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Clinical Investigation

CLINICAL INVESTIGATION

Randomized trial of near-infrared spectroscopy for personalized optimization of cerebral tissue oxygenation during cardiac surgery

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Abstract

Background. We assessed whether a near-infrared spectroscopy (NIRS)-based algorithm for the personalized optimization of cerebral oxygenation during cardiopulmonary bypass combined with a restrictive red cell transfusion threshold would reduce perioperative injury to the brain, heart, and kidneys.

Methods. In a randomized controlled trial, participants in three UK centres were randomized with concealed allocation to a NIRS (INVOS 5100; Medtronic Inc., Minneapolis, MN, USA)-based 'patient-specific' algorithm that included a restrictive red cell transfusion threshold (haematocrit 18%) or to a 'generic' non-NIRS-based algorithm (standard care). The NIRS algorithm aimed to maintain cerebral oxygenation at an absolute value of $>$ 50% or at $>$ 70% of baseline values. The primary outcome for the trial was cognitive function measured up to 3 months postsurgery.

Results. The analysis population comprised eligible randomized patients who underwent valve or combined valve surgery and coronary artery bypass grafts using cardiopulmonary bypass between December 2009 and January 2014 (n=98 patient-specific algorithm; n=106 generic algorithm). There was no difference between the groups for the three core cognitive domains (attention, verbal memory, and motor coordination) or for the non-core domains psychomotor speed and visuo-spatial skills. The NIRS group had higher scores for verbal fluency; mean difference 3.73 (95% confidence interval 1.50, 5.96). Red cell transfusions, biomarkers of brain, kidney, and myocardial injury, adverse events, and health-care costs were similar between the groups.

Conclusions. These results do not support the use of NIRS-based algorithms for the personalized optimization of cerebral oxygenation in adult cardiac surgery.

Clinical trial registration. http://www.controlled-trials.com, ISRCTN 23557269.

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Key words: cardiopulmonary bypass; cerebral oxygenation; cognitive dysfunction; spectroscopy, near-infrared

Editor's key points

- Personalized optimization of cerebral oxygen saturation during cardiac surgery may reduce perioperative neuronal injury.
- One manoeuvre for optimization is blood transfusion, which poses its own risks.
- The authors developed an optimization protocol involving a transfusion threshold of haematocrit 18%.
- Cognitive outcomes were similar with this protocol compared with a generic protocol (no near-infrared spectroscopy optimization, haematocrit threshold 23%).

Brain injury occurs in up to 40% of patients undergoing cardiac surgery with cardiopulmonary bypass (CPB), where it contributes to morbidity, mortality, and the increased use of healthcare resources.[1] This has been attributed in part to cerebral hypoperfusion and hypoxia caused by non-physiological blood flow during CPB, often in the presence of diseases that result in abnormal autoregulation.[2 3]

Near-infrared spectroscopy (NIRS) is a non-invasive method for the measurement of regional cerebral oxygenation and has been shown to reflect cerebral mixed venous oxygen saturations in cardiac surgery patients.[4] It has been hypothesized that personalized goal-directed interventions directed towards increasing regional brain oxygen saturation as measured by NIRS during CPB might lead to reductions in brain injury[4] or reductions in injury to other organs, including the heart and kidneys, as a consequence of improved overall perfusion.[5] It has also been postulated that NIRS might be used to personalize transfusion decisions, whereby red cell transfusions are used as one component of a patient-specific algorithm designed to optimize tissue oxygenation.[6]

To test these hypotheses and to address clinical uncertainty regarding the benefits of NIRS-based algorithms[7] reflected by variability in their use,[8] we performed a multicentre randomized controlled trial comparing a personalized goal-directed NIRS-based algorithm that incorporated a restrictive red cell transfusion threshold *vs* standard care in adult patients undergoing heart valve surgery with or without coronary artery bypass grafting (CABG). The primary outcome for the trial was cognitive function measured up to 3 months postsurgery. Secondary outcomes included biomarkers of brain, kidney, and myocardial injury, adverse events, and resource use.

Methods

Trial design and participants

The effects of patient-specific cerebral oxygenation monitoring as part of an algorithm to reduce red cell transfusion in patients having heart valve surgery (PASPORT) trial (registration ISRCTN 23557269 on February 27, 2009) was a parallel-group randomized controlled trial conducted at three cardiac surgery centres in the UK. Male and female adult patients undergoing open valve or combined CABG and open valve surgery were eligible. Exclusions, listed in Supplementary material Table S1, included patients with pre-existing neurological disease or inflammatory states. Participants provided written informed consent before surgery but became eligible for randomization only if they scored ≥24 on the Mini Mental State Examination (indicating no cognitive impairment). The allocated intervention was applied during CPB. Participants were followed up until discharge and at 6 weeks and 3 months after randomization. The trial complied with the Declaration of Helsinki. A UK National Health Service (NHS) Research Ethics Committee (REC) approved the study (09/H0102/13) on June 15, 2009. A detailed protocol has been reported elsewhere.[9] University Hospitals Bristol NHS Trust was the trial sponsor. Changes to the trial after commencement are described in the Supplementary material.

Randomization and blinding

Participants were randomly allocated to either the 'generic' or 'patient-specific' algorithms for optimizing tissue oxygenation during CPB in a 1:1 ratio, stratified by centre and surgical procedure (valve only or combined CABG and valve). Allocations, blocked with varying block sizes, were generated by computer and concealed using a secure password-protected internet-based randomization system. Randomization occurred before surgery after written informed consent was given and eligibility confirmed and as close to the planned surgery time as possible. Patients and outcome assessors were blinded to group allocation.

Interventions

The trial compared two algorithms for optimizing tissue oxygenation during CPB, generic and patient-specific algorithms. The interventions were defined as follows.

Generic algorithm (including a standard transfusion threshold)

This was a generic algorithm for optimizing tissue oxygenation based on global measures of oxygen utilization and including a predefined intraoperative haematocrit transfusion threshold of 23%.

Patient-specific algorithm (including a restrictive transfusion threshold)

This was a patient-specific, goal-directed algorithm based on the monitoring and optimization of regional cerebral oxygen saturation measured using the INVOS 5000 NIRS device (Somanetics, IN, USA), combined with a predefined 'restrictive' intraoperative haematocrit transfusion threshold of 18%. Optimization of cerebral oxygenation used a modified Murkin protocol[10] (see Supplementary Table S2) that aimed to maintain INVOS values at an absolute value of >50% or at >70% of baseline values obtained in the anaesthetic room before induction whilst breathing room air. If target cerebral oxygenation values were not achieved by modifying aspects of pump flow, gas exchange, or depth of anaesthesia as specified in the algorithm, red cells could be transfused above the 18% haematocrit threshold.

Details of perioperative care protocols, monitoring of protocol compliance, blinding of clinical staff, and other steps to mitigate bias are described in the Supplementary material.