

# World Journal of *Cardiology*

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# Contrast use in relation to the arterial access site for percutaneous coronary intervention: A comprehensive meta-analysis of randomized trials

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## Abstract

### AIM

To compare the amount of contrast used during percutaneous coronary intervention (PCI) *via trans*-radial access (TRA) *vs trans*-femoral access (TFA).

### METHODS

Scientific databases and websites were searched for: randomizedcontrolledtrials (RCTs). Data were extracted by two independent reviewers and was summarized as the weighted mean difference (WMD) of contrast used with a 95%CI using a random-effects model.

### RESULTS

The meta-analysis included 13 RCTs with a total of 3165 patients. There was no difference between the two strategies in the amount of contrast used (WMD = - 0.65 mL, 95%CI: -10.94-9.46 mL;  $P = 0.901$ ).

### CONCLUSION

This meta-analysis shows that in patients undergoing PCI, the amount of contrast volume used was not different between TRA and TFA.



**Key words:** Femoral; Contrast; Percutaneous coronary interventions; Radial

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**Core tip:** Adaptation of radial access for percutaneous coronary interventions in patients with chronic kidney disease is slower because of concern about contrast-induced nephropathy from the greater contrast load. Data from individual studies vary; therefore we performed a comprehensive meta-analysis of randomized controlled trials comparing the amount of contrast used between radial access and femoral access.

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## INTRODUCTION

Trans-radial access (TRA) for percutaneous coronary interventions (PCIs) results in a lower risk for bleeding and vascular complications than trans-femoral access (TFA)<sup>[1-5]</sup>. However, CathPCI registry data suggest that adaption of TRA-PCI in patients with lower glomerular filtration rates (GFRs) is lower compared to patients with higher GFRs; one wonders if this could be the result of concern over the larger amount of contrast used in TRA compared to TFA<sup>[6]</sup>. Data from individual studies have been variable: Some show larger contrast volume is used with TRA<sup>[2,7]</sup>, others show equal amounts used in both strategies<sup>[5,8]</sup>, and yet others show less contrast used with TRA<sup>[3,9]</sup>. Therefore, we performed an updated comprehensive meta-analysis of randomized controlled trials (RCTs) comparing the amounts of contrast used in TRA and TFA during PCI.

## MATERIALS AND METHODS

This meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for systematic reviews and meta-analyses<sup>[10]</sup>. We performed a systematic search of PubMed, Embase, and the Cochrane Library and cross-referenced relevant articles using various combinations of keywords such as "radial", "femoral", "cardiac catheterization", and "coronary intervention" for eligible published studies. Data were collected by two independent investigators, and disagreements were resolved by consensus. Trials were included if they enrolled patients undergoing PCI and randomly assigned them to TRA or TFA. We recorded mean contrast volume used. We also contacted corresponding authors for those articles not reporting

contrast volume or reporting the median contrast used. We were able to obtain the mean contrast used for only one additional trial<sup>[11]</sup>.

We summarized the data as the weighted mean difference (WMD) of contrast used with a 95%CI using Comprehensive Meta-Analysis (CMA) system version 3 (Comprehensive Meta-Analysis; Biostat Inc., Englewood, NJ, United States). A random-effects model was used to analyze data. The presence of heterogeneity across trials was evaluated using the Cochran Q test and the Higgins  $I^2$  test<sup>[12]</sup>. The measure of  $I^2$  can be interpreted as the percentage of variability resulting from heterogeneity between studies rather than sampling error<sup>[12]</sup>. Finally, an additional sensitivity analysis was performed where one study at a time was excluded, and the impact on the summary results of removing each was evaluated.

## RESULTS

Among 26 identified RCTs, only 15 trials reported the amount of contrast used. However, data for the mean contrast used was available for only 13 RCTs, which used 3165 patients, and these were used for final analysis<sup>[4,5,7,11,13-20]</sup>. Figure 1 shows the search flow diagram. The bias assessment for each RCT is shown in Figure 2.

The characteristics of the individual trials included in the meta-analysis are shown in Table 1. Most studies were single-center studies with broad spectra of patient populations, including patients with stable angina, acute coronary syndrome, or ST-elevation myocardial infarction. The majority of the procedures were performed by radial experts.

There was no difference in the amount of contrast used during either TRA or TFA (WMD = - 0.65 mL, 95%CI: -10.94 to 9.46 mL;  $P = 0.901$ ; Figure 3). We found significant between-trial heterogeneity ( $Q = 260.8$ ,  $df = 12$ ;  $P < 0.001$ ;  $I^2 = 95.4$ ). However, during sensitivity analysis, removal of any single study did not affect summary results (Figure 4).

## DISCUSSION

In this study, we compared a broad spectrum of 3165 patients enrolled in 13 RCTs in terms of the contrast volume used during TRA or TFA during PCI. Overall, there was no difference in contrast volume use between the two access strategies. However, most trials were single-centered, and the majority of procedures were performed by radial experts.

Acute kidney injury (AKI) is a well-recognized complication of PCI that is associated with greater risk of in-hospital mortality and poor long-term outcomes<sup>[21]</sup>. The two major causes of post-PCI AKI are contrast-induced nephropathy (CIN) and renal atheroembolus<sup>[22,23]</sup>. The reported incidence of CIN post-PCI varies widely depending on numerous clinical, demographic, and procedural

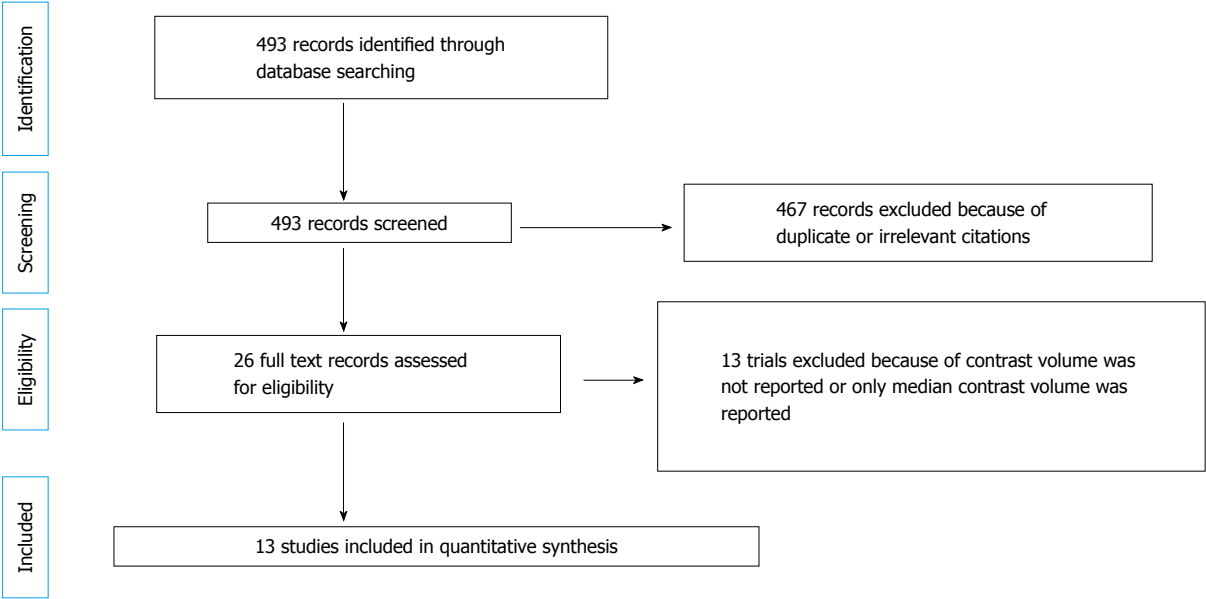


Figure 1 Flow diagram for study selection.

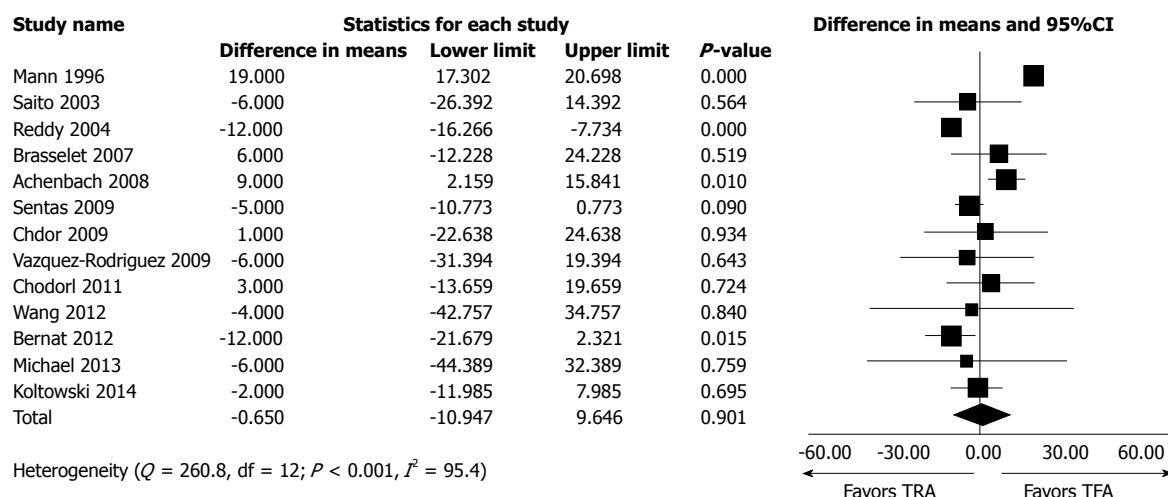


Figure 2 Risk of bias of included randomized controlled trials.

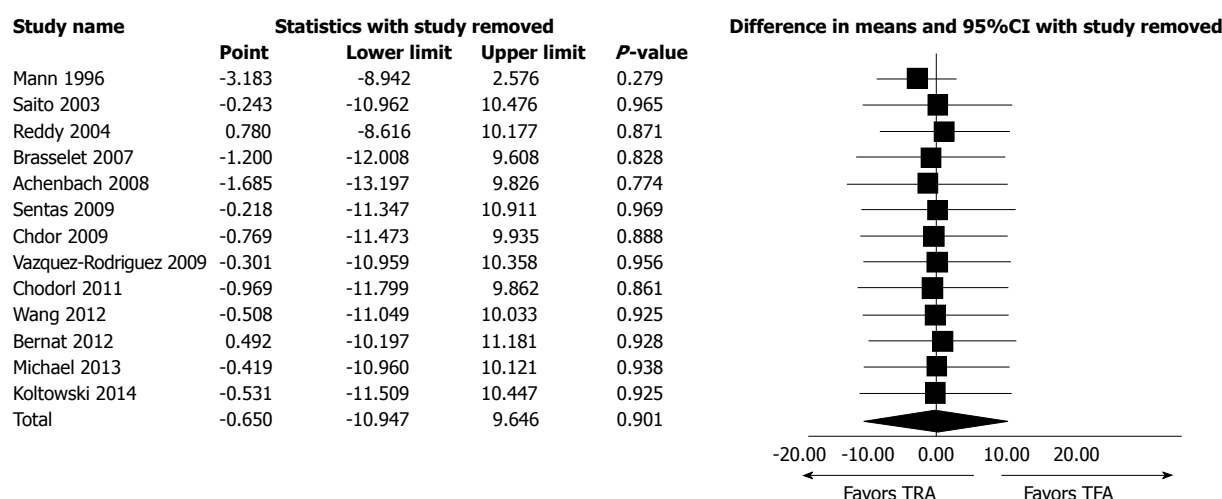
factors<sup>[22]</sup>. Among these, contrast volume is a well-established, dose-dependent, and potentially modifiable risk factor for CIN<sup>[22]</sup>. Although there have been reports of greater contrast use with TRA and concerns about possible subsequent CIN from this more extensive dye load<sup>[2,7,24]</sup>, our meta-analysis shows that the volume of contrast used is not higher among patients undergoing PCI with TRA compared to TFA.

In contrast, a report from the British Columbia Cardiac and Renal Registries that included 69214 patients after coronary catheterization and PCI showed that chronic kidney disease (CKD) onset within 6 mo was significantly lower with TRA compared to TFA (0.5% vs 2.2%,  $P < 0.001$ ) even after adjusting for baseline variables<sup>[9]</sup>. Similarly, another propensity-matched study showed that TRA, compared to TFA, was associated with a lower risk of AKI<sup>[25]</sup>. Finally, a recent meta-analysis of observational studies (adjusted by propensity score matching) showed that TRA, compared to TFA, was associated with lower risk of AKI<sup>[26]</sup>. The primary mechanism by which TRA was associated with a lower risk of kidney injury is thought to be through a reduced likelihood of renal atheroembolization because it offers the additional advantage of avoiding passage through potential atheromatous aortae and renal vessels<sup>[9,23]</sup>. The other mechanism by which TRA leads to less kidney injury is through a reduced risk of bleeding and the subsequent need for a blood transfusion. Post procedure bleeding and blood transfusion are independently associated with the development of AKI<sup>[27,28]</sup>.

The potential benefits of TRA in CRD patients is in paradox to the CathPCI registry data, which show a slow adaption of TRA-PCI in patients with lower GFRs compared to patients with higher GFRs<sup>[6]</sup>. It is not clear if this is a result of misconceptions about potential increases in contrast use with radial access<sup>[24]</sup> or due to



**Figure 3** Forest plot showing weighted mean difference of contrast use. The size of the square represents the weight that the corresponding study exerts in the meta-analysis. The larger the square, the more the study contributes to the overall estimate. Diamonds indicate the overall summary estimate for the analysis, its width representing the 95%CI. TRA: *Trans*-radial access; TFA: *Trans*-femoral access.



**Figure 4** Forest plot showing weighted mean difference of contrast use with sensitivity analysis evaluating the impact on overall summary results of removing each study. TRA: *Trans*-radial access; TFA: *Trans*-femoral access.

pressure from nephrologists who routinely recommend against using TRA in patient with CKD<sup>[29]</sup>. Even the Fistula First Initiative Coalition, sponsored by the Centers for Medicare and Medicaid Services, discourages use of the radial artery for access of the arterial vasculature in patients at risk for, or with known Stage 4 or 5 CKD<sup>[30]</sup>. This needs further investigation to assure we are not withholding beneficial intervention in these patient populations because of the theoretical possibility that dialysis access will be lost in the future.

This meta-analysis has several limitations. First, as with all meta-analyses, it is subject to various biases because data were combined from many studies with varying protocols. Second, most of the studies were single-centered, and the majority of procedures were performed by radial experts. Furthermore, in a majority of the trials, patients with coronary artery bypass grafts (CABG) were excluded. Therefore, the generalizability

of this study may be limited, particularly to operators less-skilled in radial access and to patients with CABG. Finally, apart from the AKI-MATRIX sub-study, none of the randomized studies comparing TRA and TFA has ever systematically explored the issue of renal complications<sup>[31]</sup>. Therefore, we were not able perform the meta-analysis using AKI as one of the outcomes.

In conclusion, this meta-analysis of RCTs showed that in patients undergoing PCI, the amount of contrast volume used was not different between the TRA and TFA arms.

## COMMENTS

### Background

Trans-radial access (TRA) for percutaneous coronary interventions (PCIs) results in lower bleeding and vascular complications than trans-femoral access (TFA). A recent randomized controlled trial (RCT) and several updated meta-



**Table 1** Characteristics of included trials

Ref.	Year	TRA (n)	TFA (n)	Mean contrast volume (mL)		TRA operator experience	Patient population
				TRA	TFA		
Mann <i>et al</i> <sup>[13]</sup>	1996	73	75	138	119	NR	ACS
Saito <i>et al</i> <sup>[14]</sup>	2003	77	72	180	186	Experienced	AMI
Reddy <i>et al</i> <sup>[15]</sup>	2004	25	50	123	135	Low	Elective PCI
Brasselet <i>et al</i> <sup>[14]</sup>	2007	57	57	97	91	Intermediate-experienced	ACS
Achenbach <i>et al</i> <sup>[5]</sup>	2008	152	155	88	79	Experienced	ACS, Elective PCI
Sentas <i>et al</i> <sup>[16]</sup>	2009	335	335	84	89	Experienced	ACS, Elective PCI
Chodór <i>et al</i> <sup>[17]</sup>	2009	50	50	198	197	Experienced	STEMI
Vazquez-rodriguez <i>et al</i> <sup>[18]</sup>	2009	217	222	275	281	Experienced	AMI
Chodór <i>et al</i> <sup>[19]</sup>	2011	49	59	165	162	Experienced	STEMI
Wang <i>et al</i> <sup>[20]</sup>	2012	60	59	160	164	Experienced	STEMI
Bernat <i>et al</i> <sup>[3]</sup>	2012	348	359	170	182	Experienced	STEMI
Michael <i>et al</i> <sup>[7]</sup>	2013	63	63	171	142	Experienced	NSTEMI or elective PCI with previous CABG
Kořowski <i>et al</i> <sup>[11]</sup>	2014	52	51	63	65	Experienced	STEMI

ACS: Acute coronary syndrome; AMI: Acute myocardial infarction; CABG: Coronary artery bypass graft; NSTEMI: Non-ST-elevation myocardial infarction; PCI: Percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction; TRA: *Trans*-radial access; TFA: *Trans*-femoral access.

analyses of RCTs have also shown that TRA also improves mortality compared to TFA in patients with acute coronary syndrome.

### Research frontiers

Despite the proven benefits of TRA for PCI, its adaptation for patients with chronic kidney disease has been slow because of concern about contrast-induced nephropathy from greater contrast use. Data from individual studies have been variable: Some show larger contrast volumes with TRA, but others show equal amounts of contrast use in both strategies.

### Innovations and breakthroughs

In this study, the authors investigated the amounts of contrast used in TRA compared to TFA during PCI. This is the most comprehensive meta-analysis of RCTs in this field.

### Applications

This study shows that the amount of contrast used does not differ between TRA-PCI and TFA-PCI. Therefore, TRA-PCI should not be avoided in patients with chronic kidney disease solely because of concern for increased contrast use.

### Peer-review

The authors investigated the dose of contrast volume in patients who underwent trans-radial percutaneous coronary intervention (PCI) or trans-femoral PCI, using the meta-analysis method. They showed no difference in contrast medium between the two arms. This meta-analysis seems to be interesting.

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