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Review

Impact of vascular access on acute kidney injury after percutaneous coronary intervention☆,☆☆,★

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ABSTRACT

Objectives: We performed a systematic review of the literature and a meta-analysis to examine the role of access site in affecting the incidence of acute kidney injury (AKI) after percutaneous coronary intervention (PCI).
Background: The vascular access site may play a central role among procedure-related risk factors for AKI after PCI. Transradial access is associated with reduced vascular complications and major bleeding which, in turn, is an emerging risk factor for post-procedural AKI.
Methods: Results of six observational studies, three out of six providing propensity matching adjustment, of patients undergoing PCI from the radial and the femoral access were pooled, including overall 26,185 patients. The endpoint was the incidence of study-defined AKI. A meta-regression analysis was performed to further assess the role of study-level covariates. Random-effects models were privileged.
Results: There was a significant difference in the incidence of AKI after PCI, favoring radial access (odds ratio [OR] 0.51, 95% CI 0.39–0.67, $p < 0.0001$), and the effect size was larger in studies including only patients presenting with ST-elevation myocardial infarction (STEMI) (OR 0.42, 95% CI 0.24–0.72, $p = 0.001$). The meta-regression showed a significant relationship between the benefit of radial access and the proportion of STEMI patients ($p = 0.031$) in each of the included studies.
Conclusions: Transradial intervention is associated with a reduction in the incidence of AKI after PCI, as compared to the femoral access, and this benefit is more evident in STEMI patients. These findings warrant further confirmation in randomized controlled trials.

1. Introduction

Acute kidney injury (AKI) after percutaneous coronary intervention (PCI) remains associated with significant morbidity and mortality [1], despite a controlled expansion of intravascular volume [2,3]and the minimization of contrast dose [4,5] may be effective preventive strategies. Risk factors for AKI development include both patient- and procedure-related features and, among the latter, the vascular access site may play a role.

Transradial access is associated with reduced incidence of vascular access-related major bleeding; this translated into improved clinical outcomes in some studies [6], but not in others [7]. Importantly, bleeding is an emerging risk factor for AKI [8]. In turn, radial access might reduce the occurrence of kidney injury because of complementary mechanisms, such as reduced risk of hemodynamic instability and impaired renal perfusion consequent to major bleeding [8] and reduction of cholesterol embolization (CE) in renal arteries, since the mechanical trauma to the descending aorta due to passage of catheters is avoided [9,10]. To this purpose, in a large retrospective study transradial PCI was associated with lower risk of AKI [10]. Interestingly, the lower risk of AKI with transradial access was independent from the observed reduction in bleeding complications [10]. On the contrary, data from a high volume radial center have failed to confirm previous findings [11]. Despite the growing interest about transradial coronary interventions [6], none of the randomized studies comparing radial versus femoral approach has yet systematically explored to date the issue of renal complications [12]. On this background, we performed a systematic review of the literature and a meta-analysis of the available data to examine the potential effectiveness of transradial, as compared to transfemoral access, in reducing the incidence of AKI after PCI.

2. Methods

2.1. Data search

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [13]

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and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines [14]. We searched MEDLINE, EMBASE and Cochrane databases using Internet-based engines with the search restricted to English language. The terms used for research included "radial", "transradial", "femoral", "transfemoral", "percutaneous coronary intervention", "acute kidney injury", and "contrast-induced nephropathy". Additional sources included clinicaltrials.gov, clinicaltrialresults.org, cardiosource.com, tctmd.com, Google Scholar and abstracts from major cardiovascular meetings. Furthermore, we searched the reference lists of relevant studies and reviews, editorials and letters.

We restricted our analysis to studies that met all the following inclusion criteria: i) study population consisting of patients undergoing either urgent or elective PCI, ii) study reporting the incidence of AKI as primary or secondary outcome, iii) study providing data about transradial and transfemoral vascular access. The most updated or inclusive data for a given study were chosen for abstraction. The final search was performed on September 30, 2015.

2.2. Data extraction

The outcome extracted was the incidence of AKI. Because of the varying definitions of AKI across the studies, the measure of association derived was a relative rather than an absolute risk. Odds ratio (OR) with 95% confidence intervals (CI) was therefore abstracted or calculated on the basis of the reported event rates. For studies reporting unadjusted, adjusted, or propensity-matched data, the highest-quality estimate was picked for the overall meta-analysis using the following rank order: propensity matched > adjusted > unadjusted. The quality assessment of the identified records was based on the Newcastle–Ottawa Scale (NOS) for cohort studies [15]: when a study included relevant information that could be associated with NOS, one star was added. Studies with 7–9, 4–6, and 0–3 stars were identified as good, satisfactory or unsatisfactory, respectively.

2.3. Statistical analysis

The results of all studies were pooled using a DerSimonian–Laird random-effects model [16] to minimize heterogeneity, and confirmed by a fixed-effects model to avoid overweighting of smaller studies. Statistical heterogeneity was assessed with Cochran's Q and graded using the I^2 statistic with I^2 <25%, 25%–50%, and I^2 >50% representing mild, moderate, and severe inconsistency, respectively [17]. Multiple sensitivity analysis was performed: first, the influence of individual studies on the pooled OR was assessed by excluding individual studies in order to establish the impact of each trial on the effect size; second, the pooling was restricted to studies reporting ($n = 3$) propensity-matched data or including ($n = 2$) only patients presenting with ST-elevation myocardial infarction (STEMI). The potential publication bias was assessed by visual inspection of funnel plot and by Egger's regression asymmetry test of the OR on its standard error.

In order to account for the possible high-level of heterogeneity, which means that the observed variance comes from real differences between studies and, as such, can potentially be explained by study-level covariates (moderators), weighted random-effects meta-regression modeling was used [18]. We regressed the impact of radial access effect size (log OR) against the log-transformed percentage of patients having a major bleeding or presenting with STEMI in each study, using the inverse of the variance of the log OR as weight. Such percentages can be considered surrogate indicators of the underlying hemorrhagic risk of each study population and can have the advantage of being a measure that reflects multiple factors contributing to outcome occurrence [19]. We similarly regressed log OR against the log-transformed percentage of patients with other clinical and procedural variables (Table 1), which in turn can be considered generic indicators of the risk of contrast-induced AKI.

Statistical analysis was performed using *meta* package (General Package for Meta-Analysis) [20] for R (The R Foundation for Statistical Computing) and *MetaReg* macro [21] for SPSS (Statistical Package for Social Science).

3. Results

3.1. Search results and quality assessment

We identified 46 potentially relevant studies (Fig. 1). After removing duplicates and unsuitable studies, 25 full-text studies were retrieved for detailed evaluation and among these, 19 studies were excluded: eleven studies did not report the incidence of AKI, seven studies did not report renal outcomes stratified by vascular access and in one single-center observational study of propensity-matched patients no alterations in renal function were observed within 96 h after the procedure [22]. The last 6 studies [4,8,10,11,23,24] were found to meet the inclusion criteria and were therefore included in this systematic review (Table 1). All the studies were observational, at least satisfactory at NOS (Table 2) and cumulatively reporting data from 90,055 patients. Three studies [10,11,23] out of 6 provided adjusted outcomes by propensity score matching, which were used to the purpose of quantitative synthesis according to study methodology. The present meta-analysis therefore reports data from 26,185 patients.

3.2. Effect size and publication bias

There was a statistically significant difference in the incidence of AKI (Fig. 2), favoring radial approach (OR 0.51, 95% CI 0.39–0.67, $p < 0.0001$ with random-effects model, OR 0.54, 95% CI 0.47–0.63, $p < 0.0001$ with fixed-effects model). In other words, the effect size was that the use of radial approach has approximately halved the risk of post-procedural AKI as compared to femoral approach. Visual estimation of the funnel plot (Fig. 3) suggested a minimal asymmetry, which was quantified to be statistically non-significant by means of Egger's regression test ($t = -1.23$, $p = 0.29$).

3.3. Heterogeneity, sensitivity analysis and meta-regression

There was a significant heterogeneity across the studies ($p = 0.0238$, $I^2 = 61.4\%$), which indicates that more than 60% of the observed variance came from real differences between studies and, as such, could potentially be explained by study-level covariates. However, none of the studies was found to unduly influence the significance of the estimate with study removal analysis. The pooled effect size of studies including propensity matched patients (OR 0.64, 95% CI 0.49–0.85, $p = 0.002$ with random-effects model) and only patients with STEMI (OR 0.42, 95% CI 0.24–0.72, $p = 0.001$ with random-effects model) were consistent with the main analysis.

The univariate meta-regression analysis (Table 3) showed a direct relationship of the effect size of radial access in reducing the incidence of AKI with the prevalence of STEMI ($Z = -2.95$, $p = 0.003$) and an inverse relationship with the global incidence of major bleeding ($Z = 2.67$, $p = 0.008$). No significant associations were found for age, diabetes, chronic kidney disease, heart failure and contrast volume. At multivariate meta-regression (Table 3), STEMI remained significantly associated with log OR of AKI reduction with radial access ($Z = -2.16$, $p = 0.031$, omnibus p of the model = 0.003).

4. Discussion

In this meta-analysis of observational studies of patients undergoing elective or urgent PCI, the radial approach was found to be significantly associated with a reduced incidence of AKI. In addition, the meta-regression model showed that a relationship exists between the effect size of radial access in reducing the incidence of AKI (log OR) and two