

# Apnoeic oxygenation in adults under general anaesthesia using Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) – a physiological study

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## Abstract

**Background.** Apnoeic oxygenation during anaesthesia has traditionally been limited by the rapid increase in carbon dioxide and subsequent decrease in pH. Using a Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) technique a slower increase in carbon dioxide than earlier studies was seen. Notably, apnoeic oxygenation using THRIVE has not been systematically evaluated with arterial blood gases or in patients undergoing laryngeal surgery. The primary aim of this study was to characterize changes in arterial  $P_{O_2}$ ,  $P_{CO_2}$  and pH during apnoeic oxygenation using THRIVE under general anaesthesia.

**Methods.** Adult patients, (ASA I-II), undergoing shorter laryngeal surgery under general anaesthesia, were oxygenated during apnoea using THRIVE, 100% oxygen, 40–70 litres  $\text{min}^{-1}$ . A cohort was randomized to hyperventilate during pre-oxygenation. Vital parameters and blood gases were monitored.

**Results.** Thirty-one patients, age 51 (34–76) yr, BMI 25 (4) were included. Mean apnoea time was 22.5 (4.5) min. Patients were well oxygenated,  $SpO_2$  was never below 91%. The increase in  $PaCO_2$  and end-tidal  $CO_2$  during apnoea was 0.24 (0.05) and 0.12 (0.04)  $\text{kPa min}^{-1}$ , respectively. Hyperventilation during pre-oxygenation generated no difference in  $PaCO_2$  at the end of apnoea compared with normoventilation.

**Conclusions.** This physiological study of apnoeic oxygenation using THRIVE during laryngeal surgery shows that this technique is able to keep patients with mild systemic disease and a BMI <30 well oxygenated for a period of up to 30 min. The THRIVE concept makes it possible to extend the apnoeic window but monitoring of  $CO_2$  and/or pH is recommended.

**Clinical trial registration.** NCT02706431.

**Key words:** respiration; artificial apnea hypercapnia; carbon dioxide; oxygen; pH

### Editor's key points

- Transnasal Humidified Rapid-Insufflation Ventilatory exchange (THRIVE) may be effective in delaying hypoxia and hypercapnoea, but its efficacy has not been assessed in patients undergoing laryngeal surgery.
- In non-intubated patients who were undergoing laryngeal surgery under general anaesthesia, THRIVE technique was effective in preventing hypoxia and excessive hypercapnoea.

Apnoeic diffusion oxygenation has been evaluated in humans and animals since the beginning of the 20<sup>th</sup> century, but has never served as an alternative to traditional ventilation as a result of the rapid increase of carbon dioxide (CO<sub>2</sub>) and consequential decrease in pH.<sup>1–4</sup> Recently, Transnasal Humidified Rapid-Insufflation Ventilatory exchange (THRIVE) was used to extend the apnoeic window up to 65 min in patients with difficult airways before securing the airway.<sup>5</sup> None of these patients desaturated below 90%. The rate of increase in end-tidal carbon dioxide (ETCO<sub>2</sub>) was 0.15 kPa min<sup>-1</sup>, lower than earlier findings of an increase in ETCO<sub>2</sub> or arterial carbon dioxide (PaCO<sub>2</sub>) of approximately 0.5 kPa min<sup>-1</sup>,<sup>2,6–8</sup> which indicates partial gas exchange.<sup>5</sup> With this mass flow of oxygen into an open airway there are speculations that some amount of CO<sub>2</sub> is flushed out of the airway.<sup>5</sup> Several studies have demonstrated that high-flow oxygen can be beneficial during awake fiberoptic intubation,<sup>9</sup> pre-oxygenation before emergency tracheal intubation in critically ill patients<sup>10</sup> and in patients with intracranial haemorrhage.<sup>11</sup> Taken together, apnoeic oxygenation using THRIVE seems to be a feasible alternative for shorter laryngeal procedures and might also be a safe way to pre-oxygenate patients before and during tracheal intubation, thereby extending the apnoeic window. Notably, to date apnoeic oxygenation using THRIVE has only been demonstrated in a case series of 25 patients and systematic data on arterial blood gases during THRIVE are lacking.<sup>5</sup>

The primary aim of the study was to investigate the changes in arterial oxygen, carbon dioxide and pH over time when THRIVE was used under general anaesthesia during short laryngeal procedures. The secondary aims were (1) to describe PaO<sub>2</sub>, PaCO<sub>2</sub> and pH after hyperventilation during pre-oxygenation, (2) to see whether transcutaneous carbon dioxide measurement is consistent with blood gas analysis and (3) to characterize the difference between ETCO<sub>2</sub> and PaCO<sub>2</sub> at the end of the procedure.

## Methods

### Ethics

This study conforms to the standard of the Declaration of Helsinki and was approved by the Regional Ethics Committee on Human Research at the Karolinska Institutet, Stockholm, Sweden, Dnr 2015/1839-31/2. The study was registered at the US National Institutes of Health #NCT02706431 15<sup>th</sup> Dec 2015, principal investigator Malin Jonsson Fagerlund (ClinicalTrials.gov). The trial was conducted according to Good Clinical Practice and the CONSORT guidelines (CONSORT Checklist, Appendix 1) at the ear, nose and throat operation ward, Department of Anesthesiology, Surgical Services and Intensive Care,

Karolinska University Hospital, Stockholm, Sweden, between December 2015 and May 2016.

### Study subjects

31 adult patients (>18 yr), ASA physical status I–II, presenting for elective short laryngeal procedures, such as microlaryngoscopy, were included in this prospective randomized trial. Participants were enrolled preoperatively by one of four anaesthetists responsible for data collection in the study. Exclusion criteria were ASA physical status >II, New York Heart Association class >2, body mass index (BMI) >30, pregnancy, severe gastrointestinal reflux disease and neuromuscular disease. Patients were included after oral and written informed consent.

### Monitoring

Standard perioperative monitoring including non-invasive blood pressure (NIBP), 3-lead ECG and peripheral oxygen saturation (SpO<sub>2</sub>) (Aisys CS, GE Healthcare, United States) was used throughout the procedure. The patients received an arterial line in the radial artery before induction of anaesthesia and arterial blood gases were obtained before pre-oxygenation and every five min after anaesthesia induction. Blood gases were analysed using an ABL 90 (Radiometer, Brønshøj, Denmark). Transcutaneous carbon dioxide (tcCO<sub>2</sub>) was continuously monitored (Radiometer, Brønshøj, Denmark) with the sensor placed on the left part of the chest after calibration. End-tidal carbon dioxide (ETCO<sub>2</sub>) was measured before pre-oxygenation during spontaneous breathing and on the first breath at end of apnoea. The degree of neuromuscular block was assessed by the train-of-four (TOF) ratio (Aisys CS, GE Healthcare, United States) with the neuromuscular transmission monitor placed over the ulnar nerve measuring adductor pollicis muscle activity.

### Study protocol

Patients were placed in a supine position with the head elevated approximately 10–20 degrees and received a peripheral venous cannula. Ringer-acetate solution (Ringer-Acetat®, Baxter Healthcare Ltd, Thetford Norfolk, Great Britain) was given perioperatively. Of the pre-planned 30 patients, the first 20 patients were randomized into two blocks of 10 subjects each to pre-oxygenation with or without hyperventilation using a randomization plan from <http://www.randomization.com> (last accessed November 19, 2015). Allocation according to randomization was not concealed. In both groups, pre-oxygenation was done with Optiflow™ (Fisher & Paykel Healthcare, Auckland, New Zealand) 40 litres min<sup>-1</sup>, 100% oxygen, for at least three min. In the hyperventilation group, the patients were instructed to take full vital capacity breaths for two min or until dizziness occurred. Anaesthesia was induced by target controlled i.v. infusion (TCI) (Alaris® PK Syringe pump, Cardinal health, Rolle, Switzerland) of propofol (Propofol-Lipuro®, B. Braun Melsungen AG, Melsungen, Germany) and remifentanyl (Ultiva®, GlaxoSmithKline AB, Solna, Sweden). The mean targeted induction concentration was 7.7 (0.9) µg ml<sup>-1</sup> and 6.3 (0.8) ng ml<sup>-1</sup>, and the range of maintenance concentration was 2.5–12.0 µg ml<sup>-1</sup> and 2.5–13.0 ng ml<sup>-1</sup> for propofol and remifentanyl, respectively. Neuromuscular block was achieved by i.v. injection of rocuronium (Esmeron®, MSD, Haarlem, Netherlands) 0.5–0.6 mg kg<sup>-1</sup>. With the onset of apnoea, Optiflow™ was increased to 70 L min<sup>-1</sup>, 100% oxygen, which was maintained throughout anaesthesia. The airway was kept patent by the anaesthetist using jaw thrust until the surgeons rigid tubular laryngoscope

**Table 1** Patient characteristics. Comorbidity were <sup>1</sup> denotes medicated and well controlled hypertension and <sup>2</sup> a previous lobectomy of one lung and mild chronic obstructive pulmonary disease with no need of medication. Patient #27 was excluded because of obstruction of the nasal catheter by the laryngoscope. Data are presented as mean (SD) or frequency (percentage) as appropriate. n = 30. F: female. M: male. MLS = Microlaryngeal surgery. VC = vocal cord

Pat #	Sex	Age (yr)	BMI (kg m <sup>-2</sup> )	Smoker	ASA	Co-morbidity	Reason for surgery	Performed procedure	Duration of surgery (min)	Duration of apnoea (min)	Max PaCO <sub>2</sub> (kPa)	Max tCO <sub>2</sub> (kPa)	Max ETCO <sub>2</sub>	Min pH	SpO <sub>2</sub> end of apnoea (%)
1	F	45	23.3	no	1	no	VC cyst	MLS + biopsy	13	20	9.7	9.9	7.4	7.2	99
2	M	52	24.0	no	1	no	VC papilloma	MLS + biopsy	25	25	10.6	10.8	8.5	7.18	98
3	M	47	23.9	no	1	no	VC polyp	MLS	8	14	7.9	7.9	5.2	7.3	99
4	F	43	22.3	no	1	no	VC oedema	MLS + biopsy	11	19	8.4	9.3	6.3	7.21	100
5	F	48	30.5	no	2	no	VC keratosis	MLS	24	25	10.4	9	7.4	7.16	99
6	F	41	19.0	no	1	no	VC cyst	MLS + biopsy	29	30	10.6	10.7	7.4	7.14	99
7	M	50	24.9	no	2	no	Hypo-pharyngeal cancer	MLS	10	11	7.9	8.2	5.7	7.26	98
8	M	59	25.1	no	1	no	VC papilloma	MLS + biopsy	25	26	10.7	10.4	6.9	7.16	99
9	M	64	22.8	no	1	no	VC polyp	MLS + biopsy	13	21	5.9	5.7	4.4	7.37	100
10	F	46	21.3	no	1	no	VC papilloma	MLS + biopsy	20	20	11.0	10.7	7.6	7.16	98
11	M	42	24.3	no	1	no	VC polyp	MLS	17	21	8.9	8.9	7.4	7.27	99
12	F	68	21.8	yes	2	no	VC cyst	MLS + biopsy	18	20	10.8	10.4	9.0	7.17	99
13	M	64	28.0	no	1	yes	Sinus Morgagni cyst	MLS + biopsy	24	25	11.0	10.1	6.5	7.15	99
14	M	71	23.5	no	2	no	VC keratosis	MLS + biopsy	16	20	11.1	9.9	8.5	7.19	99
15	M	76	22.1	yes	1	yes	VC keratosis	MLS + biopsy	43	25	10.8	8.9	8.4	7.14	99
16	M	48	28.8	yes	2	no	VC keratosis	MLS + biopsy	20	20	10.2	10.4	6.3	7.22	93
17	M	36	25.1	yes	2	no	VC papilloma	MLS + biopsy	15	20	9.8	9.9	7.2	7.23	99
18	M	34	22.5	no	1	no	VC papilloma	MLS + biopsy	20	20	11.8	11.7	7.0	7.15	99
19	F	76	19.5	no	2	no	VC keratosis	MLS + biopsy	20	21	11.3	11.5	6.7	7.17	98
20	M	49	32.2	no	1	yes	VC papilloma	MLS + biopsy	20	21	11.1	12.9	7.3	7.15	91
21	M	35	29.4	no	1	no	VC papilloma	MLS + biopsy	20	22	11.4	12.2	9.7	7.17	92
22	F	53	30.3	no	2	yes	VC papilloma	MLS + biopsy	22	23	9.4	9.7	6.6	7.22	98
23	M	35	24.7	no	1	no	VC papilloma	MLS + biopsy	10	20	8.8	10.1	7.3	7.25	99
24	M	69	24.5	no	1	no	VC keratosis	MLS + biopsy	16	20	10.2	10	7.1	7.22	100
25	M	51	32.2	no	2	no	VC polyp	MLS + biopsy	29	29	11.5	12.6	8.5	7.17	100
26	M	51	24.6	no	1	no	VC polyp	MLS + biopsy	20	22	9.9	9.7	7.0	7.2	100
28	M	43	26.0	no	2	no	VC cyst	MLS + biopsy	24	27	11.8	13.9	8.7	7.14	99
29	M	62	25.2	no	1	yes	Contact granuloma	MLS + biopsy	24	28	9.3	11.3	7.0	7.16	98
30	F	27	22.2	no	1	no	VC cyst	MLS + biopsy	30	33	11.6	11.2	8.6	7.13	100
31	M	44	29.6	no	1	no	VC cyst	MLS + biopsy	39	27	12.2	11.9	9.2	7.13	97
Average (SD)									20.8 (7.8)	22.5 (4.5)	10.2 (1.4)	10.3 (1.6)	7.4 (1.2)	7.2 (0.05)	98.2 (2.2)

was put in place in full suspension, ensuring that the dorsal part of the laryngeal inlet was open to oxygen flow at all times. During the procedure blood-gas analyses were assessed every five min. TcCO<sub>2</sub>, ECG, arterial BP and SpO<sub>2</sub> were measured continuously. Neuromuscular block was monitored with a TOF ratio registered every five min throughout the procedure with a mean TOF ratio of 6.0 (12.7) % during apnoea. Reversal was done with a fixed dose of 200mg of sugammadex (Bridion®, MSD, Hertfordshire, Great Britain), which was enough to reverse the neuromuscular block to a TOF ratio >90%. At the end of the procedure the airway was repossessed by the anaesthetist and the patient was mask ventilated until spontaneous breathing reoccurred. ETCO<sub>2</sub> was measured on the first breath at end of apnoea when ventilated with a mask or a tracheal tube if intubated because of discontinuation criteria below. The apnoeic time was until the procedure was completed or until a discontinuation criterium occurred.

Discontinuation criteria were a procedure duration > 40 min, PaCO<sub>2</sub> > 11 kPa, pH < 7.15, SpO<sub>2</sub> < 90% or occurrence of malignant arrhythmias. If any of the criteria was fulfilled the apnoeic period was ended by intubation with a tracheal tube and ventilated mechanically or jet ventilated.

Postoperatively patients were monitored with non-invasive BP, ECG and SpO<sub>2</sub>. Blood gases were analysed at admission and discharge. Participation in the study was concluded when the patient left the post-anaesthesia care unit (PACU).

#### Sample size calculation

The primary outcomes of this study are descriptive and therefore no power analysis was done on these and we planned for 30 patients to target the primary outcomes. Before study start, a power analysis for the effect of hyperventilation on the increase in PaCO<sub>2</sub> was designed to have a two-tailed alpha error of 0.05 and a beta error of 0.2 (power 80%). If the true difference between normoventilation and hyperventilation at 20 min was at least 1.5 kPa and a standard deviation of 1.0 kPa, a sample size of eight in each group was suggested. In order to compensate for dropouts we planned for 10 patients in each group.

#### Statistical analysis

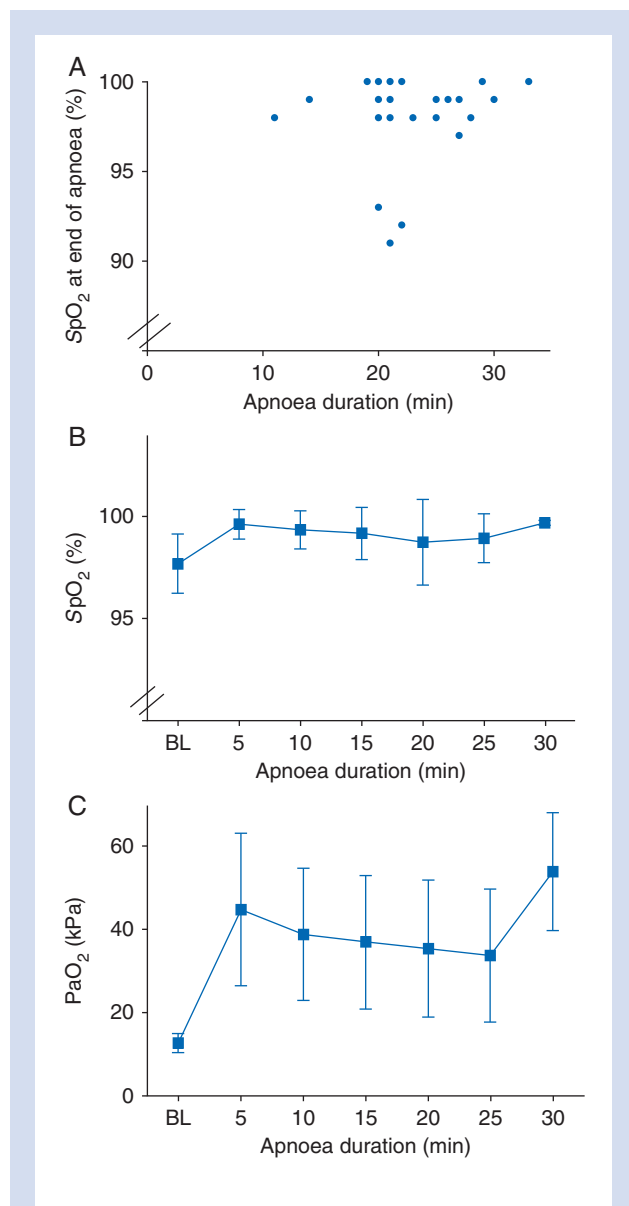
Data are presented as mean (SD) or range and pre-planned analysis was done using paired or un-paired Student's t-tests as appropriate when comparing two variables. As the duration of apnoea was different between the patients and the apnoeic time largely dependent on the surgery we decided to analyse the hyperventilation trial with an unpaired Student's t-test at the last point in time where all patients were in the trial (i.e. at 10 min). Statistical analysis and graphs were made using Prism 6.0 and Statmate 2 (GraphPad, Software Inc., La Jolla, CA, USA). A P-value of <0.05 was considered statistically significant.

## Results

### Study population

Thirty patients completed the study protocol (CONSORT flow diagram, Appendix 2). One patient was excluded from the study because of obstruction of the nasal catheter by the laryngoscope used during surgery. For two patients the pre-operative blood gas is missing as a result of technical difficulties. Patient characteristics data is presented in Table 1.

The apnoeic time was 22.5 (4.5) min. In one patient the surgery was not finished when PaCO<sub>2</sub> was 11 kPa (discontinuation

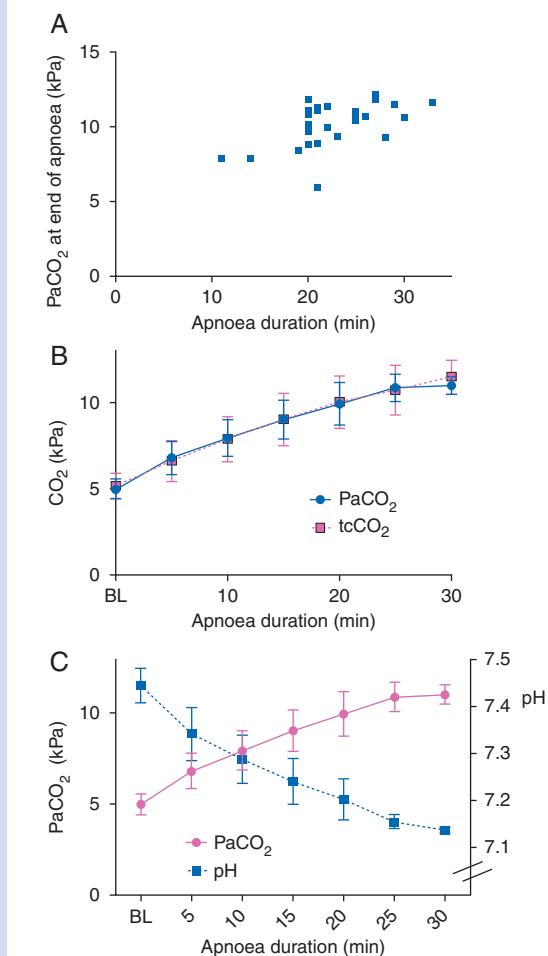


**Fig 1** Oxygenation during THRIVE. Relationship between total apnoea duration and peripheral oxygen saturation (SpO<sub>2</sub>) at the end of apnoea for each subject (A). Each point represents an individual patient. Peripheral oxygen saturation (SpO<sub>2</sub>) (B) and partial pressure of arterial oxygen (PaO<sub>2</sub>) (C) during 30 min of apnoeic oxygenation using 100% oxygen. The Y-axis in A and B has been adjusted to display maximal resolution of data (i.e. does not start from 0). Data are presented as mean (SD) (B and C), n = 30. BL = Baseline values before pre-oxygenation.

criteria), therefore supraglottic jet ventilation was initiated. For all other patients apnoea was terminated because surgery was finished. The study was terminated as planned when 30 participants had completed the protocol.

### Primary outcome: changes in PaO<sub>2</sub>, PaCO<sub>2</sub> and pH

All patients were well oxygenated throughout the procedure and none had a SpO<sub>2</sub> below 91% (Fig. 1). A summary of apnoea times and corresponding PaO<sub>2</sub> and PaCO<sub>2</sub> values at the end of



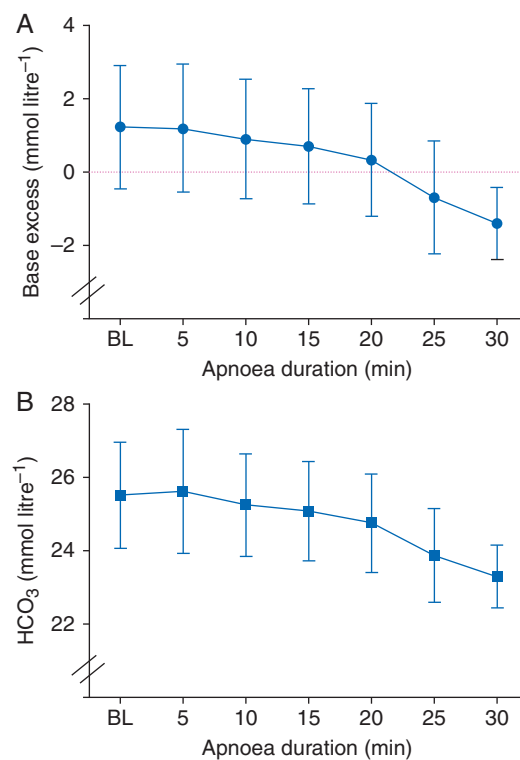
**Fig 2** Carbon dioxide and pH levels during THRIVE. Relationship between total apnoea duration and partial pressure of arterial carbon dioxide ( $\text{PaCO}_2$ ) at the end of apnoea for each subject (A). Each point represents an individual patient. Partial pressure of arterial carbon dioxide ( $\text{PaCO}_2$ ) and transcutaneous carbon dioxide ( $\text{tcCO}_2$ ) (B) and partial pressure of arterial carbon dioxide ( $\text{PaCO}_2$ ) and pH over time during apnoeic oxygenation (C). Data are presented as mean (SD),  $n = 30$ . BL = Baseline values before pre-oxygenation.

apnoea are presented in Figures 1A and 2A. The increase in  $\text{PaCO}_2$  was  $0.24$  ( $0.05$ )  $\text{kPa min}^{-1}$ . The pH decreased from  $7.44$  ( $0.04$ ) to  $7.14$  ( $0.01$ ) (Fig. 2C). Base excess and bicarbonate are presented in Figure 3.

## Secondary outcomes

### Hyperventilation

The first 20 patients were randomized to normal breathing or hyperventilation during pre-oxygenation. Immediately after hyperventilation during pre-oxygenation  $\text{tcCO}_2$  was  $4.18$  ( $0.82$ ) kPa compared with the resting value before pre-oxygenation of  $5.05$  ( $1.00$ ) kPa ( $P = 0.0001$ ),  $n = 10$ . At five min  $\text{tcCO}_2$  did not differ compared with those who normoventilated (Fig. 4C). Therefore no difference in  $\text{PaCO}_2$  and pH over time between the groups



**Fig 3** Base excess (A) and standard bicarbonate ( $\text{HCO}_3^-$ ) (B) levels during apnoeic oxygenation. Data are presented as mean (SD),  $n = 30$ . BL = Baseline values before pre-oxygenation.

with or without hyperventilation during pre-oxygenation with Optiflow<sup>TM</sup> was seen (Fig. 4).

### Comparison between arterial and transcutaneous carbon dioxide

There was no difference between  $\text{tcCO}_2$  and  $\text{PaCO}_2$  (Fig. 2B).

### Arterial-alveolar and end-tidal carbon dioxide difference before and after apnoeic oxygenation using THRIVE

In 17 of the patients a preoperative  $\text{ETCO}_2$  was measured and the difference between  $\text{ETCO}_2$  and  $\text{PaCO}_2$  was  $0.73$  ( $1.35$ ) kPa pre-operatively and increased to  $3.11$  ( $0.95$ ) kPa ( $P < 0.0001$ ) at the end of the procedure. The increase in  $\text{ETCO}_2$  was  $0.12$  ( $0.04$ )  $\text{kPa min}^{-1}$ .

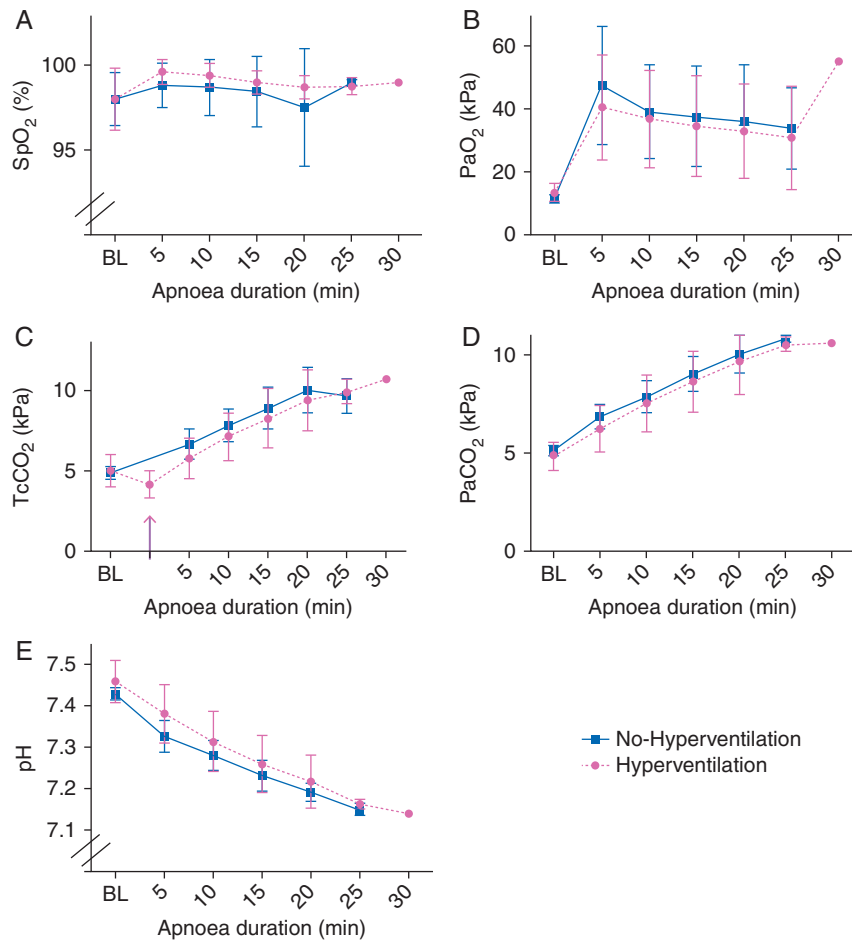
### Circulatory effects

A reduction of BP was observed during the first 10 min (Fig. 5). The heart rate was stable during apnoea and no patients experienced arrhythmias except a few single ventricular extra systoles without effect on haemodynamics.

### Subjective experience of the surgeon

The surgeons reported more favourable conditions for surgery using apnoeic oxygenation in all patients ( $n = 30$ ), compared with a traditional technique using tracheal tube, jet ventilation or apnoea combined with mask ventilation.





**Fig 4** Effect of hyperventilation on oxygenation (A and B) and carbon dioxide level (C and D) during apnoeic oxygenation using THRIVE. Transcutaneous  $\text{CO}_2$  ( $\text{tcCO}_2$ ) measured after hyperventilation during pre-oxygenation in 10 patients (arrow in the  $\text{tcCO}_2$  graph). There were no differences in  $\text{PaCO}_2$  between hyperventilation vs normoventilation at apnoea duration 10 min ( $P = 0.50$ ). Data are presented as mean (SD),  $n = 20$ . BL = Baseline values before pre-oxygenation.

### Postoperative care

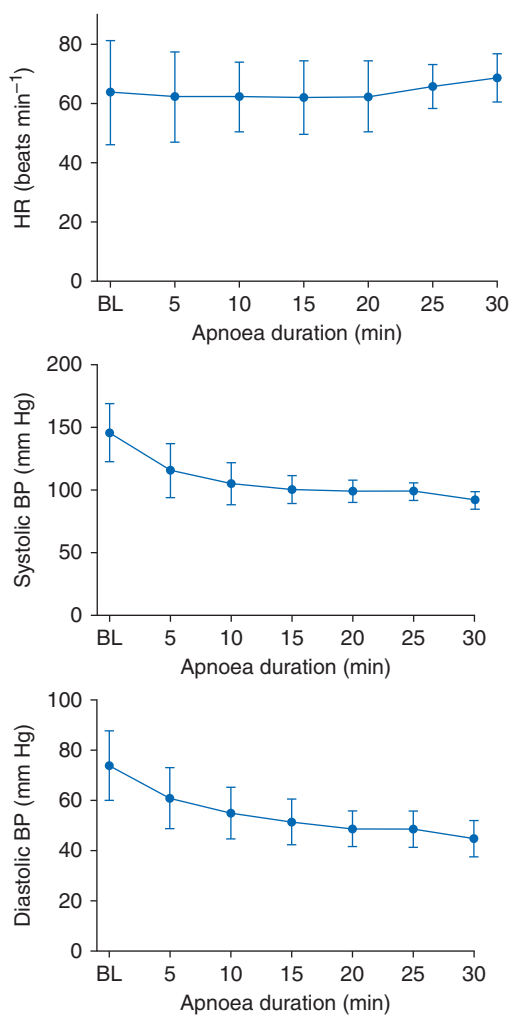
The peripheral oxygen saturation was 97 (1.8) % on arrival to PACU. No patient experienced desaturation below 91%. The  $\text{PaO}_2$  was 13.6 (4.4) kPa at admission and 11.3 (1.9) kPa at discharge. The  $\text{PaCO}_2$  was 5.79 (0.56) kPa at admission and 5.51 (0.43) kPa at discharge. All patients were routinely put on supplemental  $\text{O}_2$  on transport from operation room to PACU and 13 patients received additional nasal oxygen of 1-3 litres  $\text{min}^{-1}$  in the PACU. All patients were haemodynamically stable. Mean length of stay in the PACU was 70 (28) min.

### Discussion

In this prospective interventional trial we demonstrate that oxygenation during apnoea using THRIVE maintains the patients well oxygenated for up to 30min with arterial pH of 7.13 or above. The increase in  $\text{PaCO}_2$  was approximately  $0.24 \text{ kPa min}^{-1}$  in contrast to a less marked increase of  $0.12 \text{ kPa min}^{-1}$  when capnography was used. The increase in  $\text{ETCO}_2$  is in parallel with the study by Patel and Nouraei<sup>5</sup> but our results show that capnography underestimates the accumulation of  $\text{CO}_2$ .

### Comparison with previous studies

The prerequisite for apnoeic oxygenation is that 100% oxygen is delivered in an airway that remains open and that full denitrogenation has been accomplished. Provided that those criteria have been fulfilled, oxygen saturation has been maintained for time periods as long as 65 min.<sup>2 5 12</sup> The limiting factor for the duration of apnoeic oxygenation is not oxygenation but rather increase in  $\text{CO}_2$  and lowering of arterial pH.<sup>2 6-8 12 13</sup>  $\text{CO}_2$  moves from the bloodstream into the alveoli by passive diffusion during apnoea, but is also buffered in the blood. The increase of  $\text{PaCO}_2$  level varies between studies. In a study mimicking total airway occlusion, completely without  $\text{CO}_2$  washout, an average increase of  $\text{CO}_2$  of  $0.68 \text{ kPa min}^{-1}$  was seen.<sup>8</sup> Older studies of apnoeic oxygenation supplying a flow of oxygen of approximately  $0.2 \text{ litres min}^{-1}$  gave an average  $\text{CO}_2$  increase between  $0.43$  and  $0.56 \text{ kPa min}^{-1}$ .<sup>2 6 7</sup> Increasing the oxygen flow and delivering it endobronchially with thin catheters allowing for gas exchange outside of the lung resulted in a lower increase of  $\text{CO}_2$  ( $0.24 \text{ kPa min}^{-1}$ )<sup>12</sup> or even steady state,<sup>13</sup> thereby managing elimination of  $\text{CO}_2$  during apnoea. This was recently extended in a case series by Patel and Nouraei<sup>5</sup> using



**Fig 5** Circulatory effects, heart rate (HR), systolic blood pressure (BP) and diastolic blood pressure (BP) during apnoeic oxygenation using THRIVE under general anaesthesia. Data are presented as mean (SD),  $n = 30$ . BL = Baseline values before pre-oxygenation.

transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) with Optiflow during apnoea with the goal of securing a difficult airway. With a high flow of oxygen of 70 litres  $\text{min}^{-1}$  delivered nasally  $\text{CO}_2$  increased with a rate of  $0.15 \text{ kPa min}^{-1}$  measured by capnography.<sup>5</sup> In our study we had different rates of accumulation of  $\text{CO}_2$  depending on the method of analysis, end-tidal vs arterial and transcutaneous. As the gradient between  $\text{ETCO}_2$  and  $\text{PaCO}_2$  was increased over time capnography is clearly not a reliable method of monitoring during extended apnoea. More importantly, capnography cannot be used during apnoeic oxygenation.

In both studies the airway was kept patent at all times, but in the present study partial blocking of the laryngeal inlet created by the surgeon's tubular laryngoscope could potentially affect the mass flow of gas. As we had the same increase in  $\text{ETCO}_2$  as in the above mentioned study, gasflow around the tubular laryngoscope seems to be sufficient. Muscle activity of the diaphragm and

minimal movements can eliminate  $\text{CO}_2$  during apnoea. Therefore we aimed for full muscle relaxation and close monitoring, making sure the patients were truly apnoeic the entire study period. Blocking muscular action could lower the production of  $\text{CO}_2$  from skeletal muscle,<sup>14</sup> while minimal recovery of neuromuscular transmission resulting in spontaneous ventilation might enhance  $\text{CO}_2$  clearance. Both administration and monitoring of neuromuscular activity have varied in previous studies.<sup>2 6-8 12 13</sup>

The increase of  $\text{CO}_2$  during THRIVE in the current study presents a non-linear pattern with an initial quick increase of the  $\text{CO}_2$  that levelled off during the apnoeic period, as has been described in previous studies.<sup>6 8 15</sup> The exact mechanism behind this is not fully understood.

Hyperventilation had a limited and brief effect of lowering the  $\text{PaCO}_2$  but could not substantially affect  $\text{PaCO}_2$  to prolong the apnoeic window.

Transcutaneous  $\text{CO}_2$  showed good correlation to arterial  $\text{CO}_2$  with no detectable difference, which is in line with other studies.<sup>16</sup>

The high flow of oxygen delivered by Optiflow<sup>TM</sup> provides a slight positive airway pressure<sup>17 18</sup> that could increase functional residual capacity,<sup>19</sup> prevent atelectasis caused by anaesthesia and apnoea<sup>20</sup> and improve gas exchange. Despite this, we noted an increased arterial-alveolar  $\text{CO}_2$  difference during the apnoeic period.

### Study strengths and limitations

Repeated systematic arterial blood gas sampling during apnoeic oxygenation with THRIVE was done for the first time and correlated to  $\text{tcCO}_2$  which might be more convenient for use in a clinical situation.

Only non-obese patients of ASA class I-II were included. The conclusions may therefore not be applicable to patients with obesity or advanced cardiopulmonary disease. Randomization in the present study was done regarding hyperventilation, but was not blinded to the examiner.

### Clinical relevance and direction of future studies

The present study demonstrates that apnoeic oxygenation using THRIVE could act as an alternative to conventional ventilation techniques during short time laryngeal surgery. Potential clinical advantages using THRIVE during laryngeal surgery are higher accessibility to the operating field and less vibrations than caused by jet ventilation.

Based on this study, it is likely that the THRIVE technique could be applied to extend the time to desaturation in other situations (i.e. emergencies). As we have only studied ASA I-II patients with a BMI below 30, it is of importance to evaluate this technique in patients with more pronounced systemic disease and more importantly a higher BMI. There are older data indicating that a higher BMI, often associated with a lower functional residual capacity, shortens the time to desaturation during apnoea,<sup>21</sup> but this has not been investigated using THRIVE. Also, if there is a substantial V/Q mismatch present, even a high flow of oxygen during apnoea will not be enough to counteract hypoxia.<sup>22</sup>

Moreover, much is still unknown regarding the basic physiology of THRIVE. The effects of a progressive increase of  $\text{CO}_2$  and acidosis using THRIVE regarding other organs of the body and toxic effects of hyperoxia need to be further evaluated. Finally, the airway pressure, flow mechanics and mechanism for  $\text{CO}_2$  washout remain to be described.

## Conclusions

This physiological study of apnoeic oxygenation using THRIVE during laryngeal surgery shows that this technique is able to keep patients with mild systemic disease and a BMI <30 well oxygenated and with a pH at or above 7.13 for a period of 30 min. THRIVE makes it possible to extend the apnoeic window, but transcutaneous or arterial monitoring of CO<sub>2</sub> and/or pH should be used as capnography is not accessible during apnoea.

## Authors' contributions

Study design/planning: I.-M.G., Å.L., J.U., M.J.F.

Study conduct: I.-M.G., Å.L., J.T., J.U.

Data analysis: I.-M.G., Å.L., J.U., M.J.F.

Writing paper: I.-M.G., Å.L., J.U., M.J.F.

Revising paper: all authors

## Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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## Declaration of interest

None declared.

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