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Review

The prevention of statins against AKI and mortality following cardiac surgery: A meta-analysis

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ABSTRACT

Objective: It is universally acknowledged that acute kidney injury (AKI) often comes following cardiac surgery with severe morbidity and mortality. The impact of statins on the incidence of AKI and mortality after cardiac surgery are controversial, therefore, it is urgent to explore the source of heterogeneity via the subgroup analysis.
Methods: We searched PubMed, ISI and Elsevier to May 31st 2016 for studies which investigated the effects of statins relevant to this theme. Statistical analysis was using RevMan5.2 and Stata12.0. The outcomes were the occurrence of AKI and the mortality after cardiac surgery. For the first time, we discussed the source of heterogeneity on the basis of the characters of patients in the following subgroup analysis.
Results: A total of 17 studies with 18,684 statins and 24,033 non-statin users were included. The meta-analysis suggested that statins not only reduced the occurrence of AKI [Odds Ratio (OR) 0.72, 95% Confidence Interval (CI) 0.55–0.94)] in the subjects without high risk factors, also decreased the mortality of the patients suffering AKI (OR 0.40, 95% CI 0.22–0.72).
Conclusion: Patients undergoing cardiac surgery might benefit from statins by reducing the occurrence of AKI and the mortality of the patients suffering AKI.

1. Introduction

It is universal that cardiovascular disease is especially common in the elders and is being the top cause of death. Cardiac surgery, such as elective coronary artery bypass grafting (CABG), valvular heart surgery, and percutaneous coronary intervention (PCI) etc. is being applied more and more extensively [1]. Acute kidney injury (AKI) is the typical complication after cardiac surgery, and is up to approximately 30% of these patients [2], which increases intensive care unit length of stay and the mortality [3]. Surgical, anesthetic and critical care advancements decreased perioperative mortality but have not been confirmed in the reduction of the incidence of AKI, which increased the demand of postoperative renal replacement therapies [4–6] according to the Acute Kidney Injury Network (AKIN) and Risk-Injury-Failure (RIFLE) staging systems [7,8].

It was reported that statins benefited in delaying the incidence of coronary atherosclerosis and patients with CABG in reducing the occurrence of complications [9] and the mortality due to AKI after cardiac surgery [10]. However, the results were controversial [11]. Statins have been demonstrated with anti-inflammatory [12], endothelial stabilizing [13], and pleiotropic roles in potential renal benefits [14].

There were several meta-analyses relevant to this theme having been published in the past few years, of which the conclusions were not all the same. Some articles pointed out that statins fail to reduce AKI after cardiac surgery [15–17]. Nevertheless, the recent study revealed that statins declined the incidence of AKI [18]. There were some obvious limitations in these studies, including missing studies with large sample size [15], not all the studies were based on cardiac surgery [16] and a very small sample size with only 367 subjects [17]. Likewise, the latest article included only 6 studies in the subgroup analysis of AKI [18].

Considering the above mentioned limitations, it was thus necessary to conduct a brand-new analysis including the latest published studies with large sample size. The present meta-analysis firstly explored the characteristics of patients in the subgroup analysis, intending to further understand the effects of statins on the incidence of AKI after cardiac surgery. What's more, this article confirmed the role of statins in reducing the mortality of subjects suffering from AKI.

2. Methods

2.1. Search strategy

We searched PubMed, ISI and Elsevier databases for articles up to May 31st 2016 with comparisons about the occurrence of AKI after

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cardiac surgery and its mortality. The predefined searching key words were "cardiac surgery" or "cardiovascular surgery", "statin" or "HMGCo-Areductase inhibitor", and "acute kidney injury" or "AKI" or "acute renal injury" through keywords searching systems.

2.2. Selection criteria

The including criteria: (a) the original research, (b) articles described the occurrence of AKI with statins after cardiac surgery and its mortality, (c) articles provided exact value of events with Odds Ratio (OR) and 95% Confidence Interval (CI).

2.3. Exclusion criteria

The excluding criteria: (a) the study with differences in dosage or type of statins, (b) systemic review or meta-analysis, (c) studies without exact values.

2.4. Data extraction

Data were extracted independently according to the selection and exclusion criteria. The risk of bias assessment tool created by RevMan 5.2 was conducted according to the following bias domains: selection, performance/detection, attrition, and reporting bias (Fig. 1). Data relevant to the meta-analysis from each study were extracted by two researchers (Minxiong Li and Honghong Zou) separately. In order to avoid omissions of important studies, the authors also searched the references in systemic reviews or meta-analysis articles in terms of this topic, but those studies without exact number of AKI were dropped out. Data extracted from each article includes: the first author's name, year of publication, number of patients, number of AKI, number of death due to AKI, types of cardiac surgery, OR for AKI and mortality. The selection process details are showed in the Fig. 2.

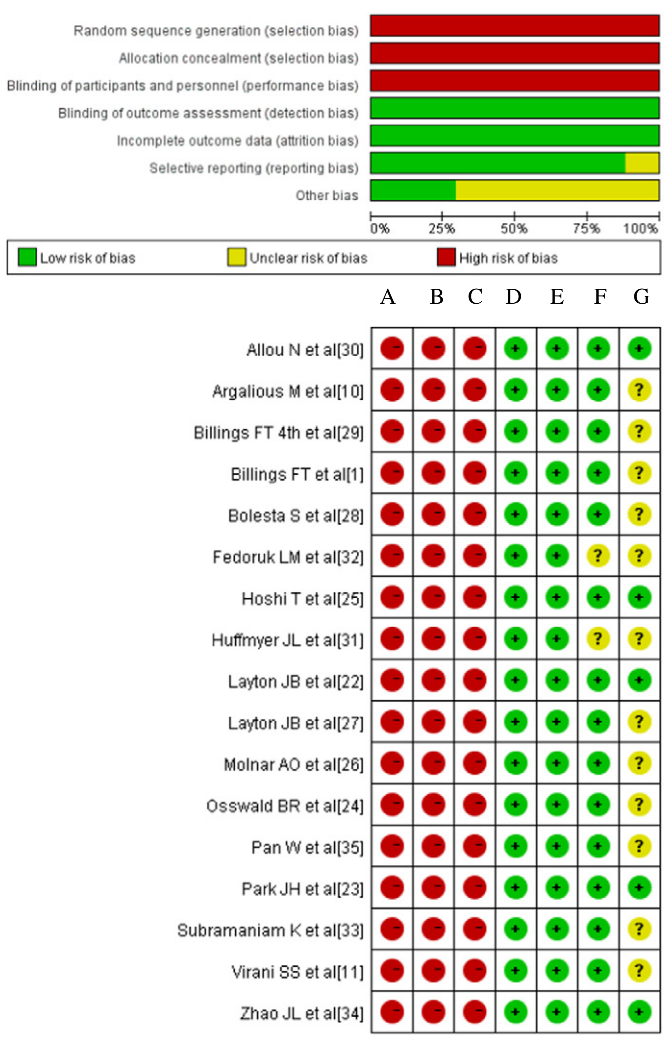

Fig. 1. Risk of bias graph and risk of bias summary (A = random sequence generation; B = allocation concealment; C = blinding of participants and personnel; D = blinding of outcome assessment; E = incomplete outcome data; F = selective reporting; and G = other bias).

2.5. Statistical analysis

Data were analyzed with RevMan 5.2 and Stata12.0. For each study, the adjusted estimated effects expressed as the OR and 95% CI were used and summarized by Forest plots. Q-statistics or I^2-statistics was performed to test for the heterogeneity among the included studies. The standard fixed effects model was selected in the absence of heterogeneity. On the contrary, the random effects model was used. It was reported that drugs taken by the patient might interact with statins to decrease its effectiveness [19,20]. Risk factors for AKI included: elderly, male, diabetes or hypertension, taking diuretics, ACE inhibitor or an angiotensin-receptor blocker and other risk factors such as chronic kidney disease and cardiopulmonary bypass (CPB) use [21]. Subgroup analysis was performed to explore the source of heterogeneity based on the types of patients. Subjects in the statin group of type A were more likely to have risk factors of AKI. Type B was their counterpart. Sensitivity analysis was conducted to test the stability of the results. Eggers' test and Begg's funnel plot were generated to assess the existence of publication bias and examine the differences in the studies.

3. Results

3.1. Characteristics of included studies

17 articles [1,10,11,21–34] with a total of 42,717 subjects (18,684 statin and 24,033 non-statin users) were eventually identified according to the search strategy, the inclusion and exclusion criteria (Table 1). All the included studies displayed the occurrence of AKI after cardiac surgery, and six of which also recorded the mortality due to AKI [10,21,25,31,32,34]. The characteristics and methodological quality of all the included studies were summarized in Table 1.

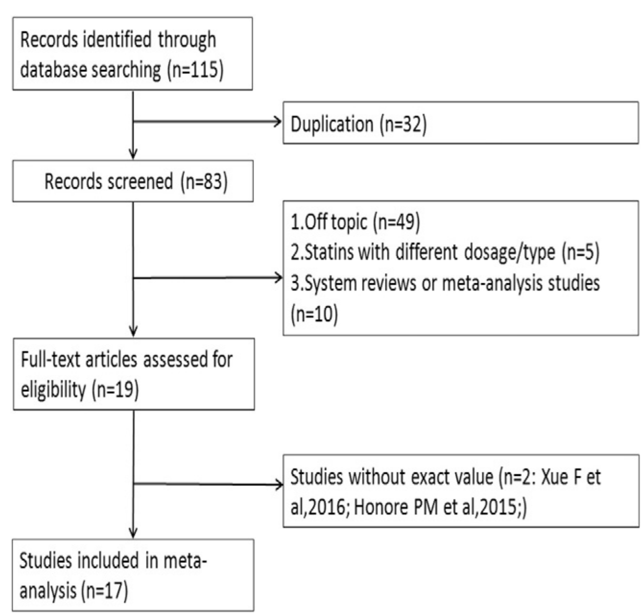

Fig. 2. Flow diagram representing the selection process.