Still without impact on adverse post-operative outcomes: pre-operative statin therapy in patients undergoing cardiac surgery

With interest we read the systematic review by Liakopoulos et al.1 In their meta-analysis of mainly observational studies, the authors conclude that the early clinical outcome is substantially improved in statin-pre-treated patients. The authors correctly address an unequal distribution of potentially confounding factors among patient groups as a limitation for the correct interpretation of their results. More explicitly, factors such as pre-operative treatment with β-blocker may indeed contribute in a substantial way to the outcome of their meta-analysis. The authors report treatment with β-blocker to be significantly 1.3-fold more frequent in the group of statin-treated patients with \( P < 0.01 \). Just to elucidate the strength of this potential confound, the precise significance level is \( P = 3 \times 10^{-127} \) based on a two-sided Fisher’s exact t-test.

Observational studies underlying this meta-analysis already report and discuss group differences in the underlying risk factors and their management2–4 as well as group differences in the emergency status of the cardiac surgery5 as significant contributors to an effect on post-operative outcomes. The studies of Ali and Buth6 (weighted with 26.62% in the meta-analysis), Clark et al.7 (18.04%) and Powell et al.8 (11.27%) statistically adjusted their odds ratios (ORs) for the respective confounds. Ali and Buth reported an unadjusted reduction in an early, all-cause mortality of \( OR = 0.50 \) (95% confidence interval (CI) = 0.38–0.67, \( P = 0.0001 \)), but an adjusted non-significant OR of 0.9 (95% CI = 0.6–1.2, \( P = 0.36 \)). Clark et al. calculate an adjusted OR of 0.55 (95% CI: 0.32–0.93) compared with an unadjusted OR of 0.43 (95% CI: 0.28–0.66) and Powell et al. reported an unadjusted OR of 0.62 (95% CI: 0.40–0.96) but a non-significant adjusted OR of 0.83 (95% CI: 0.50–1.37, \( P = 0.46 \)). Especially the studies of Ali and Buth and Powell et al. demonstrate the uncertainty of the statistical significance of pre-operative statin treatment on clinical outcomes using unadjusted data.

According to the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies,5 indication of statistical uncertainty of findings has to be presented within the result section of a meta-analysis. In the meta-analysis by Liakopoulos et al., it would therefore have been necessary to report the discrepancy between the unadjusted data that have been used in their analysis and the adjusted data of the original contributions.

Most importantly, in this particular case, a proper meta-analysis would have required complete raw data sets including information about all relevant confounding variables. This will not be possible for the topic of pre-operative statin treatment, because the original contributions largely differ in the number and type of confounding variables adjusted for.

Clinically relevant conclusions may, therefore, rely on the convincing negative outcomes of the study of Ali and Buth until randomized controlled trials may show a beneficial effect of pre-operative statin therapy on early post-operative adverse outcomes in cardiac surgery patients.

References


Letters to the Editor


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Still without impact on adverse post-operative outcomes: pre-operative statin therapy in patients undergoing cardiac surgery: reply

We appreciate the authors’ comments and thank them for emphasizing several limitations that must be considered for accurate interpretation of the reported statin treatment effects in our systematic review. As correctly stated in their comment, our analysis identified an unequal distribution of potentially confounding factors among patient groups, including a significantly higher prevalence of a β-blocker and aspirin therapy in statin pre-treated patients (\( P < 0.001 \)). In large observational trials, the use of both β-blocker and aspirin has been associated with decreased mortality and morbidity following cardiac surgery.1,2 The importance of this treatment bias with unknown impact on the presented results is highlighted in detail in the limitation section and must be taken seriously into account when interpreting the results of our meta-analysis.

Furthermore, assessment of odds ratios (ORs) was performed after a detailed review and extraction of all available raw data from the included studies. The unadjusted “crude” OR was determined when complete data sets from risk-adjusted treatment groups were not reported in the respective studies. Given the fact that adjustment for covariates and