Increased apparatus dead-space and tidal volume increases blood concentrations of oxygen and sevoflurane in overweight patients – a randomized controlled clinical study

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Abstract

Background and objective: General anesthesia impairs respiratory function in overweight patients. We wanted to determine if increased tidal volume (V_T), with unchanged end-tidal carbon dioxide partial pressure ($P_{ET}CO_2$), affects blood concentrations of oxygen and sevoflurane in overweight patients.

Methods: Prospective, randomized, clinical study. ASA physical status I and II patients with BMI over 25 scheduled for elective surgery of the lower abdomen were randomly assigned to one of two groups with 10 patients in each. One group was ventilated with normal V_T (NV_T) and one group with increased V_T (IV_T) achieved by increasing inspired plateau pressure 0.04 cm H_2O kg^{-1} above initial plateau pressure. Extra apparatus dead space was added to maintain $P_{ET}CO_2$ at 4.5 kPa. Respiratory rate was set at 15 min^{-1}, and sevoflurane was delivered to the fresh gas by a vaporizer set at 3%. Arterial oxygenation, sevoflurane tensions ($P_a$sevo, $F_i$sevo, P_{ET}sevo), P_aCO_2, $P_{ET}CO_2$**,** V_T and airway pressure were measured.

Results: The two groups of patients were similar with regard to gender, age, weight, height and BMI. Arterial oxygen tension (mean ± SD) was significantly higher in the IV_T group (15±4.3 kPa vs. 10±2.7 kPa after 60 min anesthesia, $P < 0.05$). Mean P_{ET}sevo did not differ between the groups, while arterial sevoflurane tension (mean ± SD) was significantly higher in the IV_T group (1.74 ± 0.18 kPa vs. 1.43 ± 0.19 kPa after 60 min anesthesia, $P < 0.05$).

Conclusion: Ventilation with larger tidal volumes with isocapnia maintained with added apparatus dead-space increases the tension of oxygen and sevoflurane in arterial blood in overweight patients.

Key words: anesthesia, sevoflurane, FRC, pulmonary gas exchange

Introduction

Respiratory function and pulmonary gas exchange are regularly impaired during general anesthesia. Atelectasis appears in around 90% of all patients after induction of anesthesia and Rothen and colleagues found a linear correlation between atelectasis and shunt. [1 - 4] Some authors describe a relationship between airway closure and the body constitution under general anesthesia with mechanical ventilation, i.e. the functional residual capacity and respiratory compliance decreases exponentially in the supine position with increased body mass index. [4, 5] In morbidly obese patients general anesthesia and paralysis lead to even more atelectasis and an increased risk of hypoxemia. [6]

Luttropp and Johansson demonstrated a method to ventilate with larger tidal volumes during general anesthesia with maintained isocapnia by introducing increased apparatus dead-space for partial rebreathing of CO_2. [7] In previous studies we found moderately improved oxygenation and a reduced difference between arterial and exhaled carbon dioxide tension with larger tidal volumes achieved this way in patients with BMI less than 25. [8] The results were similar to what could be expected from an increase in functional residual capacity (FRC) and also included a more efficient uptake of sevoflurane. [9] We hypothesized that larger tidal volumes would increase arterial concentration of oxygen and volatile anaesthetics in overweight patients as well. In the present study we therefore determined if larger tidal volumes affect arterial concentration of oxygen and sevoflurane in patients with BMI over 25 kg m^{-2} undergoing abdominal surgery.

Method

Ethics

Ethical approval for this study according to the standards set in the Helsinki declaration (Regional Ethics Committee, Dnr: 480/2007) was provided by Regional Ethics Committee Lund, Sweden (Chairperson L. Noltorp) on 6 November 2007. Consent to participate in the study was received from each patient.

Patients

The investigation included 20 patients, ASA physical status 1 or 2, scheduled for elective colon surgery at Skane university hospital, Lund Sweden, between September 2009 to January 2010. Patients were considered for inclusion in the trial if they were over 18 yr age and had a BMI > 25 kg m^{-2}. All procedures were estimated to last more than 60 minutes. Patients with known pulmonary or cardiovascular disease were excluded. Patients were randomized to one of two groups with 10 patients in each group via randomly mixed sealed envelope assignment at the start of the procedure in the operating theatre (Fig1).

Experimental procedure

Before start of anesthesia, an unused carbon dioxide absorber was applied (Drägersorb, Dräger Medical, Lübeck, Germany) to the anasthesia ventilator (Dräger Primus™, Dräger Medical, Lübeck, Germany). All patients were preoxygenerated with 100% oxygen for 3-4 minutes with a fresh gas flow of 5 liters $minute^{-1}$. Anesthesia was induced with 2 µg kg^{-1} fentanyl and 1.5-3.0 mg kg^{-1} propofol. Atracurium 0.6 mg kg^{-1} was administered for muscle paralysis. Ventilation was assisted manually with 100% oxygen via a semiopen circle system (4.5 L volume) until tracheal intubation and then by means of ventilator with a FiO_2 at 0.35 in nitrogen. No positive end expiratory pressure (PEEP) was applied. Propofol 8 mg kg^{-1} h^{-1} was infused until an arterial cannula had been inserted in the radial artery.

In the group with normal tidal volume (NV_T), respiratory rate was set to 15 min^{-1} and V_T was adjusted as to achieve a $P_{ET}CO_2$ at 4.5 kPa. In the group with increased tidal volume (IV_T), respiratory rate was set to 15 min^{-1}. Initial plateau pressure ($P_{plateau}$) was monitored and then V_T was increased until $P_{plateau}$ was 0.04 cm H_2O kg^{-1} over the initial $P_{plateau}$. In a previous study an increase in $P_{plateau}$ of 0.04 cm H_2O kg^{-1} was found to result in a mean increase in tidal volume of 3.3 ml kg^{-1} in adult patients. [7] The $P_{ET}CO_2$ was then adjusted to 4.5 kPa with a flexible corrugated hose (disposable plastic tube, Medcore, AB Uppsala, Sweden) placed between the Y-piece of the anesthesia circle system and the heat and moisture filter (HME) attached to the endotracheal tube.[7] This flexible corrugated hose increased the dead-space volume and provided adjustable rebreathing of carbon dioxide. In both groups, inspiratory:expiratory ratio was 1:2 including an inspiratory plateau of 10%. When stable $P_{ET}CO_2$ values reached 4.5 kPa, a control (time zero) sample of arterial blood was obtained and sevoflurane administration was started with a vaporizer (sevoflurane Dräger Vapor 2000: Medical, Lübeck, Germany) set to 3%. After 5 minutes the fresh gas flow was adjusted to 1.0 L min^{-1} with an unchanged vaporizer setting throughout the anesthesia period.

Blood samples of 3 ml were drawn from the arterial line into heparinized syringes at 0, 1, 3, 5, 10, 15, 30, 45 and 60 minutes after the start of the sevoflurane administration (totally 27 ml). Arterial oxygen tension (P_aO_2), oxygen saturation (S_aO_2) and carbon dioxide tension (P_aCO_2) were analyzed using an automatic blood gas analyzer (ABL 725™, Radiometer, Copenhagen Denmark). Sevoflurane concentration was analyzed with gas chromatography (GC) on a Perkin-Elmer 3920 gas liquid chromatograph, as previously described. [9, 10]

Patients were monitored with 3-lead ECG, heart rate, oxygen saturation, as measured by pulse oximeter (SpO_2), invasive arterial blood pressure via the arterial cannula, (Intelli Vue MP70 Anesthesia, Philips Medizin System, Boeblingen Germany), inspiratory and expiratory oxygen partial pressure (F_iO_2, $P_{ET}O_2$), sevoflurane inspiratory and expiratory partial pressure ($F_i$sevo, P_{ET}sevo) and carbon dioxide inspiratory and expiratory partial pressure (F_iCO_2, $P_{ET}CO_2$) as analyzed by the ventilator. Total ventilation min^{-1}, tidal volumes and airway pressures as peak pressure, plateau pressure and mean pressure were measured and documented at the same intervals. Static compliance of the respiratory system was calculated as tidal volume divided by the inspiratory plateau pressure.

Extra doses of fentanyl (50-100 µg) were given if mean arterial blood pressure (MAP) increased more than 20% above the initial baseline level. Hypotension (MAP < 60 mmHg) was treated with 5-10 mg ephedrine intravenously. All patients received 3-5 ml kg^{-1} h^{-1} of glucose solution 2.5% with sodium (70 mmol l^{-1}), chloride (45 mmol l^{-1}) and acetate (25 mmol l^{-1}) intravenously. Neuromuscular blockade was monitored with a neuromuscular transmission analyzer (TOF-Watch™; Organon Technology B V., Boxel Netherlands).

Additional doses of atracurium were given at the discretion of the anesthetist.

Statistics

All statistical analysis were performed with SPSS 16.0 for Windows, (SPSS Inc., Chicago, IL, USA). An initial power analysis assuming a $P_a$sevo concentration difference at 0.3 kPa with a SD of 0.2 kPa, revealed that 7 patients in each group would be needed to achieve a power of 0.8 at $P < 0.05$. Ten patients in each group were enrolled. Descriptive variables, tidal volumes, airway pressures, S_PO_2 and lung compliance are expressed as median and inter quartile range in square brackets and analyzed with a non-parametric method according to Mann-Whitney test. The values of F_iO_2, $P_{ET}O_2$, $F_i$sevo, P_{ET}sevo, $P_a$sevo and $P_{ET}CO_2$ are presented as mean ± SD and the analysis was conducted with an independent two-tailed t-test. For change of values over time, an analysis with a two-way repeated measurement ANOVA was used. The ANOVA analysis was followed by Greenhouse-Geisser *post hoc* test. A *P*-value < 0.05 was considered to indicate statistical significance.

Results

The two groups of patients were similar with regard to gender, age, weight, height and body mass index (BMI, Table 1). No 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.

Tidal volumes were significantly larger in the IV_T group, (Table 2). Peak and mean airway pressure were also significantly higher in the IV_T group compared to the NV_T group (Table 2). The median adjustable dead-space volume between the Y-piece and HME in the IV_T group was 3.0 [2.8-4.0] ml^{-1} kg and lung compliance was higher in the IV_T group throughout the observation period ($P < 0.05$, Table 2).

Mean end-tidal carbon dioxide values ($P_{ET}CO_2$) were similar in the two groups (Table 3). P_aCO_2 was, however, lower in the IV_T group throughout the observation period ($P < 0.05$, Table 3) and the difference between P_aCO_2 and $P_{ET}CO_2$ was smaller in the IV_T group compared to the NV_T group ($P < 0.05$, Table 3).

All patients received ventilation with a F_iO_2 of 35%, except three patients from the NV_T group, which received an increased F_iO_2 after a period of S_PO_2 less than 91%. The values of S_PO_2 and P_aO_2 were significantly higher in the IV_T group compared to the NV_T group ($P <$ 0.05, Table 4).

P_{ET}sevo was lower in the IV_T group between 1-5 min ($P < 0.05$, fig. 2), but not between 10 and 60 minutes (Table 5). Mean $P_a$sevo was higher in the IV_T group compared to the NV_T group from 5 minutes and the difference increased with time ($P < 0.05$, Table 5, Fig. 2). The difference between $P_a$sevo and P_{ET}sevo was smaller in the IV_T group compared to the NV_T group ($P < 0.05$, Table 5, Fig. 2).

Discussion

In the present study, mean P_aO_2 and $P_a$sevo were found to be higher in overweight patients ventilated with larger tidal volumes. This is in line with previous results obtained from patients with normal weight. [8, 9] Mean F_iO_2 and $F_i$sevo did not differ between the groups. Thus, differences in inspired concentrations could be ruled out as explanations for the increased oxygen and sevoflurane uptake in the IV_T group.

Reduced FRC makes airway closure more frequent, which is a likely explanation for the appearance of regions with a low ventilation/perfusion ratio and atelectasis during anesthesia. [4, 11] In fact, atelectasis and airway closure may explain 75% of the deterioration in PaO_2. [4] Neumann and colleagues demonstrated a significant inverse correlation between PaO_2 and atelectasis. [12] In the present study, plateau pressure did not differ between the two groups but tidal volume was considerably larger in the IV_T group compared the NV_T group resulting in larger lung compliance in the IV_T group. A plausible explanation to the increase in compliance is recruitment or decreased loss of ventilated lung tissue by the larger tidal volume. This is supported by the findings by Erlandsson and colleagues who showed that a recruitment maneuver resulted in decreased plateau pressure and increased lung compliance with a decreased shunt VD_{alv}/VT. [13]

It is reasonable to assume that the recruitment of ventilated lung tissue increased FRC in the IV_T group. This is in line with the results presented by Reinius and colleagues who showed that a recruitment maneuver followed by PEEP reduced atelectasis, improved oxygenation and increased compliance in obese patients. [14] Conversely, the lower value of lung compliance in the NV_T group could indicate more atelectasis of lung tissue in this group. This is supported by the need to increase F_iO_2 in three patients of this group in order to maintain a S_pO_2 above 90%, indicating pulmonary shunting of venous blood. Pelosi and colleagues found that an increase in BMI can be related to a reduction in FRC after induction of anesthesia, which makes atelectasis more frequent.[5] It should be noted that we did not directly assess the development of atelectasis in the present study. Thus, apart from reduced atelectasis our findings could at least partly be explained by increased alveolar ventilation in the IV_T group.

Patients in the NV_T group received an average tidal volume of 5.0 ml kg^{-1} (total weight), and apparently is developed of regions with abnormal ventilation/perfusion. Routinely, PEEP of 5-10 cmH_2O is applied in order to prevent this. The present results suggest that increasing tidal volumes might have a similar effect but at a lower expense by means of lower mean airway pressure and perhaps subsequent reduction of lung injury and circulatory impairment. A randomized study comparing PEEP with large tidal volumes during anesthesia to overweight patients is, however, needed to test this hypothesis.There is, however, one influence on the present oxygenation and arterial sevoflurane concentration in this study which has not been ruled out, a possible intrinsic PEEP. Unfortunately, our equipment did not measure intrinsic PEEP levels. This is a limitation of the study.

The P_aCO_2 levels were slightly lower in the IV_T group and could contribute to increased $P_a$sevo levels by mean of just increased ventilation. However, the $P_{ET}CO_2$ were similar between the groups and indicates that the increased levels of $P_a$sevo could be explained by increased alveolar ventilation in the IV_T group. The P_{ET}sevo – $P_a$sevo difference was greater in the group ventilated with smaller tidal volumes in the absence of PEEP. This must be kept in mind in order to avoid overestimation of depth of anesthesia when assessed on the basis of P_{ET}sevo in patients ventilated this way.

In conclusion, in patients with BMI over 25, ventilation with larger tidal volumes with isocapnia accomplished with an added apparatus dead-space improves oxygen and sevoflurane uptake in arterial blood.

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Table 1

Patient data. Values are median with interquartile range within brackets. The two groups were similar regarding gender, age, weight, height or BMI.

	NV_T	IV_T
Number of patients	10	10
Women (n)	6	5
Age, years	64 [52-78]	64 [54-68]
Weight, kg	84 [78-101]	81 [79-85]
Height, meter,	1.64 [1.60-1.75]	1.74 [1.65-1.77]
Body Mass Index, kg m^{-2}	30 [26-36]	27 [26-28]

Table 2

Comparison of tidal volumes (V_T), tidal volume kg body weight^{-1}, peak, plateau, mean airway pressures and lung compliance in the normal tidal volume group (NV_T) and increased tidal volume group (IV_T). Values are median [inter quartile range], n = 10 in each group. P-Plateau values were not statistically significantly different between the two groups The values of V_T, V_T (ml kg^{-1}), P-Peak, P-Mean and Lung Compliance were statistically significantly larger in the IV_T group compared to the NV_T group Mann-Whitney test (*, = $P < 0.05$).

		5 min	30 min	60 min
V_T (ml)	NV_T	400 [340-467]	440 [380-478]	397 [362-428]
	IV_T	777 [708-812]*	750 [703-808]*	717 [692-807]*
V_T (ml kg^{-1})	NV_T	4.6 [4.3-5.3]	4.9 [4.5-5.2]	5.0 [4.5-5.1]
	IV_T	9.3 [8.6-10]*	9.2 [8.7-9.7]*	9.0 [8.7-9.8]*
P-Peak (cmH_2O)	NV_T	16.5 [12.0-23.3]	16.0 [13.0-22.3]	15.5 [14.0-22.5]
	IV_T	24.5 [21.5-26.5]*	25.0 [23.0-25.5]*	25.5 [22.8-27.8]*
P-Plateau (cmH_2O)	NV_T	15.0 [11.8-20.3]	14.5 [11.8-17.8]	15.0 [12.8-19.8]
	IV_T	18.5 [15.0-20.0]	16.0 [11.8-17.8]	17.5 [15.0-21.5]
P-Mean (cmH_2O)	NV_T	6.0 [4.0-7.0]	5.0 [4.0-6.3]	4,0 [4.0-6.3]
	IV_T	7.0 [6.0-9.0]*	7.0 [6.0-8.3]*	7.0 [6.8-9.0]*
Lung Compliance	NV_T	28 [23-34]	29 [21-33]	27 [21-31]
(ml cmH_2O^{-1})	IV_T	41 [37-53]*	48 [36-58]*	41 [31-52]*

Table 3

Comparison of the values for the expiratory carbon dioxide ($P_{ET}CO_2$), carbon dioxide pressures in arterial blood (P_aCO_2) and P_aCO_2-$P_{ET}CO_2$ difference (P_a-$P_{ET}CO_2$) between normal tidal volume group (NV_T) and increased tidal volume group (IV_T). Values are mean ± SD (n = 10 in each group). $P_{ET}CO_2$ values were similar in the two groups. The values of P_aCO_2 and P_a-$P_{ET}CO_2$ were statistically significantly lower in the IV_T group compared to the NV_T group. Independent two-tailed t-test (*, $P < 0.05$).

		5 min	30 min	60 min
$P_{ET}CO_2$ (kPa)	NV_T	4.3 ± 0.28	4.4 ± 0.27	4.4 ± 0.22
	IV_T	4.6 ± 0.32	4.6 ± 0.33	4.5 ± 0.07
P_aCO_2 (kPa)	NV_T	5.2 ± 0.36	5.5 ± 0.25	5.5 ± 0.31
	IV_T	5.0 ± 0.32*	5.2 ± 0.36*	5.0 ± 0.20*
P_a-$P_{ET}CO_2$ (kPa)	NV_T	0.92 ± 0.32	1.1 ± 0.21	1.1 ± 0.30
	IV_T	0.42 ± 0.22*	0.57 ± 0.36*	0.53 ± 0.21*

Table 4

Comparison of the values for the inspiratory oxygen concentrations (F_iO_2), oxygen saturation, as measured by pulse oximeter (S_PO_2), oxygen tension (P_aO_2), between normal tidal volume group (NV_T) and increased tidal volume group (IV_T). Values of S_PO_2 are median [inter quartile range] and values of F_iO_2 and P_aO_2 are mean ± SD, (n = 10 in each group). F_iO_2 values were similar in the two groups. S_PO_2 and P_aO_2 were statistically significantly higher in the IV_T group compared to the NV_T group. Mann-Whitney test and independent two-tailed t-test, respectively, (*, $P < 0.05$).

		5 min	30 min	60 min
F_iO_2 (%)	NV_T	35 ± 2.1	37 ± 2.3	37 ± 5.5
	IV_T	35 ± 1.0	35 ± 1.0	35 ± 0.5
S_PO_2 (%)	NV_T	96 [92-98]	96 [93-97]	94 [91-98]
	IV_T	100 [99-100]*	100 [99-100]*	99 [98-100]*
P_aO_2 (kPa)	NV_T	11 ± 3.8	11 ± 2.9	10 ± 2.7
	IV_T	16 ± 3.0*	17 ± 3.8*	15 ± 4.3*

Table 5

Comparison of the values for the inspiratory sevoflurane concentrations ($F_i$sevo), expiratory sevoflurane concentrations (P_{ET}sevo), arterial sevoflurane tensions ($P_a$sevo) and P_{ET}sevo-$P_a$sevo difference (P_{ET}-$P_a$sevo) between normal tidal volume group (NV_T) and increased tidal volume group (IV_T). Values of $F_i$sevo, P_{ET}sevo, $P_a$sevo and P_{ET}-$P_a$sevo are mean ± SD (n = 10 in each group). $F_i$sevo and P_{ET}sevo values were not significantly different between the groups except P_{ET}sevo which was statistically significantly lower in the IV_T group before and at 5 min. Arterial sevoflurane tensions were statistically significantly higher in the IV_T group compared to the NV_T group. P_{ET}sevo-$P_a$sevo differences were statistically significantly lower in the IV_T group compared to the NV_T group. Two-Way repeated measurement ANOVA followed by Greenhouse-Geisser *post hoc* test (*, $P < 0.05$).

		5 min	30 min	60 min
$F_i$sevo (kPa)	NV_T	2.80 ± 0.28	2.24 ± 0.20	2.30 ± 0.24
	IV_T	2.64 ± 0.19	2.18 ± 0.20	2.24 ± 0.17
P_{ET}sevo (kPa)	NV_T	2.10 ± 0.15	1.82 ± 0.18	1.89 ± 0.22
	IV_T	1.88 ± 0.15*	1.76 ± 0.21	1.85 ± 0.19
$P_a$sevo (kPa)	NV_T	1.43 ± 0.20	1.37 ± 0.21	1.43 ± 0.19
	IV_T	1.60 ± 0.17*	1.65 ± 0.19*	1.74 ± 0.18*
P_{ET}-$P_a$sevo (kPa)	NV_T	0.68 ± 0.29	0.46 ± 0.19	0.46 ± 0.23
	IV_T	0.28 ± 0.17*	0.11 ± 0.12*	0.11 ± 0.13*

Legends to figures

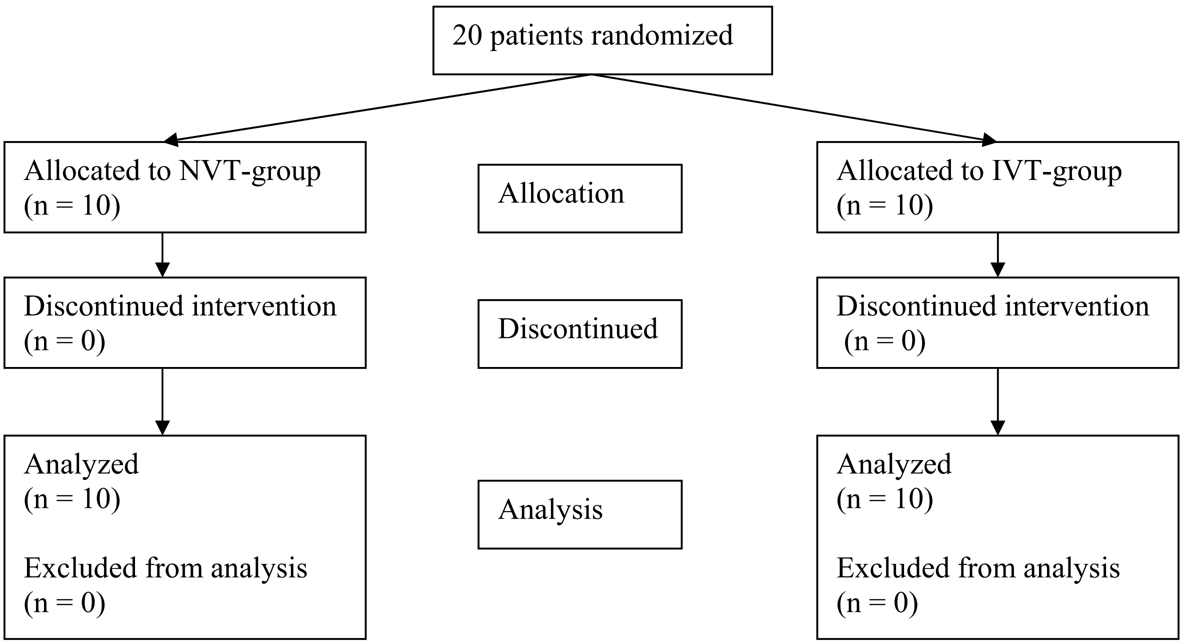
Figure 1

Patient flow of the study.

Figure 2

Comparison of the values for arterial sevoflurane ($P_a$sevo) and end-tidal sevoflurane tension (P_{ET}sevo) between the increased tidal volume group (IV_T) and normal tidal volume group (NV_T). Values are mean ± SD (n = 10 in each group). The expiratory sevoflurane concentration was similar in the two groups except before and at 5 min when it was statistically significantly lower in the IV_T group. Arterial sevoflurane tensions were statistically significantly higher in the IV_T group compared to the NV_T group and the differences increased with time. Two-Way repeated measurement ANOVA followed by Greenhouse-Geisser *post hoc* test ($P < 0.05$).

Figure 1


20 patients randomized
Allocated to NVT-group
(n = 10)
Allocation
Allocated to IVT-group
(n = 10)
Discontinued intervention
(n = 0)
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Discontinued intervention
(n = 0)
Analyzed
(n = 10)
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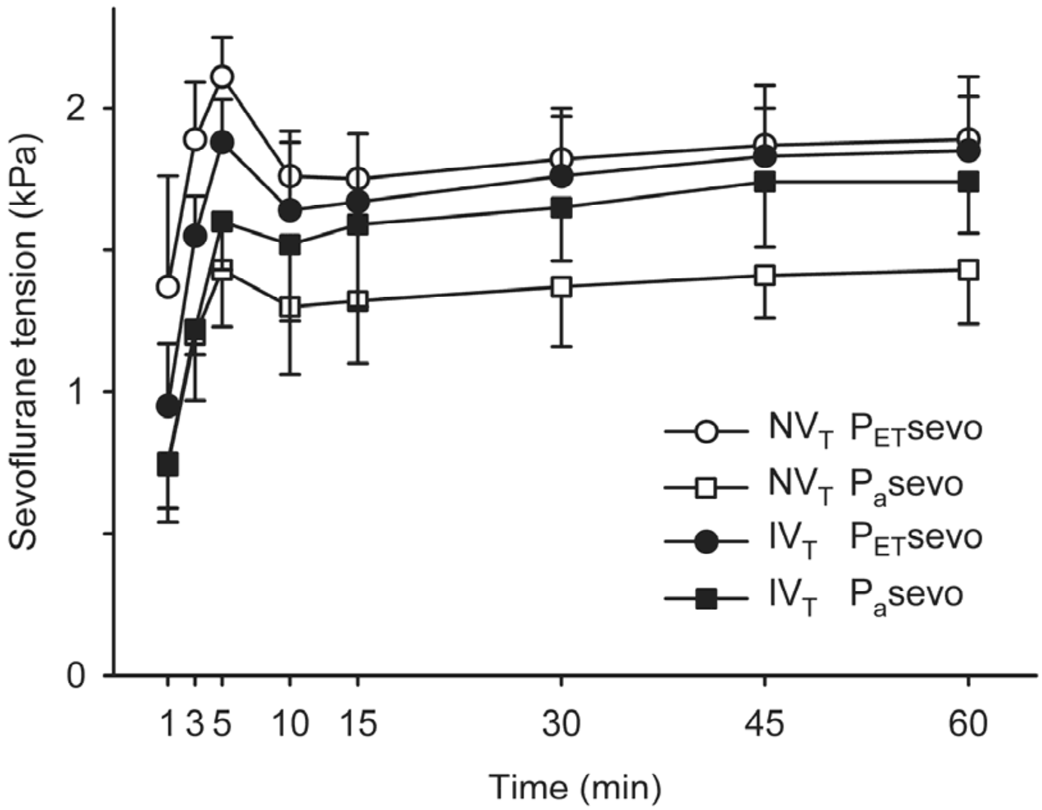
(n = 0)
Analysis
Analyzed
(n = 10)
Excluded from analysis
(n = 0)

Figure 2


Sevoflurane tension (kPa)
0
1
2
1 3 5 10 15 30 45 60
Time (min)
NV$_T$ P$_{ET}$sevo
NV$_T$ P$_a$sevo
IV$_T$ P$_{ET}$sevo
IV$_T$ P$_a$sevo