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Citation

Oliveri, F., Meretta, A., Schaerli, N., Montero-Cabezas, J., & Jukema, J. W. (2024). Statin pretreatment and cardiac surgery: end of a myth? *Journal Of Cardiovascular Medicine*, 25(2), 176-177. doi:10.2459/JCM.0000000000001584

Version: Not Applicable (or Unknown)

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Note: To cite this publication please use the final published version (if applicable).

Statin pretreatment and cardiac surgery: end of a myth?

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J Cardiovasc Med 2024, 25:176–177

Keywords: atrial fibrillation, postoperative atrial fibrillation, statin and postoperative atrial fibrillation

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Received 10 October 2023 Accepted 8 December 2023

Postoperative atrial fibrillation (POAF) is a threatening complication associated with prolonged hospitalization and increased in-hospital and long-term mortality.¹ Ischaemia–reperfusion causing oxidative stress and inflammation seems to be the cause of POAF.² Statins, known for their pleiotropic cardioprotective and antioxidant actions,³ have garnered interest for their potential in preventing POAF, with some evidence indicating enhanced effects through statin reloading.⁴ Thus, it has been hypothesized that statins might prevent POAF. However, many small randomized controlled trials (RCTs) and meta-analyses have produced varying and conflicting results, posing challenges in forming conclusive insights.⁵ Nevertheless, one of the largest RCTs, the STICS trial, unveiled an unexpectedly elevated risk of acute kidney injury (AKI) in the statin arm without any significant benefit on POAF prevention.⁶ The relatively recent publication of the START-CABG trial has enhanced our understanding of this important topic.⁷ Indeed, our study seeks to compare these RCTs, evaluating the effect of a statin and placebo for POAF prevention and AKI occurrence. Review Manager software (RevMan-5.4) was utilized when a pooled quantity assessment was performed. The odds ratio (OR) for endpoints was pooled using a random-effects model. A two-sided *P*-value of less than 0.05 was considered statistically significant. The Higgins *I*² was used to assess the studies' heterogeneity results.

Overall, the two trials involved 4328 patients.^{6,7} In the START-CABG trial, patients already taking statins received two extra doses or placebo 12 and 2 h before surgery. Conversely, in the STICS trials, patients were randomly selected to receive either rosuvastatin or a

placebo, starting up to 8 days before surgery and continuing for 5 days postsurgery. Our pooling analysis revealed a neutral effect of statins on POAF incidence [OR 0.94; confidence interval (CI): 0.79–1.13; *P*-value 0.5; *I*² 38%]. Notably, the STICS trial unveiled an unexpected elevated risk of AKI in the statin arm. Pooling data with the START-CABG study produced a neutral overall effect (OR 1.15; CI: 0.81–1.63; *P*-value 0.45; *I*² 78%).

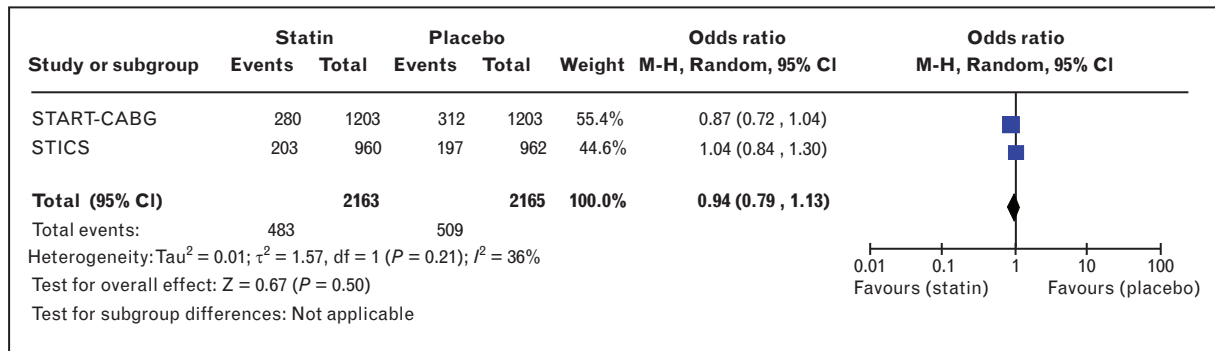
Despite statins' significantly reducing C-reactive protein after cardiac surgery (indicative of potential lowered inflammation),⁷ our pooled analysis failed to reveal a significantly lower risk of POAF. However, the heterogeneity of our results should be considered. To begin with, the STICS trial exclusively utilized a 20-mg dose of rosuvastatin only, whereas the START-CABG study included various types of statins at their highest doses, potentially affecting the heterogeneity of POAF occurrence. Furthermore, there were slight differences in the patient populations studied; whereas START-CABG focused exclusively on patients slated for coronary artery bypass grafting (CABG), the STICS trial included individuals undergoing both CABG and aortic valve replacement. Again, clinical scenarios also slightly diverged: while START-CABG focused solely on patients scheduled for CABG, STICS involved individuals undergoing both CABG and aortic valve replacement. Lastly, it is worth noting that the two studies took place in different geographic locations: China for STICS and Germany for START-CABG. The potential influence of ethnic and genetic factors on treatment response could further magnify the observed heterogeneity in results.

Our study also revealed no significant difference in the postoperative rate of AKI between both study arms. Our result aligns with the Statin in AKI Cardiac Surgery trial outcomes.⁸ Nevertheless, the STICS trial, which demonstrated a heightened occurrence of postoperative AKI in the Chinese population receiving statin treatment, emphasizes the necessity for a thorough assessment before prescribing statins to Chinese individuals shortly before cardiac surgery.

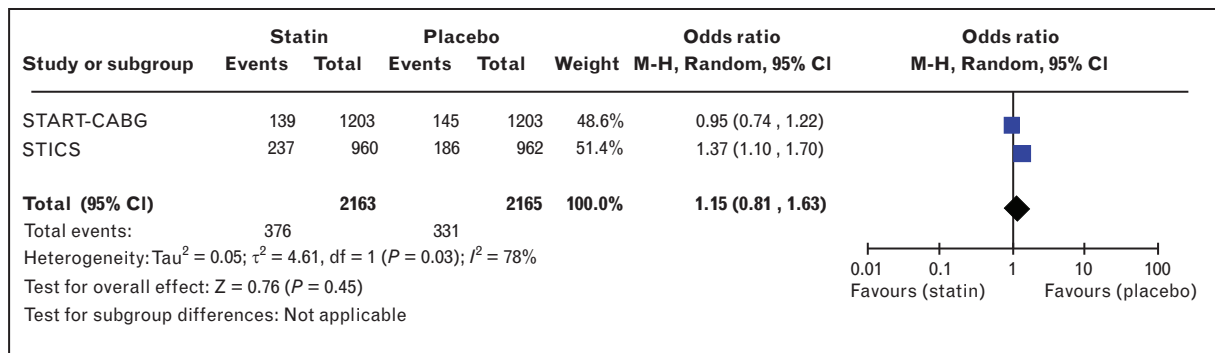
In conclusion, while statin therapy remains pivotal across numerous clinical scenarios, our study indicates its lack of benefit in POAF prevention (Fig. 1).

Fig. 1

(a) POAF



(b) AKI



Forest plots comparing statin to placebo before cardiac surgery. (a) Postoperative atrial fibrillation (POAF); (b) postoperative acute kidney injury (AKI).

Conflicts of interest

The Department of Cardiology of the Leiden University Medical Center received unrestricted research grants from Abbott Vascular, Bayer, Biotronik, Boston Scientific, Edwards Lifesciences, GE Healthcare and Medtronic. J.M.-C. received a research grant from Shockwave Medical and speaker fees from Abiomed, Boston Scientific, and Penumbra Inc. The remaining authors have no conflicts of interest to declare.

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