

# Pulse Perfusion Values to Predict Eye Opening After Intravenous Anesthesia: An Explorative Study

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*Variables measured in modern pulse oximetry apparatuses include a graphic pulse curve and a specified perfusion value (PV) that could be a sensitive marker for detecting differences in sympathetic activity. We hypothesized that there is a correlation between a reduction of PV and the time to eye opening after anesthesia with propofol-remifentanyl. This study includes 29 patients, ASA physical status 1 or 2, scheduled for elective thyroid surgery. Main outcome measures were PV measured by pulse oximetry, heart rate, and noninvasive mean arterial blood pressure recorded before anesthesia, 15 minutes after induction, and at start of surgery, end of surgery, and eye opening at the end of anesthesia. Carbon dioxide ( $P_{ET}CO_2$ ) and oxygen inspiratory ( $F_I-PO_2$ ) and expiratory ( $F_E-PO_2$ )*

*concentrations were measured at all times except before anesthesia. Results demonstrated that PVs before anesthesia and at eye opening were lower than 15 minutes after induction and at end of surgery ( $P < .05$ ). The  $P_{ET}CO_2$  and difference of  $F_I-P_{ET}O_2$  increased at eye opening compared with the end of surgery ( $P < .05$ ). We conclude that the pulse oximetry PV and the increased  $P_{ET}CO_2$  could be useful variables to predict timing of recovery in terms of eye opening after intravenous anesthesia.*

**Keywords:** Carbon dioxide, inspiratory and expiratory oxygen, intravenous anesthesia, perfusion, plethysmography, pulse oximeter.

**P**lethysmography is part of the monitoring equipment routinely used for assessment of patients during anesthesia to ensure adequate hemoglobin oxygen saturation ( $SpO_2$ ). Pulse oximetry is a method of using a noninvasive technique to measure  $SpO_2$  by the principles of spectrophotometry (eg, that the relative absorption of red and infrared light of the systolic waveform correlates to arterial blood oxygen saturations).<sup>1</sup> Pulse oximetry also provides information about heart rate and changes in arterial blood flow that may occur because of fluctuations in blood pressure during anesthesia.<sup>2,3</sup>

The plethysmography unit uses 2 light-emitting diodes with different wavelengths: 1 emitting visible red light at 660 nm and 1 infrared light at 940 nm measured by a light-sensitive phototransistor, which records the transmittance of the light in the tissue.<sup>1,4</sup> Variables measured in modern pulse oximetry apparatuses include  $SpO_2$ , a graphic pulse curve, and/or a specified perfusion value (PV). Some studies have suggested that the amplitude of the PV may be sensitive to estimate the level of sympathetic activity.<sup>5-7</sup> However, to the authors' knowledge, there are now standard values described for the awake patient, and the values probably are influenced by real-time changes caused by temperature, pain, and hypovolemia.

Earlier studies had used eye opening and/or orientation to person to verify the recovery time after anesthesia.<sup>8,9</sup>

In our previous study, the PV was found to be larger during deep anesthesia using 1.2 minimum alveolar concentration and to return toward baseline after the end of anesthesia, when the patient regains consciousness and reopens his or her eyes.<sup>10</sup> This study also demonstrates that during induction and maintenance of anesthesia, PV and bispectral index values matched each other well. However, during the recovery phase the PVs returned to baseline levels faster than the bispectral index values.<sup>10</sup>

The aim of the present study was to investigate whether PV is related to depth of anesthesia in terms of eye opening after intravenous anesthesia.

## Materials and Methods

• **Ethics.** Ethical approval for this study according to the standards set in the Helsinki Declaration was provided by the Regional Ethics Committee, Lund, Sweden, in December 2013 (Dnr: 2013/780). Patients scheduled for elective thyroid surgery were enrolled by surgery reception nurses. Consent to participate in the study was received from each patient.

• **Patients.** The investigation included 30 patients, ASA physical status 1 or 2, at Skåne University Hospital, Lund, Sweden, from November 2012 to January 2013. Patients were considered for inclusion in the trial if they were more than 18 years of age and scheduled for elective thyroid surgery. Patients with known pulmonary or

cardiovascular disease or receiving pharmacologic antihypertensive treatment were excluded. The study was prospective and descriptive.

• **Experimental Procedure.** Before the start and throughout anesthesia, all patients were monitored as described here. Before induction, the first set of values (heart rate, noninvasive blood pressure, SpO<sub>2</sub>, and PV) was recorded (time: preanesthesia). Intravenously, anesthesia was induced with propofol at 1 to 3 mg/kg and remifentanyl at 0.8 to 1 µg/kg; suxamethonium (Suxameton), 1 mg/kg, was administered for muscle paralysis. Infusion of propofol at 3 to 4 mg/kg/h and remifentanyl at 0.2 to 0.3 µg/kg/min volume was started and was measured with 2 syringe pumps (Braun Perfusor Space, B Braun Melsungen AG). Ventilation was assisted manually with 0.8 L of oxygen via a semiopen circle system (4.5 L in volume) until tracheal intubation. Then by ventilator, patients were ventilated at a respiratory rate (RR) of 10/min to 12/min, with a fraction of inspired oxygen (F<sub>I</sub>O<sub>2</sub>) at 0.35 in nitrogen by fresh gas flow of 5 L/min. The tidal volume (V<sub>T</sub>) and RR were adjusted to maintain end-tidal carbon dioxide measured at the end of the endotracheal tube (P<sub>ET</sub>CO<sub>2</sub>) at 33.8 mm Hg throughout the study. After 5 minutes, the fresh gas flow was adjusted to 0.5 L/min throughout the anesthesia period.

The second set of values (heart rate, noninvasive blood pressure, SpO<sub>2</sub>, carbon dioxide expiratory partial pressure (P<sub>ET</sub>CO<sub>2</sub>), inspiratory and expiratory oxygen partial pressure (F<sub>I</sub>O<sub>2</sub>, P<sub>ET</sub>O<sub>2</sub>) and PV was recorded 15 minutes after induction (time: anesthesia 15 minutes). Five minutes before surgical skin incision, the anesthesia provider increased the infusions of propofol to 6 mg/kg h and remifentanyl to 0.5 µg/kg/min. The values (heart rate, noninvasive blood pressure, SpO<sub>2</sub>, P<sub>ET</sub>CO<sub>2</sub>, F<sub>I</sub>O<sub>2</sub>, P<sub>ET</sub>O<sub>2</sub> and PV) were recorded a third time 5 minutes after skin incision (time: start of surgery). After 15 minutes, propofol infusion was reduced to 4 mg/kg/h and remifentanyl infusion was adjusted to 0.4 to 0.6 µg/kg/min dependent on the noninvasive mean arterial blood pressure (MAP) of patients. If MAP decreased below 55 mm Hg, patients received ephedrine, 5 to 10 mg intravenously. All patients received 3 to 5 mL/kg/h of 2.5% glucose solution with sodium (70 mmol/L), chloride (45 mmol/L), and acetate (25 mmol/L) intravenously. Thirty minutes before the expected end of the anesthesia, all patients received an opiate agonist, ketobemidone (5 mg) intravenously, to prevent postoperative pain.

At completion of the last skin suture, a third set of values was recorded (time: end of surgery). Intraoperative recovery time was defined as the time from the discontinuation of propofol-remifentanyl at the end of surgery to eye opening when a fourth set of values (heart rate, noninvasive blood pressure, SpO<sub>2</sub>, P<sub>ET</sub>CO<sub>2</sub>, F<sub>I</sub>O<sub>2</sub>, P<sub>ET</sub>O<sub>2</sub>, and PV) were recorded (time: eye opening). When the patients opened their eyes, the mechanical ventilation was suspended.

Characteristic	Value
Women (n)	21
Age, y	57 ± 18
Weight, kg	75 ± 18
Height, m	1.66 ± 0.1
Body mass index, kg/m <sup>2</sup>	26.7 ± 4.3

**Table 1. Patient Characteristics (N = 29)<sup>a</sup>**

<sup>a</sup>Values are mean ± SD.

Patients were monitored with a 3-lead electrocardiogram (ECG), heart rate, noninvasive blood pressure, SpO<sub>2</sub>, and PV as measured by the pulse oximeter probe (IntelliVue MP70, Philips Medizin System). Carbon dioxide expiratory partial pressure (P<sub>ET</sub>CO<sub>2</sub>), F<sub>I</sub>O<sub>2</sub>, and P<sub>ET</sub>O<sub>2</sub> were analyzed by the ventilator (Dräger Primus, Dräger Medical Systems). Total ventilation minutes, V<sub>T</sub>, and RR were measured and documented at the same intervals. Pulse oximeter sensor wavelength ranged from 500 to 1,000 nm, and emitted light energy was 15 mW or less.

• **Statistical Analysis.** All statistical analysis was performed with SPSS version 22.0 for Windows (SPSS Inc). A power analysis was performed for the main outcome parameter: differences between PV during anesthesia and eye opening. With a difference of 3.5 with an SD of 3, a power of 0.8 was achieved with 14 patients. All data, including demographic data (age, height, weight, and body mass index), are reported as mean and SD.

For interpreting the relationship between different variables, a multiple regression analysis with the Durbin-Watson test was used. For change of values over time, a 1-way repeated measurement analysis of variance (ANOVA) was used. The ANOVA analysis was followed by Tukey and Scheffé post hoc tests. A *P* value less than .05 was considered to indicate statistical significance for all statistical analyses.

## Results

Patient characteristics are presented in Table 1. One patient was excluded from the study because of an atrial fibrillation discovered when the patient was connected to the ECG monitoring at the start of anesthesia. No other intraoperative problems were noted during the study. All patients recovered from anesthesia and left the postoperative unit in accordance with the routines assigned for the surgical procedure.

The values of propofol and remifentanyl were significantly lower at preanesthesia compared with start of surgery and end of surgery (*P* < .05, Table 2). The values of noninvasive MAP were similar at preanesthesia vs the time point of eye opening but significantly higher compared with anesthesia 15 minutes and end of surgery (*P* < .05, Table 3). Heart rates were significantly higher at preanesthesia compared with all other time points (*P* < .05, see Table 3).

Drug	Pre anesthesia	Anesthesia 15 min	Start of surgery	End of surgery	Eye opening
Propofol (mg/kg/h)	—	3.4 ± 0.3 <sup>b</sup>	5.7 ± 0.4	4.1 ± 0.3	—
Remifentanil (µg/kg/min)	—	0.26 ± 0.04 <sup>b</sup>	0.56 ± 0.06	0.49 ± 0.07	—

**Table 2. Propofol and Remifentanil Doses Administered<sup>a</sup>**

<sup>a</sup>Values are mean ± SD (N = 29). Values of propofol and remifentanil were statistically significantly lower at anesthesia 15 minutes (15 minutes after induction) compared with start of surgery and end of surgery.

<sup>b</sup>*P* < .05 (1-way analysis of variance followed by Tukey and Scheffé post hoc tests).

Measure	Pre anesthesia	Anesthesia 15 min	Start of surgery	End of surgery	Eye opening
MAP (mm Hg)	83 ± 18	61 ± 9 <sup>b</sup>	65 ± 12 <sup>b</sup>	65 ± 10 <sup>b</sup>	76 ± 14
Heart rate (/min)	72 ± 14	62 ± 9 <sup>b</sup>	65 ± 9 <sup>b</sup>	64 ± 11 <sup>b</sup>	64 ± 10 <sup>b</sup>

**Table 3. Comparison of Noninvasive Mean Arterial Blood Pressure (MAP) and Heart Rate<sup>a</sup>**

<sup>a</sup>Values are mean ± SD (N = 29). Values of MAP and heart rate were statistically significantly larger in preanesthesia compared with anesthesia 15 minutes (15 minutes after induction), start of surgery, and end of surgery. Values of MAP were statistically significantly larger at eye opening.

<sup>b</sup>*P* < .05 (1-way analysis of variance followed by Tukey and Scheffé post hoc tests).

Value	Preanesthesia	Anesthesia 15 min	Start of surgery	End of surgery	Eye opening
Respiratory rate (/min)	—	11 ± 1.5	11 ± 1.5	10 ± 1.3	10 ± 1.3
V <sub>T</sub> (mL)	—	498 ± 144	481 ± 148	493 ± 136	492 ± 132
P <sub>ET</sub> CO <sub>2</sub> (mm Hg)	—	32.3 ± 2.3	32.3 ± 2.3	33.0 ± 1.5	35.3 ± 1.5 <sup>b,c</sup>
F <sub>I</sub> O <sub>2</sub> (%)	—	34.3 ± 5.1	33.0 ± 3.1	34.9 ± 4.1	35.1 ± 5.8
P <sub>ET</sub> O <sub>2</sub> (%)	—	29.2 ± 5.2	27.5 ± 3.2	29.3 ± 4.4	28.8 ± 6.2
Difference in F <sub>I</sub> -P <sub>ET</sub> O <sub>2</sub>	—	5.1 ± 0.7	5.6 ± 0.8 <sup>b</sup>	5.5 ± 0.7 <sup>b</sup>	6.3 ± 1.0 <sup>b,c</sup>
SpO <sub>2</sub> (%)	100 ± 1.3	100 ± 1.2	99 ± 1.8	99 ± 1.3	99 ± 1.1
Perfusion	1.7 ± 0.7	6.8 ± 3.5 <sup>d</sup>	3.6 ± 2.4 <sup>b,d</sup>	5.7 ± 2.7 <sup>d</sup>	1.9 ± 0.9 <sup>c</sup>

**Table 4. Comparison of Oximetry and Other Respiratory Values<sup>a</sup>**

Abbreviations: F<sub>I</sub>O<sub>2</sub>, fraction of inspired oxygen; P<sub>ET</sub>CO<sub>2</sub>, end-tidal carbon dioxide; P<sub>ET</sub>O<sub>2</sub>, expiratory oxygen fraction; SpO<sub>2</sub>, oxygen saturation; V<sub>T</sub>, tidal volume.

<sup>a</sup>Values are mean ± SD (N = 29). Values for respiratory rate, V<sub>T</sub>, and SpO<sub>2</sub> were similar at all time points. Values of P<sub>ET</sub>CO<sub>2</sub> were larger at time of eye opening compared with during the anesthesia period. Difference between F<sub>I</sub>-P<sub>ET</sub>O<sub>2</sub> was significantly larger at start of surgery and time of eye opening compared with Anesthesia 15 minutes (15 minutes after induction) and end of surgery. Values of perfusion were lower at preanesthesia and at eye opening compared with the total anesthesia period. Values of perfusion were lower at start of surgery compared with anesthesia 15 minutes.

<sup>b</sup>Anesthesia 15 minutes; *P* < .05 (1-way analysis of variance followed by Tukey and Scheffé post hoc tests).

<sup>c</sup>End of surgery; *P* < .05 (1-way analysis of variance followed by Tukey and Scheffé post hoc tests).

<sup>d</sup>Preanesthesia; *P* < .05 (1-way analysis of variance followed by Tukey and Scheffé post hoc tests).

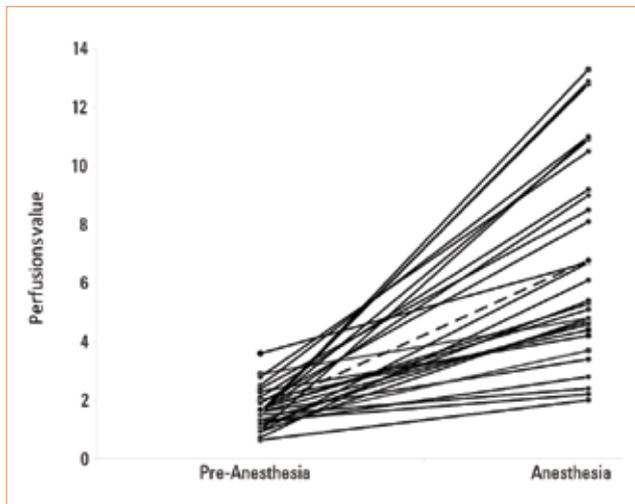
The values of P<sub>ET</sub>CO<sub>2</sub> and difference in F<sub>I</sub>-P<sub>ET</sub>O<sub>2</sub> were larger at the time point eye opening compared with anesthesia 15 minutes and end of surgery (*P* < .05, Table 4). The values of difference in F<sub>I</sub>-P<sub>ET</sub>O<sub>2</sub> were significantly larger at time point start of surgery compared with anesthesia 15 minutes (*P* < .05, see Table 4). The data of RR, V<sub>T</sub>, and SpO<sub>2</sub> was similar at all time points (see Table 4).

The PVs were lower at preanesthesia and eye opening compared with anesthesia 15 minutes, start of surgery, and end of surgery (*P* < .05, see Table 4, Figure 1). The PVs were significantly lower at start of surgery compared

with anesthesia 15 minutes (*P* < .05, see Table 3). The PV was similar at time point preanesthesia and eye opening. The ratio of PV between preanesthesia and anesthesia 15 minutes was 0.30 ± 0.16, and the ratio of PV between end of surgery and eye opening was 0.35 ± 0.16 (see Table 4, Figure 2).

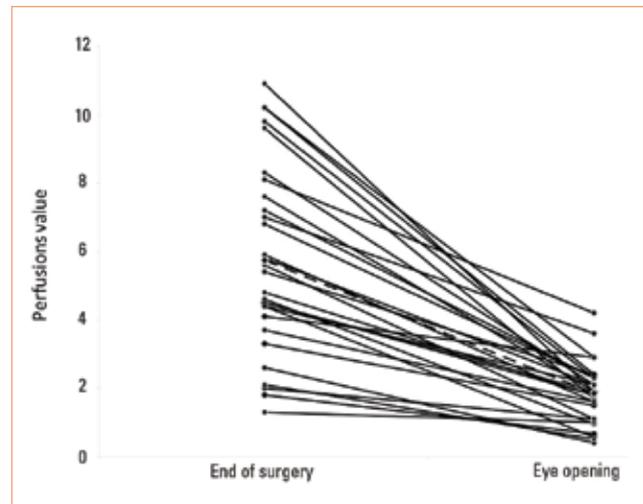
## Discussion

In the present study using propofol and remifentanil, the PVs increased between the periods of anesthesia 15 minutes and end of surgery. The PV thereafter returns



**Figure 1.** Perfusion Values (PV) Before Anesthesia Induction (preanesthesia) and 15 Minutes After Induction (anesthesia 15 minutes)<sup>a</sup>

<sup>a</sup>Mean is indicated by bolder dashed line (N = 29). Ratio of PV between preanesthesia and anesthesia 15 minutes was  $0.30 \pm 0.16$ . Perfusion values were statistically lower at preanesthesia compared with anesthesia 15 minutes ( $P < .05$ ).

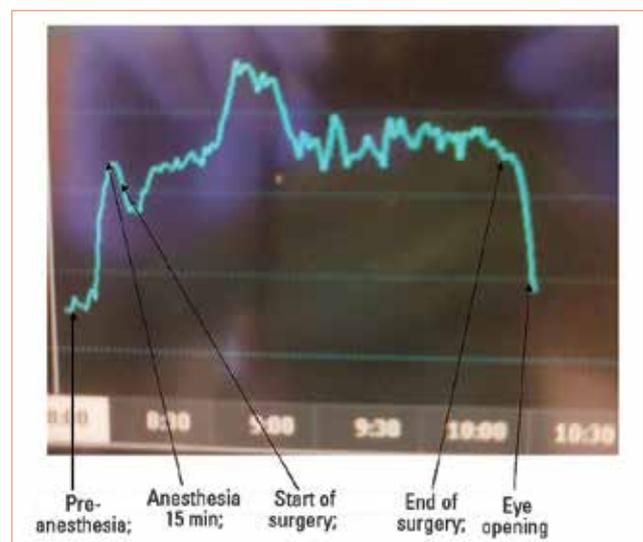


**Figure 2.** Perfusion Values (PV) at End of Surgery and After end of Anesthesia When the Patient Opens His or Her Eyes (Eye Opening)<sup>a</sup>

<sup>a</sup>Mean is indicated by bolder dashed line (N = 29). Ratio of PV between end of surgery and eye opening was  $0.35 \pm 0.16$ . Perfusion values were lower at time of eye opening compared with end of surgery ( $P < .05$ ).

to baseline once the patient regains consciousness and reopens his or her eyes (Figure 3). We also observed after the end of surgery to the time of eye opening, during unchanged ventilations modes, an increase in  $P_{ET}CO_2$  as well as an increase in the  $F_I-P_{ET}O_2$  differences, which could indicate an increased metabolism. These findings are in line with those of Elizarov and colleagues,<sup>11</sup> who observed a correlation between painful surgery and increased metabolism according to various surgical stimuli. Steinbrook and Concepcion<sup>12</sup> also demonstrated an increased hemodynamic response when epidural local anesthetic with epinephrine was given, which resulted in an increased  $CO_2$  production.

The aim of the present study was to investigate whether PV was related to the different time points during the anesthesia period. As mentioned in our results, we observed that at the start of surgery and during eye opening, the patient's PV was decreased, which might indicate an increased sympathetic activity between these time points. Other studies support these findings and demonstrate that the amplitude of the pulse curve may be a sensitive marker for changes in the sympathetic system, such as painful stimuli (eg, skin incision during anesthesia).<sup>5-7</sup> In the present study, we therefore interpret, together with the increase in the  $CO_2$  values and the increase in the oxygen consumption, that the differences in the PVs could mirror an increased adrenergic and/or metabolic response during the awakening phase. Our previous study using sevoflurane anesthesia showed a similar appearance.<sup>10</sup> This earlier study also demonstrated that there was an increase in the PV throughout



**Figure 3.** Example of Trend over the Perfusion Value in an Anesthesia Period

the anesthesia period and a strong agreement between the PV before induction of anesthesia and eye opening in the recovery phase.<sup>10</sup> However, it is notable that the PVs during the intraoperative period are decreased with use of propofol-remifentanyl in the present study (PVs of 6 to 7) vs our earlier study using sevoflurane (PVs of 9 to 10). We interpret this finding to be increased vascular dilation during use of an inhalational agent.

Our results must be interpreted with caution because changes in the plethysmographic waveform and the PV could be caused by a pharmacologic hypotension or

hypovolemia. Other researchers demonstrate a strong correlation between plethysmographic wave amplitude and the arterial pressure waveform; both the plethysmographic waveform and the arterial waveform reflect the cardiac stroke volume.<sup>13-15</sup> Other reasons could be that during a pressure ventilation technique, the amplitude of the plethysmographic waveform varies synchronously with the respiratory cycle.<sup>2,3</sup> Furthermore, administration of adrenergic drugs normally provides a drug-induced vasoconstriction that reduces the pulse amplitude, with a lower PV as a result. However, the present study involved patients with ASA physical status 1 and 2 without any history of circulatory conditions, and no hypothermia or hypovolemia was recorded and no adrenergic drugs were given. It therefore seems reasonable to assume that the observed PVs reflect different depths of anesthesia.

Another limitation in the present study could be the small number of participants. However, considering the design of the study, we believed it was still possible to achieve convincing results since the results are based on adequate statistical power. We also believe that being able to more quickly detect patients' physiologic changes could benefit patient safety, such as time of recovery phase, and presumably have an impact on patient flow according to the operating schedule. However, further studies are needed to determine if the PV is useful in other forms of anesthesia procedures to better predict recovery times by detecting adrenergic circulatory responses.

In conclusion, in hemodynamically stable patients, pulse oximetry PVs could be a useful variable to predict the timing of recovery in terms of eye opening after intravenous anesthesia.

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## DISCLOSURES

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