International Journal of Cardiology 157 (2012) 381–385

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Effect of gender on repeated coronary artery revascularization after intra-coronary stenting: A meta-analysis ☆

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ARTICLE INFO

Article history:
Received 18 September 2010
Received in revised form 16 December 2010
Accepted 22 December 2010
Available online 13 January 2011

Keywords:
Coronary artery disease
Gender
Stent
Target vessel revascularization
Major adverse cardiac events

ABSTRACT

Background: As a risk factor of coronary artery disease (CAD), gender might be associated with the prognosis of percutaneous coronary intervention (PCI). However, there are conflicting reports in the literature regarding the role of gender on repeated coronary artery revascularization after PCI.
Objective: This meta-analysis aimed to determine whether gender influenced the incidence of repeated coronary artery revascularization after intra-coronary stenting.
Methods: We performed a meta-analysis including 13 randomized controlled trials (a total of 156,798 patients, including 107,697 men and 49,101 women) that assessed the results of target vessel revascularization (TVR), target lesion revascularization (TLR) and major adverse cardiac events (MACE) after PCI. PUBMED, MEDLINE, EMBASE and the Cochrane Database were searched for articles published in the last 10 years.
Results: There was no difference in the long-term incidence of TVR between males and females after PCI (16.68% vs. 16.41%; odds ratio (OR) = 0.94; 95% confidence intervals (CI): 0.82–1.07; $P = 0.36$). However, the short-term rate of TVR after PCI was significantly higher in women than that in men (4.25% vs. 3.83%; OR = 0.91; 95% CI: 0.86–0.97; $P < 0.01$). Moreover, women had higher short-term and long-term incidences of MACE than men after PCI (short-term: 8.02% vs. 5.57%; $P < 0.01$; long-term: 16.14% vs. 13.72%, $P < 0.01$).
Conclusions: The present data suggested that female sex could increase the short-term incidence of repeated coronary revascularization after PCI. However, the long-term rate of repeated coronary revascularization was similar between male and female patients.

1. Background

As a risk factor of CAD, gender could be associated with the prognosis of coronary artery revascularization. Many previous studies found that female sex increased mortality and the incidence of cardiac events. The Euro Heart Survey of ACS [1,2] showed that among patients with ST-segment elevation ACS, the in-hospital mortality rate was 10.1% for women and 5.4% for men, with corresponding rates of 2.5% and 2.1% for patients with non-ST-segment elevation. Results from NRMI-I published in 1998 which enrolled more than 350,000 patients with acute myocardial infarction (AMI) showed that women had nearly twice the mortality rates of men, even after adjusting the age and risk factors [3]. Women also complained more frequently of angina and took more anti-angina medication after PCI [4].

In addition, previous studies indicated that female sex might increase the risk of TVR after PCI [5]. However, Mehilli and colleagues demonstrated that the 1-year rate of coronary vessel revascularization was lower in women than that in men (14.8% vs. 17.5%, $P < 0.05$) after coronary stenting for stable or unstable angina, although the incidence of MACE was higher in women than that in men (7.2% vs. 6.0%) [6]. Chiu et al. showed that there was no difference in the incidence of repeated revascularization between male and female patients (20% vs. 19%, $P > 0.05$) [7]. Therefore, we performed a meta-analysis to analyze the effect of gender on the incidence of repeated coronary artery revascularization after PCI.

2. Methods

2.1. Study objective and search strategy

The primary aim of this meta-analysis was to compare the outcomes of repeated coronary artery revascularization in randomized trials and registry studies analyzed by different sexes.

Using the key terms "gender" or "sexual" or "sex," "target vessel revascularization" or "target lesion revascularization," and "coronary intervention" or "stent," we searched PUBMED, MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials from 2000 to 2010 for all randomized controlled trials and registries reporting outcomes by sex. The search was supplemented by reviews of reference lists for all relevant studies. All

☆ Grants: National Natural Science Foundation of China (30671998 and 30901383).
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doi:10.1016/j.ijcard.2010.12.082

relevant reports identified were included without language restriction. Of the 77 relevant studies, 13 were included in this meta-analysis. (Flow chart of the study is shown in Fig. 1.)

2.2. Study identification and extraction

We performed text searches for studies that met the following criteria: (1) there was a direct comparison between males and females; (2) outcomes were published in the last 10 years; (3) the incidence of TVR or TLR was reported; and (4) the follow-up duration was at least 1 month.

The following information was collected: (1) first author's name; (2) year of publication or presentation; (3) total sample size and subgroup sample size for both men and women; (4) demographic information (mean age, hypertension, diabetes, and smoking habit); (5) the number of diseased coronary vessels; (6) the proportion of patients with single vessel diseased; and (7) the mean period of follow-up.

2.3. Study outcome

The outcomes of interest were TVR (any clinically driven repeated PCI or bypass surgery of the target vessel) and TLR (any repeated PCI of the target lesion or bypass surgery of the target vessel performed for recurrent angina, ischemia, or stenosed diameter ≥ 70% by quantitative coronary angiography). Meanwhile, the prevalence of MACE was also identified across the trials. MACE was defined as a composite of death, myocardial infarction, and TVR or TLR.

2.4. Statistical analysis

The meta-analysis was performed according to the recommendations from the Cochrane Collaboration with Review Manager 5.0. The effect of gender on the occurrence of TVR, TLR, and MACE was presented as odds ratio (OR) with 95% confidence intervals (CI) using a fixed effects model. Alternatively, random effects meta-analyses were performed when between-study variability existed. Heterogeneity was quantified using the I^2 statistic (I^2 represents the percentage of variability due to between-study variability.) We regarded I^2 of less than 25%, 25–50%, and greater than 50% as low, moderate and high amounts of heterogeneity, respectively. Publication bias was evaluated using the funnel plot. Results were considered statistically significant if $P<0.05$.

3. Results

3.1. Eligible studies and baseline characteristics

The electronic database search identified 13 studies, which fulfilled our eligibility criteria. The included studies enrolled a total of 156,798 patients (107,697 men and 49,101 women). Fig. 1 demonstrated the flow chart of study identification and extraction of the meta-analysis. The baseline characteristics of the patients in different studies [5–17] were summarized in Table 1. In male patients, the mean age ranged from 60 to 64 years, while the mean age ranged from 62 to 70 years in female patients.

3.2. Effect of gender on TVR

3.2.1. Short-term effect (30-day follow-up) on TVR

There were 8 studies reported the TVR data up to 30-day follow-up. A total of 5194 patients received repeated TVR after PCI during follow-up, with 3.83% in the male patients and 4.25% in female patients. Male sex was associated with a significant reduction in the incidence of TVR (OR = 0.91, 95% CI: 0.86–0.97; $P=0.002$; Fig. 2).

3.2.2. Long-term effect (at least 6-month follow-up) on TVR

With regard to the effect of gender on long-term incidence of TVR, there were 6352 events among 38,252 patients in nine trials. During at least 6 months follow-up, the incidence of repeated TVR was 16.68% among male patients, which was similar to the rate (16.41%) among female patients ($P=0.36$, Fig. 3).

3.3. Effect of gender on TLR

A total of 1225 patients received repeated TLR after PCI in five studies, four of which followed up for 12 months and the trial of Zhang [16] followed up for 1 month. There was no significant difference in the rate of repeated TLR between male and female patients (9.81% vs. 10.35%, $P=0.31$; Fig. 4).

3.4. Effect of gender on MACE

Nine studies reported the 30-day rate of MACE after PCI among 24,809 patients. A total of 999 events (5.57%) occurred in male patients, and 552 events (8.02%) occurred in female patients. Male sex significantly reduced the 30-day incidence of MACE after PCI (OR = 0.74, 95% CI: 0.59–0.93, $P=0.009$; Fig. 5).

Besides the favorable effect on MACE of 30 days, male sex was also associated with a significant reduction in the incidence of MACE by at

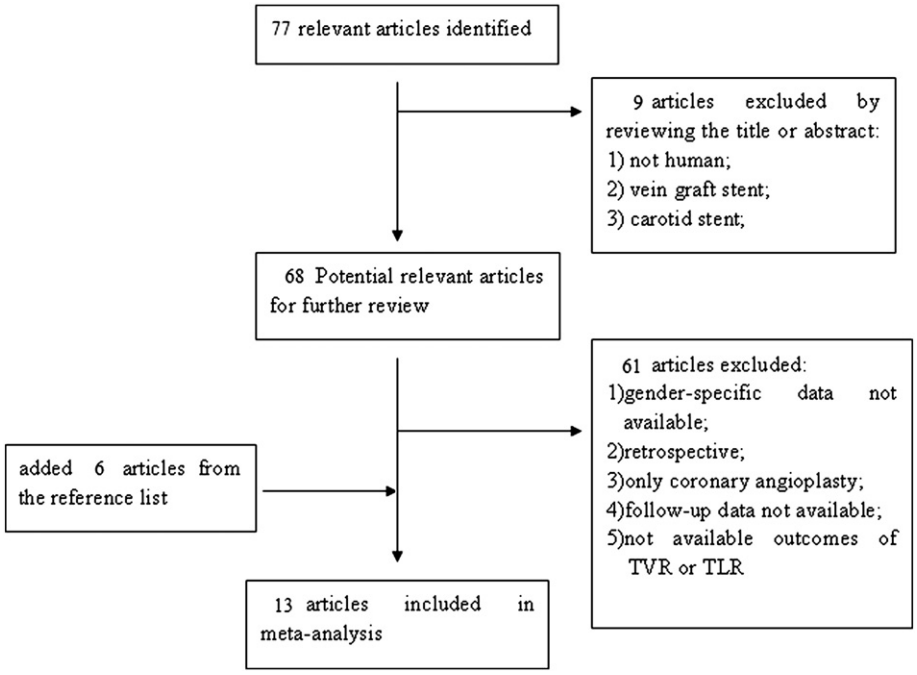

Fig. 1. Flow chart of study identification and extraction of the meta-analysis.