Flow-controlled ventilation (FCV) improves regional ventilation in obese patients – a randomized controlled crossover trial

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Abstract

Background: In obese patients, high closing capacity and low functional residual capacity increase the risk for expiratory alveolar collapse. Constant expiratory flow, as provided by the new flow-controlled ventilation (FCV) mode, was shown to improve lung recruitment. We hypothesized that lung aeration and respiratory mechanics improve in obese patients during FCV. Methods: We compared FCV and volume-controlled (VCV) ventilation in 23 obese patients in a randomized cross-over setting. Starting with baseline (BL) measurements, ventilation settings were kept identical except for the ventilation mode related differences (VCV: I:E ratio 1:2 with passive expiration, FCV I:E ratio 1:1 with active, linearized expiration). Primary endpoint of the study was the change of end-expiratory lung volume (EELV) compared to BL ventilation. Secondary endpoints were the change of mean lung volume (MLV), respiratory mechanics and hemodynamic variables and. Results: The loss of EELV and MLV compared to BL was lower during FCV compared to VCV (ΔEELV: FCV, -126 ±207 ml; VCV, -316 ±254 ml; $p < 0.001$, ΔMLV: FCV, -108.2 ±198.6 ml; VCV, -315.8 ±252.1 ml; $p < 0.001$) and at comparable plateau pressure (PPlat: BL, 19.6 ±3.7; VCV, 20.2 ±3.4; FCV, 20.2 ±3.8 cmH2O; $p = 0.441$), mean tracheal pressure was higher (Pmean: BL, 13.1 ±1.1; VCV, 12.9 ±1.2; FCV, 14.8 ±2.2 cmH2O; $p < 0.001$). All other respiratory and hemodynamic variables were comparable between the ventilation modes. Conclusions: This study clearly demonstrates that FCV in obese patients maintains lung aeration better than VCV at comparable PEEP, tidal volume, PPlat and ventilation frequency.

Background

In obese patients, the excessive adipose tissue around the thorax and the visceral organs reduces the functional residual capacity and expiratory reserve volume [1]. Obesity also leads to a low respiratory system compliance, early expiratory alveolar collapse with consecutive atelectasis, and increased airway resistance [2]. All these changes make mechanical ventilation in obese patients prone to respiratory complications [3, 4].

An emerging ventilation technique to linearise expiratory flow is flow-controlled ventilation (FCV), provided by the new ventilator Evone (Ventinova Medical B.V., Eindhoven, the Netherlands). This device provides a constant positive flow during inspiration and a constant negative flow during expiration. Thereby pressure increases linearly during inspiration [comparable to volume controlled ventilation (VCV)] and decreases linearly during expiration. Recently, we demonstrated that linearising the expiratory flow improved lung recruitment and the homogeneity of lung aeration [5, 6], and further attenuated experimental lung injury [7]. Since FCV is a new emerging technique comparative clinical studies in humans, particularly in patients with impaired respiratory system mechanics, are lacking.

We hypothesized that FCV prevents alveolar collapse and thus sustains lung recruitment in obese patients. Therefore, we compared regional ventilation using electrical impedance tomography (EIT) and respiratory system mechanics during FCV and VCV in obese patients in a randomized controlled cross-over trial.

Methods

Ethics, consent and permission

The study was approved by the Ethics Committee of the University Medical Centre of Freiburg (Engelbergstr. 21, 79106 Freiburg, Germany, Ethical Committee N° 179/18) on 29th March 2018 (Chairperson Prof. Dr. R. Korinthenberg) and registered at the German Register for Clinical Trials (DRKS00014925). Please note that this study adheres to CONSORT guidelines.

Study design and patient population

In order to cope with potential interindividual variability, the study was designed as a randomized controlled interventional cross-over trial. After obtaining written informed consent, we studied twenty-three obese patients with body mass index (BMI) $\geq$ 30 kg•m^{-2}. Patients eligible for enrolment were patients with physical status ASA $\leq$ III, undergoing elective bariatric surgery. Exclusion criteria were ASA physical status >III, age < 18 years, pregnancy, emergency procedure, cardiac pacemaker and other active implants, chronic obstructive pulmonary disease classified as GOLD stage > II and refusal of participation. The trial was conducted at the University Medical Center Freiburg, Germany. Participants were enrolled and assigned by a study related anesthesiologist. Data were collected at the University Medical Center of Freiburg, Germany.

Procedure

After obtaining written informed consent, 23 patients were included in the study. After primary recruitment and preoperative evaluation, the patients received routine monitoring (electrocardiography, SpO_2, noninvasive blood pressure measurement; Infinity Delta XL, Dräger Medical, Lübeck, Germany) and a 18-20-G intravenous catheter was established. After preoxygenation to an fraction of expired oxygen of 0.8, the anesthesia was induced with 0.3-0.5 µg•kg^{-1} predicted body weight [8] (PBW) iv sufentanil (Janssen-Cilag, Neuss, Germany) and 2-3 mg•kg^{-1} iv propofol 1% actual body weight (ABW) (Fresenius Kabi, Bad Homburg vor der Höhe, Germany). Tracheal intubation was facilitated with 0.6 mg•kg^{-1} PBW iv rocuronium (Fresenius Kabi). If the patient required a rapid sequence induction, neuromuscular blockage was performed by the administration of 1.0 mg•kg^{-1} PBW iv rocuronium. Neuromuscular blockage was monitored with a mechanomyograph (TOFscan; Dräger Medical). For tracheal intubation, we used tracheal tubes (TT) with low pressure cuffs (internal diameter of 7.0-7.5 mm for women and 8.0 mm for men; Mallinckrodt Hallo-Contour; Covidien, Neustadt an der Donau, Germany). After adequate placement of the TT, propofol was administered continuously (between 110 and 150 µg•kg^{-1}•min^{-1}).Potential hypotension (defined as mean arterial pressure < 65 mmHg) was treated with a continuous infusion of iv noradrenaline (0.03-0.2 µg•kg^{-1}•min^{-1}). Perioperative volume requirements were addressed with a

crystalloid solution (8 ml•kg^{-1}•h^{-1}, Jonosteril; Fresenius Kabi). According to our local standard, mechanical ventilation was started as volume-controlled baseline (BL) ventilation (Fabius Tiro, Dräger Medical) with a tidal volume (V_T) of 7 ml•kg^{-1} PBW, inspiration-to-expiration (I:E) ratio of 1:2, a positive end-expiratory-pressure (PEEP) of 9 cmH_2O and ventilation frequency (VF) set to maintain an end-tidal carbon dioxide partial pressure between 4.7 and 5.1 kPa. After 7 min of BL ventilation, all patients were randomly allocated to one of two cross-over groups to receive ventilation sequences either VCV-FCV or FCV-VCV for 7 min per ventilation mode. For adequate allocation, a computer generated randomisation in blocks was used. Disclosure of the randomisation was requested right after induction of anesthesia. A study related anesthesiologist conducted the randomisation in blocks, enrolled participants and assigned participants to the interventions. During the study protocol, ventilation variables were kept constant as set during the BL ventilation. To prevent from the risks of extubation and reintubation, FCV was performed by introducing the narrow-bore tracheal tube (Tribute, Ventinova Medical B.V.) into the standard TT. Blocking the cuff of the Tritube in the lumen of the TT tube provided a sufficient seal. By controlling both tube's markings, placement of the Tritube's tip exceeding that of the standard TT by 2-5 mm was ensured, and the potential risk of bronchial intubation was avoided. Respiratory data were collected from both ventilators via the respective serial communication interface and analysed offline. Electrical impedance tomography (EIT) was performed with PulmoVista 500 (Dräger Medical) in all patients to measure regional ventilation, changes in relative thoracic electrical impedance during the different ventilation phases, relative end-expiratory lung volume (ΔEELV) and to compare the expiratory decrease in intrapulmonary air [9–11].

Tritube and FCV

To perform FCV, all patient were ventilated by introducing the Tritube (Ventinova Medical B.V.) into the standard tracheal tube (Mallinckrodt Hallo-Contour; Covidien). The Tritube has a total of three lumens: One for ventilation, one for tracheal pressure measurement and one for inflating/deflating the cuff. The Tritube has a length of 40 cm and an outer diameter of 4.4 mm. The ventilation lumen has a cross sectional area of nearly 2.4 mm [12]. To ventilate patients with FCV via this tracheal tube, a specific ventilator is needed (Evone, Ventinova Medical B.V.). The Evone ventilator is currently the only ventilator to enable FCV. During FCV, patients are ventilated with a constant positive flow during inspiration and a constant negative flow during expiration. To avoid intrinsic PEEP, the intratracheal pressure is monitored continously via a dedicated pressure measurement lumen of the Tritube.

During FCV, the operator is able to adjust the inspiratory flow rate, I:E ratio, peak inspiratory pressure, end-expiratory pressure and the inspiratory concentration of oxygen. In this special ventilation mode, there is no direct way to control minute volume via tidal volumes and/or respiratory rate. However, the respiratory rate depends on the peak inspiratory pressure, the set (positive) end-expiratory pressure, the set inspiratory flow rate, the I:E ratio and the patient's lung compliance [13].

End points and data collection

ΔEELV was the primary endpoint of this study. We derived ΔEELV from adjusting end-expiratory impedance changes by V_T and tidal impedance changes as described before [6, 9]. Secondary endpoints were the respiratory system variables: plateau pressure (P_{Plat}), mean tracheal pressure (P_{mean}), respiratory system compliance (C_{RS}). Non-invasively collected hemodynamic variables included mean systolic blood pressure (RR_{sys}), mean diastolic blood pressure (RR_{dias}), mean arterial pressure (MAP) and heart rate. To compare relative intrapulmonary air distribution, baseline tidal impedance curves for ventral and dorsal lung areas were determined and compared as described before [6, 10]. The differences in mean lung volume (ΔMLV) between BL ventilation and VCV and FCV were calculated, respectively. Further, the decrease in global thoracic electrical impedance during each ventilation mode was separated into four equal sections (ΔEI_{25}, ΔEI_{50}, ΔEI_{75} and ΔEI_{100}), then matched with the correlating decrease in V_T and compared successively.

Pressure data from the Evone are based on direct tracheal pressure measurement via a dedicated lumen of the Tritube. To allow for comparability of pressure data from both ventilators, airway pressure data from the Dräger Fabius Tiro were generally converted into tracheal pressure data by calculating the flow dependent pressure drop across the respective TT and pointwise subtracting this value from airway pressure [14]. Thus all pressure data in the following refer to the respective tracheal pressure.

The datasets used and alanysed during the current study are available from the corresponding author on request. Please note that EIT data files require large memory. A separate data transfer service will be used to transfer EIT data files.

Sample size calculation and statistical analysis

In regard to the cross-over design (paired test conditions) and an assumed standardized effect size of the primary endpoint of 0.7, 19 patients were required to reach a test power of 0.8 with a desired level of significance of 0.05. To compensate for potential incomplete data sets, 23 patients were included in the study. Lilliefors tests were used to confirm that the assumed normal distribution cannot be rejected.

Values are presented as mean (standard deviation), unless indicated otherwise. Statistical analysis was done using Matlab (R2014, The MathWorks Inc., Natick, MA, USA). Linear mixed effects model analyses were performed to check for differences between the ventilation phases using R based software (jamovi project (2018), jamovi (Version 0.9.2.3), retrieved from https://www.jamovi.org). $P < 0.05$ was considered statistically significant.

Results

In total, 23 consecutive patients presenting for elective bariatric surgery were included and 19 complete data sets could be recorded. Patients were recruited from 30th July 2018 to 23rd October 2018. One patient had to be excluded due to limited size of the EIT belt, three other patients due to incomplete data collection (Fig. 1). There were no adverse events during the study procedure. The study was ended regularly after the last subject was included. Age, gender, ASA physical status, PBW, ABW and BMI were comparable between the two interventional groups (Table 1).

During mechanical ventilation, end-expiratory lung volume decreased generally (Fig. 2). ΔEELV between BL ventilation and FCV (-126 ± 207 ml) was lower than between BL and VCV (-316 ± 254 ml, $p < 0.001$). ΔMLV between BL ventilation and FCV (-108 ± 198 ml) was lower than between BL and VCV (-315 ± 252 ml, $p < 0.001$) (Fig. 3). P_{mean} was higher during FCV. No significant differences in V_T, VF, P_{Plat} and C_{RS} were found between FCV and VCV. All hemodynamic variables were comparable during FCV and VCV (Table 2).

FCV was characterized by a more even decay of impedance throughout the expiration phase (Fig. 4). ΔEI_{25}, ΔEI_{50}, ΔEI_{75} and ΔEI_{100} showed a more even decrease during FCV compared to VCV (Fig. 5). ΔEI_{25} decreases about 45% during BL ventilation and VCV and 25% during FCV. ΔEI_{50} showed no differences between the ventilation modes. ΔEI_{75} and ΔEI_{100} showed a lower decrease in global thoracic electrical impedance during BL ventilation and VCV compared to FCV (Fig. 5).

Discussion

In this study, we compared respiratory system mechanics and regional ventilation in obese patients during short application of FCV and VCV. The main findings of our study are that compared to VCV, FCV increased ΔEELV and mean lung volume without affecting respiratory or hemodynamic variables negatively.

These effects were comparable to the effects one would expect from a PEEP increase and/or a V_T increase. However, minimal and maximal airway pressure and V_T remained unchanged. Our results are consistent with and enlarge upon earlier findings on the implications of a linearized expiratory pressure decrease in lung-healthy patients, lung healthy pigs and a porcine lung-injury model [5–7].

The implications of obesity on respiratory system mechanics are well known: chest wall mechanics are impaired, and respiratory system compliance is reduced. Obese patient have an increased risk for early expiratory alveolar collapse and potential consecutive atelectrauma [4, 15–17] and thus for decreased functional residual capacity and expiratory reserve volume [4, 11, 18, 19]. Therefore, besides low V_T and optional recruitment manoeuvers, lung-protective ventilation strategies include the application of higher PEEP in these patients. However, the ideal adjustment of applied V_T, and PEEP — with respect to the potential injurious effects of alveolar overdistension — in obese patients still remain obscure [17]. In this regard, FCV improved lung recruitment without modifying PEEP or V_T.

The mechanisms behind this recruiting effects may be time dependent: when the lung volume falls below the closing capacity airway closure can occur within the expiration [4, 20]. The overall delayed expiration during FCV delays the time point at which the lung volume falls below the closing capacity. Consequently, the time until the lung volume exceeds closing capacity within the next inspiration is reduced and thus the risk of airway closure may be lowered [19]. The characterisation and correlation between the expiratory decrease in global electrical impedance and expiratory decrease in intrapulmonary air support this conjecture.

Theoretical and clinical observations predict that the linearized decrease in expiratory airway pressure has a beneficial impact on the intrapulmonary inhomogeneity [5–7, 16, 21]. However, the comparison of tidal impedance variation revealed no differences in intrapulmonary gas distribution during the different ventilation phases. The reduced accessibility of EIT images in obese and morbidly obese patients was described earlier and may be caused by the excessive volume of fat tissue around the chest wall. In horizontal supine position, this fat tissue moves laterally and may create potential shortcuts for the electrical currents of the EIT [22]. Therefore, the resolution of the EIT is limited, which may have masked differences in intrapulmonary inhomogeneity in our patients.

C_{RS} did not differ significantly between the investigated ventilation conditions. Reduced C_{RS} in obese patients may be caused mainly by excess adipose tissue around the chest wall and poor posture caused by thoracic kyphosis and lumbar hyperlordosis, aggravated through excessive abdominal fat tissue [15]. Under these conditions, the recruiting effect of FCV may have influenced C_{RS} only to a minor extent. To investigate potential effects of FCV on the C_{RS} in obese patients, longer application of FCV may be necessary.

Limitations of the study

We did not perform arterial blood gas analyses to examine the effects of FCV on gas exchange in our patients. In preclinical studies, the controlled expiration improved oxygenation and CO_2 elimination [16]. However, in contrast to other centres, placing an arterial line is not part of our standard treatment in this patient group. Therefore, we felt that such invasive approach was not justified for our study. We only investigated short ventilation periods of several minutes. The intention of our study was to investigate the potential short term recruiting effects of FCV, which we claim to have achieved. Further studies are required to investigate potential long term effects of FCV on gas exchange, respiratory system mechanics and particularly on the hemodynamics.

Conclusion:

This is the first study to investigate the influence of FCV on respiratory mechanics and lung aeration in obese and morbidly obese patients. Utilizing measurement of regional ventilation, we could demonstrate

how the linearized expiratory flow during FCV provided better maintenance of lung aeration with same VT, PPlat and PEEP, compared to VCV. The recruiting effect caused by the linearized expiratory air flow and the elevated Pmean during FCV may help prevent atelectasis and hypoxemia during mechanical ventilation in obese patients.

List Of Abbreviations

ABW, actual body weight

ASA, American Society of Anesthesiologists

BL, baseline measurements

BMI, body mass index

CRS, compliance of the respiratory system

EELV, end-expiratory lung volume

EIT, electrical impedance tomography

FCV, flow-controlled ventilation

I:E, ratio of inspiratory time to expiratory time

MAP, mean arterial pressure

MLV, mean lung volume

PBW, predicted body weight

PEEP, positive end-expiratory pressure

P_{mean}, mean airway pressure

P_{Plat}, plateau pressure

RR_{dias}, diastolic blood pressure

RR_{sys}, systolic blood pressure

SpO_2, peripheral oxygen saturation (pulse oximetry)

TT, tracheal tube

VCV, volume-controlled ventilation

VF, ventilation frequency

VT, tidal volume

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the University Medical Centre of Freiburg (Engelbergstr. 21, 79106 Freiburg, Germany, Ethical Committee N° 179/18) on 29th March 2018 (Chairperson Prof. Dr. R. Korinthenberg). Written informed consent was obtained from all participants.

Consent for publication

Not applicable

Availability of data and marterial

The datasets used and alanysed during the current study are available from the corresponding author on request. Please note that EIT data files require large memory. A separate data transfer service will be used to transfer EIT data files.

Competing interests

J.W., L.S., S.B., J.S. and S.W declare no conflicts of interest. S.S. has a consulting contract with Gründler GmbH, Freudenstadt (no relationship to this study).

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Authors contributions

Planning the study: JW, SW, SS

Conduction of the study: JW, LS, JS

Drafting the article: JW, SW, SS

Revising the article for important intellectual content: JW, LS, SB, JS, SW, SS

All authors have read and approved the manuscript.

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Tables

Table 1: Patients characteristics (n=19).

	BL_VCV_FCV (*n* = 9)	**BL_FCV_VCV (*n* = 10)**
Age (yr)	48.6 ± 6.9	43.4 ± 13.3
Gender (n), female/male	6/3	8/2
ASA I/II/III (n)	0/0/9	0/0/10
PBW (kg)	64.2 ± 12.6	59.0 ± 7.0
ABW (kg)	127.0 ± 27.6	120.0 ± 27.1
BMI ($kg \cdot m^{-2}$)	42.7 ± 4.6	42.5 ± 7.7

PBW, predicted body weight; ABW, actual body weight; BMI, body mass index.

Table 2: Respiratory and hemodynamic variables.

	BL	VCV	FCV	p vent	p order
	440.2 ± 33.0	442.0 ± 33.2	457.4 ± 50.7	0.148	0.543
(ml•kg^{-1})	7.3 ± 1.0	7.3 ± 1.0	7.4 ± 0.8	0.621	0.228
$^{-1}$)	14.2 ± 2.4	14.1 ± 2.6	14.0 ± 2.5	0.834	0.694
H_2O)	19.6 ± 3.7	20.2 ± 3.4	20.2 ± 3.8	0.441	0.275
$ıH_2O$)	12.9 ± 1.2	13.1 ± 1.1	14.8 ± 2.2	< 0.001[1]	0.388
cmH_2O^{-1})	46.6 ± 17.0	47.2 ± 16.6	44.6 ± 16.3	0.272	0.297
te (•min^{-1})	60.0 ± 11.8	57.5 ± 10.4	57.7 ± 10.0	0.261	0.158
ıHg)	135.0 ± 15.6	131.0 ± 19.2	131.0 ± 12.6	0.343	0.791
ıHg)	75.8 ± 12.1	74.4 ± 10.4	71.0 ± 11.4	0.132	0.726
nHg)	95.5 ± 12.0	93.4 ± 12.8	91.0 ± 10.2	0.167	0.731

Values are stated as mean (SD). BL, baseline (consisting of volume-controlled ventilation); VCV, volume-controlled ventilation; FCV, flow-controlled ventilation; V_T, tidal volume; V_T PBW, tidal volume per predicted body weight; VF, ventilation frequency; P_{Plat}, plateau pressure; P_{mean}, mean tracheal pressure; C_{RS}, respiratory system compliance; RR_{sys}, mean systolic blood pressure; RR_{dias}, mean diastolic blood pressure; MAP, mean arterial pressure. P vent, p for ventilation mode; p order, p for randomization (BL-VCV-FCV and BL-FCV-VCV). [1] = $p < 0.001$ for BL vs. FCV and for VCV vs. FCV (linear mixed effect analysis).

Figures

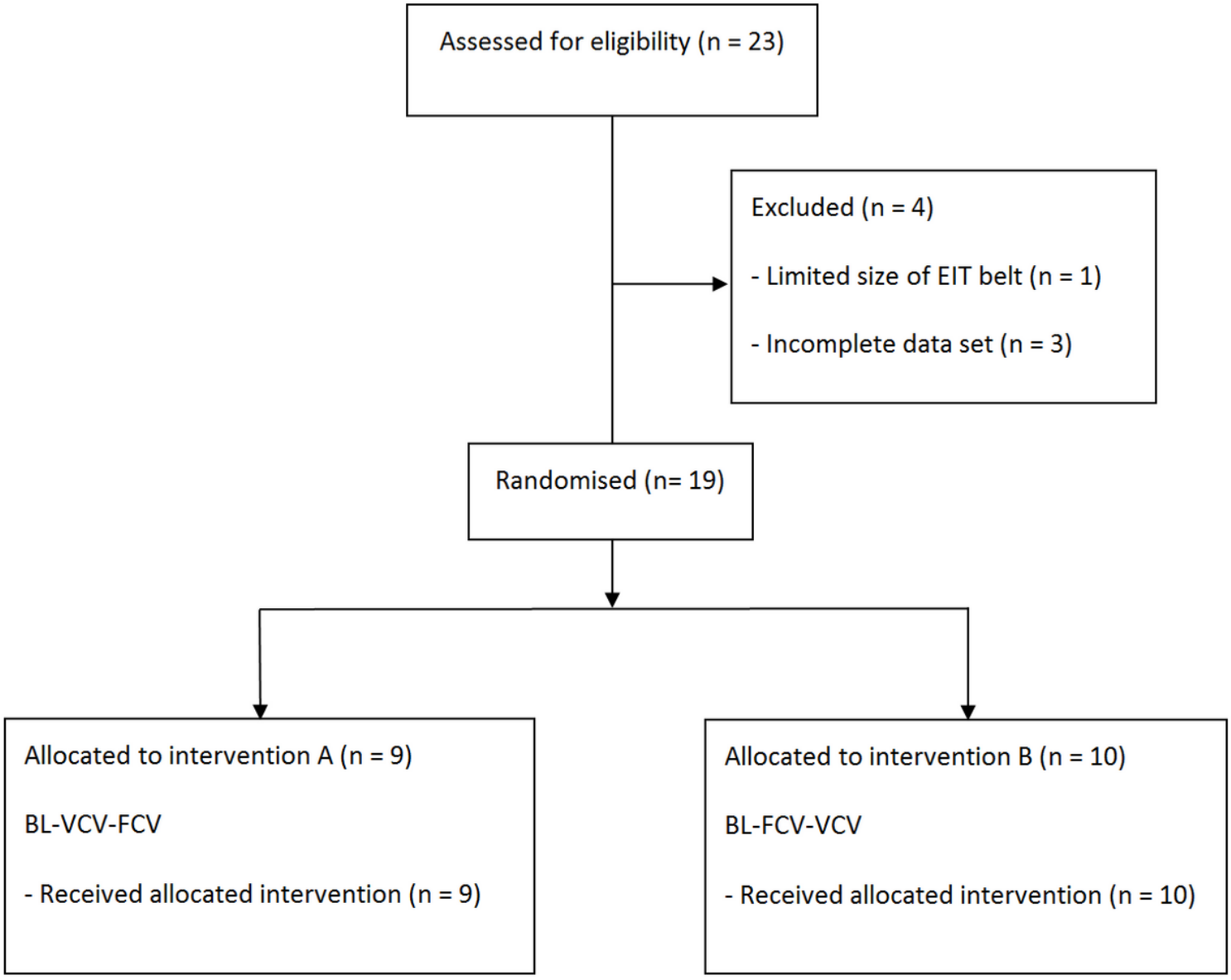

Figure 1

Flow diagram of the study population

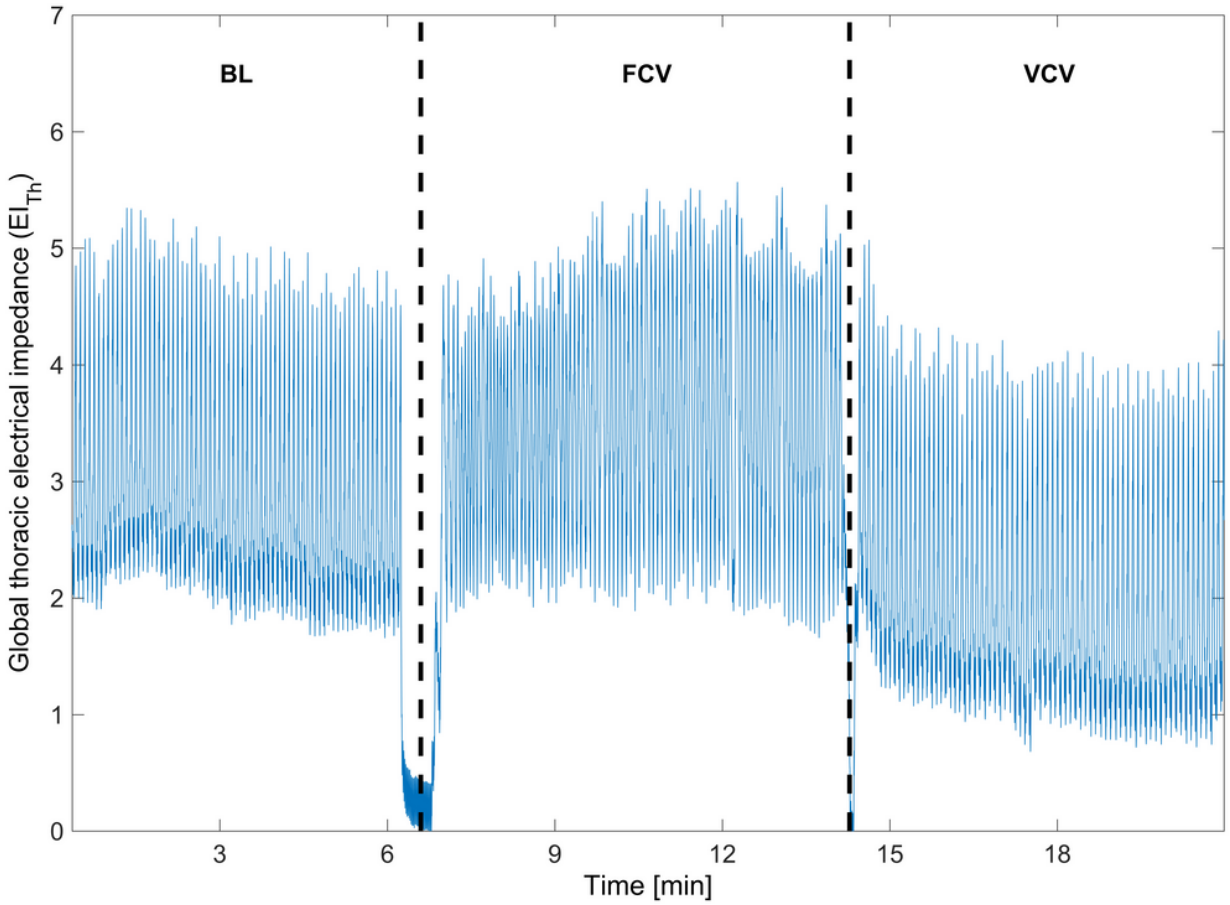

Figure 2

Exemplary relative global thoracic electrical impedance (EITh) of one patient during the study protocol. BL, baseline (volume-controlled) ventilation; VCV, volume-controlled ventilation; FCV, flow-controlled ventilation. The first slope represents the insertion of the Tritube® into the standard tracheal tube. The second slope represents the remove of the Tritube and re-connecting to the Dräger Fabius Tiro ventilator. The dotted lines indicate the switch between the respective ventilation modes.

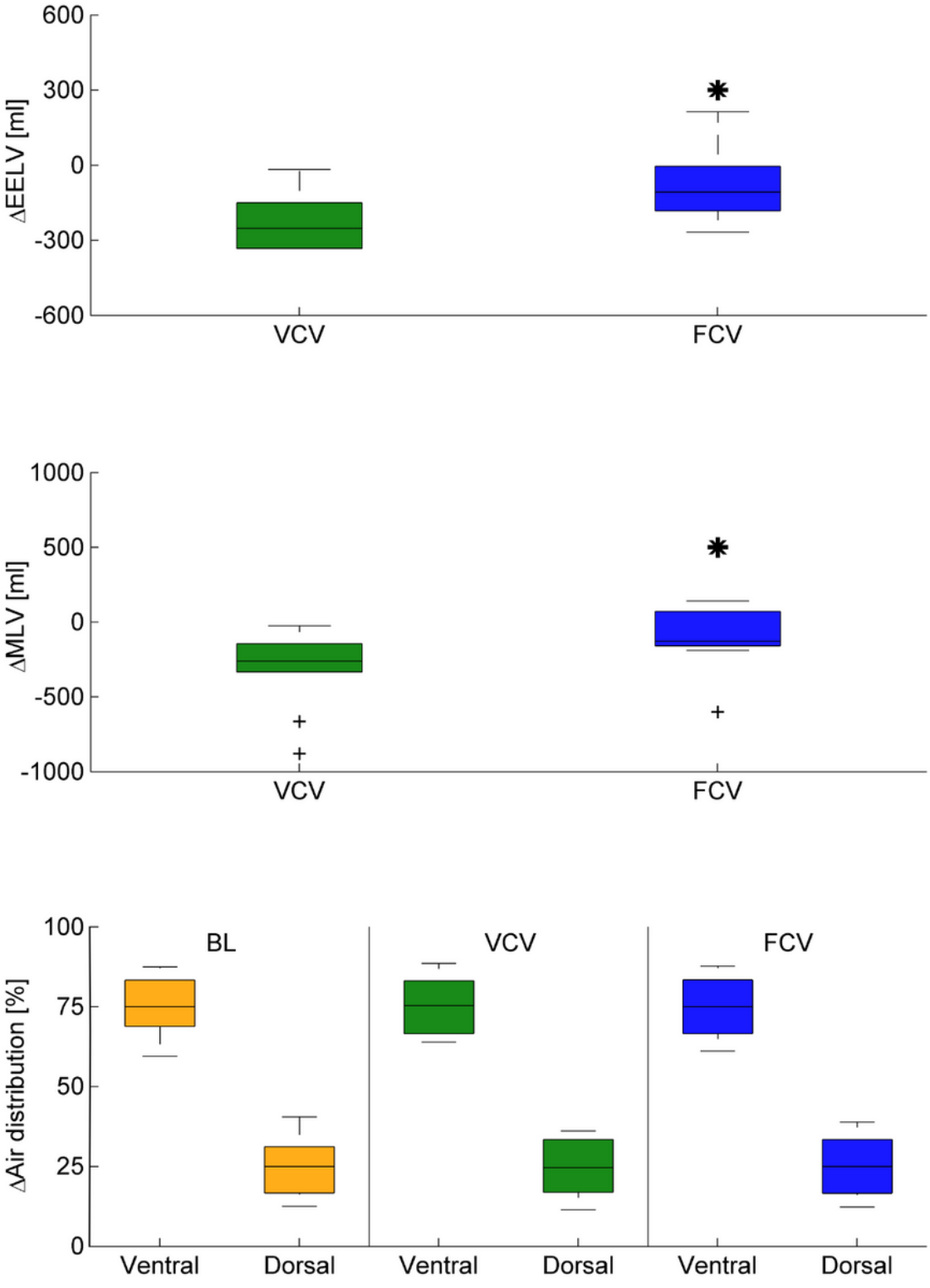

Figure 3

Alteration of end-expiratory lung volume ΔEELV, mean lung volume ΔMLV and comparison in percentage air distribution between ventral and dorsal lung areas. BL = volume-controlled baseline ventilation, VCV = volume-controlled ventilation and FCV = flow-controlled ventilation. On each box, the central mark indicates the second quartile, the bottom and top edges indicate quartiles (25th percentile and 75th percentile). * = $p \leq 0.001$ for FCV vs. VCV.

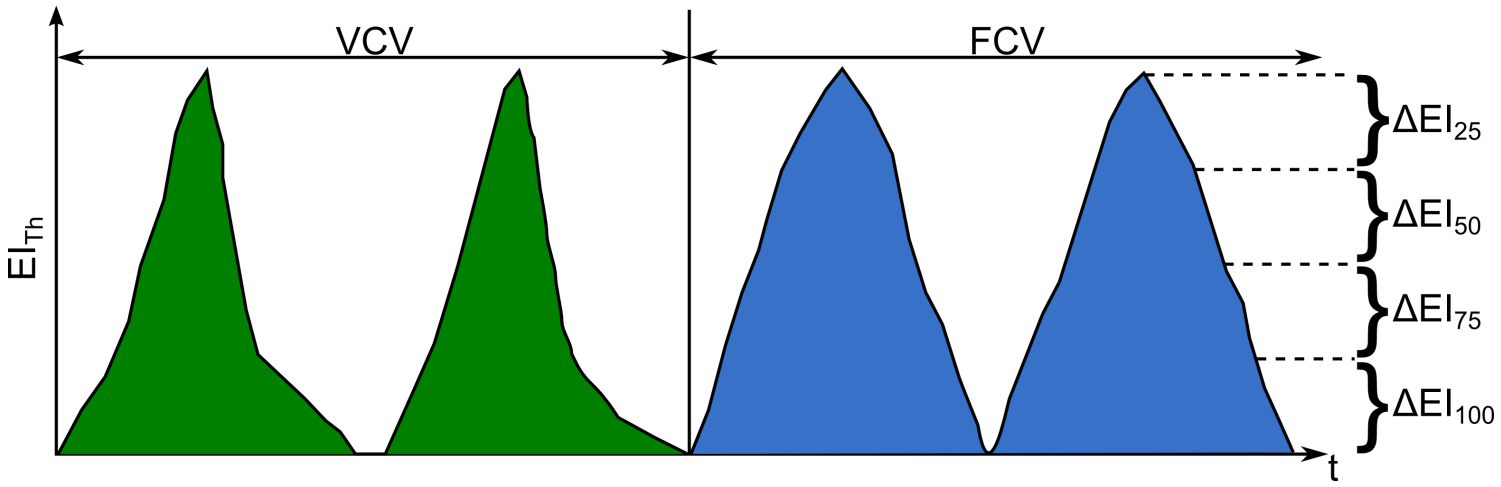

Figure 4

Exemplary global thoracic electrical impedance (EITh) during two tidal breathes of flow-controlled ventilation (FCV) and volume-controlled ventilation (VCV) in one obese patient. For further comparison, decrease in impedance during expiration was separated into four equal sections (ΔEI25, ΔEI50, ΔEI75 and ΔEI100) and matched with simultaneous tidal changes (comp. Fig. 5).

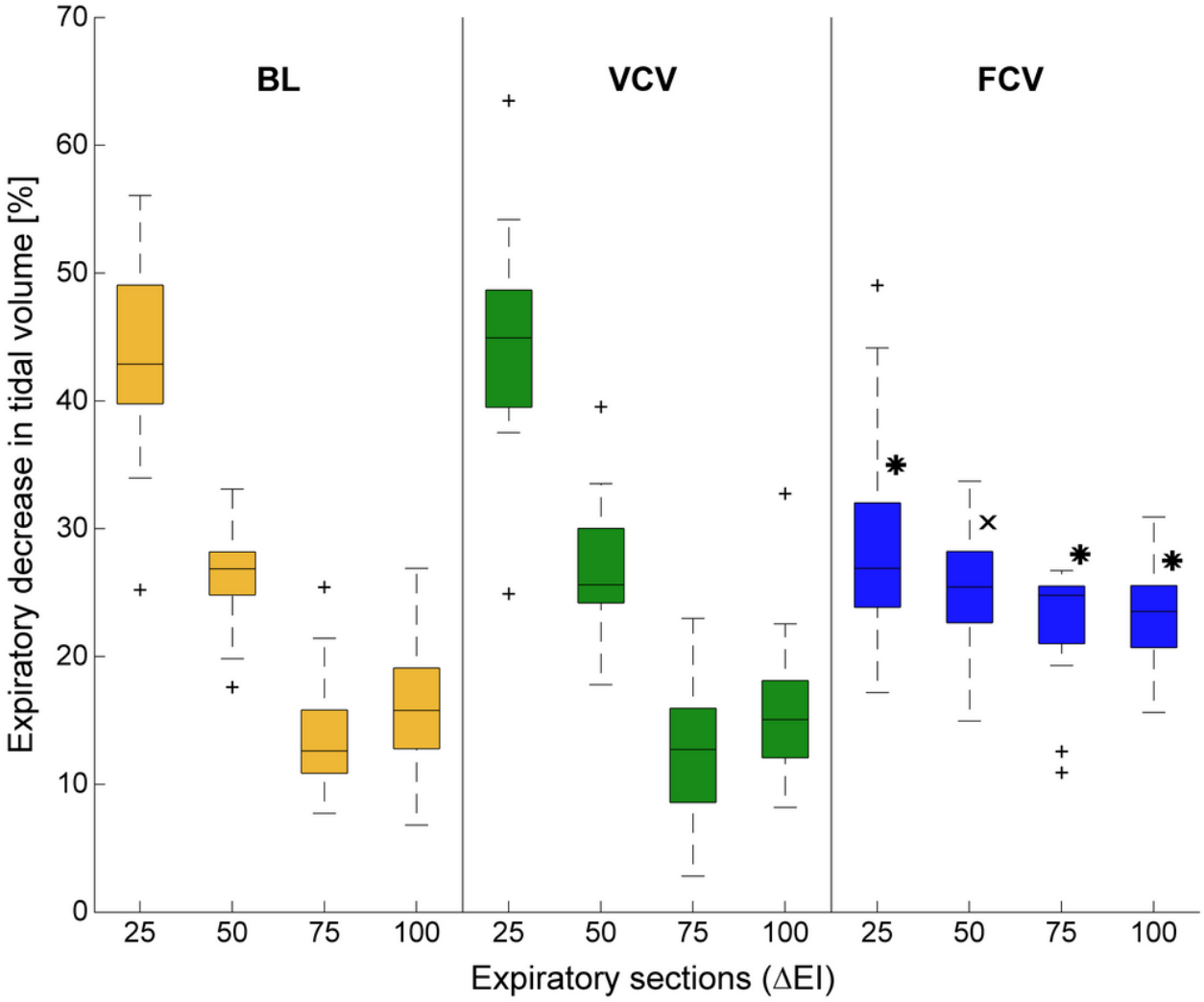

Figure 5

Relative expiratory decrease in tidal volume during the previously defined sections using the electrical impedance tomography (EIT) for volume-controlled baseline ventilation (BL), volume-controlled ventilation (VCV) and flow-controlled ventilation (FCV). In brief: the decline in global electrical thoracic impedance was separated into four equal sections (ΔEI25, ΔEI50, ΔEI75 and ΔEI100) (compare Fig. 4) and matched with the tidal changes simultaneously. On each box, the central mark indicates the second quartile, the bottom and top edges indicate quartiles (25th percentile and 75th percentile). On each box, the whiskers indicate the most extreme data points. Outliers are plotted individually ('+'). * = $p < 0.001$ for BL vs. FCV and VCV vs. FCV, x = $p > 0.05$ for BL vs. FCV and VCV vs. FCV.

Supplementary Files

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- supplement1.doc