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Age and other perioperative risk factors for postoperative systemic inflammatory response syndrome after cardiac surgery

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Abstract

Background. The inflammatory response to surgery varies considerably between individual patients. Age might be a substantial factor in this variability. Our objective was to examine the association of patient age and other potential risk factors with the occurrence of a postoperative systemic inflammatory response syndrome, during the first 24 h after cardiac surgery.
Methods. This was a retrospective cohort study, using linked data from the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) Database and the Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database. Data from patients who underwent coronary artery bypass grafting and/or valve surgery were used. The association between age and postoperative SIRS was analysed using Poisson regression, and corrected for other risk factors. Restricted cubic splines were used to determine relevant age categories. Results are expressed as risk ratios (RR) with 95% confidence intervals (CI).
Results. Data from 28 513 patients were used. In both univariable and multivariable models, increased patient age was strongly associated with reduced postoperative SIRS prevalence. Using 73–83 yr as the reference category, the RRs (95% CI) for the age categories were 1.38 (1.28–1.49) for ≤43 yr, 1.15 (1.09–1.20) for 44–63 yr, 1.05 (1.00–1.09) for 64–72 yr, and 1.03 (0.94–1.12) for >83 yr, respectively. The predictive value for postoperative SIRS of the final model, however, was moderate (c-statistic: 0.61).
Conclusions. We have demonstrated that advanced patient age is associated with a decreased risk of postoperative SIRS among cardiac surgery patients, where patients aged over 72 yr had the lowest risk.

Key words: cardiac surgical procedures; systemic inflammatory response syndrome

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Editor's key points

- Occurrence of a postoperative systemic inflammatory response can increase risk of adverse outcomes.
- In a retrospective cohort study of 28 513 patients undergoing cardiac surgery, increased age was associated with reduced inflammatory response in the first postoperative day.
- These findings support the concept of reduced acute immune responsiveness with advanced age, and might explain the greater benefit of anti-inflammatory prophylaxis in younger patients undergoing cardiac surgery.

The systemic inflammatory response to cardiac and major non-cardiac surgery is known to vary substantially between individual patients, both at clinical and biochemical levels.[1 2] Patients who develop a more severe systemic inflammatory response, that has the potential to derange and complicate the postoperative course, might have increased risk of adverse outcomes.[3 4] The underlying causes for this variation are likely multifactorial, and are probably a result of genetic and other patient susceptibilities, and the degree of intensity of the perioperative stimuli that activate the systemic immune response.

For many decades, multiple strategies have been used and investigated to prevent, and treat patients with, excessive systemic inflammation after surgery and trauma, and during sepsis. Despite promising clinical experiences with many of these strategies, results of clinical evaluation studies have thus far been largely disappointing,[5–9] with heterogeneous treatment effects throughout study populations. Of particular interest, in a large randomised controlled trial of dexamethasone in cardiac surgery,[5] a predefined subgroup analysis on the effects of steroids on mortality in different age groups indicated benefit in patients <65 yr, but potential harm in patients >80 yr. It has been speculated that this differential effect of dexamethasone could be a result of changes in the intensity of the immune response related to advancing age.[10 11] Younger patients might be able to generate a more intense inflammatory response to surgery compared with elderly patients, and so could receive benefit from anti-inflammatory prophylaxis.

The concept of the potential benefits of more targeted treatment of patients who develop a more severe inflammatory response is further supported by recent findings from studies in severe community-acquired pneumonia.[12 13] It is increasingly recognized that in order to achieve an objectively demonstrable benefit of prophylactic treatment to prevent patients from developing an exaggerated inflammatory response, tools are needed to target treatment more precisely to only those patient groups at highest risk of developing a severe, clinically important SIRS.[5 14] The setting of elective surgery and perioperative medicine provides favourable clinical circumstances for the application of such targeted strategies for anti-inflammatory prophylaxis and treatment.

Using data from a large population of patients undergoing cardiac surgery, we examined the association of patient age and other potential risk factors with occurrence of postoperative systemic inflammatory response syndrome (pSIRS) during the first 24 h after cardiac surgery.

Methods

The study was approved by the Ethics Committee of The Alfred Hospital, Melbourne, Victoria, Australia, and the need for informed consent was waived.

Study cohort

Analyses were carried out using a linked patient dataset from the Australian and New Zealand Intensive Care Society Adult ICU Patient Database (ANZICS-APD), and the Australian and New Zealand Society of Cardiac and Thoracic Surgeons Cardiac Surgery Database (ANZSCTS-CSD), which has been described.[15] The ANZSCTS-CSD was developed in 2001 and includes data from both public and private hospitals. For all cardiac surgical procedures occurring at the participating hospitals (1) patient characteristic data, (2) preoperative, intraoperative, and postoperative data, (3) outcomes and (4) derived scores are recorded. The ANZICS-APD is one of four registries run by the ANZICS Centre for Outcome and Resource Evaluation. The ANZICS-APD contains de-identified patient data on >1.4 million intensive care unit (ICU) admissions from 85% of ICUs in Australia and New Zealand. It contains (1) patient characteristic, (2) diagnostic, and (3) physiologic data from the first 24 h of ICU admission for calculation of severity of illness scores such as the Acute Physiological and Chronic Health Evaluation (APACHE) III score,[16] and can therefore provide information on the immediate postoperative period. Both databases are structurally audited to assess reliability of submitted data.[17–19]

For the current analysis, we included all patients from the linked dataset who underwent coronary artery bypass grafting and/or valve replacement or repair from 2008 to 2013, and who had data recorded in both databases (Fig. 1). Only data from centres that contributed >400 patients to the combined database were used. Patients younger than 18 yr, and patients with unreliable values for BMI (<14 kg m^{-2}), height (<135 cm), or weight (<30 kg), were excluded from the analysis.

Patient involvement

Patients were not involved in the design of this study.

Outcome definition

For this study, postoperative SIRS (p-SIRS) was defined as the presence of any two (or more) SIRS criteria at any time within the first 24 h after cardiac surgery (Supplementary Table S1).[20] We used the original SIRS criteria,[20] but adapted the temperature criterion by using hyperthermia only, as hypothermia in the immediate postoperative period is likely a result of intraoperative cooling during cardiopulmonary bypass and body heat loss after decannulation, rather than a specific sign of SIRS.

Risk factors

Potential risk factors for p-SIRS were selected from the linked study database based either on a known association between a risk factor and p-SIRS, or on pathophysiologic plausibility of a risk factor's effect on p-SIRS (i.e. generally accepted effects). We were primarily interested in the association of age with p-SIRS. We expected this association to be nonlinear; hence the shape and strength of the multivariable relation between age and p-SIRS were evaluated using a flexible model-fitting approach involving restricted cubic spline functions (by visual inspection of plots and assessment of model fit) and fractional polynomials. Based on the observed knots in these functions, five age categories were defined for the final modelling approach.[21 22] Besides patient age, multiple other preoperative and intraoperative risk factors were included in the multivariable model (given in Table 1).