TITLE
Preoperative inflammatory biomarkers are associated with adverse postoperative events in patients undergoing cardiac surgery: a systematic review and meta-analysis

AUTHORS
Rachel Heo[1, 2], Michael Wang[2, 3, 4], Pascal Meyre[5], Lauren Birchenough[6], Louis Park[6], Kiven Vuoung[7], PJ Devereaux[2, 3], Steffen Blum[5], Bertil Lindahl[8], Gregg Stone[9], David Conen[2, 3, 4]

1. Michael G. DeGroote, School of Medicine, McMaster University, Hamilton, Canada.
2. Population Health Research Institute, McMaster University, Hamilton, Canada.
3. Department of Medicine, McMaster University, Hamilton, Canada.
4. Department of Health Research Methods, Evidence & Impact, McMaster University, Hamilton, Canada.
5. Division of Cardiology and Cardiovascular Research Institute Basel, University Hospital Basel, Basel, Switzerland.
6. Faculty of Health Sciences, McMaster University, Hamilton, Canada.
7. Faculty of Health Sciences, Western University, London, Canada.
8. Department of Medical Sciences, Uppsala University and Uppsala Clinical Research Center, Uppsala, Sweden.
9. The Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, USA.

BACKGROUND
Patients undergoing cardiac surgery have a high risk of adverse postoperative outcomes. While inflammation is strongly associated with the occurrence of cardiovascular events in the nonsurgical setting, it is currently unclear whether biomarkers of inflammation measured prior to cardiac surgery are associated with adverse postoperative outcomes. This systematic review and meta-analysis aimed to evaluate these relationships.

METHODS & RESULTS
We searched MEDLINE, EMBASE, and CENTRAL for studies reporting preoperative inflammatory biomarker levels in patients undergoing cardiac surgery. Studies were included if they enrolled ≥100 patients and reported the association between ≥1 preoperative inflammatory biomarker and ≥1 postoperative outcome of interest. Only studies reporting multivariable adjusted data were included. Screening and data extraction was conducted in duplicate. Studies were pooled using random-effects models and reported as summary odds ratios (ORs) of all individual risk estimates comparing the highest versus the lowest biomarker category in each study. We used the I^2 statistic to assess heterogeneity.
Of 12,176 citations identified, 18 studies with 23,862 participants met the eligibility criteria. The average follow-up time was 36.7 months with 11 studies having a follow-up period ≥30 days. Preoperative C-reactive protein (CRP) levels were associated with a higher risk of all-cause mortality (OR 1.49, 95% CI 1.28-1.73, 12 studies), albeit with a high degree of between-study heterogeneity (I^2=88%) (Figure 1). A sensitivity analysis among studies using a high-sensitivity CRP assay yielded similar results (OR 2.00, 95% CI 1.30-3.06, I^2=83%, 7 studies). Higher preoperative CRP levels were associated with greater mortality risk in studies including only isolated coronary artery bypass graft surgery (OR 1.44, 95% CI 1.23-1.68, I^2=89%, 10 studies)

and those including multiple surgery types (OR 2.09, 95% CI 1.25-3.29, I^2=0%, 2 studies). Results were similar for studies with a follow-up period ≥30 days (OR 1.84, 95% CI 1.35, 2.50, I^2=89%, 10 studies). Higher preoperative CRP levels were also associated with a greater risk of major adverse cardiovascular events (OR 1.73, 95% CI 1.34-2.24, I^2=0%, 3 studies). Finally, higher preoperative levels of interleukin-6 (OR 1.36, 95% CI 1.00-1.86; I^2=0%, 2 studies) and fibrinogen (OR 2.39, 95% CI 1.03-5.55, 1 study) were associated with a greater risk of mortality.

CONCLUSIONS

Preoperative inflammatory biomarkers were independently associated with mortality and major adverse cardiovascular outcomes in patients undergoing cardiac surgery. Studies are warranted to determine whether anti-inflammatory therapy may prevent postoperative complications.

FIGURE

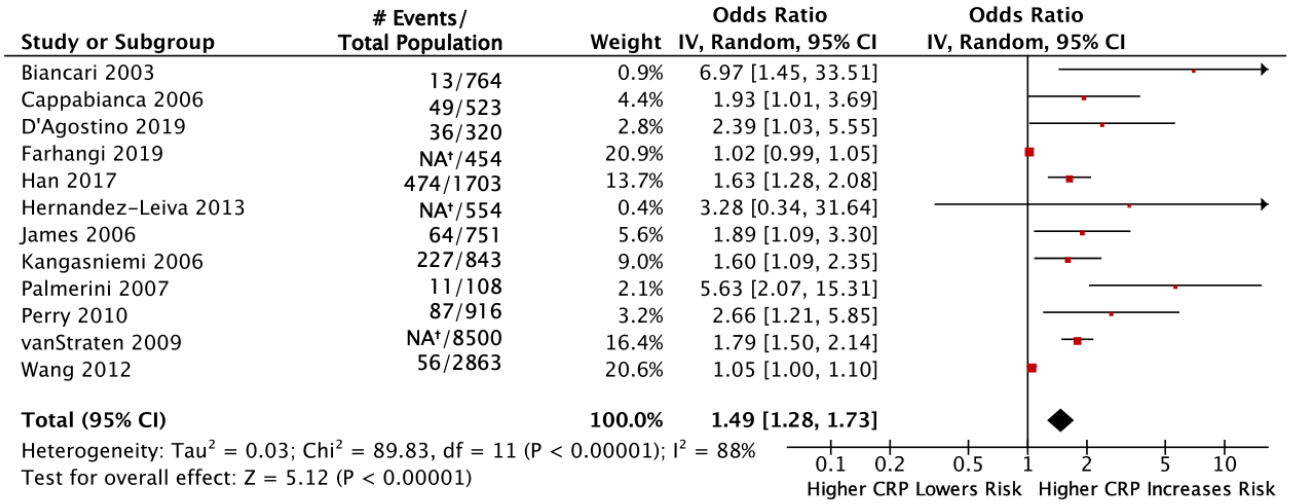

Figure 1. Forest plot of studies demonstrating the association of preoperative CRP and all-cause mortality.
†Raw number of events not reported.