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ORIGINAL ARTICLE

Intravenously administered propofol and sufentanil and radial free forearm flap tissue perfusion: A retrospective study

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Introduction

Microvascular reconstruction with a radial free forearm flap (RFFF) is frequently performed for functional and aesthetic restoration after ablative head and neck surgery.[1-3] Despite high overall success rates, however, vascular flap compromise may occur, with terminal flap failure leading to both functional and aesthetic impairment.[4-6]

Postoperative flap monitoring is therefore of paramount importance in the timely detection of vascular flap compromise, as a prolonged time interval between its onset and correction is associated with terminal flap failure.[7,8] For the purpose of postoperative flap monitoring, the O2C analysis system is often used as a technical procedure that relies on measuring flap tissue perfusion in relation to predefined thresholds indicative of vascular flap compromise, with attached surface probes enabling continuous flap monitoring.[9-12]

However, postoperative patient care after microvascular head and neck reconstruction regularly necessitates the intravenous administration of propofol and fentanyl derivates for sedation and analgesia.[13-15] Although hemodynamic effects on the general circulation (eg, changes in systemic blood pressure and vascular resistance) are generally known for both medications, their potential influence on tissue perfusion of microvascular free flaps remains unclear.[16-23] Studies

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Abbreviations and Acronyms: RFFF, radial free forearm flap; O2C, Oxygen-to-see.

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investigating the influence of medication on flap tissue perfusion have mainly focused on vasopressors, without paying particular attention to RFFFs in the head and neck region.[24-27] An influence on the part of intravenously administered propofol and sufentanil on RFFF tissue perfusion in the head and neck region would be of particular interest regarding the absolute thresholds for blood flow and hemoglobin oxygen saturation used with the O2C analysis system to detect vascular flap compromise and may also improve the understanding of microvascular free flap physiology.[9,11,12,28]

Therefore, this retrospective pilot study aimed to investigate the influence of intravenously administered propofol and sufentanil on early postoperative RFFF tissue perfusion during continuous flap monitoring after head and neck reconstruction.

Material and methods

Study population

This retrospective study was conducted after receiving approval from the local ethics committee of the Medical Faculty at RWTH Aachen University (EK 22-358; October 10, 2022) and was based on a subset of data that were analyzed in a previous study; with the current study and the previous study being part of a project to evaluate the influence of perioperative blood pressure and medication on free flap tissue perfusion in the context of postoperative flap monitoring.[29] Informed consent to participate was waived. All methods were in accordance with the relevant guidelines and regulations.

The study population consisted of 8 patients undergoing microvascular head and neck reconstruction with an RFFF in our Department of Oral and Maxillofacial Surgery between 2020 and 2022 after ablative surgery for squamous cell carcinoma ($n = 7$) or sarcoma ($n = 1$). The inclusion criteria were continuous postoperative flap monitoring and continuous intravenous administration of propofol and sufentanil, complete data sets, and age greater than 18 years.

The surgical procedures were performed under general anesthesia, and patients were monitored postoperatively in the intensive care unit with mechanical ventilation and analgosedation until at least the following morning.

The data for the baseline and surgical characteristics of the study population were obtained from clinical and surgical records. Surgery duration was calculated as the time interval between the first incision and the last suture, and flap ischemia duration was calculated as the time interval between the cessation of flap tissue perfusion at the donor site and the onset of flap tissue perfusion after anastomosis release at the recipient site.

The data on intravenously administered propofol and sufentanil doses as well as systemic blood pressure values during the first 8 postoperative hours were extracted from the IntelliSpace Critical Care and Anesthesia (ICCA) data management system (Philips Medizin Systeme Boeblingen GmbH, Boeblingen, Germany). The propofol and sufentanil doses were calculated in µg/min per kg body weight. The absolute values for systolic, diastolic, and mean arterial blood pressure were measured invasively with an arterial catheter at 5-minute intervals with the IntelliVue X2 M3002A device (Philips Medizin Systeme Boeblingen GmbH, Boeblingen, Germany) or calculated using the following formula: mean arterial blood pressure = diastolic blood pressure + 1/3 x (systolic blood pressure – diastolic blood pressure).[30] The relative values for systolic, diastolic and mean arterial blood pressure were determined by subtracting the average of all available preoperative blood pressure measurement values, which were taken before induction of anesthesia in the operating room, from the postoperative blood pressure measurement values.

Flap perfusion measurement data

The data for flap tissue perfusion during the first 8 postoperative hours were extracted from the O2C analysis system (O2C Oxygen-to-see, LEA Medizintechnik, Giesen, Germany).

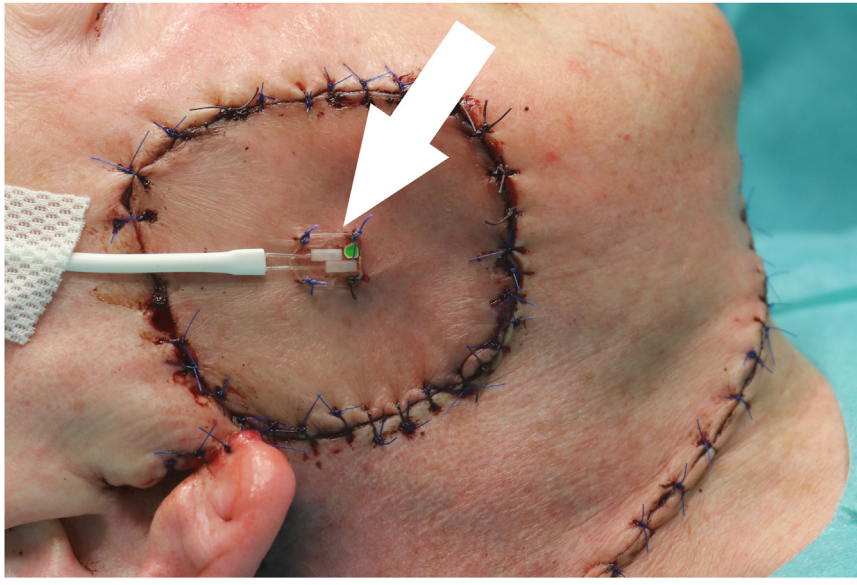


Fig. 1. Measurement of flap perfusion: Measurement of perfusion of a radial free forearm flap with an attached surface probe (white arrow) in a patient reconstructed in the right cheek region.

The measurement of flap tissue perfusion was performed continuously with a surface probe that was attached with 4 sutures in the middle of the flap (Fig. 1). The measurement depth was 3 mm. The flap tissue perfusion parameters blood flow (arbitrary units) and hemoglobin oxygen saturation (%) were recorded in 1-minute intervals. Blood flow was quantified using Doppler spectroscopy (830 nm; 30 mW) as the product of erythrocyte quantity, based on the analysis of the sum of light absorbances, and velocity, based on the analysis of the Doppler shift of light wave frequencies due to the movement of the erythrocytes in the blood vessel.[9,31] Hemoglobin oxygen saturation was quantified using white light spectroscopy (500-800 nm; 50 W) as the color change of light absorbances in comparison to prerecorded hemoglobin spectra with defined oxygen saturation.[9,31] Flap flow conductance was calculated as the ratio of flap blood flow and mean arterial blood pressure.[24]

Statistical analysis

The data were presented as numbers (with percentage) or medians (with interquartile range [IQR]). The data for propofol and sufentanil doses and tissue perfusion values were analyzed as mean calculated over 15-minute time intervals (32 intervals per patient over a measurement period of 8 hours).

The testing for associations between the measured flap tissue perfusion parameters blood flow and hemoglobin oxygen saturation, as well as the calculated flap tissue perfusion parameter flap flow conductance and intravenously administered propofol and sufentanil doses, was based on linear mixed models (autoregressive covariance structure for repeated measures and unstructured covariance structure for random effects; restricted maximum likelihood method) ($n = 256$), with controlling for absolute and relative systolic, diastolic and mean arterial blood pressure values as well as intravenously administered norepinephrine and sufentanil (for propofol) or propofol (for sufentanil) doses in case of significance. *P*-values were two-tailed and considered statistically significant <0.05. The statistical analysis was performed using SPSS Version 28 (SPSS, IBM, New York, NY).

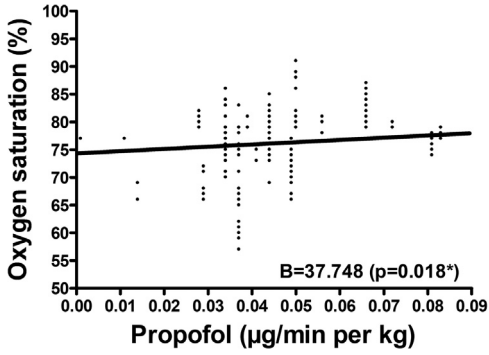


Fig. 2. Association of flap hemoglobin oxygen saturation with propofol: Data shown as scatter plot for hemoglobin oxygen saturation and propofol dose; B coefficient and *P*-value corresponding to the calculation of a linear mixed model (intercept y = 74.358); $^{*}P < 0.05$ upon controlling for blood pressure (absolute systolic blood pressure [$P = 0.011$]; absolute diastolic blood pressure [$P = 0.009$]; absolute mean arterial blood pressure [$P = 0.010$]; relative systolic blood pressure [$P = 0.012$]; relative diastolic blood pressure [$P = 0.011$]; relative mean arterial blood pressure [$P = 0.011$]) and medication (norepinephrine [$P = 0.043$]; sufentanil [$P = 0.025$]).

Results

Baseline and surgical characteristics of the study population

The study population comprised a total of 8 patients, 3 (37.5%) men and 5 (62.5%) women (Table 1). The median age was 67 years (IQR 24 years), and the median body mass index was 27.8 kg/m² (IQR 10.0 kg/m²). The median surgery duration was 508.5 minutes (IQR 122.0 minutes), and the median flap ischemia duration was 87.5 minutes (IQR 25.0 minutes).

Association between flap tissue perfusion and propofol

The flap tissue perfusion parameters blood flow and flap flow conductance were not associated with propofol dose (B = 168.788, $P = 0.568$; and B = −1.207, $P = 0.922$; respectively) (Table 2). The flap tissue perfusion parameter hemoglobin oxygen saturation was positively associated with propofol dose (B = 37.748, $P = 0.018$) (Table 2 and Fig. 2). This association was consistent while controlling for blood pressure (absolute systolic [$P = 0.011$], diastolic [$P = 0.009$], and mean arterial blood pressure [$P = 0.010$], as well as relative systolic [$P = 0.012$], diastolic [$P = 0.011$], and mean arterial blood pressure [$P = 0.011$]) and intravenously administered medication (norepinephrine [$P = 0.043$] and sufentanil [$P = 0.025$]).

Association between flap tissue perfusion and sufentanil

The flap tissue perfusion parameters blood flow, hemoglobin oxygen saturation, and flap flow conductance were not associated with sufentanil dose (B = 416.610, $P = 0.779$; B = 13.228, $P = 0.917$; B = 3.496, $P = 0.915$; respectively) (Table 2).

Discussion

This retrospective pilot study investigated the relationships between early postoperative tissue perfusion in RFFFs and intravenously administered propofol and sufentanil during continu-

Table 1
Characteristics of the study population.

Patient	*Parameters*				
Baseline characteristics					
Number	*Sex*	*Age (years)*	*BMI (kg/m²)*	*ASA*	*Diagnosis*
1	Female	53	24.5	II	Squamous cell carcinoma
2	Male	63	35.3	II	Sarcoma
3	Female	63	21.5	III	Squamous cell carcinoma
4	Female	74	28.6	III	Squamous cell carcinoma
5	Male	49	27.1	III	Squamous cell carcinoma
6	Female	81	32.3	III	Squamous cell carcinoma
7	Male	82	24.5	III	Squamous cell carcinoma
8	Female	71	44.2	III	Squamous cell carcinoma

Surgical characteristics				
Number	*Flap location*	*Anastomosis recipient vessel (arterial/venous)*	*Surgery duration (min)*	*Ischemia duration (min)*
1	Intraoral (mouth floor)	Facial artery/Internal jugular vein	548	72
2	Extraoral (buccal)	Superior thyroid artery/Internal jugular vein + HNCV	469	91
3	Intraoral (mandibula)	Facial artery/Internal jugular vein + Anterior jugular vein	550	84
4	Intraoral (mandibula)	Facial artery/Internal jugular vein	430	103
5	Intraoral (tongue)	Facial artery/Internal jugular vein	566	80
6	Intraoral (tongue)	Superior thyroid artery/Internal jugular vein	415	81
7	Extraoral (buccal)	Facial artery/Internal jugular vein	469	106
8	Intraoral (tongue)	Superior thyroid artery/Facial vein	640	108

Parameters are indicated individually for each patient.
ASA, American Society of Anesthesiologists score; BMI, body mass index; HNCV, hypoglossal nerve comitans vein

Table 2
Association between flap tissue perfusion and propofol or sulfentanil.

Medication	*Blood flow (AU)*		*Hemoglobin oxygen saturation (%)*		*Flow conductance (AU/mmHg)*	
	B	*P-value*	*B*	*P-value*	*B*	*P-value*
Propofol	168.788	0.568	37.748	**0.018***	−1.207	0.922
Sulfentanil	416.610	0.779	13.228	0.917	3.496	0.915

Data presented as B coefficient (with *P*-value) corresponding to linear mixed models separately calculated for testing the association between propofol and blood flow, hemoglobin oxygen saturation or flow conductance (calculated as ratio of blood flow and mean arterial blood pressure) as well as sulfentanil and blood flow, hemoglobin oxygen saturation or flow conductance (calculated as ratio of blood flow and mean arterial blood pressure) ($n = 256$).
Significant *P*-values are bold; $^{*}P<0.05$ upon controlling for blood pressure (absolute systolic blood pressure [$P = 0.011$]; absolute diastolic blood pressure [$P = 0.009$]; absolute mean arterial blood pressure [$P = 0.010$]; relative systolic blood pressure [$P = 0.012$]; relative diastolic blood pressure [$P = 0.011$]; relative mean arterial blood pressure [$P = 0.011$]) and medication (norepinephrine [$P = 0.043$]; sufentanil [$P = 0.025$]).
AU, arbitrary units.

ous flap monitoring with an O2C analysis system with attached surface probes, as both medications are often administered postoperatively after microvascular head and neck reconstruction, may influence RFFF tissue perfusion, and thus may confound the monitoring of RFFFs with the O2C analysis system in view of the absolute thresholds indicative of vascular flap compromise.[9-15,21]

The O2C analysis system used for postoperative flap monitoring relies on the measurement of flap tissue perfusion in relation to absolute thresholds indicative of vascular flap compromise (eg, blood flow <60 AU and hemoglobin oxygen saturation <40% for monitoring RFFFs with attached surface probes that measure tissue perfusion at a 3-mm tissue depth).[9-12] In view of these absolute thresholds, influences on the part of both medications on tissue perfusion in RFFFs could interfere with postoperative continuous flap monitoring with the O2C analysis system, resulting in the delayed detection of vascular flap compromise.[7-12,21] While the mechanisms, rather than the existence of a hemodynamic effect on the part of both medications on the general circulation, are actually discussed (eg, hypotension due to a vasodilatory effect), the existence of a hemodynamic effect on the part of both medications on tissue perfusion in microvascular free flaps remains unclear.[16-23] A potential hemodynamic effect on the part of both medications on RFFF tissue perfusion (eg, a reduction of perfusion pressure or an decrease in flap vessel diameter) should be even stronger in microvascular free flaps, as these are susceptible to blood pressure changes and vasoactive medication effects due to denervation.[5,17]

Nevertheless, prior studies addressing the influence of intravenously administered medications on microvascular free flap tissue perfusion focused on vasopressors and also included flap types other than RFFFs and flap locations other than the head and neck region, which is why conclusions regarding RFFFs appear to be difficult to draw.[24-27]

In general, beyond a potentially confounding effect on the part of intravenously administered propofol and sufentanil on the postoperative continuous monitoring of RFFFs with the O2C analysis system, the investigation of their hemodynamic effect could contribute to the understanding of microvascular free flap perfusion and, in the context of flap tissue perfusion being a prerequisite for flap viability and survival, further improvements in the postoperative care of patients undergoing microvascular head and neck reconstruction.[9-12,17,28]

The study showed that hemoglobin oxygen saturation was positively associated with propofol dose, while blood flow and flap flow conductance and propofol dose as well as blood flow, hemoglobin oxygen saturation, and flap flow conductance and sufentanil dose were not associated.

A positive association between blood flow and both medications may have been expected based on a vasodilatory effect on the part of both medications on the local flap vasculature, which should increase blood flow, as vessel diameter is a major determinant of tissue perfusion in terms of blood flow.[16-23] In contrast, a vasodilatory effect on the part of both medications on

the general vasculature, leading to lower systemic blood pressure, should decrease blood flow, as perfusion pressure is also a major determinant of tissue perfusion in terms of blood flow.[16-23] However, no association was observed for blood flow or flap flow conductance and both medications. In this context, the observed and while controlling for several other parameters such as blood pressure persisting positive association between hemoglobin oxygen saturation and propofol is noteworthy. Since hemoglobin oxygen saturation is dependent on blood flow in RFFFs, as the measured hemoglobin oxygen saturation mainly represents hemoglobin oxygen saturation in the venous capillaries of the flap vasculature after oxygen extraction by the flap tissue, the positive association might raise the hypothesis that propofol has a depressant effect on flap tissue oxygen consumption.[9,16,17] However, this hypothesis cannot be explored by the current study design.

In general, regarding the physiology of RFFF tissue perfusion and its measurement for the purpose of postoperative continuous flap monitoring, intravenously administered propofol and sufentanil had in general no influence on early postoperative tissue perfusion in RFFFs in the head and neck region.[28] This suggests robustness of the predefined thresholds for flap tissue perfusion used to detect vascular flap compromise.[9-12] It should further be noted that based on the dosage range of intravenously administered propofol (0-0.1 µg/min per kg body weight), a maximum change in hemoglobin oxygen saturation would be 3.77 percent, unlikely to affect decision making in early postoperative continuous flap monitoring.[9-12]

The strengths of the study (including only RFFFs in the head and neck region and controlling for potential confounders) are associated with the weaknesses of the study (including only a small number of patients and investigating a short postoperative time interval, which was due to the limited availability of data on blood pressure and medication).[17,21] In addition, due to a lack of data, several other patient-related factors that also influence flap tissue perfusion (ie, flap pedicle vessel length) were not considered. Also, despite controlling for each medication studied (ie, for sufentanil when analyzing the influence of propofol and for propofol when analyzing the influence of sufentanil), a separate analysis of the effect of each medication studied could not be performed. In general, the extrapolation of the study results to patients with lower sedation or other postoperative protocols appears to be limited.

This retrospective pilot study investigated the influence of intravenously administered propofol and sufentanil on RFFF tissue perfusion in the context of postoperative continuous flap monitoring with an O2C analysis system using attached surface probes and found that the tissue perfusion in RFFFs was generally not associated with intravenously administered propofol or sulfentanil, except for an association between hemoglobin oxygen saturation and propofol. Further prospective studies based on a larger study cohort and a longer study interval are needed.

Conclusion

This retrospective pilot study showed that early postoperative RFFF tissue perfusion was generally not associated with intravenously administered propofol or sulfentanil. The observed association between hemoglobin oxygen saturation and propofol should be confirmed in further prospective studies with larger study cohorts and longer study intervals with regard to an interference with early postoperative continuous monitoring of RFFFs after head and neck reconstruction.

Credit authorship contribution statement

Mark Ooms: Conceptualization, Methodology, Data Curation, Formal Analysis, Visualization, Writing—Original Draft Preparation; **Philipp Winnand:** Data Curation, Formal Analysis, Writing—Review & Editing; **Marius Heitzer:** Data Curation, Formal Analysis, Writing—Review & Editing; **Nils Vohl:** Validation, Writing—Review & Editing; **Marie Sophie Katz:** Validation,

Writing—Review & Editing; **Johannes Bickenbach:** Resources, Validation, Writing—Review & Editing; **Frank Hölzle:** Resources, Supervision, Validation, Writing—Review & Editing; **Ali Modabber:** Conceptualization, Methodology, Resources, Supervision, Project Administration, Validation, Writing—Review & Editing.

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Declaration of competing interests

The authors declare that they have no conflict of interest.

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