



Systematic review of near-infrared spectroscopy determined cerebral oxygenation during non-cardiac surgery

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Near-infrared spectroscopy (NIRS) is used to monitor regional cerebral oxygenation (rScO₂) during cardiac surgery but is less established during non-cardiac surgery. This systematic review aimed (i) to determine the non-cardiac surgical procedures that provoke a reduction in rScO₂ and (ii) to evaluate whether an intraoperative reduction in rScO₂ influences postoperative outcome. The PubMed and Embase database were searched from inception until April 30, 2013 and inclusion criteria were intraoperative NIRS determined rScO₂ in adult patients undergoing non-cardiac surgery. The type of surgery and number of patients included were recorded. There was included 113 articles and evidence suggests that rScO₂ is reduced during thoracic surgery involving single lung ventilation, major abdominal surgery, hip surgery, and laparoscopic surgery with the patient placed in anti-Tredelenburg's position. Shoulder arthroscopy in the beach chair and carotid endarterectomy with clamped internal carotid artery (ICA) also cause pronounced cerebral desaturation. A >20% reduction in rScO₂ coincides with indices of regional and global cerebral ischemia during carotid endarterectomy. Following thoracic surgery, major orthopedic, and abdominal surgery the occurrence of postoperative cognitive dysfunction (POCD) might be related to intraoperative cerebral desaturation. In conclusion, certain non-cardiac surgical procedures is associated with an increased risk for the occurrence of rScO₂. Evidence for an association between cerebral desaturation and postoperative outcome parameters other than cognitive dysfunction needs to be established.

Keywords: tissue oxygenation, brain, muscle, cerebral cortex, intraoperative monitoring

With the introduction of near infrared spectroscopy (NIRS) for intraoperative evaluation of regional cerebral oxygenation (rScO₂), focus on maintaining cerebral blood flow (CBF) has lead to intervention algorithms to support cardiac stroke volume and central venous oxygen saturation in addition to mean arterial pressure (MAP), arterial hemoglobin O₂ saturation, and arterial carbon dioxide pressure (Bundgaard-Nielsen et al., 2007a). Several commercial NIRS-devices provide for a cerebral oximetry evaluation of rScO₂ reflecting changes in CBF (Madsen and Secher, 1999). During cardiac surgery NIRS is used for anesthetic management of the circulation (Murkin and Arango, 2009) while, as indicated by the number of review papers there is no standard recommendation for the use of NIRS in non-cardiac surgical procedures other than in carotid endarterectomy (CEA; ref. Pennekamp et al., 2009, 2011). In non-cardiac surgery hypotension and in turn a decrease in rScO₂ may arise when the blood loss challenges the central blood volume or when it is compromised during head-up tilt (Madsen et al., 1995) as used for both abdominal and orthopedic surgery. Thus rScO₂ may decrease when pressure is reduced below the lower limit of cerebral autoregulation as during cardiac surgery requiring cardiopulmonary by-pass (Ono et al., 2013). Maintained regional tissue blood flow is, however, important for limiting postoperative complications such as acute kidney failure (Chenitz and Lane-Fall, 2012), wound

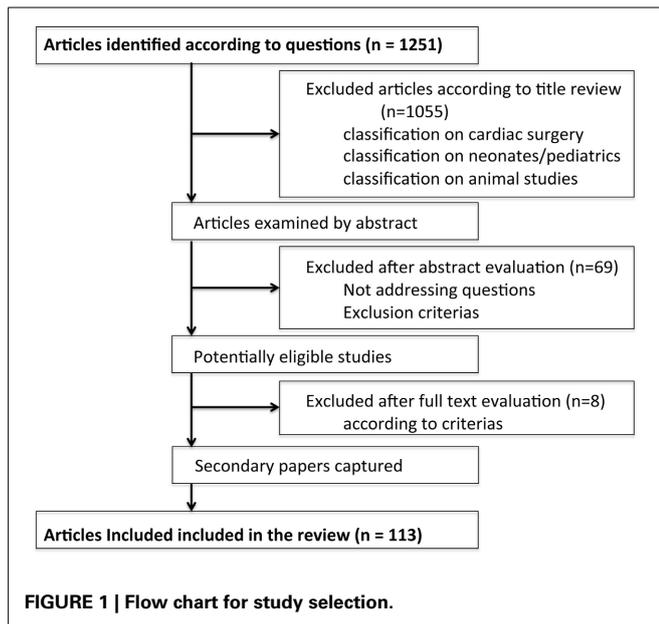
infection (Sørensen, 2012), and cognitive dysfunction (Murkin et al., 2007; Slater et al., 2009) both in cardiac and non-cardiac surgery.

A systematic review was undertaken (i) to determine the non-cardiac surgical procedures that provoke a reduction in rScO₂ and (ii) to evaluate whether an intraoperative reduction in rScO₂ influences postoperative outcome such as cognitive dysfunction. Publications included for the review are presented in a table with inclusion of the surgical speciality, the number of patients included in each article, the NIRS device used, and whether cerebral oxygenation was changed intraoperatively.

METHODS

Relevant publications were found by searching the PubMed and Embase database from inception through April 30, 2013. The search strategy combined the following MeSH (medical subject headings) terms and keywords: (NIRS or NIS or near infrared spectroscopy or oximetry), (oximetry or saturation or oxygenation or desaturation or oxygen), (brain or cerebral or muscle), and (surgery or surgical or perioperative).

Publications were included in the review if they addressed monitoring of tissue oxygenation by NIRS for intraoperative monitoring during non-cardiac and non-head-trauma surgery in adult patients (**Figure 1**). Each title and/or abstract identified was



screened for eligibility. Publications were excluded if they did not include original data (e.g., review, commentary), or if they were not published as a full-length article in a peer-reviewed journal. Non-English articles were also excluded and articles evaluating non-brain tissue only were excluded as well. If articles included animals, pediatric patients or cardiac surgical patients they did not fulfill inclusion criteria and they were therefore not considered eligible for inclusion in the study. Articles reporting changes in rScO₂ before or after surgery were also excluded. Data regarding the number of patients, type of surgery, and type of NIRS for determination of cerebral oxygenation were noted. The articles were grouped according to the predominant surgical procedure.

RESULTS

Figure 1 is a summary of the search with the initial strategy resulting in 1251 citations. According to title review, 1055 papers did not meet the inclusion criteria: 321 papers were on cardiathoracic and/or pediatric/fetal issues, 54 articles addressed studies in animals, and 99 papers were reviews and/or comments predominantly addressing cardiac surgical patients, 67 articles included head-trauma or neurological patients, 149 articles were in non-English language and 145 papers did not address intraoperative issues. In total 196 articles were included for abstract review. Additional 69 abstracts were excluded for not meeting the main inclusion criteria of this review. After full review additional papers were excluded. NIRS results from 113 papers are presented (**Table 1**).

NEUROSURGERY AND SURGERY ON THE SPINE

During neurovascular procedures (aneurysm clipping, bypass procedures, or balloon occlusion testing), rScO₂, and the NIRS-determined concentration of oxygenated hemoglobin (HbO₂) decrease (Calderon-Arnulphi et al., 2007) and rScO₂ reflects the success of surgical resection of a cerebral arterio-venous malformation (Asgari et al., 2003). While induction of anesthesia does

not change brain oxygenation tracheal intubation increases HbO₂ (Paisansathan et al., 2007). In contrast the head up tilted position provokes a decrease in rScO₂ (69 vs. 71%) (Fuchs et al., 2000) and also the NIRS-determined total Hb becomes reduced (Lovell et al., 2000).

MAXILLO-FACIAL-EYE SURGERY AND BREAST SURGERY

Minor reduction in rScO₂ is observed immediately after peribulbar block for eye surgery (Fodale et al., 2006) and with MAP reduced to 60 mmHg during orthognathic surgery rScO₂ decreases 5% (Choi et al., 2008). Such changes do not provoke postoperative cognitive dysfunction (POCD) as determined by a decrease in the minimal mental state examination (MMSE) score =2 points from baseline (Choi et al., 2008).

In patients scheduled for mastectomy induction of anesthesia with subsequent hypotension, rScO₂ increases (from 67 to 72%) to remain stable during surgery (Nissen et al., 2009a, 2010). While ephedrine preserves rScO₂, phenylephrine is reported to decrease rScO₂ 14% (Nissen et al., 2010).

THORACIC SURGERY

During open thoracotomy or thoracoscopy, about half of the patients present at least one rScO₂ value that is lower than 80% of the baseline value (Tobias et al., 2008) and during surgery with single lung ventilation up to 75% of the patients suffer from a more than a 20% decrease in rScO₂ (Hemmerling et al., 2008; Kazan et al., 2009; Tang et al., 2012). Risk factors for a reduction in rScO₂ are age, weight, and ASA class III (Tobias et al., 2008) and the minimum rScO₂ value predicts postoperative complications as evaluated by the Clavien and SOFA scoring systems (Kazan et al., 2009). The exposure time to rScO₂ values below <65% correlates with occurrence of POCD (Tang et al., 2012). This study used MMSE for evaluation of cognitive function before surgery and several days after surgery. A decrease >2 points from baseline was defined as POCD.

SHOULDER SURGERY

During arthroscopic shoulder surgery in the lateral decubitus position, rScO₂ is maintained (Murphy et al., 2010) but when the patient is placed in the beach chair position rScO₂ may decrease (Fischer et al., 2009; Dippmann et al., 2010; Tange et al., 2010; Lee et al., 2011; Yadeau et al., 2011; Jeong et al., 2012; Ko et al., 2012; Moerman et al., 2012; Salazar et al., 2013a,b) with different incidence of intraoperative cerebral desaturation (0 vs. 27%) (Tange et al., 2010; Jeong et al., 2012). The duration of cerebral desaturation episodes range from 1 min to 1 h or longer (Jeong et al., 2012). In the recent study by Salazar et al. (2013a), it is stated that mean maximal desaturation is 32% with each desaturation event lasting an average of 3 min 3 s. Lowered rScO₂ coincides with low MAP (<70 mmHg; 30, 33, 36) and raised MAP restores rScO₂ (Lee et al., 2011). In a case report including one patient it is noted that the α_1 -agonist phenylephrine increases both MAP and rScO₂ (Fischer et al., 2009). Large body mass index is reported to be associated with a reduction in rScO₂ (Salazar et al., 2013a).

The influence of intravenous (propofol) anesthesia vs. inhalational (sevoflurane) anesthesia on rScO₂ has also been evaluated

Table 1 | Studies included in the systematic review grouped in accordance to surgical procedures.

Paper	Patients	Apparatus	Intended tissue	Change in oxygenation
NEUROSURGERY AND SPINE SURGERY				
Asgari et al., 2003	N = 20 Cerebral arteriovenous malformations	Multiscan OS 30	Cortical surface	∧
Calderon-Arnulphi et al., 2007	N = 25 Neurovascular procedures	Oxiplex	Brain	∨
Fuchs et al., 2000	N = 74 Lumbar discectomy Healthy volunteers CEA	INVOS 4100	Frontal lobe	∨
Lovell et al., 2000	N = 20 Micro discectomy Healthy volunteers	NIRO 500	Frontal lobe	∨
Paisansathan et al., 2007	N = 13 Spinal or peripheral nerve surgery	Oxiplex	Frontal lobe	∧
MAXILLO-FACIAL-EYE SURGERY				
Choi et al., 2008	N = 60 Orthognathic surgery	INVOS 5100	Frontal lobe	∨
Fodale	N = 66 Ophthalmic procedures	INVOS 5100B	Frontal lobe	∨
BREAST SURGERY				
Nissen et al., 2009a	N = 71 mastectomy, thyroidectomy or parathyroidectomy	INVOS	Frontal lobe* Skeletal muscle	∧
Nissen et al., 2010	N = 78 Mastectomy, thyroidectomy or parathyroidectomy	INVOS	Frontal lobe*	∨
THORACIC SURGERY				
Tobias et al., 2008	N = 40 Open thoracotomy and thoracoscopy	INVOS 3100A	Frontal lobe	∨
Hemmerling et al., 2008	N = 20 Open thoracotomy	FORE-SIGHT	Frontal lobe	∨
Kazan et al., 2009	N = 50 Thoracic surgery	FORE-SIGHT	Frontal lobe	∨
Tang et al., 2012	N = 76 Thoracic surgery	FORE-SIGHT	Frontal lobe	∨
ORTHOPEDIC SURGERY				
Dippmann et al., 2010	N = 2 Arthroscopic shoulder surgery	INVOS 5100	Frontal lobe	∨
Fischer et al., 2009	N = 1 Arthroscopic shoulder surgery	FORESIGHT	Frontal lobe	∨
Jeong et al., 2012	N = 56 Arthroscopic shoulder surgery	INVOS 5100B	Frontal lobe	∨
Han et al., 2006	N = 56 Major orthopedic surgery	INVOS 4100	Frontal lobe	∨
Lee et al., 2011	N = 28 Arthroscopic shoulder surgery	INVOS 5100	Frontal lobe	∨
Lin et al., 2013	N = 46 Total hip arthroplasty	INVOS 5100B	Frontal lobe	∨
Ko et al., 2012	N = 50 Arthroscopic shoulder surgery	INVOS 5100	Frontal lobe	∨
Moerman et al., 2012	N = 20 Arthroscopic shoulder surgery	INVOS 5100	Frontal lobe	∨
Murphy et al., 2010	N = 124 Arthroscopic shoulder surgery in beach chair and LDP	FORE-SIGHT	Frontal lobe	∨
Papadopoulos et al., 2012	N = 69 Hip fracture repair	INVOS 5100C	Frontal lobe	∨

(Continued)

Table 1 | Continued

Paper	Patients	Apparatus	Intended tissue	Change in oxygenation
Salazar et al., 2013a	N = 51 Arthroscopic shoulder surgery	INVOS 5100	Frontal lobe	✓
Salazar et al., 2013b	N = 50 Arthroscopic shoulder surgery	INVOS 5100	Frontal lobe	✓
Song et al., 2012	N = 28 Total knee replacement	INVOS 5100	Frontal lobe	–
Tange et al., 2010	N = 30 Arthroscopic shoulder surgery	NIRO-200	Frontal lobe	–
Tzimas et al., 2010	N = 1 Hip fracture repair	INVOS 5100	Frontal lobe	^
Yadeau et al., 2011	N = 99 Arthroscopic shoulder surgery	INVOS 5100C	Frontal lobe	✓
Yoshitani et al., 2005	N = 42 Total hip arthroplasty	INVOS 4100	Frontal lobe	✓
UROLOGY				
Bundgaard-Nielsen et al., 2007b	N = 12 Open prostatectomy	INVOS	Frontal lobe Biceps muscle	–
Burkhart et al., 2011	N = 104 Non-epidural major surgery	NIRO-200	Frontal lobe	✓
Kalmar et al., 2012	N = 31 Robot prostatectomy	FORE-SIGHT	Frontal lobe	–
Meng et al., 2012	N = 29 Predominant patients for robot prostatectomy	Oxiplex	Frontal lobe	✓
Meng et al., 2011	N = 14 Predominant patients for robot prostatectomy	Oxiplex	Frontal lobe	✓
Park et al., 2009	N = 32 Robot prostatectomy	INVOS 5100	Frontal lobe	–
GYNECOLOGY				
Berlac and Rasmussen, 2005	N = 38 Caesarean section	INVOS 3100	Frontal lobe	✓
Fassoulaki et al., 2006	N = 44 Hysterectomy	INVOS 3100	Frontal lobe	✓
Kondo et al., 2013	N = 42 Caesarean section	NIRO pulse	Brain	✓
Lee et al., 2006	N = 24 Laparoscopic gynecology	INVOS 4100	Frontal lobe	✓
Morimoto et al., 2000	N = 45 Gynecologic surgery	NIRO-500	Frontal lobe	^
GASTRO-INTESTINAL SURGERY				
Casati et al., 2005	N = 122 Major abdominal surgery	INVOS 4100	Frontal lobe	✓
Casati et al., 2007	N = 60 Major abdominal surgery	INVOS 4100	Frontal lobe	✓
Gipson et al., 2006	N = 70 Laparoscopic herniorrhaphy, cholecystectomy, gastric bypass	INVOS 3100A	Frontal lobe	✓
Green, 2007	N = 46 Major abdominal surgery: whipple, hepatectomy, prostatectomy, cystectomy, aortic aneurysm repair	INVOS	Frontal lobe	✓
Harrison, 2001	N = 13 Surgery for gastrointestinal or gynecological malignancy	INVOS 3100	Frontal lobe	✓
Kitajima et al., 1998	N = 12 Laparoscopic cholecystectomy	NIRO-500	Brain	✓

(Continued)

Table 1 | Continued

Paper	Patients	Apparatus	Intended tissue	Change in oxygenation
Kurukahvecioglu et al., 2008	N = 60 Laparoscopic cholecystectomy	INVOS 5100	Frontal lobe	✓
Madsen et al., 2000	N = 48 Liver transplantation	INVOS 3100	Frontal lobe	✓
Madsen and Secher, 2000	N = 1 Liver transplantation	INVOS 3100	Frontal lobe	✓
Morimoto et al., 2009	N = 20 Laparotomy or laparoscopic surgery	INVOS 3100	Frontal lobe	✓
Nissen et al., 2009b	N = 33 Liver transplantation	INVOS	Frontal lobe	✓
Plachky et al., 2004	N = 16 Liver transplantation	INVOS 3100A	Frontal lobe	✓
Zheng et al., 2012	N = 9 Liver transplantation	INVOS (Somanetics)	Frontal lobe	✓
VASCULAR SURGERY				
Liu et al., 1999 ^{††}	N = 12 AAA patients	INVOS-3100	Frontal lobe	✓
Kuroda et al., 1996a	N = 5 Balloon occlusion test of ICA	OM-100 (Shimadzu Co.)	Frontal lobe	✓
Torella et al., 2002 ^{**}	N = 30 Aortic surgery	INVOS-4100	Frontal lobe Calf muscle	✓
Torella et al., 2003 ^{***}	N = 29 Aortic surgery (n = 21)	INVOS-4100	Frontal lobe Calf muscle	^
Torella and McCollum, 2004 ^{****}	Spinal surgery (n = 8)	INVOS-4100	Frontal lobe Calf muscle	
CAROTID SURGERY				
Ali et al., 2011	N = 10 Aortic surgery	INVOS	Frontal lobe	✓
Beese et al., 1998	N = 49 CEA, LA	INVOS-3100	Frontal lobe	✓
Carlin et al., 1998	N = 137 CEA, GA	INVOS-3100	Frontal lobe	✓
Cho et al., 1998	N = 16 CEA, LA	INVOS-3100A NIRO500 (n = 20)	Frontal lobe	✓
Cuadra et al., 2003	N = 29 CEA, GA	INVOS-4100	Frontal lobe	✓
Duncan et al., 1995	N = 40 CEA, GA	–	Frontal lobe	✓
Duffy et al., 1997	N = 22	INVOS-3100	Frontal lobe	✓
Espenell et al., 2010	N = 72 CEA, GA	FORE-SIGHT	Frontal lobe	✓
Fassiadis et al., 2006	N = 35 CEA, GA	INVOS	Frontal lobe	✓
Fearn et al., 2000	N = 40 CEA, LA	INVOS-3100A	Frontal lobe	✓
Friedell et al., 2008	N = 100 CEA	INVOS	Frontal lobe	✓
Giustiniano et al., 2010	N = 323 CEA, GA	INVOS-5100B	Frontal lobe	✓
Grubhofer et al., 1997	N = 104 CEA, GA	INVOS-3100A	Frontal lobe	✓
Grubhofer et al., 2000	N = 12 CEA, GA	INVOS-3100	Frontal lobe	✓

(Continued)

Table 1 | Continued

Paper	Patients	Apparatus	Intended tissue	Change in oxygenation
Ishigaki et al., 2008	N = 59 CEA, GA	TOS96	Frontal lobe	✓
Kacprzak et al., 2012	N = 41 CEA, GA	Selfconstruct	Frontal lobe	✓
Kawada et al., 2002	N = 16 CEA	TOS	Frontal lobe	✓
Kobayashi et al., 2009	N = 3 Extracranial ICA Aneurysm	TOS96	Frontal lobe	✓
Komoribayashi et al., 2006	N = 171 CEA, GA	TOS96	Frontal lobe	✓
Kragsterman et al., 2004	N = 89 CEA, GA	INVOS4100	Frontal lobe	✓
Kuroda et al., 1996b	N = 62 CEA, GA	OM100/110	Frontal lobe	✓
Laffey et al., 2000	N = 22 CEA, GA	INVOS3100	Frontal lobe	✓
Lee et al., 2008	N = 1 CEA, GA	INVOS4100	Frontal lobe	✓
de Letter et al., 1998	N = 37 CEA, GA	–	Frontal lobe	✓
McCleary et al., 1996	N = 102 CEA, GA	Critikon	Frontal lobe	✓
Manwaring et al., 2010	N = 65 CEA, LA/GA	INVOS	Frontal lobe	✓
Mason et al., 1994	N = 104 CEA, GA	NIRO500	Frontal lobe	✓
Mead et al., 1996	N = 11 CEA, GA	INVOS	Frontal lobe	✓
Matsumoto et al., 2009	N = 16 CEA	INVOS5100	Frontal lobe	✓
Mille et al., 2004	N = 64 CAS, LA	INVOS 3100/4100	Frontal lobe	✓
Moritz et al., 2007	N = 594 CEA, GA	INVOS3100	Frontal lobe	✓
Moritz et al., 2010	N = 48 CEA, LA	INVOS3100	Frontal lobe	✓
Nakamura et al., 2009	N = 96 CEA, LA/GA	INVOS3110A/ OMM2000	Frontal lobe/Global brain	✓
Ogasawara et al., 2003	N = 1 CEA	TOS96	Frontal lobe	✓
Pedrini et al., 2012	N = 50 CEA, GA	INVOS4100	Frontal lobe	✓
Pennekamp et al., 2012a	N = 473 CEA, GA	INVOS	Frontal lobe	✓
Pennekamp et al., 2012b	N = 11 CEA, GA	INVOS	Frontal lobe	✓
Pugliese et al., 2009	N = 151 CEA, GA	INVOS	Frontal lobe	✓
Rigamonti et al., 2005	N = 40 CEA, LA	INVOS4100	Frontal lobe	✓
Ritter et al., 2011	N = 50 CEA, LA	INVOS4100	Frontal lobe	✓

(Continued)

Table 1 | Continued

Paper	Patients	Apparatus	Intended tissue	Change in oxygenation
Samra et al., 1996	N = 83 CEA, LA	INVOS3100	Frontal lobe	✓
Samra et al., 2000	N = 38 CEA, LA	INVOS3100	Frontal lobe	✓
Samra et al., 1999	N = 99 CEA, LA	INVOS3100	Frontal lobe	✓
Sehic and Thomas, 2000	N = 34 CEA, LA	INVOS3100A	Frontal lobe	✓
Shang et al., 2011	N = 1 CEA, GA	DCS flow-oximeter	Frontal lobe	✓
Stilo et al., 2012	N = 11 CEA, GA	INVOS4100	Frontal lobe	✓
Stoneham et al., 2008	N = 100 CEA, LA	INVOS4100	Frontal lobe	✓
Takeda et al., 2000	N = 16 CEA, LA	INVOS3100	Frontal lobe	✓
Tambakis et al., 2011	N = 24 CEA	INVOS4100	Frontal lobe	✓
Uchino et al., 2012	N = 56 CEA, GA	INVOS5100C	Frontal lobe	✓
Vets et al., 2004	N = 20 CEA, GA	NIRS	Frontal lobe	✓
Williams et al., 1999	N = 14 CEA	Critikon2020	Frontal lobe	✓
Yamamoto et al., 2007	N = 45 CEA, LA	OM-220	Frontal lobe	✓
Zogogiannis et al., 2011	N = 43 CEA, GA	INVOS4100	Frontal lobe	✓

For changes in oxygenation during vascular surgical procedures see text for specific results. LA, local anesthesia; GA, general anesthesia. The full papers by Williams et al. (1994a,b,c) could not be retrieved. As these papers are among the first to report rScO₂ in patients undergoing CEA the papers are cited in the text but not in the table.

**Following 30 min acute normovolemic hemodilution decreased tissue oxygenation that reduced the hemoglobin concentration from 14.5 to 10.8 g/dl.

***Increased tissue oxygenation following blood transfusion.

****Reduced tissue oxygenation following blood loss equivalent to 650 ml or 16% of the patients' blood volume.

††Decreased cerebral oxygenation with aortic cross-clamping and following declamping increased oxygenation.

(Jeong et al., 2012). During surgery in the beach chair patients in sevoflurane anesthesia have higher internal jugular venous O₂ saturation (SjvO₂) than patients in propofol anesthesia (minimum SjvO₂ 63 vs. 42%), rScO₂ is similar in the two groups and rScO₂ and SjvO₂ correlate. As MAP also is higher with sevoflurane anesthesia, despite a less frequent use of vasopressors, the authors conclude that sevoflurane anesthesia may be a better choice in patients undergoing surgery in beach chair position (Jeong et al., 2012).

An influence of cerebral desaturation on the occurrence of POCD after shoulder surgery in the beach chair is evaluated by Salazar et al. (2013b). Based on a Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) score the authors conclude that POCD is almost identical in subjects with intraoperative cerebral desaturation compared to those in the cohort who did not (Salazar et al., 2013b). The findings are supported by Moerman et al. (2012) who report that neurological

or cognitive dysfunction does not occur after surgery in the beach chair.

OTHER TYPES OF ORTHOPEDIC SURGERY

Major orthopedic surgery (hip surgery) reduces rScO₂ ≈10% below baseline, with esmolol induced hypotension, rScO₂ becomes even lower (Han et al., 2006) and also the NIRS-determined deoxygenated hemoglobin (Hb) concentration decreases (Yoshitani et al., 2005). During hip fracture repair rScO₂ <50 or 75% of baseline occurs in 38% of patients (Papadopoulos et al., 2012) and rScO₂ decreases independently of the anesthesia used (propofol vs. sevoflurane; ref. Yoshitani et al., 2005). During knee surgery rScO₂ remains stable (Song et al., 2012).

Before surgery neurocognitive dysfunction is associated to low rScO₂ (44%) (Tzimas et al., 2010) and in patients with cerebral desaturation during major orthopedic surgery the occurrence of

POCD is reported to increase (Papadopoulos et al., 2012; Lin et al., 2013). Following surgery for hip fracture, patients with POCD have lower intraoperative rScO₂ (55 vs. 65%) compared to non-POCD patients (Papadopoulos et al., 2012). In this study cognitive function was assessed by the MMSE preoperatively and on the 7th postoperative day and compared to baseline, a reduction of MMSE score by >2 points indicated POCD. Lin et al. (2013) used MMSE, digit span test, digit symbol substitution test, trail making test, verbal fluency test, and word recognition tests and it was noted that in patients with POCD the intraoperative rScO₂ drop (14 vs. 8%) was more marked compared to non-POCD patients (Lin et al., 2013). The authors suggest that an intraoperative decrease in rScO₂ max >11% is to be considered a warning signal for development of POCD (Lin et al., 2013).

UROLOGY

In patients undergoing robotic assisted prostatectomy in the Trendelenburg position rScO₂ is reported to increase (Park et al., 2009; Kalmar et al., 2012). However, the elderly patient may demonstrate profound intraoperative desaturation (to 20% or more below baseline) (Burkhart et al., 2011). Also hemodilution may lower rScO₂ (Bundgaard-Nielsen et al., 2007b) and a reduction in rScO₂ correlates to development of hypotension (Burkhart et al., 2011). The use of phenylephrine to preserve MAP reduces rScO₂ and this effect is intensified by hypocapnia and blunted by hypercapnia (Meng et al., 2012). Importantly, rScO₂ remains unchanged after bolus ephedrine (Meng et al., 2011).

GYNAECOLOGICAL AND OBSTETRIC PROCEDURES

During gynecological laparoscopic procedures in the Trendelenburg position rScO₂ decreases from 66 to 57% with MAP at 80 mmHg (Lee et al., 2006). Different gas anesthesia (desflurane vs. sevoflurane) results in similar rScO₂ values and larger anesthetic depth increases rScO₂ (66 vs. 72%) (Fassoulaki et al., 2006). Also spinal anesthesia reduces rScO₂ (>5%) related to development of hypotension (Berlac and Rasmussen, 2005). The use of hyperbaric rather than isobaric bupivacaine for spinal anesthesia decreases HbO₂ (6 vs. 3 mmol/L) as also hypotension is more severe (Kondo et al., 2013). In contrast, tracheal extubation increases HbO₂ (Morimoto et al., 2000). The authors also demonstrate that compared with a control nicardipine and diltiazem inhibited an increase in MAP and further enhanced the increase in HbO₂ (Morimoto et al., 2000).

In a patient with an intraoperative reduction in rScO₂ to below 50% is reported to be the likely explanation for postoperative headache (Lee et al., 2006).

GASTRO-ABDOMINAL SURGERY

Laparoscopic cholecystectomy in the head-up position is reported to decrease HbO₂ even when MAP is maintained above 80 mmHg (Kitajima et al., 1998) and up to one-fifth of the patients present at least one rScO₂ value of less than 80% of baseline (Gipson et al., 2006). Even in the supine position, rScO₂ tends to be reduced while the head-down position maintains rScO₂ (Harrison, 2001). A lowered rScO₂ can be restored by intermittent sequential compression of the lower extremities (Kurukahvecioglu et al., 2008).

A 15% decrease in rScO₂ correlates with the blood loss (Green, 2007) and in the elderly patient minimum rScO₂ (49 vs. 55%), mean rScO₂ (61 vs. 66%) and area under curve rScO₂ are higher with interventions that improve rScO₂ (Casati et al., 2005). In liver patients high bilirubin (icterus) interfere with NIRS measurements (Madsen et al., 2000), however, an intraoperative decrease in rScO₂ by up to 13% correlates to release of neuron-specific enolase (Plachky et al., 2004). NIRS is also used for investigation of cerebral autoregulation during a liver transplantation (Nissen et al., 2009b; Zheng et al., 2012) and rScO₂ decreases markedly after clamping the caval vein (Plachky et al., 2004).

A possible relationship between intraoperative cerebral desaturation and development of POCD was first described in a case report (Madsen and Secher, 2000). In randomized clinical trial Casati et al. (2005) included a total of 122 patients from 5 participating hospitals randomly allocated to an intervention group (with a NIRS visible and rScO₂ maintained at =75% of preinduction values) or a control group. No differences in MMSE score were observed. However, at the seventh postoperative day those patients of the control group who had intraoperative desaturation showed lower value of MMSE (26 vs. 28) as compared with patients of the treatment group. Patients of the control group who had intraoperative desaturation also showed a longer hospital stay as compared with patients of the treatment group. These findings were confirmed by another study by Casati et al. (2007) and the authors further report that up to one in every four patients demonstrate cerebral desaturation. Furthermore, in patients with postoperative delirium intraoperative rScO₂ is lower compared to patients with no delirium (57 vs. 60%; ref. Morimoto et al., 2009).

VASCULAR SURGERY

Open aortic repair of an abdominal aortic aneurysm affects rScO₂ (Liu et al., 1999) with a reduction in proportion to the blood loss (Torella and McCollum, 2004) and hemodilution (Torella et al., 2002) while blood transfusions increase rScO₂ (Torella et al., 2003). Several report rScO₂ during carotid surgery (Williams et al., 1994a,b,c, 1999; Duncan et al., 1995; Kuroda et al., 1996a; Mead et al., 1996; Samra et al., 1996; Duffy et al., 1997; Beese et al., 1998; Carlin et al., 1998; de Letter et al., 1998; Fearn et al., 2000; Takeda et al., 2000; Kawada et al., 2002; Cuadra et al., 2003; Ogasawara et al., 2003; Vets et al., 2004; Komoribayashi et al., 2006; Yamamoto et al., 2007; Ishigaki et al., 2008; Lee et al., 2008; Stoneham et al., 2008; Kobayashi et al., 2009; Giustiniano et al., 2010; Moritz et al., 2010; Ali et al., 2011; Ritter et al., 2011; Pedrini et al., 2012; Uchino et al., 2012).

During CEA clamping the internal carotid artery (ICA) decreases ipsilateral rScO₂ (Williams et al., 1994a,b,c, 1999; Duncan et al., 1995; Mead et al., 1996; Samra et al., 1996; Duffy et al., 1997; Beese et al., 1998; Carlin et al., 1998; de Letter et al., 1998; Fearn et al., 2000; Takeda et al., 2000; Cuadra et al., 2003; Ogasawara et al., 2003; Vets et al., 2004; Komoribayashi et al., 2006; Yamamoto et al., 2007; Ishigaki et al., 2008; Lee et al., 2008; Stoneham et al., 2008; Kobayashi et al., 2009; Giustiniano et al., 2010; Moritz et al., 2010; Ali et al., 2011; Ritter et al., 2011; Pedrini et al., 2012; Uchino et al., 2012) corresponding to a drop in HbO₂ (Kuroda et al., 1996b; Cho et al., 1998; Shang et al., 2011) and

the contralateral rScO₂ remains largely unchanged (Samra et al., 1999). Clamping the external carotid artery may decrease rScO₂ 1–3% (Kuroda et al., 1996b; Samra et al., 1999; Fearn et al., 2000) and after ICA clamp a decrease in rScO₂ often exceeds 20% (Pedrini et al., 2012). An influence of anatomic irregularities in skull shape and cerebral venous drainage needs to be considered. In a case report it is described that inability to obtain a monitorable signal may be attributed to abnormal frontal sinus ipsilateral to the endarterectomy site (Sehic and Thomas, 2000). Another factor of importance is that diabetic patients are more likely to demonstrate a drop in rScO₂ >20% (Stilo et al., 2012).

With clamped ICA a change in rScO₂ also reflects a change in the transcranial doppler determined cerebral perfusion (Mason et al., 1994; Fearn et al., 2000; Grubhofer et al., 2000; Vets et al., 2004; Fassiadis et al., 2006; Pugliese et al., 2009; Shang et al., 2011) and also in the reperfusion phase changes in rScO₂ correlate to measures of CBF (Ogasawara et al., 2003; Matsumoto et al., 2009). Similarly, rScO₂ correlates to SjvO₂ (Williams et al., 1994b; Grubhofer et al., 1997; Espenell et al., 2010) and a correlation to stump pressure is also reported (Kragsterman et al., 2004; Yamamoto et al., 2007; Lee et al., 2008; Manwaring et al., 2010; Tambakis et al., 2011) so that a low stump (<40 mmHg) results in a large change in rScO₂ (Tambakis et al., 2011) but the relationship might be absent in a large series of patients (Pedrini et al., 2012). rScO₂ and systemic blood pressure correlate, with higher pressures leading to better oxygenation values (Williams et al., 1994c; Ritter et al., 2011). The use of multichannel NIRS with 8 lightsource fibers and 8 detectors providing 24 source-detector pairs supports that following application of ICA cross clamp, HbO₂, and Hb change in the border region between the right middle and posterior cerebral supply areas (Nakamura et al., 2009) with distinct changes in Hb and HbO₂ of the ipsilateral brain cortex (Kacprzak et al., 2012).

Oxygen breathing (Stoneham et al., 2008) and the use of ephedrine (Pennekamp et al., 2012a) increase rScO₂ while it declines following administration of phenylephrine (Pennekamp et al., 2012a). The most effective approach to increase rScO₂ during CEA, however, is to use a shunt (Cuadra et al., 2003; Ali et al., 2011; Ritter et al., 2011; Pedrini et al., 2012). Especially patients with rScO₂ drop >20% require shunting (Ritter et al., 2011; Stilo et al., 2012) and NIRS has a sensitivity of ≈75% and specificity ≈98% of the need for shunting (Ali et al., 2011; Ritter et al., 2011). The criterion for establishing a shunt is (i) a 20% drop in ipsilateral rScO₂ from baseline (Zogogiannis et al., 2011) or (ii) a change in rScO₂ greater than 25% or a delta rScO₂ greater than 20% that is not improved within 3 min by increasing blood pressure (Pedrini et al., 2012), or (iii) a cut-off of 21 or 10% reduction from the baseline (Tambakis et al., 2011). In patients operated under cover of local anesthesia (LA), it is the awake testing procedure that determines when a shunt is needed (Stilo et al., 2012).

Neurological deterioration relates to a decrease in rScO₂ (Williams et al., 1999; Samra et al., 2000; Moritz et al., 2007) and the anesthetic approach might be important (McCleary et al., 1996; Moritz et al., 2010). In symptomatic patients rScO₂ decreases from 63 to 51% compared to a rScO₂ drop from 66 to 61% in non-symptomatic patients (Williams et al., 1999; Samra et al., 2000). About 10% of patients have neurologic changes

after carotid clamping (Moritz et al., 2007). Indices of cerebral ischemia (amplitude transcranial motor evoked potentials, electroencephalographic evaluation, cortical somatosensory evoked potentials) correlate to rScO₂ (Beese et al., 1998; Rigamonti et al., 2005; Uchino et al., 2012) and rScO₂ needs to decrease >10% for cerebral ischemia to be detected by somatosensory evoked potentials (Duffy et al., 1997) or electroencephalography (Friedell et al., 2008).

Importantly, in patients with focal cerebral ischemia with an embolic event in the territory of the middle cerebral artery ipsilateral frontal lobe rScO₂ is unchanged (Laffey et al., 2000). However, a reduction in an ischemic ratio (the lowest rScO₂ value during clamping of the ICA divided by the mean rScO₂ value in the last 2 min before ICA clamping) predicts new neurological deficit following CEA (Kobayashi et al., 2009) and a large decrease in intraoperative rScO₂ reflects a change in cerebral metabolism (Espenell et al., 2010). The cerebral release of matrix metalloproteinase correlates to development of cerebral ischemia as determined by NIRS (Ishigaki et al., 2008). rScO₂ criteria for cerebral ischemia is (i) a rScO₂ drop of 10 index points from a stable baseline (ii) a rScO₂ decrease below an absolute value of 50%, (iii) a relative rScO₂ decrease by 20–25%, and (iv) an interhemispheric rScO₂ difference of >25% (Friedell et al., 2008). Using NIRS during CEA neurological deficit is predicted 5–10 s before the clinical observation of neurological complications (Pugliese et al., 2009).

Postoperative neurological complications may rise following an early drop in rScO₂ by more than 20% (Mille et al., 2004) and rScO₂ reduction of at least 15% relates to neurologic, cardiac or renal postoperative complications (Rigamonti et al., 2005; Giustiniano et al., 2010). Thus a fall of larger than 10% from baseline rScO₂ is dangerous but less than 5% is safe (Takeda et al., 2000). The postoperative cerebral hyperperfusion syndrome (CHS) can also be predicted by the intraoperative change in rScO₂ during clamping and unclamping ICA (Cho et al., 1998; Komoribayashi et al., 2006). After declamping a change in rScO₂ >20% predicts CHS (Pennekamp et al., 2012b) and patients with CHS exhibit a larger increase in rScO₂ (Matsumoto et al., 2009).

DISCUSSION

The present study aimed (i) to determine the non-cardiac surgical procedures that provoke a reduction in rScO₂ and (ii) to evaluate whether an intraoperative reduction in rScO₂ influences postoperative outcome. A literature search was conducted and several articles were reviewed. The Results section provides an overview of different non-cardiac surgical procedures affecting rScO₂ and the included articles representing case reports, observational studies, interventional studies, and randomized clinical trials with inclusion of single patients up to a population of 594 patients. The studies also differ in terms of patient categories, interventions applied and the NIRS device used for the evaluation of rScO₂. Taken the heterogeneous material into consideration the included articles provide answer to the primary aim of the present study. Based on the Results section it is concluded that some but not all non-cardiac surgical procedures may decrease rScO₂. While rScO₂ appears to be maintained in

patients undergoing minor non-cardiac surgery such as mastectomy, rScO₂ is reported to decrease during surgery involving procedures such as the anti-Trendelenburg body position often used for shoulder surgery and laparoscopic surgery. Hip surgery, single lung ventilation in thoracic surgery, and clamped ICA also appear to be associated with a reduction of rScO₂.

Concerning the second aim of the present review, only a limited number of studies report that the occurrence of cerebral desaturation is linked to bad postoperative outcome: (i) a randomized clinical trial including elderly patients for major abdominal surgery suggests that in patients with intraoperative optimization of rScO₂ the occurrence of POCD and length of stay in hospital become reduced, (ii) a study on patients undergoing thoracic surgery reports an association between low rScO₂ and scores of postoperative complications, and (iii) low rScO₂ may predict POCD in patients undergoing thoracic surgery, major orthopedic surgery, and major abdominal surgery. Also in patients undergoing carotid endarterectomy low rScO₂ coincides with measures of bad outcome: indices of cerebral ischemia during surgery and the occurrence of the CHS after surgery. However, pronounced intraoperative cerebral desaturation does not lead to POCD after shoulder surgery in the beach chair. Furthermore, an association between cerebral desaturation and outcome parameters such as acute kidney failure, postoperative wound infection, myocardial infarction remains to be established. So the overall conclusion is that the available evidence points toward an increase in the occurrence of POCD in patients with severe cerebral desaturation under certain types of non-cardiac surgery but more studies are needed to demonstrate a clear association between low rScO₂ and bad postoperative outcome.

In the studies supporting a potential association between rScO₂ and bad postoperative outcome, a 20–25% decline in rScO₂ appears to predict POCD and in accordance to the reviewed articles the recommendation is that in order to prevent reaching this potentially injurious level, a less extreme threshold of perhaps 10% should be an indicator for therapeutic intervention to raise cerebral O₂ saturation. Thus, with a NIRS probe attached to the forehead enables the anesthetist to follow changes in regional CBF changes both in local and global cerebral oxygenation can be monitored. The obtained value for tissue oxygenation reflects a balance between O₂ delivery and extraction measurements. Therefore factors influencing regional blood flow (Madsen and Secher, 1999; Boushel et al., 2001) such as hemoglobin concentration, blood volume, cardiac output, arterial hemoglobin O₂ saturation, and for the brain arterial carbon dioxide pressure (PaCO₂) need to be considered when NIRS is incorporated for clinical evaluations. For most of the studies included in the present review it is not obvious how such factors were controlled.

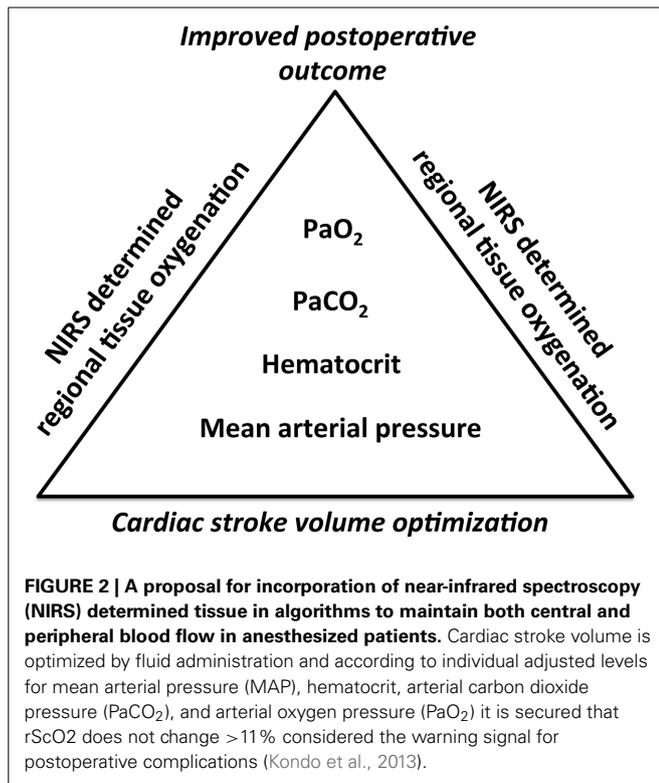
Importantly, an influence from the skin to the NIRS signal is not trivial. The NIRS devices used for clinical purposes provide light absorption into a depth of 3–4 cm. Extra-cranial tissue as indicated by dermal tissue flow, however, appears to contribute as much as 20% to rScO₂, at least with the use of two commonly applied NIRS systems (Sørensen, pers. commun.). For estimation of muscle oxygenation light only needs to traverse skin and subcutaneous tissue that may be 2–3 mm thick (Kjeld et al., 2014) but subcutaneous tissue may, obviously be vast in obese

patients. The penetration depth for light is proportional to the emitter-detector distance (Germon et al., 1999) of importance for light to reach brain tissue. Forehead skin is relatively thin in both adipose and lean patients, but the frontal sinuses in addition to the superior sagittal veins need to be considered (Sehic and Thomas, 2000). Also forehead skin blood flow is supplied with blood from both the internal and external carotid arteries (Hove et al., 2006) and with a headband preventing blood to enter the scalp, the rScO₂ decreases (Davie and Grocott, 2012). This study clearly showed that three different NIRS devices weighed changes in skin flow differently of importance when NIRS is used to guide clinical interventions.

Vasopressor medication and its influence on NIRS deserve attention. Depending on the NIRS device used up to 1/3 of changes in rScO₂ e.g., in response to administration of noradrenaline can be accounted for by change in skin blood flow (Sørensen et al., 2012). Thus, the INVOS cerebral oximeter appears more sensitive to changes in skin blood flow compared to the Foresight cerebral oximeter (Davie and Grocott, 2012). This could explain why ephedrine does not change rScO₂ while strict α -adrenergic receptor stimulation such as treatment with norepinephrine (Brassard et al., 2009) or phenylephrine may decrease rScO₂. In the case with hypotension causing cerebral deoxygenation, however, raised pressure with vasopressor medication may result in increased rScO₂. When a low rScO₂ is the combined effect of hypotension and lowered central blood volume, the use of α_1 -agonists such as phenylephrine may result in further cerebral desaturation due to a possible increase in cardiac afterload. Thus, a low cardiac output appears to influence CBF (van Lieshout et al., 2003) and phenylephrine might exert a different impact on cardiac output depending on preload to the heart (Cannesson et al., 2012). Furthermore, individual α - and β -adrenergic receptor sensitivity might be of importance and related to a genetic polymorphism (Snyder et al., 2006; Rokamp et al., 2013). When a vasopressor is administered the effect on rScO₂ depends on individual factors and the NIRS technology used.

It remains that rScO₂ responds to CO₂ (Madsen and Secher, 1999) implying a contribution from the cerebrum since skin (and muscle) blood flow does not demonstrate “CO₂ reactivity.” For clinical interventions directed to protect rScO₂ it may, however, be less relevant whether the intervention is directed to address flow to the skin or the brain or both as long as the intervention improves postoperative outcome (Casati et al., 2005, 2007; Kazan et al., 2009; Slater et al., 2009; Papadopoulos et al., 2012; Stilo et al., 2012; Tang et al., 2012; Lin et al., 2013) including renal complications (Murkin et al., 2007) and wound infections (Ives et al., 2007). In addition, intraoperative severe cerebral desaturation may provoke postoperative vision loss (Pohl and Cullen, 2005; Roth, 2009). Thus, intraoperative rScO₂ is an index for the systemic circulation reflecting changes in blood flow to other organs than the brain as the skin and kidney (Murkin and Arango, 2009).

Obviously, MAP should not be allowed to decrease to a level below the lower limit of cerebral autoregulation (60 mmHg). However, vasodilatation and reduction in intravascular volume challenge rScO₂. While the spinal anesthesia induced vasodilatation causes only minor cerebral desaturation (Berlac and



Rasmussen, 2005), the decrease in rScO₂ is aggravated when hypotension is pronounced by the use of, e.g., hyperbaric bupivacaine (Kondo et al., 2013). On the other hand, the vasodilatation provoked by GA to minor surgery does not seem to affect rScO₂ (Nissen et al., 2009a) may be because an effect on CBF is outweighed by a reduction in cerebral metabolism. In contrast, when GA is combined with procedures reducing cardiac output such as the anti-Trendelenburg body positions or the use of β -receptor antagonists, rScO₂ decreases even at MAP at 80 mmHg (Lee et al., 2006).

The majority of papers included in this review did not include a measurement of cardiac output but one study did find that rScO₂ decreased 10% as cardiac output was reduced from 5 to 4 L/min (Lee et al., 2006). In addition, the use of phenylephrine reduces rScO₂ secondary to a drop in cardiac output while ephedrine raises MAP without an effect on cardiac output (Meng et al., 2011). Thus, as mentioned vasopressors appear to affect rScO₂ differently and before a vasopressor is used, it seems an advantage that the central blood volume is secured by optimization of, e.g., stroke volume or cardiac output by administration of fluid (Bundgaard-Nielsen et al., 2007b). Such so-called individualized goal directed fluid therapy reduces postoperative complications (Bundgaard-Nielsen et al., 2007a) as is the case for algorithms directed to maintain rScO₂ (Casati et al., 2005; Murkin et al., 2007; Slater et al., 2009). Which of the two recommendations to manage circulation during anesthesia is most profitable remains to be evaluated, but the algorithms used to support the circulation could be combined as illustrated in **Figure 2**. Here it is recommended that management of a patients under GA includes not only NIRS monitoring of the brain but

also a determination of cardiac output that can be derived easily, both non-invasively and invasively from the use of, e.g., model flow technology (van Lieshout et al., 2003).

In conclusion, this review on the use of NIRS to monitor changes in cerebral oxygenation of patients scheduled for non-cardiac surgery indicates that while rScO₂ appears to be maintained in patients undergoing minor non-cardiac surgery such as mastectomy, rScO₂ may decrease during surgery involving procedures such as the anti-Trendelenburg body position often used for shoulder surgery and laparoscopic surgery. Hip surgery, single lung ventilation in thoracic surgery, and clamped ICA also appear to be associated with a reduction of rScO₂. An association of cerebral desaturation to postoperative outcome parameters such as acute kidney failure, postoperative wound infection, and myocardial infarction remains to be evaluated. After certain types of non-cardiac surgery severe cerebral desaturation might be associated with an increase in the occurrence of POCD.

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