Int J Clin Exp Med 2015;8(10):17151-17166
www.ijcem.com /ISSN:1940-5901/IJCEM0009558

Original Article

Radial versus femoral artery access for percutaneous coronary angiography and intervention: a systematic review and meta-analysis of randomized controlled trials in Chinese population

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Received April 24, 2015; Accepted August 19, 2015; Epub October 15, 2015; Published October 30, 2015

Abstract: To compare the feasibility, efficiency and safety of coronary angiography (CAG) and interventional procedures between the radial and femoral catheterization approaches in Chinese population using systematic review and meta-analysis, we conducted a search of the studies comparing radial and femoral catheterization approaches in patients underwent either CAG or percutaneous coronary intervention (PCI) in Chinese population. Fixed-effect relative risk (RR) for the primary end points and the second end points were compared between the two approaches. A total of 27 studies (n=8,749 patients) were finally included in the analysis. The success rate of radial approach was slightly lower than that of femoral approach in patients receiving CAG (*P*=0.004), but similar in patients receiving a further PCI treatment (*P*=0.11). The risk of major adverse cardiovascular events (MACEs) was similar between two approaches (*P*=0.27). Radial catheterization had a significantly lower rate of puncture site complications (*P*<0.00001), but a lower rate of puncture success rate (*P*=0.02). In patients with acute myocardial infarction (AMI), there was no difference in neither the risk of MACEs nor PCI success rate between two approaches (*P*=0.23 and 0.45, respectively), but a board line decrease of puncture success rate was observed in radial catheterization group (*P*=0.04). There were no significant differences in the volumes of contrast media, X-ray exposure time and operation time between the two approaches (all P>0.05). Thus, we concluded that radial approach is a safe method for CAG or PCI compared to traditional femoral approach in Chinese population due to their similar success rate of the procedure and risk of MACEs, and a decreased risk of puncture site complications.

Keywords: Radial artery; femoral artery, acute myocardial infarction (AMI), coronary disease, coronary angiography (CAG), percutaneous coronary intervention (PCI), systematic review, meta-analysis

Introduction

The radial catheterization technique was firstly used in coronary artery disease (CAD) patients undergoing percutaneous coronary intervention (PCI) by Campeau et al. in 1989 [1, 2]. Nowadays, it has gained increasing popularity worldwide. Compared with traditional transfemoral artery approach, radial catheterization technique has less common incidence of bleeding and does not require patient remain immobile [3-12]. Therefore, radial catheterization is now much more frequently performed in Europe and Asia [13, 14].

However, there are also several disadvantages of this non-traditional approach of cardiac catheterization. First of all, the failure of artery access using radial approach is not uncommon due to the tortuosity and anatomic variation of radial artery between individuals. Second, certain device such as 8 F catheter which requires kissing balloon is not practical to be used in trans-radial technique. In addition, traditional femoral approach has less common thrombotic complications and large-diameter devices during PCI are much easier and more practical to be inserted using femoral approach. Last, most of the cardiologists are well-trained and experiences with the traditional approach. Due to the advantage and disadvantage of both catheterization approaches, physicians and scientists have started to address the issue of which cardiac catheterization approach would be a bet-

ter choice for patients in several large-scale clinical trials. However, the results are controversial and a systematic analysis of the two approaches specifically in Chinese population is still absent [4, 5, 9, 11]. Therefore, the ultimate purpose of this systematic review and meta-analysis is to compare the feasibility, efficiency and safety of these two different cardiac catheterization approaches in Chinese population.

Material and methods

Search strategy

Studies published from 1989 to 2012 in one of the following databases, including China National Knowledge Infrastructure Database (CNKI), Chinese Biomedical Literature Database (CBM), Cochrane Library and Pubmed, were carefully searched in either Chinese or English language. The key words include "trans-radial", "radial access", "radial approach", "radial artery", "trans-femoral", "femoral access", "femoral approach", "femoral artery" and "coronary artery". Studies with key words of "randomized controlled trial*", "pseudo-randomized control* trial*", "quasi-randomized control* trial*" and "comparative study" were excluded. Using above searching strategy, studies about catheterization approach for CAG or PCI in Chinese population which potentially could be included in this meta-analysis were systematically and completely searched.

Study inclusion and exclusion criteria

The inclusion of a certain study to the final meta-analysis should meet the below inclusion criteria including, (1) a randomized controlled study comparing radial versus femoral approach for either percutaneous coronary angiography or intervention (either CAG or PCI); (2) study should include CAD patients that were older than 18 years old; and (3) study should have intention-to-treat analysis. Studies meet one of the below criteria were excluded. The exclusion criteria were: (1) study type was case reports, case series or retrospective case-control studies; (2) study included patients of malignant arrhythmia, serious hepatic, kidney dysfunction or cancer; (3) study had incomplete follow-up (<80% of the whole population investigated).

Data abstraction and quality assessment

Data abstraction was independently performed by two unblinded reviewers and quality of each study was evaluated according to the risk of the bias table from Cochrane handbook 5.1.7 [15], criteria including: (1) generation of random sequence; (2) allocation concealment; (3) blinding of participants and personnel assessments; (4) blinding outcome assessment; (5) integrity of final data; (6) selection bias and other bias. Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to evaluate the quality of the conclusion regarding primary end-point between radial and femoral approaches. High quality evidence was defined as that further research was very likely to change our confidence in the estimate of effect. Moderate quality evidence was defined as that further research was like to have an important impact on our confidence in the estimate of effect and might change the estimate. Low quality evidence was defined as that further research was very like to have an important impact on our confidence in the estimate of effect and its likelihood of changing the estimate or any estimate of effect was very uncertain. The quality of the evidence was downgraded if it had one of the following situations, including (1) serious risk of bias, (2) serious inconsistence between studies, (3) serious indirectness, (4) serious imprecision and (5) likely publication bias. In contrast, the quality of the evidence was upgraded if it had one of the following features, including (1) large effect size, (2) does-response gradient, (3) all plausible confounding would reduce a demonstrated effect, and (4) all possibility on findings would suggest a spurious effect when the actual results show no effect.

Study characteristics

The primary end points in this meta-analysis were stated below. (1) success of the procedure, including puncture success and CAG and/or PCI success, defined as sheath smooth implantation after punctuating the artery with <20% residual stenosis of targeted vessel after stenting and without dissection and thrombosis. If there was any procedural failure including failure to puncture the entry site of the artery, failure to cannulate the coronary artery, impossibility to perform the planned percutaneous

Table 1. Characteristics of all 27 studies included in the meta-analysis

Trials and Year	Regions	Number of Study	Objects	Clinical Intervention	Outcome Indicator	Length of follow-up
Fu Xiang-Hua et al. 2003	Hebei	208	AMI	TRI 106	Puncture time; Puncture success rates	One month
				TFI 102	PCI time; PCI Success rates; The access artery complications	
Tian Jun et al. 2003	Henan	400	Elderly CHD	TRI 200	Puncture time; Operation time; Compressing time; Fluoroscopy time; Immobilization time; Cannulation success time; The access artery complications rate; MACEs	In-hospital
				TFI 200		
Liu Jing-Hua et al. 2005	Beijing	153	CHD	TRI 76	CAG or PCI time; CAG or PCI Success rates; The access artery complications; X-ray exposure time	In-hospital
				TFI 77		
Wu Yan-Mei et al. 2005	Sichuan	486	CHD	TRI 243	Puncture time; Puncture success rates	In-hospital
				TFI 243	The access artery complications; X-ray exposure time; Contrast volumes	
Hu Xin-Quan et al. 2005	Hunan	384	CHD	TRI 185	Puncture success rates; PCI time; CAG or PCI Success rates; The access artery complications; X-ray exposure time; Contrast volume	In-hospital
				TFI 189		
Jin Quan-Min et al. 2005	Liaoning	774	CHD	TRI 382	Puncture time; Puncture success rates; PCI time; PCI Success rates; The access artery complications; X-ray exposure time; Contrast volumes	In-hospital
				TFI 382		
Hu Jiang-Biao et al. 2005	Zhejiang	90	CHD	TRI 46	PCI success rates; Puncture time	In-hospital
				TFI 44	Operation time; Compressing time Fluoroscopy time; The access artery complications rate	
Yu Zhun et al. 2006	Guangdong	132	CHD	TRI 44	Puncture success rates; Operating success rates; Hospital time	In-hospital
				TFI 44		
				TBI 44		
Xiao Hua et al. 2007	Guangdong	107	AMI	TRI 56	Puncture time; Puncture success rates; PCI time; PCI success rates; Recanalyzing time; The access artery complications	In-hospital
				TFI 51		
Wang Ping et al. 2007	Shaxi	126	CHD	TRI 63	Puncture time; Puncture success rates; PCI time; PCI Success rates; The access artery complications; Hospitalization time	In-hospital
				TFI 51		
Li Wei-Min et al. 2007	Heilongjiang	370	AMI	TRI 184	Puncture success rate; Cannulation time; Total procedures time; The access artery complications rates; Stent implanted; Final TIMI III flow	Unclear
				TFI 186		
Liu Xiao-Kun et al. 2008	Hebei	172	Elderly AMI	TRI 84	SAS, SDS; MACEs	One month
				TFI 88		
Feng Min et al. 2008	Shandong	196	Elderly AMI	TRI 94	PCI success rates; Puncture time; Operation time; Fluoroscopy time; The access artery complications rate; Post-operation comfort level; MACEs	One month
				TFI 102		
Pan Gang et al. 2008	Hunan	60	AMI	TRI 32	Puncture time; Puncture success rate; GW cannulation time; Total operation time; PCI success rates	Three months
				TFI 28	IRA rate; The access artery complications rates; Days in hospital; Immobilization time; MACEs	
Yan Zhen-Xian et al. 2008	Beijing	103	AMI	TRI 57	Puncture time; Puncture success rate; Cannulation time; Reperfusion time; Total time of procedures; Procedures success rate; The access artery complications rates; Hospital stay; MACEs; Temporary pacemaker; IABP	In-hospital and one month
				TFI 46		
Gan Li-Jun et al. 2009	Hubei	195	AMI	TRI 90	Puncture success rate; Cannulation time; Cannulation-to-balloon; Inflation time; Total procedures time; Operation success rates; The access artery complications rates; Hospital stay; MACEs; GP II b/III a inhibitor; Final TIMI flow	In-hospital and six month
				TFI 105		
Hou Lei et al. 2010	Shanghai	200	AMI	TRI 100	Puncture time; Puncture success rate; Cannulation time; Reperfusion time; Total time of procedures; Procedures success rates; vascular complications rates; Hospital stay; MACEs; Stent used; Tirofiban usage	One month
				TFI 100		

Yin Zuo-Min et al. 2010	Shandong	225	AMI	TRI 123 TFI 102	PCI success rates; Operation time; Door-to-balloon time; The access artery complications rates; Fluoroscopy time; The post-operation immobilization time; Days in hospital; MACEs	In-hospital
Xiong Yong-Hong et al. 2010	Beijing	1236	CHD	TRI 618 TFI 618	Puncture time; Puncture success rate; PCI success rate; Total operation time; IRA patency time; Fluoroscopy time; The access artery complications rate; MACEs	One month
Fan Hua et al. 2011	Sichuan	62	CHD	TRI 30 TFI 32	Puncture success rates; CAG success rate; Operation time; Fluoroscopy time; Days in hospital; Expense of in-hospital; The access artery complications rate; Post-operation comfort level	In-hospital
Li Xing-Sheng et al. 2011	Chongqing	1637	Elderly CHD	TRI 909 TFI 728	PCI success rate; Puncture time; Puncture success rate; CAG time; Fluoroscopy time; The access artery complications rate; Days in hospital; MACEs	3 months
Chen Yue-Wu et al. 2011	Hainan	261	CHD	TRI 139 TFI 122	Puncture time; Puncture success rates; PCI time; PCI success rates; The access artery complications rates; Fluoroscopy time; Contrast media volumes; in-hospitalization time	In-hospital
Yang Yi et al. 2011	Guangdong	90	Elderly CHD	TRI 45 TFI 45	Puncture time; PCI time; PCI success rates; The access artery complications rates; Fluoroscopy time In-hospitalization time	In-hospital
Xue Cheng-Bin et al. 2011	Tianjin	594	AMI	TRI 300 TFI 294	Cannulation; success rate; PCI success rates; Operation time; The access artery complications rates; Days in hospital of post-operation	In-hospital
Zuo Jing et al. 2011	Jilin	169	AMI	TRI 85 TFI 84	Compressing time; PCI success rates; The access artery complications rates; Post-operation comfort level	In-hospital
Ding Shu et al. 2012	Jiangsu	254	AMI	TRI 182 TFI 72	PCI time; Puncture to balloon time; PCI success rates; The access artery complications rates; MACEs; In-hospitalization time	In-hospital and 6 months
Ji Yue 2012	Liaoning	230	AMI	TRI 115 TFI 115	The access artery compression time PCI time; PCI success rates; The access artery complications rates	In-hospital

Table 2. Evaluation of Methodology Quality of each 27 studies

Trials and Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other Bias
Fu Xiang-Hua et al. 2003	Unclear risk	Unclear risk	High risk	High risk	Unclear risk	Unclear risk	Unclear risk
Tian Jun et al. 2003	Unclear risk	Unclear risk	High risk	High risk	Unclear risk	Unclear risk	Unclear risk
Jin Quan-Min et al. 2005	Unclear risk	Unclear risk	High risk	High risk	High risk	Low risk	Unclear risk
Liu Jing-Hua et al. 2005	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Hu Xin-Quan et al. 2005	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Hu Jiang-Biao et al. 2005	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Wu Yan-Mei et al. 2005	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Yu Zhun et al. 2006	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Wang Ping et al. 2007	Unclear risk	Unclear risk	High risk	High risk	High risk	Low risk	Unclear risk
Xiao Hua et al. 2007	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Low risk
Li Wei-Min et al. 2007	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Low risk
Pan Gang et al. 2008	Unclear risk	Unclear risk	High risk	High risk	Low risk	High risk	Unclear risk
Feng Min et al. 2008	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Unclear risk
Liu Xiao-Kun et al. 2008	Unclear risk	Unclear risk	High risk	High risk	High risk	Unclear risk	Unclear risk
Yan Zehn-Xuan et al. 2008	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Unclear risk
Gan Li-Jun et al. 2009	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Unclear risk
Hou Lei et al. 2010	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Unclear risk
Yin Zuo-Min et al. 2010	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Xiong Yong-Hong et al. 2010	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Unclear risk
Xue Cheng-Bin et al. 2011	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Jing Zuo et al. 2011	Unclear risk	Unclear risk	High risk	High risk	High risk	Unclear risk	Unclear risk
Yang Yi et al. 2011	Unclear risk	Unclear risk	High risk	High risk	Low risk	High risk	Unclear risk
Fan Hua et al. 2011	Low risk	Unclear risk	High risk	High risk	High risk	Low risk	Unclear risk
Li Xing-Sheng et al. 2011	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Unclear risk
Chen Yue-Wu et al. 2011	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk
Ding Shu et al. 2012	Unclear risk	Unclear risk	High risk	High risk	Low risk	Low risk	Low risk
Ji Yue 2012	Unclear risk	Unclear risk	High risk	High risk	High risk	High risk	Unclear risk

transluminal coronary angioplasty (PTCA) or stenting the coronary artery, an alternative artery access was performed. (2) Punctuation site complications included major bleeding complications which required prolonged hospitalization, surgical intervention or blood transfusion), existence of pseudo-aneurysm which required surgical or percutaneous intervention, arterio-venous fistulas which required surgical or percutaneous intervention, vascular dissection which required surgical or percutaneous intervention, vasovagal reflex, arterio-spasm or vascular occlusion, limb ischemia and nerve damage which required vascular surgery. (3) Major adverse cardiovascular events (MACEs) included death, myocardial infarction and targeted vessel revascularization. The secondary end points were operation time, X-ray exposure time, volumes of contrast media used, days in hospital and overall hospitalization expense.

Statistical analysis

Statistical analysis was performed using the Review Manager 5.1.7 freeware package [13]. Dichotomous variables were reported as proportions and percentages, and continuous variables were reported as mean. Trial heterogeneity was estimated using the Cochrane Q statistic. The I^2 statistic, which was the proportion of total variation among studies that was likely to be explained by between-study heterogeneity rather than chance, together with degree of freedom (df) and *P* values were reported. Meta-analysis of parameters was performed using either Mantel-Haenzel fixed effect model or a combined Der Simonian and Laird random effects model. When the hypothesis of homogeneity was not rejected, a Mantel-Haenzel fixed-effects model was used. Otherwise, a random-effects model combining Der Simonian and Laird random effects model with inverse variance weighting was used. Sensitivity analysis was conducted under all circumstances when heterogeneity was observed to assess the potential possibility of introducing bias towards the analysis. The relative risk (RR) and 95% confidence interval (CI) were reported in the comparison of dichotomous variables

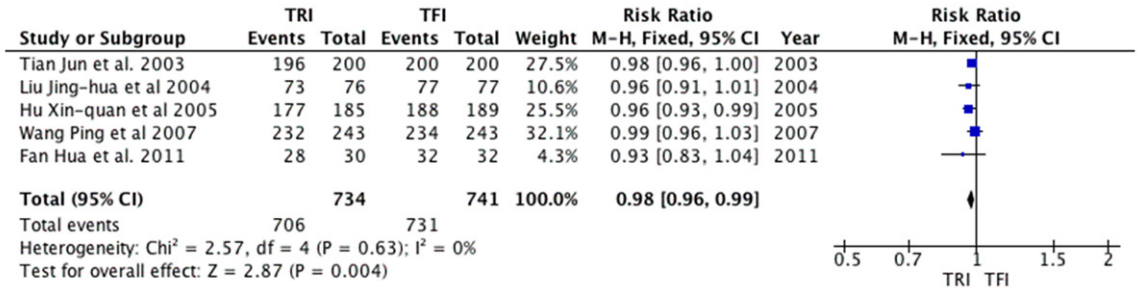

Figure 1. Forest plot comparing success rate of CAG between radial and femoral approaches in 5 studies of patients with CAD. RRs and 95% confidence intervals are shown for individual studies and the pooled population.

between the radial and femoral approaches. The mean difference (MD) and 95% CI were used for continuous variables. Two-tailed analysis was performed in all the statistical analysis and $P<0.05$ was considered as statistically significant.

A subgroup analysis of primary end points were further performed using the following categories: (1) elder group and young/middle aged group; (2) CAG and PCI; (3) selective and emergency procedures. Overall, this study was performed according to established methodology from Cochrane handbook 5.1.7.

Results

Studies and patient characteristics included in the final meta-analysis

A total of 98 clinical studies comparing the efficiency, safety and outcome of the radial approach in CAG and/or PCI in Chinese population with femoral approach were obtained from CNKI, CBM, Cochrane and Pubmed databases, among which 27 studies [14-40] were prospective, randomized and controlled studies. After a careful quality assessment, all the 27 studies were finally included in the meta-analysis. Data were extracted from the original paper or by obtaining original data from principle investigators.

These 27 studies included 8,749 patients among which 4,540 received radial catheterization and the remaining 4,209 received femoral catheterization. Characteristics of these 27 studies and the evaluation of methodology quality of each study were summarized and listed in **Tables 1** and **2**, respectively. Briefly, four of these studies [21, 24, 29, 30] were published in English language and one [40] was reported in the form of an abstract. 4 out of the 27 studies [16, 18, 22, 32] had recruited 1,322 patients for diagnostic CAG, while patients in the remaining 23 studies [14, 15, 17, 19-21, 23-40] had received PCI. Patients from 13 studies of these 23 studies [14, 21, 23, 24, 26-30, 36-39] received emergency interventional treatment due to acute myocardial infarction (AMI). The 27 studies were carried out in multiple centers throughout China with 6 in the north, 5 in the east, 4 in the northeast, central and south, 3 in southwest and 1 in northwest part of China.

In the four studies that had patients for only diagnostic CAG, 5 F diagnostic catheter with 6 F guiding catheter was used in 2 studies and 4 F guiding catheter was use in the other 2 studies. A relatively bigger-sized catheter was used in trans-femoral approach, including 6 F or 7 F introducer, 5 F or 6 F diagnostic catheter and 6 F guiding catheter.

Before PCI, all patients were pre-treated with aspirin and clopidogrel (of 300 mg~600 mg). During the procedures, unfractionated heparin was administered intravenously in all patients undergoing either radial or femoral approach according to their body weight (100 U~150 U/kg with maximum of 10000 U). Low molecular-weight heparin after PCI was administrated to patients in a case-to-case manner. Glycoprotein IIb/IIIa inhibitors were used in only four studies [26, 28, 29, 38] with a total of 709 patients (n=60, 195, 200 and 254 in each study, respectively). The follow-up of MACEs after discharge from hospital and the incidence of in-patient MACEs after the PCI procedure were reported in 9 of the studies (n=3,982) [24, 26-31, 34, 38]. The length of follow-up varies from one month to six months [24, 26-29, 31, 34].

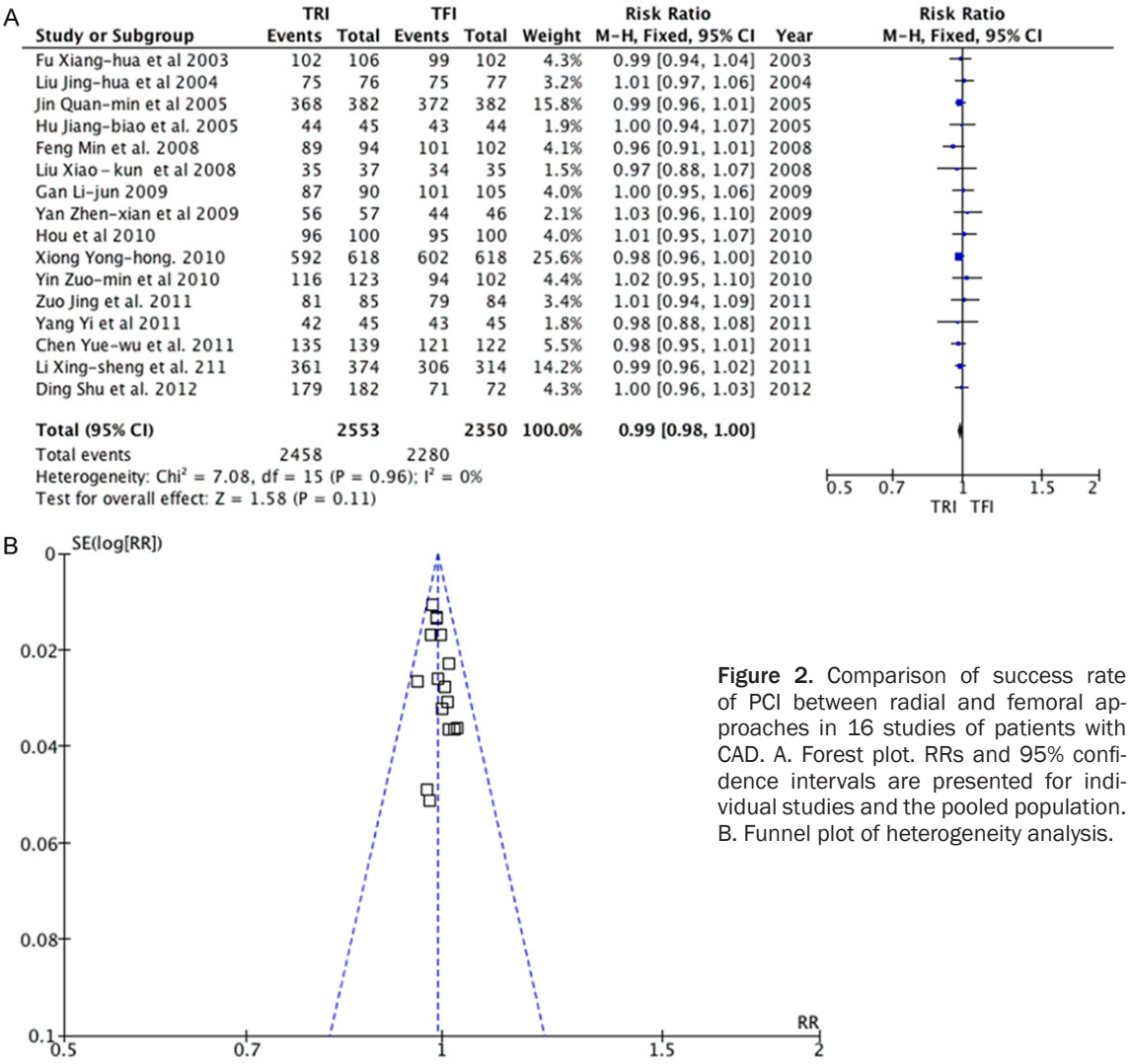

Figure 2. Comparison of success rate of PCI between radial and femoral approaches in 16 studies of patients with CAD. A. Forest plot. RRs and 95% confidence intervals are presented for individual studies and the pooled population. B. Funnel plot of heterogeneity analysis.

There were 13 studies with a total of 2,787 patients eligible for further systematic review and meta-analysis in patients with acute myocardial infarction (AMI). 64.5% of these 13 studies had studied patients with average age of 60 years old, while two studies had subjects of an average age of around 65-year-old and 75-years-old, respectively.

Meta-analysis of primary end point events between radial and femoral catheterization approaches in all patients with CAD

The success rate of CAG by radial approach was slightly lower than that of femoral approach (RR 0.98; 95% CI 0.96 to 0.99, *P*=0.004) (**Figure 1**). The success rate of PCI through radial artery was similar as that of the femoral approach (RR 0.99; 95% CI 0.98 to 1.00, *P*=0.11) (**Figure 2**). Patients received catheterization through either radial or femoral approaches also had similar incidence of MACEs during follow-ups, with 51 out of 2,148 (2.37%) patients in radial approach groups and 51 out of 1,834 (2.78%) patients in femoral approach group (data not shown). The risks of MACEs were similar between the two approaches (RR 0.81; 95% CI 0.57 to 1.17, *P*=0.27) (**Figure 3**). Radial approach was associated with a significantly lower rate of puncture site complications (RR 0.26; 95% CI 0.22 to 0.31, *P*<0.00001) (**Figure 4**), while it had a slightly lower success rate of catheterization procedure (RR 0.99; 95% CI 0.99 to 1.00, *P*=0.02) (**Figure 5**).

To check the existence of publication bias in this systematic review and meta-analysis, we

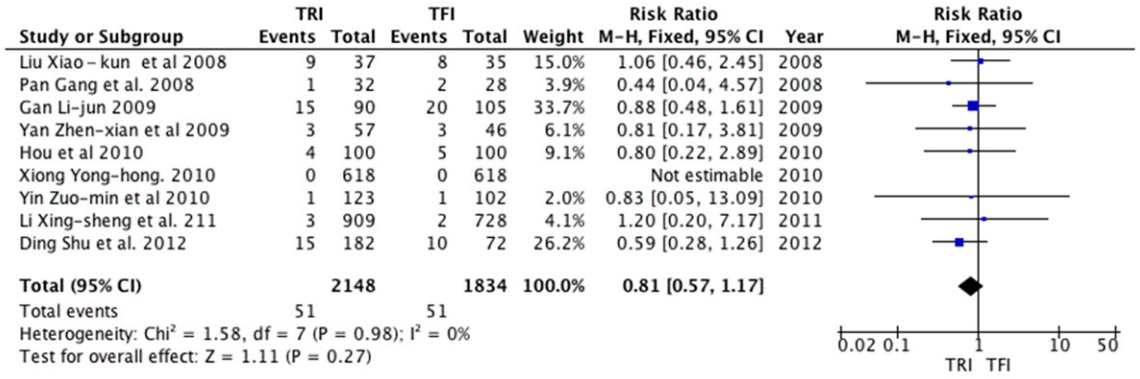

Figure 3. Forest plot comparing major adverse cardiac events (MACEs) between radial and femoral approaches in 9 studies of patients with CAD. RRs and 95% confidence intervals are shown for individual studies and the pooled population.

studied the heterogeneity and the funnel plot was shown in their corresponding figures. Except that the puncture site complications which had a significant statistic heterogeneity (P<0.00001, I^2=73%) (**Figure 4B**), all other primary end point events did not have publication bias (**Figures 2B**, **5B**). Sensitive analysis did not show an obvious publication bias introduced by a certain study in primary end point event of puncture site complication.

Meta-analysis of primary end point events between radial and femoral catheterization approaches in patients with AMI

We further compared the efficiency and safety between radial and femoral catheterization approaches in patients with AMI who mostly required emergent interventional treatment. Similar to what we obsered in the overall CAD population, there was no difference in the success rate of PCI (RR 0.99; 95% CI 0.98 to 1.01, P=0.45) (**Figure 6**) and incidence of MACEs (RR 0.80; 95% CI 0.55 to 1.15, P=0.23) (**Figure 7**) between radial and femoral catheterization approaches in AMI patients. However, puncture site complications (RR 0.20; 95% CI 0.15 to 0.26, P<0.00001) (**Figure 8**) was significantly lower in radial approach. There was also a slightly lower puncture success rate of radial approach compared with femoral approach (RR 0.99; 95% CI 0.98 to 1.00, P=0.04) (**Figure 9**) in patients with AMI. No heterogeneity has been found in any of the first end point events in AMI patients (**Figures 6B**, **8B**).

Subgroup meta-analysis of primary end point events comparing radial and femoral catheterization approaches in patients with CAD

Stratification analysis comparing procedure success rate, vascular complications and MACE between radial and femoral approaches was further performed in subgroup according to age, type of procedure received (angiography only or interventional treatment/PCI) or the feature of the procedures (emergency or non-emergency/selective) and were summarized in (**Table 3**). Patients received diagnostic angiography (CAG) and selective PCI had a slightly but significant lower procedure success rate for radial catheterization when compared with trans-femoral catheterization (RR 0.98; 95% CI 0.96 to 0.99, P=0.004 for diagnostic angiography, and RR 0.99; 95% CI 0.97 to 1.00, P=0.02 for selective PCI, respectively) (**Table 3**). However, patients had similar risk of puncture site complication and MACEs in both catheterizations approaches regardless of their age (elder or young/middle age), type of procedure they received (CAG or PCI) and type of PCI they received (selective or emergency PCI) (**Table 3**). Besides, heterogeneity analysis showed that χ^2 for Chinese language studies were 94.55 (df=22, P<0.00001) and I^2=77% (P<0.00001), similar to the characteristics of the overall population in this meta-analysis.

Heterogeneity of secondary end point events in CAD patients

There were variations in second end points between studies, including operation time (in

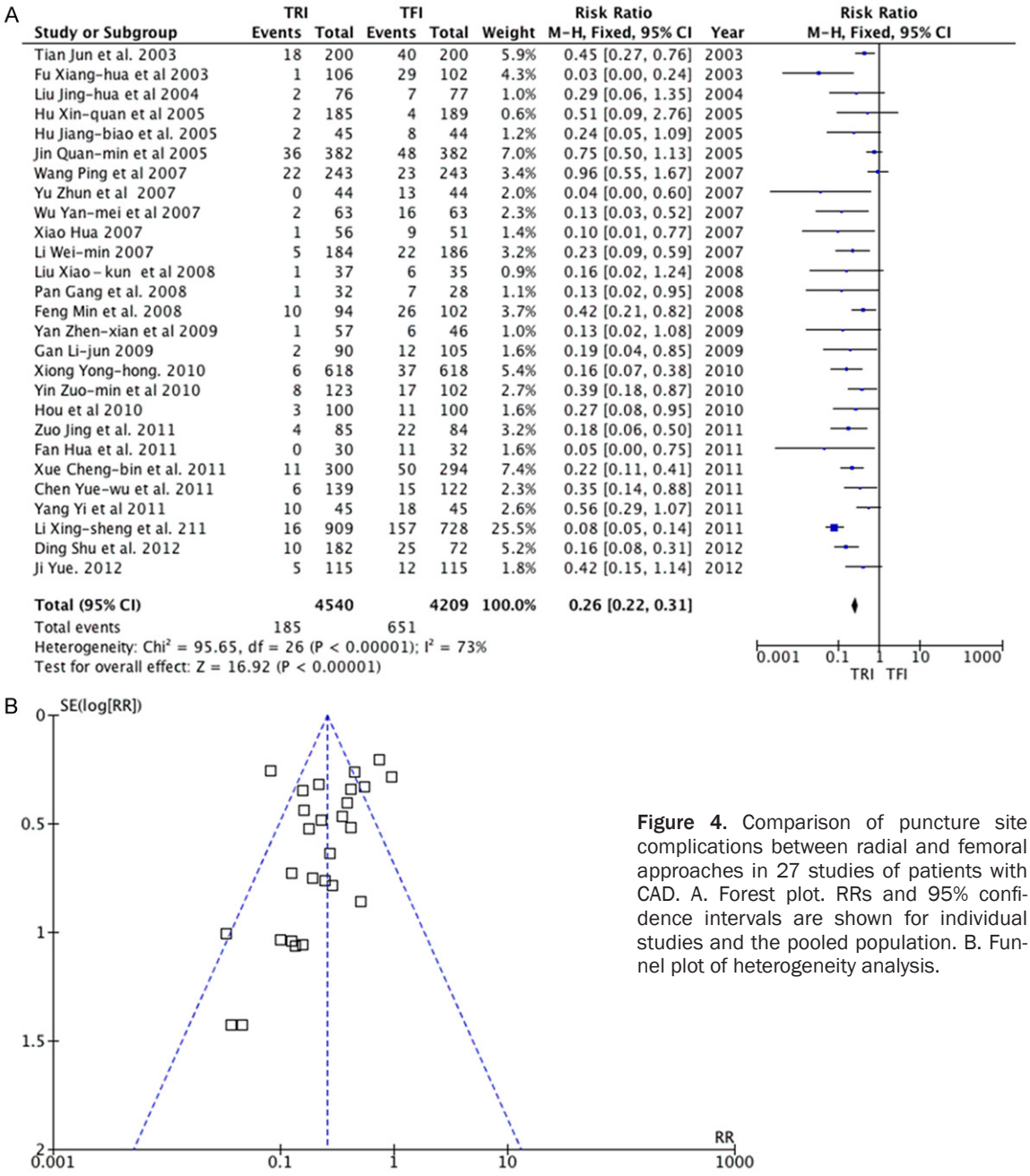

Figure 4. Comparison of puncture site complications between radial and femoral approaches in 27 studies of patients with CAD. A. Forest plot. RRs and 95% confidence intervals are shown for individual studies and the pooled population. B. Funnel plot of heterogeneity analysis.

minutes), X-ray exposure time (in minutes), volumes of contrast media used (in milliliter), length of in hospital staying (in days) and overall hospitalization expense judged by heterogeneity testing. After effort to compromise this shortcoming by using a random effect model, the heterogeneity test still remained significant in parameters including operation time (χ^2=60.25, df=17, P<0.00001), X-ray exposure time (χ^2=29.72, df=7, *P*=0.0001), volumes of contrast media used (χ^2=431.29, df=9, *P*<0.00001), and days of in hospital staying (χ^2=0.83, df=2, *P*=0.66). Therefore, sensitivity analysis was performed to evaluate the result stability of crude results and to investigate the influence of an individual study on overall risk estimate. Sensitivity analysis was carried out by sequentially omitting one study in each turn. The corresponding pooled MDs were substantially altered when any single study was deleted, suggesting that the results of this meta-analysis might introduce some publication

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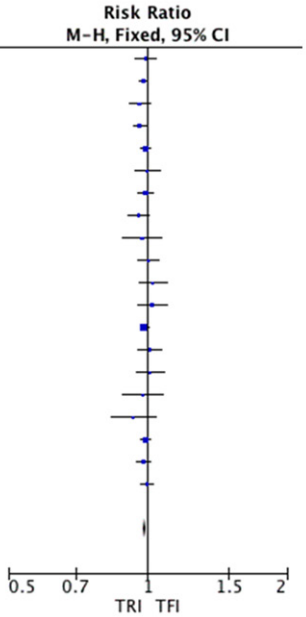
Study or Subgroup	TRI Events	TRI Total	TFI Events	TFI Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Fu Xiang-hua et al 2003	102	106	99	102	3.4%	0.99 [0.94, 1.04]	2003
Tian Jun et al. 2003	196	200	200	200	6.7%	0.98 [0.96, 1.00]	2003
Liu Jing-hua et al 2004	73	76	77	77	2.6%	0.96 [0.91, 1.01]	2004
Hu Xin-quan et al 2005	177	185	188	189	6.2%	0.96 [0.93, 0.99]	2005
Jin Quan-min et al 2005	368	382	372	382	12.4%	0.99 [0.96, 1.01]	2005
Hu Jiang-biao et al. 2005	44	45	43	44	1.4%	1.00 [0.94, 1.07]	2005
Wang Ping et al 2007	232	243	234	243	7.8%	0.99 [0.96, 1.03]	2007
Feng Min et al. 2008	89	94	101	102	3.2%	0.96 [0.91, 1.01]	2008
Liu Xiao-kun et al 2008	35	37	34	35	1.2%	0.97 [0.88, 1.07]	2008
Gan Li-jun 2009	87	90	101	105	3.1%	1.00 [0.95, 1.06]	2009
Yan Zhen-xian et al 2009	56	57	44	46	1.6%	1.03 [0.96, 1.10]	2009
Yin Zuo-min et al 2010	116	123	94	102	3.4%	1.02 [0.95, 1.10]	2010
Xiong Yong-hong. 2010	592	618	602	618	20.0%	0.98 [0.96, 1.00]	2010
Hou et al 2010	96	100	95	100	3.2%	1.01 [0.95, 1.07]	2010
Zuo Jing et al. 2011	81	85	79	84	2.6%	1.01 [0.94, 1.09]	2011
Yang Yi et al 2011	42	45	43	45	1.4%	0.98 [0.88, 1.08]	2011
Fan Hua et al. 2011	28	30	32	32	1.0%	0.93 [0.83, 1.04]	2011
Li Xing-sheng et al. 211	361	374	306	314	11.1%	0.99 [0.96, 1.02]	2011
Chen Yue-wu et al. 2011	135	139	121	122	4.3%	0.98 [0.95, 1.01]	2011
Ding Shu et al. 2012	179	182	71	72	3.4%	1.00 [0.96, 1.03]	2012
Total (95% CI)		**3211**		**3014**	**100.0%**	**0.99 [0.98, 1.00]**	
Total events	3089		2936				

Heterogeneity: $Chi^2 = 11.21$, df = 19 (P = 0.92); $I^2 = 0\%$

Test for overall effect: Z = 2.80 (P = 0.005)



B

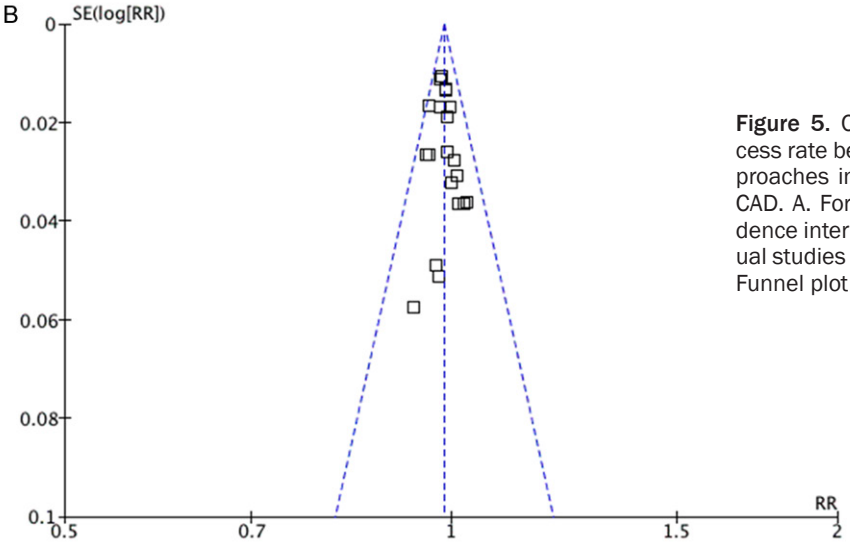


Figure 5. Comparison of puncture success rate between radial and femoral approaches in 15 studies of patients with CAD. A. Forest plot. RRs and 95% confidence intervals are presented for individual studies and the pooled population. B. Funnel plot of heterogeneity analysis.

bias. Therefore, although further meta-analysis was performed and reported in the secondary end points, the result should be interpreted with caution. Besides, since only three studies had mentioned about the overall hospital or relevant catheters expense (in the currency of the RMB), we were not able to carry out meta-analysis in this second end point event.

Meta-analysis of secondary end point events between radial and femoral catheterization approaches in patients with CAD

There was a significant difference in the mean operation time of PCI between two groups (MD=1.49, 95% CI 0.27 to 2.72, *P*=0.02). The X-ray exposure time of angiography and/or intervention procedures, which had been assessed in 13 studies (n=6,039), was not significant difference between the femoral approach group and the radial approach group (MD=-0.53, 95% CI -1.14 to 0.09, *P*=0.10). However, subgroup analysis of patients received PCI showed that the X-ray exposure time was significant shorter when using radial catheterization approach (MD=-1.11, 95% CI -2.14 to -0.08, *P*=0.03). There was also no difference in X-ray exposure time between radial and femoral approaches in patients receiving diagnostic CAG without further PCI (MD=0.46, 95% CI-0.12 to 1.04, *P*=0.12).

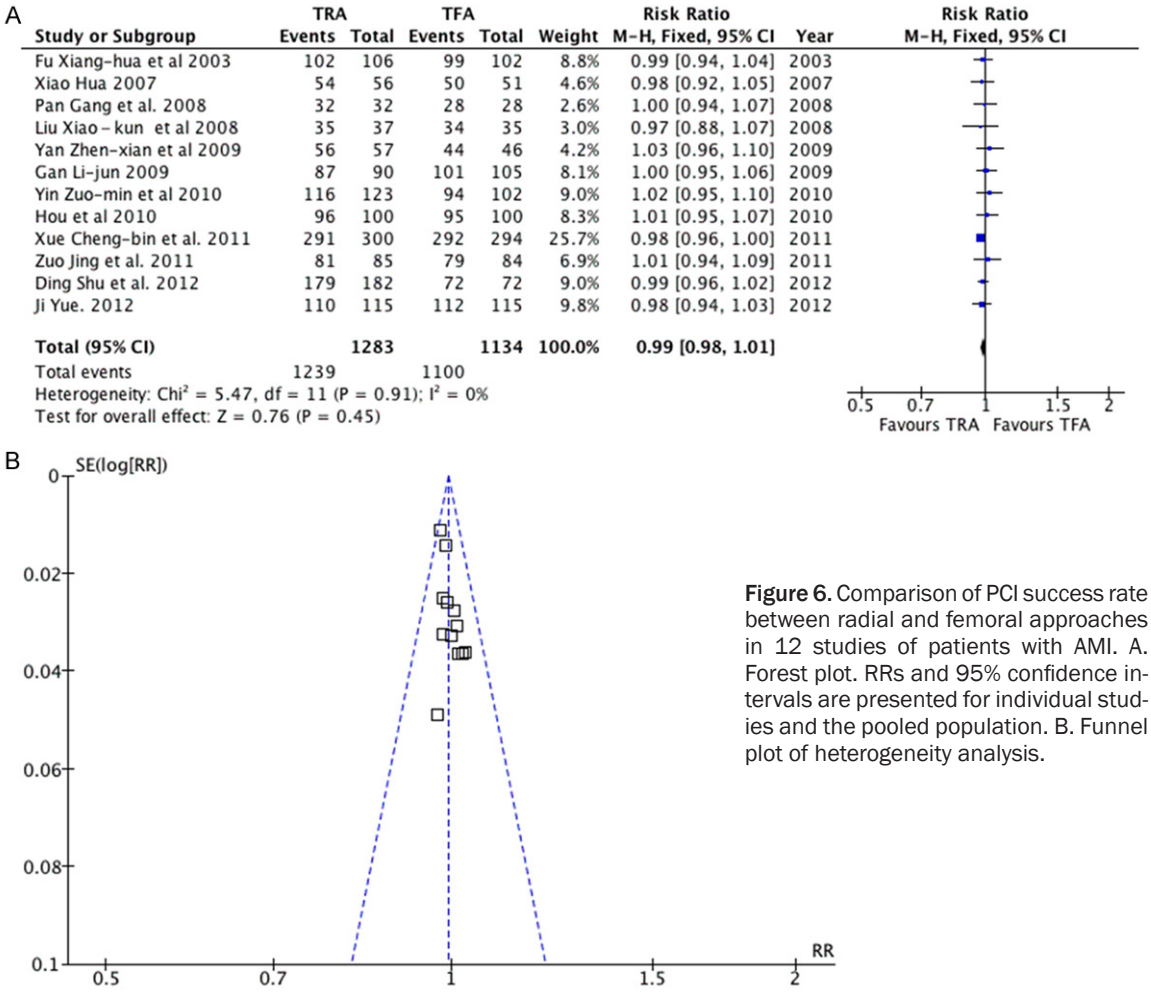


Figure 6. Comparison of PCI success rate between radial and femoral approaches in 12 studies of patients with AMI. A. Forest plot. RRs and 95% confidence intervals are presented for individual studies and the pooled population. B. Funnel plot of heterogeneity analysis.

The volumes of contrast media used was only evaluated in 4 studies (n=1,885) and there was no difference between the two approaches (MD 0.62; 95% CI-0.83 to 2.07, *P*=0.40). From a total of 11 studies, the average length of hospital staying was 7.44 days for patients receiving trans-radial catheterization, whereas the number was 9.07 days for patients receiving transfemoral catheterization (MD=-1.58, 95% CI -2.97 to -0.18; *P*=0.03). Last, the meta-analysis was not further carried out in comparing the total in hospital expenses and catheter costs because of the small number of studies available for analysis (3 studies with a total of 1,784 patients).

Discussion

Since the radial catheterization technique firstly used in clinics in 1989, this new technique has gained its popularity from both physicians and patients. As radial approach could be a substitution for traditional catheterization approach through femoral artery, the comparison between radial approach and femoral approach for diagnostic angiography and intervention is necessary and unavoidable. The result of the first large-scale randomized clinical trial RIVAL released in 2011 suggested that both radial and femoral approaches were safe and effective for PCI, while radial approach had less puncture site complications [10]. Afterwards, several other randomized controlled clinical trials were announced and are right now in the process, such as MATRIX (NCT 01433627). We believe that in the near future, results from these clinical studies would provide both physicians and patients with more solid data regarding the safety, efficiency and preference of these two approaches of catheterization.

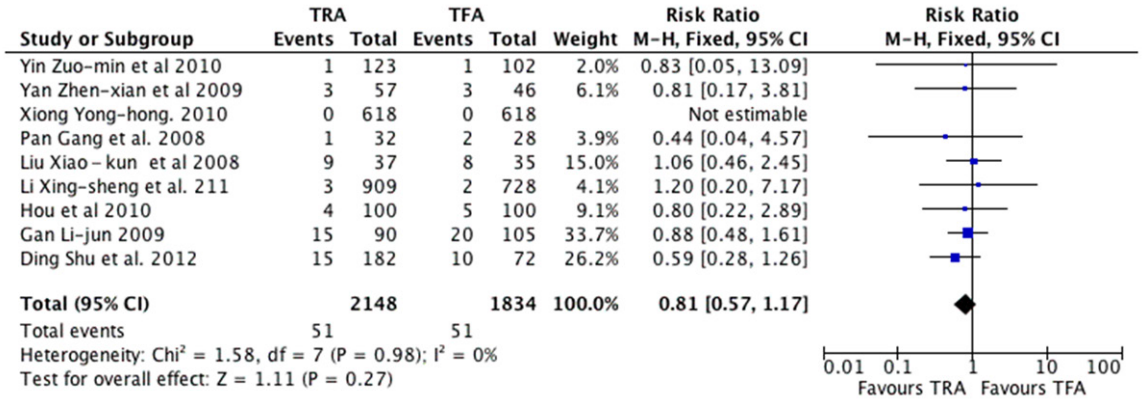


Figure 7. Forest plot comparing major adverse cardiac events (MACEs) between radial and femoral approaches in 7 studies of patients with AMI. RRs and 95% confidence intervals are presented for individual studies and the pooled population.

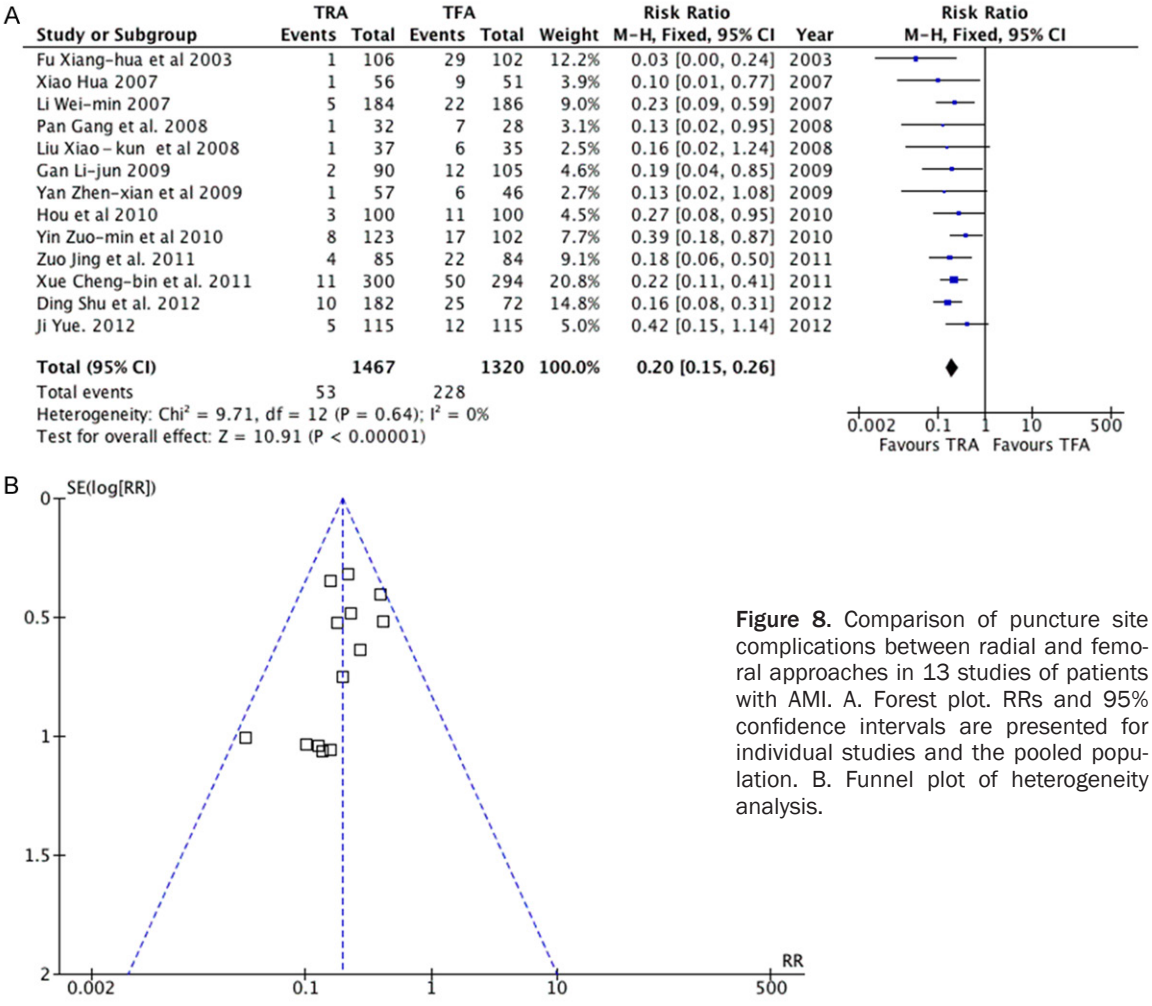


Figure 8. Comparison of puncture site complications between radial and femoral approaches in 13 studies of patients with AMI. A. Forest plot. RRs and 95% confidence intervals are presented for individual studies and the pooled population. B. Funnel plot of heterogeneity analysis.

However, all these studies have focuses on the populations other than Asian especially Chinese. With the increasing incidence of CAD and the dramatic increased number of patients received angiography and PCI every year in China, more and more patients and physicians

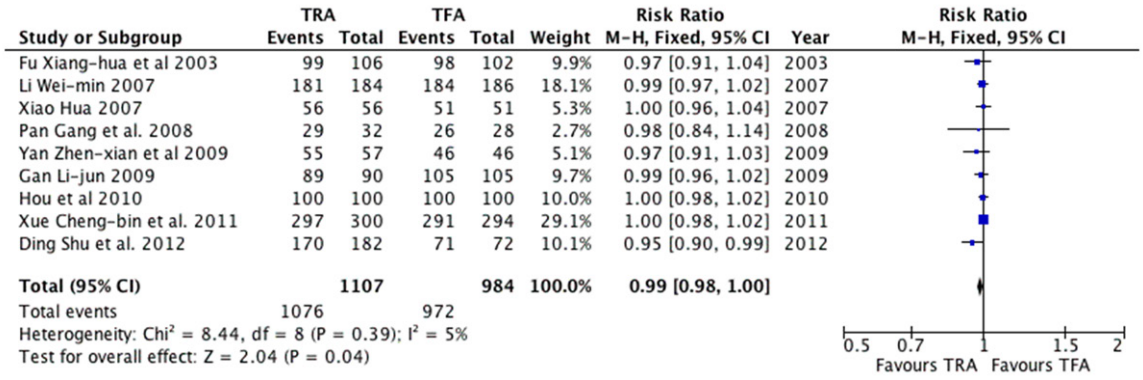


Figure 9. Forest plot comparing puncture success rate between radial and femoral approaches in 9 studies of patients with AMI. RRs and 95% confidence intervals are presented for individual studies and the pooled population.

Table 3. Subgroup analysis of primary end points (fixed-effect model)

Subgroup analysis	No. of studies	RR (95% CI) *P* value		
		Procedure success rate	Vascular complication rate	MACEs
Total population	27	0.99 (0.98-1.00) P=0.007	0.26 (0.22-0.31) P<0.00001	0.81 (0.57-1.17) P=0.27
Age				
The elder group (mean age >60 ys)	17	0.99 (0.98-1.00) P=0.07	0.28 (0.24-0.34) P<0.00001	0.78 (0.49-1.24) P=0.29
The young & middle aged group	10	1.00 (0.98-1.02) P=0.96	0.21 (0.15-0.30) P<0.00001	N/A
Procedure type (CAG with or without PCI treatment)				
Angiography (CAG)	5	0.98 (0.96-0.99) P=0.004	0.52 (0.36-0.73) P=0.0002	N/A
Intervention (PCI)	16	0.99 (0.98-1.00) P=0.11	0.23 (0.19-0.27) P<0.00001	0.81 (0.57-1.17) P=0.27
PCI type (selective of emergency procedure)				
Selective PCI	10	0.99 (0.97-1.00) P=0.02	0.24 (0.20-0.30) P<0.00001	N/A
Emergency PCI	12	0.99 (0.98-1.01) P=0.45	0.20 (0.15-0.26) P<0.00001	0.80 (0.55-1.15) P=0.23

would like to know which approach is more beneficial for patients from a large-scale evidence-based study in Chinese population. Therefore, the ultimate goal of this review and meta-analysis was to provide physicians with a systematic and objective view of the comparison between the traditional femoral catheterization and the relatively new radial catheterization in patients undergoing angiography or PCI.

Based on the 27 published randomized controlled studies comparing radial and femoral catheterization approaches in Chinese population and after a careful and standard quality control process in data selection, we found that radial approach was a safe and efficient technique for both CAG and PCI in Chinese population. Radial approach had similar rate of MACEs but a significantly lower rate of punctuated site complications in comparison to the traditional femoral approach in Chinese population.

In a previous study carried out shortly after the radial technology was first introduced to the

field [13], researchers and physicians believed that the success rate of radial approach was much lower than that of femoral approach [7]. However, with more and more physicians been trained to use this new technique for decades, they have become more experienced and confident with such technique. Current study showed that radial and femoral catheterization approaches share similar operative success rate [10, 11].

This meta-analysis showed that the percentage of punctuated site complications in the radial group was 4.1% (185 out of 4540 patients), much lower than that of the femoral group (15.5%, 651 out of 4209 patients), consistence with the founding of large-scale clinical trial RIVAL in other populations [25, 29-31, 33, 34, 38]. Besides patients with CAD, radial PCI was also associated with a similar success rate but fewer punctuation site complications compared with femoral PCI in patients with AMI. The further subgroup analysis suggested that the majority of patients undergoing coronary angiography and intervention could be benefit from both radial and femoral approaches regardless of whether they received selective or emergency treatment. However, as patients became older, the success rate of trans-radial procedures reduced gradually, with the percentage of the puncture site complications slightly increased. Despite of this, physician would still need to consider the benefit of radial approach for elder patients because it does not require long time of remaining immobile on bed and has similar MACEs incidence and lower vascular complications compared to trans-femoral approach.

Our study also showed that there were no significant difference between two approaches in terms of secondary end points including operation time, X-ray exposure time and volumes of contrast media used. However, the majority of the second end points were heterogeneous, except volumes of contrast media. Even though the random-effect model was used, operation time, X-ray exposure time, in hospital staying time and expenses in hospital were the parameters that still had a significant heterogeneity. Therefore, data interpretation should be carried out with caution. There could be several reasons for the significant heterogeneity in the secondary end points in this study. First of all, the definition of operation time differed among studies. Operation time could be CAG time, door-to-balloon time, PCI time, according to the specific aims of different studies included in this meta-analysis. Second, the heterogeneity could also reflect the variation of physician's experience and skills in operation which is unavoidable.

Last, this meta-analysis has several limitations. First, some studies could not be included due to the inaccessibility of the detailed data from the investigators. Second, due to the significant heterogeneity of most secondary end points parameters even after the adjustment methods, the finding needs to be verified and interpreted with caution.

Conclusion

This systematic review and meta-analysis shows that radial approach catheterization in CAG/PCI is a safe and effective technique compared with femoral approach catheterization in Chinese population. For skilled and experienced physicians, the radial approach had the advantage of less punctuated site complications. Besides, radial approach provides rapidly access to the artery and a potential early reopening of the occluded coronary artery particularly in patients with AMI. Last, radial approach could still be beneficial for elderly patients despite of its less success rate, considering that elderly patients do not have to be in immobilization after the procedure which could bring other complications in these people.

Acknowledgements

We thank the support of Department of Cardiology, Hebi City People's Hospital in our research.

Disclosure of conflict of interest

None.

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