Postoperative cognitive dysfunction (POCD) following coronary artery bypass grafting has a negative impact on patients physically and psychologically. Of increasing interest is the role that cerebral autoregulation plays in postoperative neurologic outcomes. We sought evidence examining the usefulness of cerebral oximetry data in preventing POCD. Three hundred eighty potential evidence sources were located. Twelve evidence sources (8 randomized controlled trials, 2 retrospective reviews, and 2 prospective cohort studies with a retrospective cohort control) met inclusion criteria. Although the neurologic assessment tools, desaturation definitions, and interventional protocols varied, strong statistical significance links the use of cerebral oximetry information to the prevention of POCD.

Keywords: Cerebral oximetry, interventional protocols, postoperative cognitive dysfunction.

Postoperative cognitive dysfunction (POCD) is a poorly understood yet potentially devastating event. A wide variety of factors, both patient- and procedure-related, have been suggested to influence POCD. Identifying preventive measures could greatly improve patient morbidity. Optimizing cerebral oxygenation is one example of a preventive measure.

A noninvasive method to monitor cerebral oxygenation and thereby infer cerebral blood flow and regional cerebral tissue saturation is now available. Using cerebral oximetry information to guide intervention may lessen the severity of POCD or prevent it. This systematic review of the literature examines the evidence surrounding the use of cerebral oximetry in preventing POCD in patients undergoing coronary artery bypass grafting (CABG).

Review of the Literature

- History. The first reports of cognitive dysfunction following open heart surgery appeared in the literature in the 1950s. Postoperative cognitive dysfunction is defined as a negative change in cognitive ability following a surgical procedure. For proper diagnosis of POCD, a person’s preoperative and postoperative cognitive test scores from at least 2 different psychometric tools must be compared. The gold standard for a positive diagnosis of POCD is a test score decline of at least 1 standard deviation from preoperative to postoperative score. Thus, patients are compared with their “normal,” not a group norm. Although the exact incidence of POCD is unknown, specific deficits are well documented. Postoperative cognitive changes typically involve memory loss, decreased concentration, and altered psychomotor performance.

Short-term POCD (commonly less than 1 month in duration) is associated with longer hospital stays, an increased need for rehabilitative services, and a slower return to the workforce, all of which economically burdens the healthcare system and negatively affects patients and their family. Longer episodes of POCD (1-3 months’ duration) are associated with early retirement and an increased mortality rate. Understanding the possible pathophysiological causes of POCD could be beneficial in preventing POCD and its consequences.

Historically, POCD was theorized to be caused by exposure to the cardiopulmonary bypass circuit and embolic particles from the surgical field. However, current studies have demonstrated that there is no difference in the occurrence of POCD in patients undergoing surgery on or off cardiopulmonary bypass. Most recently, interest has focused on patient-related risk factors such as advanced age, preexisting diagnosis of dementia, observable abnormalities on magnetic resonance images, or a history of alcohol abuse. Of increasing interest is the role that cerebral autoregulation plays in cerebral perfusion and oxygenation.

Cerebral autoregulation conceptually ranges from 70 to 150 mm Hg mean arterial pressure (MAP). Autoregulation allows cerebral blood flow to increase or decrease based on the need of localized areas of the brain. Factors involved in cerebral autoregulation include oxygen levels, carbon dioxide levels, and serum pH. Outside these ranges, cerebral blood flow theoretically becomes dependent on systemic blood pressure, and the brain is susceptible to ischemia. During cardiopulmonary bypass, a common goal is to maintain MAP around 60 mm Hg. In certain patients, including elderly in-
vivors, hypertensive patients, and those with cerebral vascular disease, 60 mm Hg is commonly thought to be excessively low. In addition, manipulation of the heart before and after bypass often results in hypotension because of altered cardiac output. In the 1990s, Harris et al.10 reported magnetic resonance imaging studies that demonstrated the common occurrence of cerebral edema following cardiac bypass surgery. If cerebral edema is present, the resulting increased intracranial pressure will decrease cerebral perfusion pressure. This decrease in cerebral perfusion pressure provides a second possible pathophysiological cause of altered cerebral oxygenation. Abnormalities in cerebral oxygenation, whether from ischemia or edema, could precipitate POCD.14

Currently, there is no widely available, simple method to directly measure cerebral blood flow or cerebral oxygenation. However, techniques do exist to measure frontal cortical oxygenation using near-infrared spectroscopy (NIRS).3 Cerebral NIRS technology, although similar to pulse oximetry, processes wavelengths between 730 and 810 nm and reflects venous oxygen reserve instead of arterial saturation. In essence, cerebral NIRS data may demonstrate an imbalance between oxygen supply and demand.11 Such an imbalance may indicate insufficient cerebral blood flow, thereby linking cerebral desaturation to POCD. A review of evidence-based literature will help to determine whether the use of cerebral oximetry can assist the anesthesia provider in preventing POCD in patients undergoing CABG.

• The PICO Question. The PICO question12 (patient/problem, intervention, comparison, outcome) guiding the search for evidence was as follows: In patients undergoing CABG (P), does the use of cerebral oximetry (I) help prevent postoperative cognitive dysfunction (O)?

• Search Strategy. The following online databases were searched for relevant evidence from 2000-2014: PubMed (including the related citations tool), The Cochrane Database, and Google Scholar. The level of evidence was appraised based on the method discussed by Melnyk and Fineout-Overholt.13

The inclusion criteria included full-text, English-language articles related to the query that were published in peer-reviewed journals. Evidence was evaluated using the title, abstract, and full text to ensure that the evidence met the inclusion criteria. The query included the following search terms (alone or in combination): coronary artery bypass grafting, cerebral oximetry, and postoperative cognitive dysfunction. An ancestry approach to obtaining references was used.

Results

The search yielded 380 potential sources, and 12 met the inclusion criteria: 8 randomized controlled trials (RCTs),14-21 2 retrospective reviews,22,23 and 2 prospective cohort studies with a retrospective cohort control24,25 (Figure). Subjects were typically 60 to 70 years old with similar demographic characteristics and medical histories. Two RCTs documented statistically significant differences between groups for age14 (P = .017) and history of atrial fibrillation15 (P = .05). Subjects underwent preoperative neurologic testing with a variety of assessment tools, including the Mini-Mental Status Exam (MMSE). Three studies did not preoperatively evaluate subjects but simply recorded postoperative stroke.19,22,24 One study failed to document what type of neurologic assessment tool was used preoperatively.23 All subjects underwent CABG with a general endotracheal anesthetic, standard monitoring, and heparinization. All subjects recovered in an intensive care unit (ICU). Cardiopulmonary bypass itself was not considered an inclusion criterion because its relationship to POCD had already been shown to be noncontributory.

The 8 RCTs14-21 published between 2002 and 2014 evaluated 990 subjects in total (Table). Three RCTs16-18 demonstrated no predictive value between cerebral oximetry and POCD. Although each study observed postoperative cognitive decline in some subjects, statistically significant differences were not observed. Negargar et al.16 examined 48 subjects using only the MMSE 1 day postoperatively. Interestingly, they observed POCD only in subjects who desaturated. In this study, no subjects exhibited cognitive decline without intraoperative desaturation, leading the authors to conclude that cerebral oximetry, although not exhibiting a statistically significant difference, was still “useful.” Studies by Reents et al.17 and Kok et al.18 were well blinded and randomized but were both underpowered, which may have contributed to a lack of statistical significance.

The remaining 5 RCTs14,15,19-21 documented statistically significant evidence relating cerebral oximetry desaturation data to POCD. These studies included a total of 832 subjects. Murkin et al.19 noted 6 subjects in the control group who had prolonged desaturations, which correlated to more frequent morbidity and mortality (including stroke); in contrast, no subjects in the treatment group experienced prolonged desaturation (P = .014). Slater and colleagues15 suggested that a cerebral desaturation threshold below 50% was associated with a “significantly” higher risk of POCD before discharge (P = .024). In addition, prolonged desaturations were linked to increased hospital stays (P = .007). In a study by de Tournay-Jetté and associates,20 POCD developed in almost 81% of subjects. Subjects whose cerebral saturation declined to less than 50% were significantly more likely to have POCD develop (P = .04). This study also documented that deep declines in saturation (> 30% from baseline) were associated with POCD lasting 1 month postoperatively (P = .03). Although encompassing only 61 patients, the study validated POCD data from similar studies with elderly patients who underwent CABG. In
2013, Mohandas et al\textsuperscript{21} reported a study of 100 subjects. The control group had a significant decline in cerebral oxygenation while on bypass ($P < .001$) and in the amount of time spent in the area under the curve ($P < .0001$). Following neurocognitive assessment, 68% and 44% of control patients demonstrated POCD at 1 week and 3 months, respectively. However, only 2 subjects in the intervention group tested positive for cognitive decline at 1 week, which had resolved by the 3-month follow-up. Most recently, Colak et al\textsuperscript{14} published a study of 200 subjects. Seven days following surgery, subjects who had experienced cerebral desaturation had a 52% occurrence of POCD compared with 28% in the intervention group ($P = .002$).

Retrospective reviews\textsuperscript{22,23} performed in 2009 and 2005 involved a total of 1,132 subjects. Although Schoen et al\textsuperscript{22} found cerebral oximetry to be nonpredictive for POCD, their analysis did document that subjects in the intervention group needed a shorter amount of “high dependency care” and a shorter length of hospitalization ($P < .0001$). The authors’ conclusion was that cerebral oxygenation monitoring is associated with a “relative” improvement. The second retrospective review, published in 2005 by Edmonds\textsuperscript{23} evaluated 332 subjects. Whereas 42% of subjects experienced periods of cerebral hypoxia, neurologically injured patients were far more likely to have experienced cerebral desaturation ($P = .02$) than their uninjured counterparts. Edmonds also reported a decrease in “serious” brain injury from an expected 6.1% to 3.0% ($P = .03$) when using cerebral oximetry monitoring. The final 2 studies\textsuperscript{24,25} were prospective cohort designs with a retrospective cohort as a control. In both studies, the prospective arm implemented cerebral oximetry monitoring; the retrospective cohort underwent CABG before the availability of cerebral oximetry. The studies evaluated a total of 2,921 subjects: 1,478 in the retrospective control groups and 1,443 in the prospective treatment groups. In the study by Goldman and colleagues,\textsuperscript{24} 2.5% of control subjects but only 0.97% of the intervention group ($P < .044$) had permanent intraoperative strokes. Palmberger et al\textsuperscript{25} demonstrated a decrease in the incidence of POCD from 13.3% to 7.3% after introduction of cerebral oximetry monitoring. The authors did mention that the prospective set of subjects underwent a more extensive preoperative workup than did the control group, which could have introduced some bias into their results.\textsuperscript{23}

**Discussion**

Some studies evaluated for this literature review strongly linked cerebral desaturation with POCD. More importantly, the evidence suggests that by treating the cerebral desaturation, POCD is either decreased or prevented altogether.\textsuperscript{14,15,19-21,23-25} Although not reaching statistical significance, results of 2 additional studies led their authors to conclude that cerebral oximetry was useful.\textsuperscript{16,22}

- **Neurologic Assessment.** Any assessment of POCD hinges on the exclusion of patients who have neurologic abnormalities preoperatively. Patients in the RCTs and in the prospective arms of the cohort studies were evaluated preoperatively for cognitive dysfunction. Among the wide variety of assessment tools used (Table), the MMSE was the most commonly used instrument. The MMSE was first described in 1975 and is thought to be clinically relevant and easy to use. Reliability has been proved in a test-retest situation as close as 24 hours apart and as late as 28 days.\textsuperscript{26} Five of the 12 studies included the MMSE. Seven of the 12 studies (See Table) used more than 1 type of assessment to capture greater specificity concerning preoperative psychomotor ability (related to memory, speed, and attention).

- **Interventions.** The studies we examined varied both in the definition of abnormal regional cerebral tissue saturation and in the treatment of the abnormality. Definitions of abnormal cerebral oxygen saturation varied among researchers and often included 2 variables. Several researchers used a 20% to 30% variation from baseline\textsuperscript{14,16,20-21,23} or a nadir of 40% to 50%,\textsuperscript{15,17,22} and 4 researchers further defined “abnormal” as area under the curve in minutes.\textsuperscript{14,18-20} Again, some authors used more than 1 definition of cerebral desaturation.

A variety of interventions exist to elevate cerebral blood flow and improve oxygenation. These interventions include measures that eliminate mechanical obstruction, increase cerebral oxygen delivery, raise MAP and cardiac output, or decrease cerebral oxygen consumption.\textsuperscript{11} Specific interventions may include increasing delivered fraction of inspired oxygen, transfusing packed red blood cells, administration of vasopressors, or increasing PaCO\textsubscript{2}. The choice of intervention or interventions was provider dependent. No evidence-tested interventional protocols...
<table>
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<tr>
<th>Evidence source</th>
<th>N</th>
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<tr>
<td>Reents et al, 2002</td>
<td>50</td>
<td>D2-letter, Halstead-Reitan, Benton visual block design, digit span</td>
<td>1, 3, 6 days</td>
<td>&lt; 25% baseline or &lt; 40%</td>
<td>No statistical significance ($P = .70$)</td>
<td>Well-blinded study, anesthesiologists saw no oximetry data; no interventions made related to rScO2, no power analysis</td>
</tr>
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<td>Goldman et al, 2004</td>
<td>2,279</td>
<td>Documented “stroke”</td>
<td>Not documented</td>
<td>“declined”</td>
<td>Fewer permanent strokes ($P = .044$)</td>
<td>Enrolled patients for 18 months, well powered, intervention group significantly “sicker” than controls, significantly longer postoperative ventilation and hospital stay in control group</td>
</tr>
<tr>
<td>Edmonds, 2005</td>
<td>332</td>
<td>Not documented</td>
<td>Not documented</td>
<td>&lt; 20% baseline</td>
<td>↓ “serious brain injury” ($P = .03$)</td>
<td>Well-powered study, correlated EEG with cerebral oximetry and transcranial Doppler flow, additional intraoperative assessment might limit generalizability</td>
</tr>
<tr>
<td>Murkin et al, 2007</td>
<td>206</td>
<td>Documented “stroke”</td>
<td>Not documented</td>
<td>AUC = 70%</td>
<td>↑ stroke ($P = .014$) and morbidity/mortality in control group vs intervention ($P = .017$)</td>
<td>Well randomized and blinded, adequately powered, used an interventional protocol</td>
</tr>
<tr>
<td>Negargar et al, 2007</td>
<td>48</td>
<td>MMSE</td>
<td>1 day</td>
<td>&lt; 20% baseline</td>
<td>No statistical significance ($P = .26$)</td>
<td>No statistical significance but may have been underpowered (no power analysis), no control group: on-pump compared with off-pump, authors believed cerebral oximetry “useful”</td>
</tr>
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<td>Schoen et al, 2011</td>
<td>800</td>
<td>Documented “stroke”</td>
<td>Not documented</td>
<td>&lt; 50%</td>
<td>↓ rScO2 = more pulmonary complications ($P &lt; .0001$) and “high dependency unit” ($P = .04$)</td>
<td>Hypoperfusion a risk factor for CRRT, not predictive for POCD, authors believed that “higher risk patients” would benefit from cerebral oximetry monitoring</td>
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<td>Slater et al, 2009</td>
<td>265</td>
<td>MMSE, HVLT, grooved pegboard</td>
<td>Before discharge, 3 months</td>
<td>&lt; 50%</td>
<td>A “significant” rScO2 ↓ causes POCD ($P = .024$, OR = 2.22)</td>
<td>Statistically significant results, subjects enrolled over 25 months, well randomized and blinded, had an interventional plan</td>
</tr>
<tr>
<td>de Tourney-Jetté et al, 2011</td>
<td>61</td>
<td>MMSE, Rey Auditory, Rivermead battery</td>
<td>4-7 days, 1 month</td>
<td>&lt; 30% baseline or AUC 50%</td>
<td>rScO2 &lt; 50% ↑ early POCD ($P = .04$), rScO2 &lt; 30% baseline ↑ late POCD ($P = .03$)</td>
<td>Well blinded during neurologic assessment, interventional protocol in place, more severe cerebral desaturation linked to prolonged POCD</td>
</tr>
<tr>
<td>Palmbergen et al, 2012</td>
<td>642</td>
<td>Modified Rankin score, DOS Scale</td>
<td>Before ICU discharge</td>
<td>&lt; 20% baseline</td>
<td>POCD ↓ from 13.3% to 7.3% ($P = .019$, OR = 0.37, 95% CI = 0.16-0.86)</td>
<td>Statistically significant results, no statistical demographic differences, higher risk patients intentionally chosen for prospective arm, noted decreases in ICU and hospital stay, preoperative interventions could have affected outcomes</td>
</tr>
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</table>
Postoperative cognitive dysfunction (POCD) after coronary artery bypass grafting (CABG) surgery can negatively affect patients physically, emotionally, and economically. To date, no protocols have been developed involving neurologic assessment tools, ideal desaturation thresholds, or interventional order. Currently, interventional protocols for cerebral desaturation rely on the anesthesia provider’s choice. A cost-benefit analysis has not been attempted. Despite these concerns, significant evidence exists to support the link between cerebral desaturation and POCD. Multiple studies have shown that attempts to raise cerebral blood flow when desaturation occurs effectively reduces or prevents POCD. Studies have also shown that POCD lengthens hospitalization, extends intubation time, and prolongs ICU stay. Unnecessarily increasing acute care days decreases available resources for other patients and increases healthcare costs.

**Conclusion**

Evidence obtained from future RCTs would be improved if a universally accepted definition of abnormal regional cerebral tissue saturation were available. Studies evaluating interventional protocols might provide evidence on the efficacy of the interventions and the order in which interventions are best implemented. Providers interested in incorporating the use of cerebral oximetry
into their practice must consider the cost of these devices along with gaps in the current body of knowledge.

REFERENCES


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DISCLOSURES

The authors have declared they have no financial relationships with any commercial interest related to the content of this activity. The authors did not discuss off-label use within the article.