with the help of an online translator.

The parameters being studied were access site complications, ambulation time, crossover rate, death rate, access site hematoma rate, length of hospital stay, major bleeding, procedural time, pseudoaneurysm formation and contrast dose.

3.1. Effect of access site on pseudoaneurysm formation, access site hematoma formation and access site complications – Fig. 1

Four trials reported the rates of pseudoaneurysms. Only 1 patient in the radial group (1/804) versus 29 patients in the femoral group (29/893) developed a pseudoaneurysm. The heterogeneity for the above comparison was “zero” and P -value=0.010. The femoral group patients had an 90% higher chance of pseudoaneurysm development and the MH risk ratio was 0.10 (95% CI 0.03–0.34) times in the radial group.

Access site hematoma rates were reported in 7 trials. Only 27 patients (27/993) in the radial group and 82 (82/1277 patients) in the femoral group developed a hematoma. The odds of hematoma development was significantly lower in the radial group by 0.39 (95% CI 0.25–0.60), $P < 0.001$.

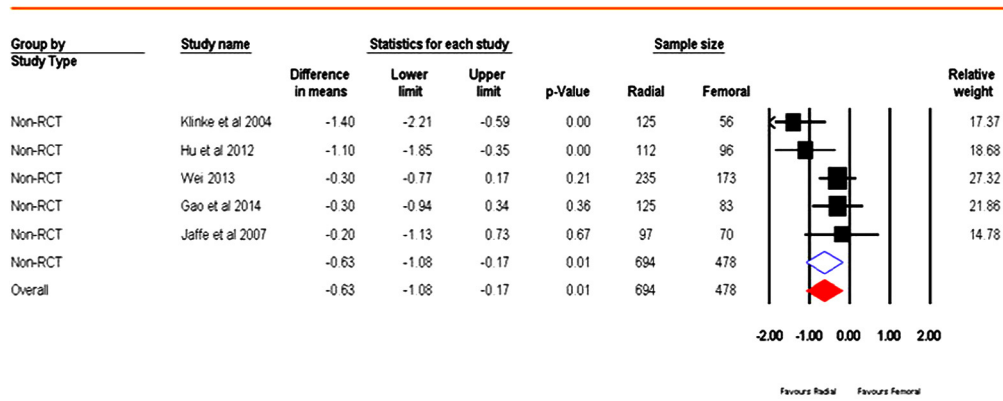
Similarly for access site complications, a total of 7 trials reported this variable, which included 883 patients in the radial group and 1178 patients in the femoral group. The overall risk of access site complications was lower by 85% in the radial group and the MH risk ratio for complications in the radial group was 0.14 (95% CI 0.10–0.23). The heterogeneity for the above result was 32.23% and had a P value of < 0.001 .

3.2. Effect of access site on crossover rate, procedural time, ambulation time, contrast dose and fluoroscopy time – Fig. 2

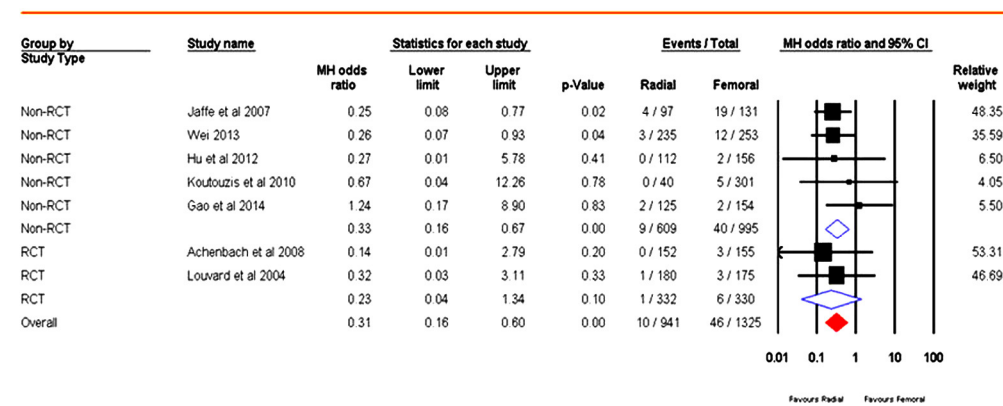
The likelihood of access site crossover was nearly 345% higher in the radial group than the femoral group. The MH risk ratio for crossover in the radial group was 4.45 (1.90–10.42) with a $P < 0.001$. The heterogeneity for the above comparison was 74.23%. The values were reported in 706 patients in the radial group and 1072 patients in the femoral group in 6 trials.

Procedural time was 2.64 min (1.56–2.64 min) longer in the radial group in comparison to the femoral group. Four trials reported this value with 607 patients and 884 patients in radial and femoral groups respectively. I2 for above was “zero” and P value was < 0.001 . Given the slight increase in procedural time Fluoroscopy time was also evaluated. Six trials reported the fluoroscopy times in minutes for a total of 706 patients in radial and 1072 patients in the femoral group. The heterogeneity for the above comparison was 67.70% and the P value failed to attain a statistically significant value ($P = 0.70$).

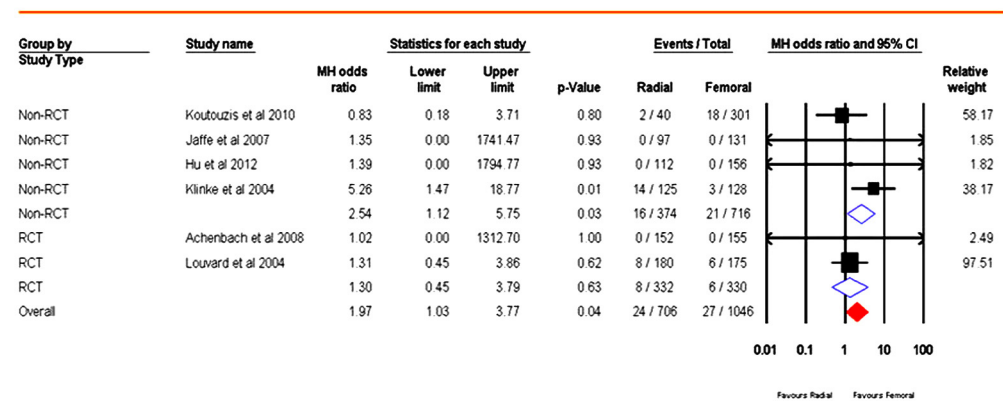
The ambulation time was reported in four trials including 569 patients in radial and 694 patients in the femoral groups. The pooled mean ambulation time in the radial group was lower by 14.25 h (8.86–19.56 h). The heterogeneity for the above comparison was 99.67%. On sensitivity analysis by “single study removal method” the heterogeneity dropped by only 0.93%.



Pooled mean difference in Length of Stay (Radial Vs Femoral)



MH Odds ratio for Major Bleed (Radial Vs Femoral)



MH Odds ratio for "In Hospital Mortality"(Radial Vs Femoral)

Fig. 3. Forest plot showing pooled mean differences for (from top to bottom) length of stay, major bleed and in-hospital mortality. Randomized and nonrandomized controlled trials are shown separately with the summary represented by the empty diamond in the graphs. Solid diamonds at the bottom of comparisons denote the final net effect.

Contrast dose was reported in 6 studies that included 761 and 1150 patients in the radial and femoral groups respectively. The heterogeneity for the above comparison was 98.44% The P value for the above-pooled results was 0.01 achieving statistical significance showing approximately 9 mL of extra contrast being used in the radial approach.

3.3. Effect of access site selection on length of stay, periprocedural MI, major bleeding and in-hospital death – Fig. 3

Five studies reported the length of stay in 694 and 822 patients in radial and femoral groups respectively. The pooled mean length of stay was shorter in the radial group by 0.64 days (95% CI 0.18–

1.10) days. The heterogeneity for the above was 67.21% and the *P*-value was 0.01.

Peri-procedural MI was reported in 4 trials wherein 34 (of 486 patients) and 47 (of 596 patients) suffered MI. Pooled risk ratio for MI in the radial group was lower being 0.98 (1.47–0.66). The heterogeneity of comparison was “zero” but statistical significance could not be achieved (*P*=0.940).

The incidence of major bleeding was lower in the radial group. Ten patients (10/941) in the radial group and 46 patients (46/1325) in the femoral group reported major bleeding in 7 trials. The incidence of major bleeding in the radial group was lower by 67.9%. The MH risk ratio in the radial group for bleeding was 0.32 (95% CI 0.16–0.60) with a “zero” heterogeneity.

We pooled the in hospital/peri-procedure mortality described consistently across trials. The MH risk ratio of death was 0.66 (95% CI being 0.32–1.34) in radial group compared to the femoral group. The likelihood of mortality in femoral group was higher by 44%. Death rates were reported in 6 trials. In radial group 13 deaths (in 706 patients) and in the femoral group 38 deaths (of 1046 patients) were reported. The heterogeneity for the pooled result was 0%. As the number of non-RCT studies were higher a statistically significant advantage was seen with radial group (*P*=0.05), however the overall result and the RCT groups failed to achieve a statistical significance. 30 day and 1 year mortality could not be evaluated as all the trials did not report this.

Publication bias was evaluated using funnel plot for each of the above variables and was further quantified using the Egger's test. No statistically significant publication bias was found in any of the above comparisons.

4. Discussion

The elderly population is a special demographic category who is at risk of higher rates of access site bleeding, post-procedural deconditioning and delirium. Age-related increase in the atherosclerotic burden and long standing metabolic abnormalities like diabetes are likely contributing factors, therefore coronary angiography techniques that are likely to reduce the frequency or severity of any post-procedural adverse event are to be welcomed.

Until 2008, radial approach to PCI (r-PCI) was utilized in only 1.32% of total procedures.¹⁶ The authors found a significantly reduced incidence of bleeding complications in comparison to femoral approach, with comparable procedural success rates.

One of the most significant results of our meta-analysis pertains to the crossover rates, which is an important factor where radial artery cannulation is the first preferred puncture site. In our meta-analysis, crossover from the radial to the femoral site was 3 times (345%) higher than the femoral group. These results are in sharp contrast to the crossover rates in patients under the age of 75 years, which is 7–10%.¹⁷ In a single center study involving 582 consecutive patients, the crossover rate for radial to femoral access was 5%, while for the transfemoral access it was 0.8%.¹⁸ Gokhroo et al., in another retrospective study of 4195 patients revealed that after 100 procedures, the average puncture time is reduced by 600% and the total procedure time by 500%.¹⁹ It remains to be seen if decrease in crossover rate could be achieved in the elderly with user experience in this age group.

Some of the factors responsible for higher failure rates, longer procedure times and greater crossover rates with trans-radial cannulation in patients 75 years or older are luminal narrowing, increased atherosclerotic burden, arterial tortuosity and a low threshold to abandon the transradial attempt. An increase of 2.64 min in terms of procedure time that we found is in contrast to similar procedure times in younger population.²⁰ A related finding is the increased use of contrast in the transradial group. It is

conceivable that at least in part it is related to longer procedure times. Limiting the quantum of dye injected is important to reduce the risk of contrast-induced nephropathy.²¹ As stated earlier, as experience is gained, this difference is likely to become insignificant however, one may not state this with confidence in the elderly, due to the age related changes in anatomy as stated above.

In keeping with the results of other studies, our meta-analysis demonstrates an increased risk of major bleeding (~70% more likely) in patients undergoing coronary angiography via femoral access.³ As a result, it is likely that need for blood transfusion is higher in the transfemoral group along with an increase in the cost of hospitalization and morbidity.^{22,23} Ease of application of pressure to reduce post-procedure bleeding and reduction of access site complications like pseudoaneurysm are additional benefits of trans-radial cannulation even in the elderly age group. This is clearly demonstrated in our meta-analysis.

In our meta-analysis, transradial approach led to earlier ambulation by an average of 14.25 h. A reduction in post-procedure ambulation time is a major benefit of trans-radial cannulation in terms of a reduction in pneumonia, deep vein thrombosis rates and pulmonary embolus. Shorter post-procedure ambulation times are also protective against deconditioning and delirium that facilitate an earlier discharge home in the elderly population.²⁴

Among the major adverse events, in-hospital death, based on analysis of non-randomized trials, was more likely via the femoral approach (risk ratio of 0.38, *P*-value 0.05). Stated differently, elderly patients (≥ 75 years) undergoing procedures via femoral approach were 62% more likely to die. When randomized controlled trials were included the incidence of in hospital death was 1.8 for the radial group and 3.6 for the femoral group but there was no statistical difference between the two groups. More studies are required in this age group to form a definite conclusion and its effect on mortality.

4.1. Limitations

A certain degree of heterogeneity is inevitable in any published meta-analysis.²⁵ An effort was made to address this particular limitation by single study removal method. Inter-institutional differences in cannulation approaches and outcomes are possible contributing factors to high heterogeneity. Another limitation is that not all included trials are “randomized controlled trials”. After independent assessment of trials by different reviewers we included these non-RCTs as the values of desired parameters were documented. Prior to inclusion quality assessment was made for possible bias and if two independent reviewers agreed – the trial was included. However, the effect of bias in non-RCT cannot still be negated, thus we presented our results split up into “RCT” and “non-RCT”. Radial approach is known to have a limitation that it is believed to have higher occlusion rates in elderly. Despite attempts to analyze this parameter, no mathematical pooling was possible as the consistent documentation of numbers across trials was not there. Level of experience of the procedurist is bound to influence the results. Variables like peri-procedural myocardial infarction failed to achieve levels of statistical significance. Such events are fortunately rare; however, this was a limitation of our study. Another limitation is the risk of death to a large extent is influenced by Klink et al., however, propensity matched data was not used in the calculation which may lead to selection bias. In addition, in-hospital mortality was calculated as opposed to 30 day or 1 year mortality. This was due to lack of availability of the data in the trials.

5. Conclusions

Overall, transradial access for cardiac catheterization is associated with significant benefits even in the elderly (≥ 75

years). Reductions access site related morbidity, length of stay, major bleeding and shorter time to ambulation are some of the major benefits. However, longer procedure time, greater crossover rates and increased contrast dose are substantial drawbacks. They are likely to be addressed with better technical skills which emanate with experience

Conflicts of interest

The authors have none to declare.

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