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# $O_2$ supplementation to secure the near-infrared spectroscopy determined brain and muscle oxygenation in vascular surgical patients: a presentation of 100 cases

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This study addresses three questions for securing tissue oxygenation in brain ($rScO_2$) and muscle ($SmO_2$) for 100 patients (age 71 ± 6 years; mean ± SD) undergoing vascular surgery: (i) Does preoxygenation (inhaling 100% oxygen before anesthesia) increase tissue oxygenation, (ii) Does inhalation of 70% oxygen during surgery prevent a critical reduction in $rScO_2$ (<50%), and (iii) is a decrease in $rScO_2$ and/or $SmO_2$ related to reduced blood pressure and/or cardiac output? Intravenous anesthesia was provided to all patients and the intraoperative inspired oxygen fraction was set to 0.70 while tissue oxygenation was determined by INVOS 5100C. Preoxygenation increased $rScO_2$(from 65 ± 8 to 72 ± 9%; $P < 0.05$) and $SmO_2$ (from 75 ± 9 to 78 ± 9%; $P < 0.05$) and during surgery $rScO_2$ and $SmO_2$ were maintained at the baseline level in most patients. Following anesthesia and tracheal intubation an eventual change in $rScO_2$ correlated to cardiac output and cardiac stroke volume (coefficient of contingence = 0.36; $P = 0.0003$) rather to a change in mean arterial pressure and for five patients $rScO_2$was reduced to below 50%. We conclude that (i) increased oxygen delivery enhances tissue oxygenation, (ii) oxygen supports tissue oxygenation but does not prevent a critical reduction in cerebral oxygenation sufficiently, and (iii) an eventual decrease in tissue oxygenation seems related to a reduction in cardiac output rather than to hypotension.

**Keywords: blood pressure, cardiac output, cerebral oxygenation, muscle oxygenation**

## INTRODUCTION

Monitoring regional cerebral oxygenation ($rScO_2$) by near infrared spectroscopy (NIRS) is used for both cardiac and non-cardiac surgery (Casati et al., 2005; Murkin and Arango, 2009) and suggested as an index for how well the circulation is managed (Murkin, 2011). A decrease in intraoperative $rScO_2$ to less than 80% of the preoperative value, or to a level lower than 50% have been associated with postoperative complications such as cognitive dysfunction (Casati et al., 2005; Slater et al., 2009), stroke (Olsson and Thelin, 2006) and increased length of stay in hospital (Casati et al., 2005). Furthermore, patients with a preoperative $rScO_2$ below 50% demonstrate increased probability for 1-year postoperative mortality (Heringlake et al., 2011). Thus, it appears to be an advantage to maintain $rScO_2$ during surgery but with induction of general anesthesia subsequent reduction in blood pressure may affect regional blood flow and in turn tissue oxygenation (Petrozza, 1990). Yet, in patients undergoing minor surgery such as mastectomy, thyroidectomy or parathyroidectomy, a low blood pressure does not appear to affect $rScO_2$ as determined by NIRS (Nissen et al., 2009). During surgery mean arterial pressure (MAP) is maintained often above 60 mmHg that is considered to represent the level that secures cerebral autoregulation (Paulson et al., 1990). On the other hand, during certain types of surgery deliberate reduction of MAP to below 60 mmHg may be initiated to limit hemorrhage (Martin and Galliano, 1965; Beaussier et al., 2000; Boonmak et al., 2013).

Patients undergoing vascular surgery are supplemented with $O_2$ to prevent arterial desaturation (Dixon et al., 2005) and a high intraoperative inspired $O_2$ fraction has the potential to improve postoperative outcome (Niinikoski, 1969; Hunt and Pai, 1972; Greif et al., 2000; Fries et al., 2005; Turtiainen et al., 2011). Raised inspired $O_2$ fraction might affect regional blood flow to the brain (Nielsen et al., 1999; Smith et al., 2012) and skeletal muscle (Welch et al., 1977; Pedersen et al., 1999) and we aimed to assess influence of $O_2$ supplementation on $rScO_2$ and muscle oxygenation ($SmO_2$) in a cohort of vascular surgical patients. It was addressed whether (i) preoxygenation (inhaling 100% oxygen before anesthesia) increases tissue oxygenation, (ii) inhalation of 70% oxygen during surgery prevents a critical reduction in $ScO_2$ to below 50%, and (iii) a decrease in $rScO_2$ and/or $SmO_2$ is related to reduced blood pressure or cardiac output (CO).

## MATERIALS AND METHODS

Using a non-randomized single-center retrospective study-design we included vascular surgical patients enrolled in a cohort as approved by the Danish Data Protection Agency (2009-41-3617) and by the local ethical committee (H-4-2012-FSP). The evaluation included, arbitrarily, 100 patients (71 males; age 71 ± 6 years,

height 171 ± 12 cm, weight 75 ± 16 kg; mean ± SD) in whom vascular surgery was performed between March 2009 and August 2011. Patients were planned for open ($n = 23$) or endovascular aortic repair (EVAR) ($n = 56$) of an abdominal aortic aneurysm, lower limb by-pass surgery ($n = 6$), an iliaco-femoral ($n = 9$) or axillo-femoral bypass ($n = 1$), open surgery for arterial mesenteric stenosis ($n = 2$), or EVAR of a thoracic aortic aneurysm ($n = 3$). Fifty-nine patients were in treatment for arterial hypertension and medication included an ACE antagonist ($n = 36$), adrenergic β-receptor blockade ($n = 23$), a calcium channel inhibitor ($n = 18$), and diuretics ($n = 25$). Ten patients were diabetics and for 14 patients suffered from chronic obstructive lung disease.

The patients were exposed to at least 6 h of fast and orally intake of clear fluids was stopped 2 h before surgery. Three-lead electrocardiography monitored heart rate (HR) and pulse oximetry assessed arterial hemoglobin $O_2$ saturation ($SpO_2$). A peripheral vein was used for administration of fluid and anesthetics. In accordance to local guidelines, a radial artery catheter (20 gauge; 1.1 mm) was, after local anesthesia, inserted in the arm with the highest non-invasively determined systolic blood pressure. The catheter was kept patent by isotonic saline (3 ml/h) through to a transducer (Edwards Life Sciences, Irving, CA, USA) positioned at the level of the heart. A two channel cerebral oximeter (INVOS 5100C, Somanetics, Troy, MI, USA) was used to detect $rScO_2$ and $SmO_2$. The reported values are taken to represent hemoglobin oxygen saturation in the tissue beneath the sensor as the ratio between deoxygenated hemoglobin and the sum of deoxygenated and oxygenated hemoglobin. Thus, as approved by the US Food and Drug Administration (510k-080769), the INVOS 5100C- determined $rScO_2$ is considered a trend monitor of the hemoglobin $O_2$ saturation for skin, scalp, and cortical tissue. With the NIRS-probe applied to the forehead it is assumed that capillaries within the frontal lobe contribute most to light absorbance (Madsen and Secher, 1999) but the skin, subcutaneous tissue and the scalp also contribute to change the INVOS-determined $rScO_2$ (Davie and Grocott, 2012; Soerensen et al., 2012). The $rScO_2$ was determined with a sensor attached to the forehead as least 2 cm above the eyebrows and that position is considered to limit an influence from the frontal sinus on $rScO_2$ (Tubbs et al., 2002). Monitoring a change in NIRS-determined $SmO_2$ indicates an early warning of an acute blood loss (Madsen et al., 1995) but the decision to apply a NIRS sensor to the middle part of the right biceps muscle was made by the anesthesiologist in charge and $SmO_2$ is therefore reported for only 61 patients. The $SmO_2$ value reflects both hemoglobin/oxyhemoglobin and myoglobin (Madsen and Secher, 1999).

Modelflow methodology (Nexfin, bmeye B.V, Amsterdam, The Netherlands) (Bogert and van Lieshout, 2005) was used to assess CO and cardiac stroke volume (SV) from the pressure curve and heart rate (HR) and MAP were monitored through the arterial line. Neuromuscular blockade was evaluated with "train of four" (Organon Dublin, Ireland). Lactated Ringer and Macrodex (Fresenius Kabi, Bad Homburg, Germany) were administered to support the central blood volume according to a goal-directed strategy (Bundgaard-Nielsen et al., 2007) as guided by SV and CO and by central venous $O_2$ hemoglobin saturation in patients instrumented with a central venous catheter (via the internal jugular vein as guided by an ultrasound image). Administration of red blood cells was initiated in bleeding patients when hemoglobin was below 6 mmol/L.

The patients received no sedating drugs and in accordance to local guidelines inhalation of $O_2$ was introduced using a bilateral nasal catheter. Thereafter a facial mask was applied for continued $O_2$ breathing until anesthesia was induced with propofol (1 mg/kg) and fentanyl (1 μg/kg). Cisatracurium (0.1–0.15 mg/kg) facilitated oral tracheal intubation and anesthesia was maintained with propofol (0.08 mg/kg/min) and remifentanil (0.3–0.4 μg/kg/min). For ventilation a Dräger CATO (M32040, Lübeck, Germany) in volume-controlled mode was adjusted to an end-tidal $CO_2$ tension of 4–4.5 kPa and a positive end-expiratory pressure of 5 cm $H_2O$ was used. When the patient was intubated, the inspiratory $O_2$ fraction was set to 0.7 for maintenance of tissue oxygenation whereby the incidence of surgical site infections may decrease (Greif et al., 2000; Turtiainen et al., 2011). In 16 patients arterial blood was obtained for immediate blood gas analysis (ABL 725; Radiometer, Copenhagen, Denmark) to secure that changes in $SpO_2$ reflected those in $SaO_2$.

Values were recorded: (a) with the patient breathing room air, (b) after breathing $O_2$ enriched air, (c) following induction of anesthesia, and finally (d) after tracheal intubation. Reported values during surgery represent the lowest noted $rScO_2$ with the associated values for $SmO_2$, HR, SV, CO, and MAP.

### STATISTICS

For normally distributed data, One-Way analysis of variance (ANOVA) with repeated measures was used. In the case of a significant main effect, a Tukey-test based *post-hoc* evaluation was applied. Correlations among variables were evaluated by Spearman's test. A GLM matrix analysis was use to locate the factor that had the statistically strongest influence on $rScO_2$. A $P$-value $< 0.05$ was considered statistical significant.

## RESULTS

Breathing $O_2$ enriched air increased arterial $O_2$ tension (from 10 ± 2 to 34 ± 12 kPa), $SpO_2$ (95.3 ± 2.4 to 99.7 ± 1.1%), arterial hemoglobin $O_2$ saturation (from 96.2 ± 2.0 to 99.7 ± 0.2%), and the arterial $CO_2$ tension (from 5.1 ± 0.6 to 5.4 ± 0.7 kPa; all $P < 0.05$). In all patients $O_2$ breathing increased $rScO_2$ (**Figure 1**) and $SmO_2$ while there was no effect on cardiovascular variables (**Table 1**). Statistically, $SpO_2$ contributed most to $rScO_2$ ($P < 0.0001$): changes in tissue oxygenation correlated to those in $SpO_2$ ($rScO_2$, $r = 0.50$; $SmO_2$, $r = 43$. $P < 0.05$) as provoked by breathing $O_2$ enriched air before anesthesia.

Following induction of anesthesia, MAP, HR, and CO lowered, while $rScO_2$ and $SmO_2$ remained elevated. For three patients $rScO_2$ was reduced by more than 10% indicative of a potentially critical reduction in regional cerebral $O_2$ supply. During surgery with an end-tidal $CO_2$ pressure of 4.4 ± 0.4 kPa, SV, and CO were at the levels before anesthesia, $SmO_2$ remained elevated and $rScO_2$ was not significantly changed as compared to the preoperative level. In seven patients, however, $rScO_2$ decreased by more than 10% and for five of these patients $rScO_2$ was below 50%. In the patients demonstrating a significant drop in $rScO_2$, CO

was reduced by 1.6 ± 1.2 L/min but $rScO_2$ appeared independent of MAP when CO was maintained or increased (**Figure 2**). Thus, there was no statistical significant relation between $rScO_2$ and MAP but $ScO_2$ was correlated to SV and CO (**Table 2**). Also $rScO_2$ correlated to age, while $SmO_2$ correlated only to SV and CO before but not after induction of anesthesia ($P = 0.0025$).

## DISCUSSION

This study aimed to answer three questions: (i) Does preoxygenation (inhaling 100% oxygen before anesthesia) increase tissue oxygenation? (ii) Does inhalation of 70% oxygen during surgery prevent a reported critical reduction in $ScO_2$ to 50%? and (iii) When $ScO_2$ and/or $SmO_2$ decrease, is the decrease then related to reduced blood pressure and/or cardiac output? In vascular surgical patients, administration of elevated inspiratory $O_2$ fraction increased oxygenation of both the cerebral frontal lobe ($rScO_2$) and skeletal muscle ($SmO_2$) (by 10 and 3%, respectively). Importantly, this increase in tissue oxygenation appeared protective for development of tissue hypoxemia following induction of anesthesia, although the incidence of critical reduction in $rScO_2$ remained 5%. The third important observation was that during anesthesia a correlation between tissue oxygenation and a decrease in MAP was not observed indicating

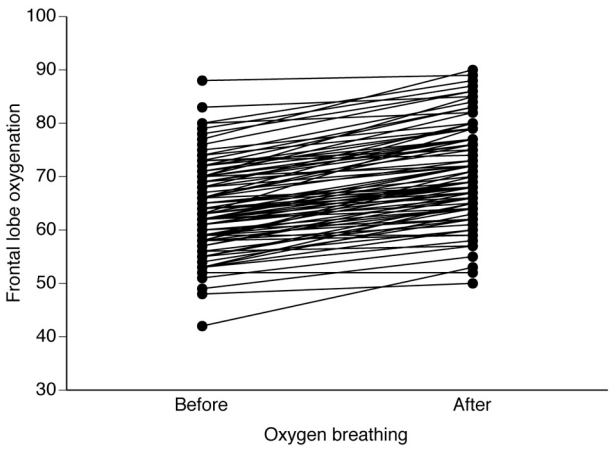


**FIGURE 1 | Effects of $O_2$ breathing on NIRS determined frontal lobe oxygenation.** Data are individual responses from vascular surgical patients exposed to preoperative facial mask breathing with 100% $O_2$.

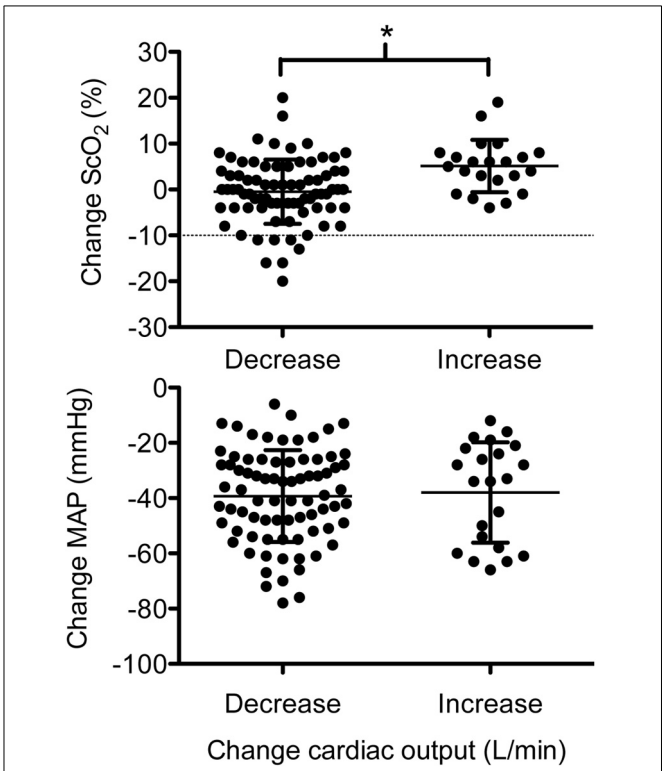


**FIGURE 2 | The surgical changes in frontal lobe oxygenation ($ScO_2$) and mean arterial pressure (MAP) related to cardiac output (CO; decrease is CO below the preoperative level and increase is CO above the preoperative level).** The dotted line straight line (upper panel) at −10% represents the change in $ScO_2$ considered to be critical. *Different value; $P < 0.05$.

**Table 1 | Cardiovascular and blood gas variables for vascular surgical patients.**

| | Before anesthesia | | During anesthesia | | |
|---|---|---|---|---|---|
| | $-O_2$ | $+O_2$ | Induction | Intubation | Surgery |
| $SpO_2$ (%) | 95.3 ± 2.4 | 99.7 ± 1.1* | 99.8 ± 1.1* | 99.8 ± 0.9* | 99.9 ± 0.2* |
| $ScO_2$(%) | 65 ± 8 | 72 ± 9* | 70 ± 10* | 75 ± 8* | 66 ± 7† |
| $SmO_2$(%) | 75 ± 9 | 78 ± 9* | 80 ± 7* | 79 ± 7* | 80 ± 8* |
| HR (b $min^{-1}$) | 73 ± 13 | 72 ± 14 | 65 ± 13* | 72 ± 16 | 61 ± 11*† |
| MAP (mmHg) | 103 ± 18 | 102 ± 18 | 69 ± 18* | 86 ± 25* | 64 ± 11*† |
| SV (ml) | 67 ± 16 | 66 ± 16 | 60 ± 17* | 59 ± 17* | 69 ± 15† |
| CO (L $min^{-1}$) | 4.9 ± 1.3 | 4.8 ± 1.3 | 4.1 ± 1.2* | 4.3 ± 1.3* | 4.1 ± 1.1* |

*Values are means ± SD with ($+O_2$) and without ($-O_2$) preoxygenation and following induction of anesthesia, immediately after the patient was intubated, and during surgery 47 ± 24 min after intubation. CO, cardiac output; HR, heart rate; MAP, mean arterial pressure; SV, cardiac stroke volume; $SpO_2$, puls oximetry determined hemoglobin $O_2$ saturation in arterial blood; $SmO_2$ and $ScO_2$, near infrared determined muscle and frontal lobe oxygenation, respectively.*

**Different from before anesthesia without $O_2$ supplementation.*

*†Different between intubation and surgery; $P < 0.05$.*

**Table 2 | Relationship between frontal lobe oxygenation and cardiovascular variables.**

| | Breathing atm | Breathing $O_2$ | Anesthesia | Intubation | Surgery |
|---|---|---|---|---|---|
| HR | $-0.02/P = 0.8529$ | $0.01/P = 0.9451$ | $0.02/P = 0.8689$ | $0.01/P = 0.8987$ | $-0.06/P = 0.5814$ |
| MAP | $-0.01/P = 0.9258$ | $-0.01/P = 0.9532$ | $0.21/P = 0.8689$ | $0.11/P = 0.2565$ | $0.11/P = 0.2917$ |
| SV | $0.36/P = 0.0002$* | $0.34/P = 0.0006$* | $0.23/P = 0.0392$* | $0.29/P = 0.0032$* | $0.30/P = 0.0724$ |
| CO | $0.40/P < 0.0001$* | $0.40/P < 0.0001$* | $0.32/P = 0.0013$* | $0.36/P = 0.0003$* | $0.20/P = 0.0513$ |
| $SpO_2$ | $0.10/P = 0.3433$ | $0.07/P = 0.5195$ | $0.02/P = 0.8116$ | $0.04/P = 0.7232$ | $0.04/P = 0.7262$ |
| Age | $-0.20/P = 0.0415$* | $-0.19/P = 0.0599$ | $-0.18/P = 0.0697$ | $-0.20/P = 0.0420$* | $0.09/P = 0.3985$ |
| $FiO_2$ | | | | | $0.16/P = 0.1133$ |
| $CO_2$ | | | | | $-0.16/P = 0.1183$ |

*Correlations are evaluated by Spearmans Rank Test and the included numbers are the coefficient of contingence with its level of statistical significance as determined by two-tailed t-test. CO, cardiac output; $FiO_2$, inspired $O_2$ fraction; HR, heart rate; MAP, mean arterial pressure; SV, cardiac stroke volume; $SpO_2$, pulse oximetry determined hemoglobin $O_2$ saturation in arterial blood.*

**Marks the variable with statistical significance at $P < 0.05$.*

that for vascular surgical patients, as for patients scheduled for other types of surgery (Nissen et al., 2009), a transient drop in blood pressure to below what is often considered the lower limit of cerebral autoregulation does not affect $rScO_2$. On the other hand, $rScO_2$ correlated to a reduction in CO and SV.

It has not been evaluated whether it is profitable to control flow-related variables (SV, CO, or $SvO_2$) in conjunction with an effort to maintain $rScO_2$ during surgery. With fluid administration according to an "individualized goal-directed regime," SV and hence CO is optimized to a level considered to represent normovolemia (Bundgaard-Nielsen et al., 2010). In the present study, the cardiovascular variables reported during surgery represent situations where $rScO_2$ reached a minimum and the associated CO may reflect that fluid resuscitation was about to be initiated.

A correlation between $rScO_2$ and CO supports a link to blood flow (Ide et al., 1999) and as cardiovascular capacity decline with advancing age (Proctor and Joyner, 1997), this view is further supported by a correlation between $rScO_2$ and age. Seven patients suffered a critical reduction in $rScO_2$ when CO dropped (**Figure 2**) and if $O_2$ supplementation had not induced a 10% increase in $rScO_2$, it is likely that $rScO_2$ would have been reduced to a critical level in more patients. We did not find indication for that a low MAP affected $rScO_2$ and in ASA class I patients, a 30% reduction in MAP with a minimum MAP of 50 mmHg, is considered acceptable (Yamada et al., 1988; Petrozza, 1990). In this evaluation 32 of 100 patients undergoing vascular surgery at one stage of the operation developed a MAP < 60 mmHg, apparently without affecting $rScO_2$. Even when MAP was below 50 mmHg ($n = 12$), $rScO_2$ was maintained.

Administration of an $O_2$ enriched atmosphere was introduced to reduce the incidence of complications after colorectal surgery (Greif et al., 2000) and vascular surgery (Turtiainen et al., 2011). Yet, not all follow-up studies support that a high $O_2$ fraction reduces surgical site infections (Pryor et al., 2004; Belda et al., 2005; Meyhoff et al., 2009; Bustamante et al., 2011) and $O_2$ supplementation may provoke formation of $O_2$ free radicals (García-de-la-Asunción et al., 2011). Furthermore, surgical site infection, atelectasis, pneumonia, and respiratory failure occur at similar frequencies in patients with an inspired $O_2$ fraction of 0.80 compared to 30% $O_2$ (Meyhoff et al., 2009). The tendency for $O_2$ breathing to provoke pulmonary atelectasis (Hedenstierna, 2012) suggests the use of positive end expiratory pressure as applied in this evaluation. Also the relevance for using $O_2$ supplementation is likely to vary among groups of patients. For vulnerable patients a reduction in tissue oxygenation may provoke ischemic stroke after surgery (Waggoner et al., 2001; Cheng-Ching et al., 2010). Importantly, vascular surgical patients often present with coronary artery or cerebrovascular disease (Hertzer et al., 1984) and hypotension may become critical for maintained tissue oxygenation. We suggest that $O_2$ supplementation is important for perioperative preservation of tissue oxygenation.

This study is limited by several factors: a retrospective design often fails to extract dynamic cardiovascular variables in patients exposed to surgery. Furthermore, for the patients included in the present cohort, the recommendation to use NIRS to guide the circulation during surgery may not have been followed and a placebo-controlled randomized design is in need. A third reservation relates to the NIRS used for interpretation of changes in tissue oxygenation as the INVOS cerebral oximeter appears to be sensitive to changes in skin blood flow (Davie and Grocott, 2012).

From this retrospective evaluation of tissue oxygenation including 100 patients undergoing vascular surgical procedures, it is concluded that $O_2$ supplementation increases the NIRS-determined oxygenation of the cerebral frontal lobe and skeletal muscles. Furthermore, the data suggest that an elevated inspired oxygen fraction is not efficient to prevent a critical reduction in cerebral oxygenation since a decrease seems to be related to a reduced cardiac output.

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