HHS Public Access
Author manuscript
Anesth Analg. Author manuscript; available in PMC 2017 July 13.

Published in final edited form as:
Anesth Analg. 2016 June ; 122(6): 1786–1793. doi:10.1213/ANE.0000000000001275.

A Multicenter Pilot Study Assessing Regional Cerebral Oxygen Desaturation Frequency During Cardiopulmonary Bypass and Responsiveness to an Intervention Algorithm

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Conflict of Interest: See Disclosures at the end of the article.

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DISCLOSURES

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Conflicts: Balachundhar Subramanian reported no conflicts of interest.
Attestation: Balachundhar Subramanian has seen the original study data, reviewed the analysis of the data, and is the author responsible for archiving the study files.
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Conflicts: Gayane Yenokyan reported no conflicts of interest. **Attestation:** Gayane Yenokyan has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files. **Name:** Charles W. Hogue, MD.
Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Conflicts: Charles W. Hogue consulted for Covidien and received research funding from Covidien.
Attestation: Charles W. Hogue has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

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Abstract

BACKGROUND—The purpose of this multicenter pilot study was to: (1) determine the frequency of regional cerebral oxygen saturation ($rSco_2$) desaturations during cardiac surgery involving cardiopulmonary bypass (CPB); (2) evaluate the accuracy of clinician-identified $rSco_2$ desaturations compared with those recorded continuously during surgery by the near-infrared spectroscopy (NIRS) monitor; and (3) assess the effectiveness of an intervention algorithm for reversing $rSco_2$ desaturations.

METHODS—Two hundred thirty-five patients undergoing coronary artery bypass graft and/or valvular surgery were enrolled at 8 US centers in this prospective observational study. NIRS (Invos™ 5100C; Covidien) was used to monitor $rSco_2$ during surgery. The frequency and magnitude of $rSco_2$ decrements >20% from preanesthesia baseline were documented, and the efficacy of a standard treatment algorithm for correcting $rSco_2$ was determined. The data from the NIRS monitor were downloaded at the conclusion of surgery and sent to the coordinating center where the number of clinician-identified $rSco_2$ desaturation events was compared with the number detected by the NIRS monitor.

RESULTS—The average $rSco_2$ obtained at baseline (mean ± SD, 61% ± 11%; 99% confidence interval, 57%–65%) and during CPB (62% ± 14%; 57%–67%) was not different. However, $rSco_2$ after separation from CPB (56% ± 11%; 53%–60%) was lower than measurements at baseline and during CPB ($P < 0.001$). During CPB, $rSco_2$ desaturations occurred in 61% (99% confidence interval, 50%–75%) of patients. The area under the curve for product of magnitude and duration of the $rSco_2$ was (mean ± SD, 145.2; 384.8% × min). Clinicians identified all patients with an $rSco_2$ desaturation but identified only 340 (89.5%) of the 380 total desaturation events. Of the 340 clinician-identified $rSco_2$ desaturation events, 115 resolved with usual clinical care before implementation of the treatment algorithm. For the remaining 225 events, the treatment algorithm resulted in resolution of the $rSco_2$ desaturation in all but 18 patients.

CONCLUSIONS—This multicenter pilot study found that 50% to 75% of patients undergoing cardiac surgery experience one or more $rSco_2$ desaturations during CPB. Nearly 10% of desaturation events were not identified by clinicians, suggesting that appropriate alarming systems should be adopted to alert clinicians of such events. The intervention algorithm was effective in reversing clinically identified $rSco_2$ desaturations in the majority of events.

Near-infrared spectroscopy (NIRS) is used increasingly during cardiac surgery to monitor regional cerebral oxygen saturation ($rSco_2$) as an indicator of cerebral perfusion adequacy, particularly during cardio-pulmonary bypass (CPB).[1,2] Unlike pulse oximetry, NIRS monitoring does not distinguish arterial from venous blood. Because approximately 70% to 75% of cerebral blood volume is venous blood, $rSco_2$ provides an indicator of O_2 supply versus-demand balance.[3] Case reports and observational studies have linked episodes of $rSco_2$ desaturation during coronary artery bypass graft (CABG) surgery with risk for stroke and postoperative cognitive dysfunction.[1,2] These studies, although, have limitations that confound the ability to interpret whether decrements in $rSco_2$ during surgery are clearly linked with adverse neurologic outcomes.[1,2] Low $rSco_2$ may merely serve as an epiphenomenon identifying patients with cerebral vascular disease or limited cardio-pulmonary reserve who are at high risk of complications.[4] Importantly, limited data are available on the effectiveness of interventions aimed at correcting $rSco_2$ desaturations and whether such interventions lead to improved patient neurologic outcomes.[5–10]

Many clinicians, administrators, and health care payers may desire a higher level of evidence than what is currently available on the benefits of NIRS monitoring before it is adopted for routine use in patients undergoing cardiac surgery. Such evidence would ideally come from multicenter prospective studies that compare the effect of interventions to correct $rSco_2$ desaturations with the effect of current standard of care on the frequency of neurologic complications. As a first step to achieve this goal, in this pilot study, we assembled a group of investigators at 8 US institutions to: (1) determine the frequency of $rSco_2$ desaturations during cardiac surgery with CPB; (2) compare the accuracy of clinician-identified $rSco_2$ desaturations with that of continuous NIRS monitoring during surgery; and (3) assess the effectiveness of an intervention algorithm for reversing $rSco_2$ desaturations. We hypothesized that $rSco_2$ desaturations are frequent during CPB and that a multicenter network of investigators can successfully follow an intervention algorithm and accurately report their data to a central data-coordinating center. As a proof of concept construct, the intent of the study was not to link desaturations or their correction to specific outcomes. However, these data may be of value to clinicians for establishing reference ranges of $rSco_2$ and for evaluating potential interventions for treating $rSco_2$ desaturations.

METHODS

The procedures of this study were approved by The Johns Hopkins Medical Institutions Human Research Review Board. The procedures further met with the approval of the IRBs of 7 other enrolling sites: Beth Israel Deaconess Hospital, Harvard Medical School, Boston, MA; Brigham and Women's Hospital/Cape Cod Hospital, Harvard Medical School, Hyannis, MA; Duke University School of Medicine, Durham, NC; Emory University School of Medicine, Atlanta, GA; Mayo University School of Medicine, Rochester, MN; University of Virginia School of Medicine, Charlottesville, VA; and University of Maryland School of

Medicine, Baltimore, MD. All study procedures were performed only after receiving individual written informed patient consent.

Data Collection and Patient Monitoring

From November 8, 2013, to March 4, 2015, 239 patients were enrolled at the 8 study sites; this analysis focuses on 235 patients with nonmissing demographic and medical history data. Male and female patients were eligible for inclusion if they were >50 years old and undergoing primary or reoperative CABG and/or cardiac valve surgery. Enrolled patients at each research site were assigned a sequential 3-digit study number and a 4-character alpha code. Study data were collected on a paper case report form provided by the coordinating center (The Johns Hopkins University School of Medicine). The collected data included preoperative demographics and medical history. Medical conditions such as hypertension, prior stroke or transient ischemic attack, congestive heart failure, and other diseases were based on diagnosis by the patient's primary medical team.

The patients received institutionally standard anesthesia and surgery care, including direct arterial blood pressure monitoring. Before the induction of general anesthesia, the patients were connected to an NIRS monitor (Invos™ 5100C; Covidien, Boulder, CO). The forehead was cleansed with an alcohol swab, and 2 self-adhesive probes were attached according to manufacturer's guidelines. Baseline $rSco_2$ readings were obtained, while the patients were breathing room air. Nonpulsatile CPB flow was maintained between 2.0 and 2.4 L/min/m^2. The patients were managed with α-stat pH management. There was no standardized algorithm for blood transfusion.

$rSco_2$ Data Collection and Intervention Algorithm

An episode of $rSco_2$ desaturation was defined as a >20% decline from baseline detected from either the right or the left sensor. During surgery, the time of any $rSco_2$ desaturation was recorded on the study data sheet. Management of these $rSco_2$ desaturations followed an algorithm as proposed by Murkin et al.[11] and Denault et al.[12] (Fig. 1). Clinicians and perfusionists were instructed on the study procedures and the treatment algorithm for $rSco_2$ desaturation. They then recorded each sequential intervention and the time when the $rSco_2$ desaturation was corrected. Subsequent $rSco_2$ desaturations were similarly treated and recorded when they occurred. At the conclusion of the surgery, $rSco_2$ data files from the NIRS monitor were downloaded to a USB driver.

Study demographic and other data were recorded onto the case report forms, which was then transferred to an Excel spreadsheet (Microsoft, Inc., Redmond, WA) format. Once completed, the electronic case report form was uploaded onto an Internet, study-specific, encrypted Web site supported by MedDium, Inc. (Bethesda, MD, https://www.meddium.com/). The $rSco_2$ data from the NIRS monitor were also uploaded to the same Web site. Only deidentified data for a patient assigned a study number and alpha code were uploaded. The study data could be reviewed only by authorized personnel at the coordinating center.

Sample Size Calculation and Data Analysis

The primary outcome of this pilot study was the combined frequency of $rSco_2$ desaturations from all enrolling centers. The frequency of this event is not known and was the aim of this study. We sought to enroll 28 patients at each site or a total of 225 patients. We added an additional 14 patients to this sample size as a buffer in case any protocol was incomplete. This sample size was chosen to be similar to that reported by Murkin et al.[11] who observed $rSco_2$ desaturation in 56% of 200 patients. In that study, the interventions to correct the $rSco_2$ desaturations were effective in 80.4% of episodes. Thus, we expected 126 episodes of $rSco_2$ desaturation during surgery in this pilot study.

Demographic, prior medical, and preoperative data are presented as mean ± SD or median (range) for continuous variables and frequencies for categorical variables and compared using 1-way analysis of variance, Kruskal-Wallis, or χ^2 tests across the study sites. Pairwise comparisons after significant overall test were performed considering multiple comparisons using the Tukey method. The overall proportion of desaturation events was estimated for the entire sample and for each site. Ninety-nine percent confidence intervals (CI) are reported for all estimates; they were calculated using generalized linear models with site-specific robust variance estimates to account for potential nonindependence of observations within sites. $rSco_2$ at baseline, the start of CPB, and the end of CPB was summarized and compared using generalized linear model with time (start and end of CPB versus baseline) as the primary independent variable. The model was estimated using generalized estimating equations with exchangeable working correlation structure to account for within-patient correlation of $rSco_2$ levels over time. We evaluated the accuracy of clinician-identified $rSco_2$ desaturations by comparing the number and the frequency of investigator-reported $rSco_2$ saturations to the number recorded continuously by the NIRS monitor during surgery. The severity of $rSco_2$ desaturations was determined as the area under the curve of magnitude and duration of $rSco_2$ desaturations. The latter was determined off-line at the coordinating center from the uploaded $rSco_2$ data. The number and specific type of each sequential intervention for $rSco_2$ desaturation were determined. Compliance with the intervention algorithm for $rSco_2$ desaturation was defined as a clinician's successful correction of each $rSco_2$ desaturation episode identified by retrospective review of the patient's NIRS monitor data file.

RESULTS

Data were successfully collected from 235 patients. The medical and operative characteristics of the enrolled patients are shown in Table 1 and the Supplemental Table 1 (Supplemental Digital Content, http://links.lww.com/AA/B408). There were differences among the enrolling sites in some characteristics, including patient age, race, history of congestive heart failure, type of surgical procedure, and duration of CPB and aortic cross-clamping.

Baseline $rSco_2$ and results obtained during and after separation from CPB are shown in Figure 2. Average baseline $rSco_2$ for the left, right, and the average of the left and right frontal lobes, respectively, were (mean ± SD; 99% CI) 61% ± 11% (57%–65%), 61% ± 12% (58%–65%), and 61% ± 11% (57%–67%). During CPB, the average $rSco_2$ measurements were 62% ± 14% (57%–66%), 62% ± 15% (57%–67%), and 62% ± 14% (57%–67%) for the left, right, and the average of the left and right sides, respectively. After CPB, these results were 56% ± 11% (53%–60%), 56% ± 12% (52%–60%), and 56% ± 11% (53%–60%). The average $rSco_2$ during CPB was no different than baseline ($P = 0.338$), but $rSco_2$ after separation from CPB was lower than that at baseline and that recorded during CPB after adjustment for site ($P < 0.001$). $rSco_2$ values differed among enrolling sites. The average $rSco_2$ was lower at Duke University Hospital than that at the Mayo Clinic before ($P < 0.001$), during ($P = 0.001$), and after CPB ($P = 0.004$). The average $rSco_2$ also was lower at Duke University Hospital than that at The Johns Hopkins Hospital before CPB ($P = 0.001$). Thirty-one (15%; 99% CI, 5%–41%) patients had baseline left-sided $rSco_2$ <50%, and 34 (15%; 99% CI, 6%–37%) had baseline right-sided $rSco_2$ <50%, while breathing room air.

The frequency of $rSco_2$ desaturations during CPB for all patients, as well as that observed at each enrolling site, is shown in Table 2. One or more $rSco_2$ desaturations occurred in 61% (99% CI, 50%–75%) of patients during CPB. A total of 380 desaturation events were detected from data downloaded from the NIRS monitor at the conclusion of surgery. The frequency of desaturation varied among enrolling sites ($P = 0.023$). After adjusting for multiple comparisons, we identified a difference in the frequency of $rSco_2$ desaturation between the Mayo Clinic and Duke ($P = 0.004$), Emory University and the Mayo Clinic ($P = 0.027$), and the Mayo Clinic and the University of Virginia ($P = 0.032$). Clinicians detected all patients with at least 1 $rSco_2$ desaturation during CPB, but they identified 340 (89.5%) of the 380 desaturation events.

The effectiveness of each intervention for reversing $rSco_2$ desaturation is shown in Table 3. There was spontaneous resolution of the desaturation in 115 events. For the remaining 225 events, treating hypotension was the most effective strategy for correcting $rSco_2$ desaturation. Desaturations remained unresolved during CPB in 18 (5%; 99% CI, 3%–10%) of the 340 events. Of the patients with resolved desaturations, 1 intervention was needed in 70 events, 2 interventions in 57 events, 3 interventions in 28, and >3 interventions were needed in 65 events.

DISCUSSION

In this study, we observed that the average $rSco_2$ during CPB was no different from that at baseline. However, average $rSco_2$ decreased after separation from CPB compared with values measured at baseline and during CPB. Desaturation in $rSco_2$ occurred in 61% (99% CI, 50%–75%) of patients. NIRS monitoring recorded 380 desaturation events, of which clinicians identified 340 (89.5%). In all but 5% (99% CI, 3%–10%) of patients, there was either resolution of $rSco_2$ desaturations with usual clinical care or they were corrected by the intervention algorithm.

Many clinicians have embraced $rSco_2$ monitoring as a means for judging the adequacy of cerebral perfusion during CPB in an effort to reduce the risk for adverse neurologic events. Currently, only a low level of evidence supports the use of $rSco_2$ monitoring for this purpose. In a previously published systematic review, our group identified 43 articles involving 6399 patients that evaluated the relationship between $rSco_2$ monitoring and adverse neurologic outcomes after cardiac surgery.[1] The identified citations included 13 case reports and 27 observational studies. These reports provided anecdotal evidence that $rSco_2$ desaturations can be indicative of rare CPB cannula malposition, allowing for timely surgical adjustments. Although the data were not consistent, some observational studies linked $rSco_2$ desaturations during CPB and postoperative cognitive dysfunction or stroke. Interpretation of these studies, however, is confounded by small sample sizes, the use of a limited psychometric testing battery in many of the studies, the lack of patient testing after hospital discharge, use of historical controls, the failure to risk adjust in the data analysis, and the use of monitors from multiple manufacturers.

In our systematic review, we identified 2 studies in which patients were prospectively randomized to an intervention to treat $rSco_2$ desaturations during CPB.[11,13] Poor adherence to the intervention protocol in the study by Slater et al.,[13] however, limits interpretation of those results. Murkin et al.[11] randomly assigned 200 patients undergoing CABG surgery to 2 groups. In one, patients with $rSco_2$ desaturations >30% below baseline were treated with a stepped intervention algorithm. These patients were compared with a control group for whom $rSco_2$ data were collected but not displayed to clinicians. In that study, the patients in the control group had longer $rSco_2$ desaturations ($P = 0.014$), a higher frequency of a composite organ complication end point (death, ventilation >48 hours, stroke, myocardial infarction, return for re-exploration [$P = 0.048$], and longer hospitalization in the intensive care unit [$P=0.029$]) than did patients in the intervention arm. Episodes of $rSco_2$ desaturation were observed in 56 of 100 patients in the intervention group, and the success rate of the $rSco_2$ desaturation intervention was 80.4%. The study by Murkin et al. did not have adequate power to detect a difference in neurologic complications. Moreover, the sample size calculations assumed a complication rate in the control arm of 40%, whereas the observed rate was 30%.

A higher level of evidence than is currently available seems desirable to justify routine $rSco_2$ monitoring for the approximately 600,000 patients who undergo CABG and/or valvular surgery annually in the United States.[14] Its use may be justified given the devastating consequences of stroke and cognitive complications after cardiac surgery, including high costs of care for affected patients. For example, postoperative stroke alone adds an average of 15 days to the length of hospitalization after cardiac surgery, increases hospital costs by > $35,000, and increases the likelihood of discharge to an extended care facility after surgery.[15–17] In this study, we demonstrated the frequency of $rSco_2$ desaturations, the feasibility of multicenter collection of $rSco_2$ monitoring data, and the application of an intervention algorithm for desaturations. These results would be useful in the design of a comparative effectiveness trial that evaluates the cost-benefit relationship of $rSco_2$ monitoring in patients undergoing cardiac surgery.

There is no universal definition of $rSco_2$ desaturation. Widely reported definitions are based largely on older data obtained from patients undergoing carotid endarterectomy surgery. In those studies, decrements in $rSco_2$ between 5% and 20% from baseline or values <50% ipsilateral to carotid artery cross-clamping were associated with reductions in transcranial Doppler–measured cerebral blood flow velocity, electroencephalogram slowing, alterations in somatosensory-evoked potentials, or mental status changes when surgery was performed under regional anesthesia.[1] In this study, we defined $rSco_2$ desaturation as a >20% decline from baseline but did not use a threshold value such as decrements <50%. Many patients have baseline $rSco_2$ <50% that may result from factors other than acute reduction in cerebral oxygenation, such as low cardiac output, pulmonary disease, cerebral vascular disease, and anemia. Indeed, in this study, baseline $rSco_2$ <50% was observed on the left side in 13% of patients and on the right side in 14% of patients, before induction of anesthesia. We observed a baseline averaged $rSco_2$ of 61% ± 11% (99% CI, 57%–65%). In a single-center study of 250 CABG surgery patients, the reported ranges of $rSco_2$ before cardiac surgery varied between 47% and 83%.[5] In a larger prospective study of 1178 patients, preoperative room air $rSco_2$ ranged from 57% to 67% for survivors but 47% to 62% for nonsurvivors after CABG surgery.[4] We did observe differences in the baseline $rSco_2$ value among enrolling sites that might be explained by differences in patient age, race, or preoperative medical conditions among the centers. Differences in the frequency of desaturation and greater responsiveness to interventions in our study compared with those reported by Murkin et al.[11] might be explained, in part, by the different definitions of desaturation (>20% from baseline versus >30% decrement).

In our study, clinicians were not blinded to $rSco_2$ data. We observed that there was resolution of the clinician-identified $rSco_2$ desaturation in 115 (34%) of 340 events with usual clinical care. We did not include a threshold duration in our definition of desaturation. Thus, many of these events with resolution before implementation of the treatment algorithm were likely of short duration. Clinicians might have further intervened with corrective maneuvers (e.g., increasing CPB flow after transient reduction) before institution of the algorithm. Furthermore, our intent was to simulate a usual clinical environment of NIRS monitoring to enhance the external validity of our findings. Thus, we did not specify a protocol for setting the alarms on the NIRS monitor. Regardless, the treatment of hypotension was the most effective intervention at reversing $rSco_2$ desaturations. In the randomized study by Murkin et al., raising blood pressure was effective in 62% of cases, and increasing CPB flow was the second most effective intervention.[18] We did not record which medications were used to raise blood pressure. Drugs with vasoconstrictive properties potentially could influence $rSco_2$ readings indirectly as a result of their effects on the scalp circulation. This potential effect is related to the imprecise subtraction algorithms used by NIRS monitors, whereby light absorption from superficial tissue is subtracted from absorption in deeper tissue to yield frontal lobe $rSco_2$.[1,19,20] Hypothetically, vasoconstriction of scalp blood vessels could reduce $rSco_2$ readings regardless of any benefit of higher blood pressure on cerebral blood flow. However, in this investigation, we observed correction of $rSco_2$ desaturation with raised blood pressure. Regardless of these theoretical concerns, investigations during carotid endarterectomy surgery found that changes in $rSco_2$ were 87.5% sensitive and 100% specific for identifying changes in transcranial Doppler blood flow velocity during selective clamping of the internal carotid artery. At the same time, $rSco_2$ monitoring had 0% sensitivity and specificity for identifying laser Doppler blood flow velocity of the scalp during selective clamping of the external carotid artery.[21]

We observed that 57% (i.e., 193 of 340) of clinician-detected $rSco_2$ desaturations were unilateral. This observation may explain why 3% of desaturation events responded to a repositioning of the head to the midline. Presumably, head position away from the midline might impede cerebral venous return and reduce cerebral perfusion pressure. Malposition of CPB venous or arterial cannulae might also explain some cases of unilateral $rSco_2$ desaturation. Repositioning of CPB cannulae was effective in 8% of cases. The most effective interventions for $rSco_2$ desaturation collectively were those aimed at improving cerebral oxygen delivery included increasing the FIo_2% of gas delivery, avoiding the cerebral vasoconstrictive effects of hypocapnia by decreasing gas flow to the membrane oxygenator (i.e., decreasing "sweep speed"), ensuring appropriate CPB flow, and increasing oxygen-carrying capacity with red blood cell transfusion. These efforts were effective in 55% of desaturation events that were not spontaneously corrected with usual clinical care.

In this study, we did not relate $rSco_2$ desaturations or their treatment to patient outcomes. The small sample size and limited funding available did not permit our team to collect such outcomes. Regardless, this study was meant as a pilot to establish feasibility for performing such a study. Finally, our definition of desaturation did not include the duration that $rSco_2$ was >20% below baseline. Although short and long desaturations were considered equally, we did quantify severity by calculating area under the curve of events.

In conclusion, in this multicenter pilot study, we found that between 50% and 75% of patients undergoing cardiac surgery experience one or more $rSco_2$ desaturations during CPB. Nearly 10% of desaturation events were not identified by clinicians, suggesting that appropriate alarming systems should be adopted to alert clinicians of such events. Acute $rSco_2$ desaturation events either spontaneously corrected with usual clinical care or in response to the intervention algorithm in all but 18 (5%) of 340 clinician-identified events.

Acknowledgments

Funding: Supported, in part, by an unrestricted grant from Covidien, Inc. (Medtronic/Covidien, Boulder, CO), by individual institutional funds, and by National Institutes of Health (NIH) grant R01 94600 to Dr. Hogue. We would like to acknowledge support for the statistical analysis from the National Center for Research Resources and the National Center for Advancing Translational Sciences (NCATS) of the NIH through grant number 1UL-1TR001079.

References

1. Zheng F, Sheinberg R, Yee MS, Ono M, Zheng Y, Hogue CW. Cerebral near-infrared spectroscopy monitoring and neurologic outcomes in adult cardiac surgery patients: a systematic review. Anesth Analg. 2013; 116:663–76. [PubMed: 23267000]
2. Steppan J, Hogue CW Jr. Cerebral and tissue oximetry. Best Pract Res Clin Anaesthesiol. 2014; 28:429–39. [PubMed: 25480772]
3. Bickler PE, Feiner JR, Rollins MD. Factors affecting the performance of 5 cerebral oximeters during hypoxia in healthy volunteers. Anesth Analg. 2013; 117:813–23. [PubMed: 24023027]
4. Heringlake M, Garbers C, Käbler JH, Anderson I, Heinze H, Schön J, Berger KU, Dibbelt L, Sievers HH, Hanke T. Preoperative cerebral oxygen saturation and clinical outcomes in cardiac surgery. Anesthesiology. 2011; 114:58–69. [PubMed: 21178669]
5. Taillefer MC, Denault AY. Cerebral near-infrared spectroscopy in adult heart surgery: systematic review of its clinical efficacy. Can J Anaesth. 2005; 52:79–87. [PubMed: 15625262]
6. Goldman S, Sutter F, Ferdinand F, Trace C. Optimizing intra-operative cerebral oxygen delivery using noninvasive cerebral oximetry decreases the incidence of stroke for cardiac surgical patients. Heart Surg Forum. 2004; 7:E376–81. [PubMed: 15799908]

7. Edmonds HL Jr, Ganzel BL, Austin EH III. Cerebral oximetry for cardiac and vascular surgery. Semin Cardiothorac Vasc Anesth. 2004; 8:147–66. [PubMed: 15248000]
8. Edmonds HL Jr. Protective effect of neuromonitoring during cardiac surgery. Ann N Y Acad Sci. 2005; 1053:12–9. [PubMed: 16179501]
9. Edmonds HL Jr. Pro: all cardiac surgical patients should have intraoperative cerebral oxygenation monitoring. J Cardiothorac Vasc Anesth. 2006; 20:445–9. [PubMed: 16750751]
10. Murkin JM, Arango M. Near-infrared spectroscopy as an index of brain and tissue oxygenation. Br J Anaesth. 2009; 103(suppl 1):i3–13. [PubMed: 20007987]
11. Murkin JM, Adams SJ, Novick RJ, Quantz M, Bainbridge D, Iglesias I, Cleland A, Schaefer B, Irwin B, Fox S. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. Anesth Analg. 2007; 104:51–8. [PubMed: 17179242]
12. Denault A, Deschamps A, Murkin JM. A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy. Semin Cardiothorac Vasc Anesth. 2007; 11:274–81. [PubMed: 18270192]
13. Slater JP, Guarino T, Stack J, Vinod K, Bustami RT, Brown JM III, Rodriguez AL, Magovern CJ, Zaubler T, Freundlich K, Parr GV. Cerebral oxygen desaturation predicts cognitive decline and longer hospital stay after cardiac surgery. Ann Thorac Surg. 2009; 87:36–44. [PubMed: 19101265]
14. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, Ferguson TB, Ford E, Furie K, Gillespie C, Go A, Greenlund K, Haase N, Hailpern S, Ho PM, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott MM, Meigs J, Mozaffarian D, Mussolino M, Nichol G, Roger VL, Rosamond W, Sacco R, Sorlie P, Roger VL, Thom T, Wasserthiel-Smoller S, Wong ND, Wylie-Rosett J. American Heart Association Statistics Committee, Stroke Statistics Subcommittee. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. Circulation. 2010; 121:e46–215. [PubMed: 20019324]
15. Hogue CW Jr, Palin CA, Arrowsmith JE. Cardiopulmonary bypass management and neurologic outcomes: an evidence-based appraisal of current practices. Anesth Analg. 2006; 103:21–37. [PubMed: 16790619]
16. Speir AM, Kasirajan V, Barnett SD, Fonner E Jr. Additive costs of postoperative complications for isolated coronary artery bypass grafting patients in Virginia. Ann Thorac Surg. 2009; 88:40–5. [PubMed: 19559186]
17. Tarakji KG, Sabik JF III, Bhudia SK, Batizy LH, Blackstone EH. Temporal onset, risk factors, and outcomes associated with stroke after coronary artery bypass grafting. JAMA. 2011; 305:381–90. [PubMed: 21266685]
18. Murkin JM, Martzke JS, Buchan AM, Bentley C, Wong CJ. A randomized study of the influence of perfusion technique and pH management strategy in 316 patients undergoing coronary artery bypass surgery. I. Mortality and cardiovascular morbidity. J Thorac Cardiovasc Surg. 1995; 110:340–8. [PubMed: 7637351]
19. Germon TJ, Young AE, Manara AR, Nelson RJ. Extracerebral absorption of near infrared light influences the detection of increased cerebral oxygenation monitored by near infrared spectroscopy. J Neurol Neurosurg Psychiatry. 1995; 58:477–9. [PubMed: 7738560]
20. Davie SN, Grocott HP. Impact of extracranial contamination on regional cerebral oxygen saturation: a comparison of three cerebral oximetry technologies. Anesthesiology. 2012; 116:834–40. [PubMed: 22343469]
21. Al-Rawi PG, Smielewski P, Kirkpatrick PJ. Evaluation of a near-infrared spectrometer (NIRO 300) for the detection of intracranial oxygenation changes in the adult head. Stroke. 2001; 32:2492–500. [PubMed: 11692006]

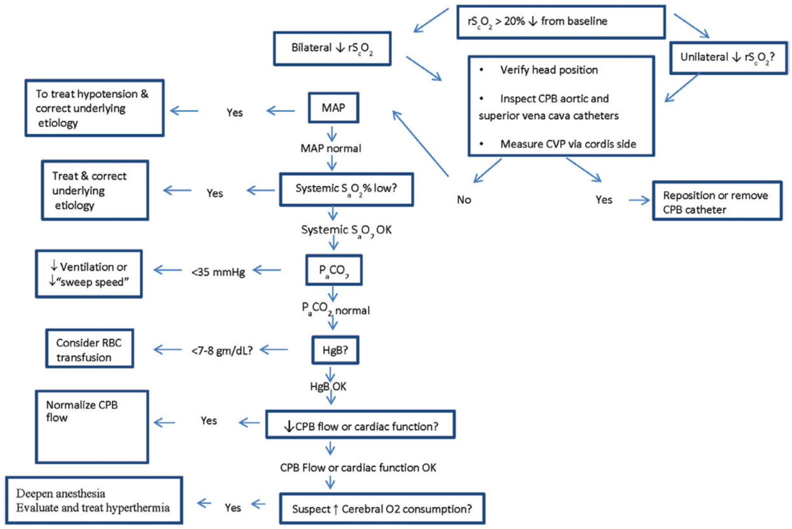

Figure 1.

Treatment algorithm for regional cerebral oxygen saturation ($rSco_2$) desaturations (>20% decline from baseline) during cardiopulmonary bypass. Adopted from Denault et al.[12] CPB = cardiopulmonary bypass; MAP = mean arterial pressure.

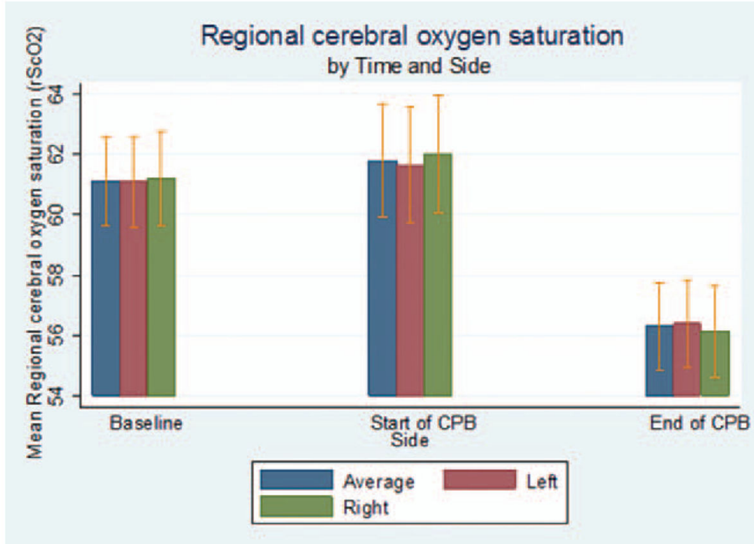

Figure 2.

Regional cerebral oxygen saturation ($rSco_2$) at baseline, the start of cardiopulmonary bypass (CPB), and the end of CPB. The data (mean ± SD) were combined from all enrolling sites.

Table 1

Patients' Medical History and Operative Data

Characteristic	***n* = 235**	***P* value between sites**
Age[a] (y)	68.3 ± 9.1	0.036
Male/female[b]	161 (68.5)/74 (31.5)	0.117
Height[a] (cm)	171.5 ± 9.6	0.792
Weight[a] (kg)	85.6 ± 20	0.043
Race[b]		<0.001
Caucasian	204 (86.8)	
African American	25 (10.6)	
Asian	3 (1.3)	
Prior stroke[b]	17 (7.2)	0.160
Prior transient ischemic attack[b]	11 (4.7)	0.154
Hypertension[b]	180 (76.6)	0.800
Diabetes[b]	72 (30.6)	0.921
Insulin[b]	25 (10.6)	0.922
Chronic obstructive pulmonary disease[b]	31 (13.2)	0.806
Congestive heart failure[b]	63 (26.8)	<0.001
Tobacco smoking[b]		0.414
Current	20 (8.5)	
Former	108 (46.0)	
Atrial fibrillation[b]	49 (20.9)	0.213
Prior myocardial infarction[b]	57 (24.3)	0.249
Medication[b]		
Aspirin	181 (77.0)	0.319
Clopidogrel	30 (12.8)	0.108
Prasugrel	1 (0.4)	
Ticagrelor	3 (1.3)	
Coumadin	19 (8.1)	0.862
β-adrenergic receptor blockers	171 (72.8)	0.081
Angiotensin-converting enzyme inhibitor	78 (33.2)	0.524
Surgical procedure[b]		
CABG surgery	129 (54.9)	0.003
1-vessel	24 (10.2)	0.038
2-vessel	27 (11.5)	
3-vessel	49 (20.9)	
4-vessel	27 (11.5)	
5-vessel	2 (0.9)	
Aortic valve replacement	85 (36.2)	0.777

Characteristic	*n* = 235	*P* value between sites
Mitral valve replacement/repair	61 (26.0)	0.008
Tricuspid valve replacement/repair	13 (5.5)	0.020
Prior cardiac surgery	24 (10.2)	0.006
Duration of CPB (min)[c]	102.0 (31.0–329)	0.002
Duration of aortic cross-clamping (min)[c]	74.0 (0–242)	0.110
Patients at each enrolling site[b]		
Beth Israel Deaconess Hospital	28 (11.9)	
Cape Cod Hospital	28 (11.9)	
Duke University Hospital	28 (11.9)	
Emory University Hospital	28 (11.9)	
Johns Hopkins Hospital	37 (15.7)	
Mayo Clinic	28 (11.9)	
University of Maryland Hospital	30 (12.9)	
University of Virginia	28 (11.9)	

CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass.

[a]Mean ± SD.

[b]Number (%).

[c]Median (range).

Table 2

The Number and Frequency of One or More $rSco_2$ Desaturations (>20% Decline from Baseline) and the Area Under the Curve (AUC) for Cumulative Duration of Desaturations (% × min) Occurring During Cardiopulmonary Bypass

	Total $rSco_2$ desaturations	Unilateral desaturation	Bilateral desaturation	Left AUC[a]	Right AUC[a]	Left and right AUC[a]
Total number of patients with at least one event	138 (61%)	193	187	140.7 (358.0)	149.7 (462.9)	145.2 (384.8)
Beth Israel Deaconess	14 (50%)	20	19	74.3 (164.6)	30.8 (66.6)	52.6 (97.7)
Cape Cod Hospital	15 (54%)	14	13	141.8 (321.9)	138.2 (303.3)	140.0 (308.4)
Duke University	18 (64%)	26	28	106.2 (288.2)	90.0 (134.2)	98.1 (193.4)
Emory University	23 (82%)	31	36	173.2 (281.8)	137.1 (187.9)	155.1 (202.1)
Johns Hopkins	23 (79%)	34	25	199.2 (313.5)	239.4 (459.6)	219.3 (328.3)
Mayo Clinic	12 (43%)	25	19	107.6 (174.6)	71.1 (142.8)	89.4 (156)
University of Maryland	15 (54%)	18	24	219.3 (754)	235.4 (819.7)	227.3 (785.3)
University of Virginia	18 (64%)	25	23	101.1 (218.8)	250.0 (811.1)	175.5 (510.1)

[a]Mean (SD).

$rSco_2$ = Regional cerebral oxygen saturation

Table 3

Efficacy of Interventions to Correct Decrements in Regional Cerebral Oxygen Saturation ($rSco_2$) of >20% from Baseline for the 340 Clinician-Identified Events

	Intervention-corrected $rSco_2$ desaturation
Treat hypotension	67 (29.8%)
Increase Fio_2%	35 (15.6%)
Normalize CPB flow	32 (14.2%)
RBC transfusion	31 (13.8%)
Decrease CPB “Sweep Speed”	25 (11.1%)
Deepen anesthesia	24 (10.7%)
Adjust CPB cannula	18 (8.0%)
Reposition head to midline	6 (2.7%)

There was resolution of 115 desaturation events with usual clinical care and not the treatment algorithm. The data are listed as the number of desaturation of events that were not spontaneously corrected with percentage based on the event effectiveness versus all events that responded to any intervention (n = 225). In 18 (8%) patients, the $rSco_2$ was unresolved despite interventions.

CPB = cardiopulmonary bypass; RBC = red blood cell.