Protocols for a systematic review and network meta-analysis of antithrombotic therapy strategies for atrial fibrillation patients undergoing percutaneous coronary intervention Version 2

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Abstract

Objective: To evaluate the comparative efficacy and safety of antiplatelet agents, vitamin K antagonist (VKA) and non-VKA oral anticoagulants (NOACs) in patients with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI).

Methods: PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials will be searched to identify clinical trials comparing antiplatelet drugs with VKA and NOACs or their combination in AF patients undergoing PCI with a mean/median follow-up of at least 12 months. A network meta-analysis will be conducted to directly and indirectly compare the efficacy and safety of competitive antithrombotic regimens with a Bayesian random-effects model.

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Protocol

Inclusion and exclusion criteria

Step 1.

Inclusion criteria:

(1) clinical trials with at least one compared group;

(2) study population of coronary artery disease patients with paroxysmal, persistent, or permanent AF undergoing PCI;

(3) treatment with antiplatelet drugs (aspirin and P2Y12 inhibitors) and/or anticoagulants (warfarin and new oral anticoagulants such as dabigatran, rivaroxaban, apixaban and edoxaban) with a target international normalized ratio (INR) of 2.0-3.0 if warfarin is used to reflect present standard practice;

(4) outcomes involving main adverse cardiac and cerebrovascular events (MACCEs) and major bleeding;

(5) mean or median follow-up period no less than 12 months.

Exclusion criteria:

(1) articles published only in the form of abstracts or in non-English languages;

(2) antithrombotic therapies change differently in post-PCI;

(3) vague compared treatments such as VKA *vs.* non-VAK.

Identify all possible records through databases

Step 2.

Search databases: PubMed, Embase and Cochrane Central

Search key words: (“atrial fibrillation” or “AF”) and (“percutaneous coronary intervention” or “PCI” or “coronary stent implantation”) and (“aspirin” or “$P2Y_{12}$ antagonist” or “$P2Y_{12}$ inhibitor” or “clopidogrel” or “ticagrelor” or “warfarin” or “vitamin K antagonist” or “VKA” or “dabigatran” or “rivaroxaban” or “apixaban” or “edoxaban” or “novel oral anticoagulant” or “new oral anticoagulant” or “NOAC”)

Two reviewers search key words independently from the earliest possible search date till March 2017.

Remove duplicate records by titles and abstracts.

Step 3.

Exclude irrelevant studies and non-English language articles based on titles and abstracts.

Step 4.

Get all qualified studies included in this network meta-analysis after full-text assessment.

Step 5.

Remove unqualified studies after assessment of full-text studies:

(1) article type: clinical trial designs, reviews, meta analyses, letters, case reports, comments, editorials, survey and investigation;

(2) without at least a control group or non-AF patients underwent PCI included;

(3) obviously changed treatments in peri-PCI;

(4) without MACCEs or major bleeding endpoints;

(5) mean/median follow-up periods less than 1 year.

Data extraction

Step 6.

Collected data: study design, sample size (all and in compared arms), follow-up duration, antithrombotic strategies in post-PCI, efficacy and safety outcomes, baseline characteristics of the patients including mean age, male percentage, mean $CHADS_2$/CHA_2DS_2-VASc and HAS-BLED scores, the number and percentage of MACCEs (including all-cause mortality, cardiac death, myocardial infarction, target lesion revascularization and stroke) as primary outcome and major bleeding outcomes (defined by TIMI or the Bleeding Academic Research Consortium [BARC] criteria) as

secondary outcome both in around 1-year follow-up in every arm.

Quality assessment

Step 7.

Assess the qualities of observational studies by the Newcastle-Ottawa Scale (NOS, evaluation of selection, comparability and outcome) and randomized controlled trials (RCTs) by Jadad Scale (judgment of randomization, double blind, withdrawals and dropouts) respectively.

Statistical analysis

Step 8.

Treat results for endpoint events as dichotomous data. Use risk ratio (RR) and 95% confidence interval (CI) to estimate pooled results from studies. Conduct a Bayesian network meta-analysis in Addis 1.16.8 software by Markov chain Monte Carlo methods, which provides direct and indirect evidence for any given treatments in one joint analysis and a possible ranking distribution of 2 endpoints for all regimens. If 95% CI of inconsistency factors median contains 0 and *p* value of node split model is over 0.05, inconsistent model will be considered not significant. Then use consistent model for further analysis.