Early View

Original article

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Particle flow rate from the airways as fingerprint diagnostics in mechanical ventilation in the intensive care unit: a randomized controlled study

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Take home message: Particle flow rate (PFR) from the airways may be used to continuously monitor the small airways in real time. A low PFR during mechanical controlled ventilation is likely to correspond to a protective ventilation.

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Abstract

Introduction: Mechanical ventilation (MV) can be monitored by analysing particles in exhaled air as measured by particle flow rate (PFR). This could be a potential method of detecting ventilator induced lung injury (VILI) before changes in conventional parameters can be detected. The aim of this study was to investigate PFR during different ventilation modes in patients without lung pathology.

Method: A prospective study was conducted on patients on MV in the cardiothoracic intensive care unit (ICU). A PExA 2.0 device was connected to the expiratory limb on the ventilator for continuous measurement of PFR in 30 patients randomized to either volume-controlled ventilation (VCV) or pressure-controlled ventilation (PCV) for 30 minutes including a recruitment manoeuvre (RM). PFR measurements were continued as the patients were transitioned to pressure regulated volume control (PRVC) and then pressure support ventilation (PSV) until extubation.

Results: PRVC resulted in significantly lower PFR while those on PSV had the highest PFR. The distribution of particles differed significantly between the different ventilation modes.

Conclusions: Measuring PFR is safe after cardiac surgery in the ICU and may constitute a novel method of continuously monitoring the small airways in real time. A low PFR during mechanical ventilation may correlate to a gentle ventilation strategy. PFR increases as the patient transitions from controlled MV to autonomous breathing, which most likely occurs as recruitment by the diaphragm opens up more distal airways. Different ventilation modes resulted in unique particle patterns and could be used as a fingerprint for the different ventilation modes.

Introduction

Ventilator induced lung injury (VILI) can be an adverse consequence of mechanical ventilation (1-4). Adopting ventilator strategies which reduce VILI is an important goal in ventilatory management. In acute respiratory distress syndrome (ARDS), lung protective ventilation with low tidal volumes and limited airway pressure has significantly reduced mortality among those patients (1, 5). Among the different ventilation modes, pressure-controlled ventilation (PCV) is often suggested to reduce the risk of developing VILI due to the potential ramifications of high pressure when compared to the use of volume-controlled ventilation (VCV) (6, 7). However, in metanalysis studies, there is yet to be a definitive conclusion regarding the advantage of either PCV or VCV (4). The benefits relative to the potential damage incited by recruitment manoeuvres (RM) is also an area of continuous debate especially in the most vulnerable groups of patients, such as those with ARDS. To this day, the evidence for the benefits without causing any additional harm are not conclusive (8, 9). There is still ongoing debate surrounding the optimal RM to use in both methods of ventilation and at what time during the course of mechanical ventilation the RM should be performed (10, 11). Patients with severe ARDS, who are responders to RM, should be treated according to the open lung concept (OLC) with low tidal volumes and high PEEP after a RM. Conversely, patients who are not responders should be treated with reduced PEEP without any RM's to avoid overdistension of alveoli (1). However, despite pronounced ventilation strategies, VILI still occurs, indicating that clinicians need new or improved diagnostic tools to monitor mechanical ventilation in avoidance of VILI.

Exhaled breath particles (EBPs) are thought to originate from the respiratory tract lining fluid (RTLF) that covers the epithelial surface of the distal parts of the lung (12-15). EBPs are transmitted in exhaled air during the opening and closing of small airways and can be measured as particle flow rate (PFR) using a PExA machine. The identity of particles collected using the PExA technique has shown to be consistent with the particles collected from bronchoalveolar lavage (BAL) fluid, indicating that EBPs originate from the RTLF (15). In a recent publication, increased PFR was strongly connected to lung injury (16). The PFR significantly increased indicating lung injury prior to other clinical indicators of injury, including respiratory parameters and the cytokine response in the blood. The implication is that PFR could be used as an early signal of lung injury (16).

The present study was designed to explore if and how PFR could be used to monitor mechanical ventilation in different ventilation modes. We further explored if different ventilator settings resulted in different PFR patterns in postoperative patients on mechanical ventilation without lung pathology. Furthermore, the effect of RM during different ventilation modes was investigated.

Method

A prospective randomized controlled clinical study was performed in patients on mechanical ventilation at Lund University Hospital in Sweden during 2019. The study was approved by the local ethics committee, EPN Dnr 2018/129. The study consisted of 30 patients (22 males, 8 females) undergoing elective open heart surgery: coronary artery bypass grafting (CABG) (n=15), aortic valve replacement surgery (AVR) (n=10) or a combination of CABG and AVR (n=5). The mean age was 69 years of age, ranging from 44 to 83. All patients enrolled in the study were presented with information regarding the study and signed an informed consent form.

All patients were initially sedated using Propofol-®Lipuro (B Braun Medical AB, Danderyd, Sweden) 20 mg/ml at an infusion rate of 2-3 mg/kg/h during the time in ICU. Norepinephrine (Pfizer AB, Sollentuna, Sweden) 40 μg/ml, at infusion rates between 0.05 – 2 μg/kg/min was used to maintain mean, arterial pressure (MAP) above 65 mmHg. MAP above accepted levels were treated with Nitroglycerin Abcur (Abcur AB, Helsingborg, Sweden) 1 mg/ml, at infusion rates between 0.25-5 μg/kg/min. In the case of postoperative pain and shivering, intravenous Oxycodone 10 mg/ml (Mundipharma AB, Göteborg, Sweden), Petidine 50 mg/ml (Meda AB, Solna, Sweden) or Clonidine 150 μg/ml (Boehringer Ingelheim AB, Stockholm, Sweden) were administered.

Inclusion criteria's

Patients included in the study were those with normal lung function undergoing elective open-heart surgery who would receive post-operative treatment with mechanical ventilation at the cardiothoracic intensive care unit (ICU).

Exclusion criteria's

Patients were excluded if they had COPD stage 1-4, pulmonary fibrosis, or other kinds of lung pathology. They were also excluded if they were currently a smoker or a recent smoker (< 6 month). Other exclusion criteria included an ejection fraction (EF) less than 45%, chronic renal failure, or chronic liver failure.

PExA device and measurements

A customized PExA 2.0 device (PExA, Gothenburg, Sweden) was connected on the expiratory limb of the respiratory circuit. A mouthpiece containing a one-way valve was used to prevent mixture of inspiratory and expiratory air. Particle flow rate (PFR) was measured continuously from the airways by the PExA device during the entire period during which the patient was intubated in the ICU. The PExA device conducts measurements using an optical particle counter (OPC) and by impaction on a filter. It can thereby analyse exhaled particle flow and exhaled particle size distribution, as described in detail in previous studies (17, 18). The PExA device measures particles in the size range 0.41 μm to 4.55 μm by the OPC and divides them into eight different size groups, as following: particle 1; 0.48 (0.41-0.55) μm, particle 2; 0.59 (0.55-0.70) μm, particle 3; 0.75 (0.70-0.92) μm, particle 4; 0.98 (0.92-1.14) μm, particle 5; 1.22 (1.14-1.44) μm, particle 6; 1.67 (1.44-2.36) μm, particle 7; 2.52 (2.36-2.98) μm, particle 8; 3.37 (2.98-4.55) μm (17).

A study timeline is shown in figure 1. Upon arrival into the ICU, patients were randomized to either volume-controlled ventilation (VCV) or pressure-controlled ventilation (PCV) during the first 30 minutes after arrival at the ICU including a RM 15 minutes after initiation of ventilation. The RM was performed over one minute using a PEEP of 10 cmH_2O, a respiratory rate of 4 breaths per minute and an inspiratory-expiratory ratio (I:E) of 2:1. All other settings were kept unchanged during the RM. A representative measurement of three minutes before and three minutes after the RM was chosen for statistical analysis of PFR during the RM. PFR was measured during VCV and PCV at two time periods, before and after RM to obtain a representative value.

When the patient awoke from anaesthesia the ventilator mode was set to PSV to allow spontaneous breathing. Train-of-four (TOF) was analysed in close proximity to the RM to assure that the muscle relaxation drugs (Rocuronium bromide) given during surgery didn't have any impact on the measurements.

Vital parameters and ventilatory settings

Vital parameters were measured, in addition to the standard monitoring at the ICU; at arrival, before RM, after RM and before extubation. Measurements are presented in *Table 1*. The ventilator settings at arrival were individual according to local guidelines (tidal volume (V_t) of 6-8 mL/kg, PEEP of 5 cmH_2O, FiO_2 of 30-50%, peak inspiratory pressure (PIP) <25 cmH_2O and end tidal CO_2 between 34,5 - 45 mmHg, respiratory parameters during measurements are presented in *Table 2*.

Statistics

A power analysis was performed prior to the study. Descriptive statistics with mean and standard error of the mean (SEM) were used in results and figures. GraphPad Prism 8 was used for statistical analysis. Mann-Whitney test and Kruskal-Wallis test were performed (depending on data distribution) to analyse if statistically significant difference was achieved among particles in exhaled air. Statistical significance was defined as $p < 0.0001$ (****) $p < 0.001$ (***), $p < 0.01$ (**), $p < 0.05$ (*) and $p > 0.05$ (not significant, ns).

Results

Of the thirty-six patients assessed for eligibility, 6 did not meet the inclusion criteria and were therefore excluded from the study. The remaining thirty patients were subsequently randomized to either volume-controlled ventilation (VCV) or pressure-controlled ventilation (PCV) during the first 30 minutes upon arrival at the ICU. After this thirty-minute period, which included a RM at 15 minutes, patients were placed on pressure regulated volume control (PRVC) until they have gained consciousness and are then placed on pressure support ventilation (PSV) until extubation. All randomized patients received allocated interventions. No patients were lost to follow-up. Patient demographics are shown in table 3.

Ventilation with Pressure regulated volume control (PRVC) resulted in the lowest Particle flow rate (PFR).

When comparing different ventilation mode, PRVC produced the lowest PFR at a rate of 77.2 ± 34.4 particles/min compared to VCV 83.7 ± 16.8 (p = 0.0285) and PCV 439.1 ± 153 (p = 0.0149). However, there were no significant difference between the VCV and PCV group (p=0.3980) The results are shown as mean and SEM. *(figure 2).*

Ventilation with pressure support ventilation (PSV) resulted in significant higher particle flow rate (PFR) compared to all other ventilation modes used.

When the patient awoke from anaesthesia, the ventilator mode was set to PSV to allow spontaneous breathing. The PFR significantly increased during PSV compared to all other ventilation modes studied.

The PFR during PSV was 2249 ± 426 particles/min compared to PFR during PRVC 77.2 ± 43.4 particles/min (p < 0.0001) *(Figure 2).*

Recruitment manoeuvre did not result in increased PFR.

A recruitment manoeuvre (RM) was conducted in both patients VCV and PCV mode but within a patient, did not result in any significant changes in PFR before or after the manoeuvre. For example, the PFR in VCV before the RM was 77.6 ± 19.3 particles/min and after the RM 89.8 ± 28 particles/min (p = 0.6529). *(Figure 3).*

Distribution of particles according to size did reflect significant differences between the different ventilation modes implying that PExA device could be used as a fingerprint diagnostic in mechanical ventilation.

The PExA device divides particles according to particle impaction and can thereby analyse size by distribution into eight different size groups, described in detail in previous studies (17, 18). Studying the particle size distribution between the ventilation modes, we discovered a significantly higher number of particles seen in PSV for all particle size groups (1-8) compared to the other ventilation modes (p < 0.0001). (*Figure 4).*

When analysing particle size separately we found a significant lower PFR in particle 1-4 comparing PRVC to PCV and also a significant lower PFR in particle 1-3 comparing PRVC to VCV. No difference was found for particle size 5-8. (*Figure 5*).

Discussion

Conventional monitoring of mechanical ventilation in the ICU is unable to detect subtle changes or stressors in the lung which precede the onset of lung injury. New techniques – and ideally those which

are non-invasive – should strive to detect early changes in the lung with the goal of optimising mechanical ventilation. Such strategies could be personalised for the patient to reduce ventilator induced lung injury (VILI). Considering that one contributing factor to VILI may be the repeated opening and closing of the distal airways during mechanical ventilation (2), a method of monitoring the activity of these airways would be clinically useful. The PFR as measured by the PExA device reflects the EBPs transmitted by these small airways and thus, a low PFR is theorized to correlate with reduced opening and closure of the airways and consequently gentler ventilation.

It is proposed that PFR in the clinic is a tool to measure changing conditions which a clinician could then utilize to gain a clearer picture of the clinical scenario. For example, increasing or decreasing PFR could be secondary to a change in ventilatory settings, which would be readily apparent to a clinician, or could be the result of patient transitioning from mechanical breathing to spontaneous breathing, or lung pathology. The clinician could use PFR as a tool to monitor lung status and thus, the relationship of PFR to ventilation mode was examined here. In this study, changes in ventilation mode and comparison between modes was correlated to changes in PFR.

A previous clinical study on lung transplant patients showed no difference in PFR using the ventilation modes VCV and PCV (19). This same observation was reproduced in the present study. According to clinical guidelines, PRVC is considered a gentle ventilation mode when a specific volume is desired as it also maintains the lowest possible pressure. A previous study compared PRVC to VCV and found significantly lower PIP when ventilating with PRVC (20). In the present study, a significantly lower PFR was observed when using PRVC relative to both PCV and VCV.

Additionally, this study found that PSV as a mode resulted in a higher PFR compared to all other modes. In theorizing the cause of such higher rates, the mechanics of breathing should be considered. While the patient is sedated, both the diaphragm and the accessory muscles are affected by sedatives relative to conscious breathing. Post-operatively, as sedation wears off and the ventilation mode is transitioned to PSV, the patient takes over increasingly more of the respiratory work. In this transition from controlled mechanical breathing to more conscious control by the patient with support from the ventilator, there is a significant increase in PFR. This increase is hypothesized to be attributed to the relative work of increasingly active respiratory muscles as active breathing seems to open previously closed alveoli. This reiterates the result of higher PFR in spontaneously breathing patients relative to ventilated patients, as previously published (19).

A recent study has demonstrated an increase in PFR preceding clinical signs of ARDS in a large animal model (16), and another study in lung transplanted patients has additionally shown higher PFR as a clinical indicator of primary graft dysfunction, a type of acute lung injury (19). This would appear

to indicate that particles in exhaled breath increase with pathology of the lung and resultantly may be an early indicator of damage to the lung. None of the patients in the present study showed signs of increased PFR during the time of the study and there were no other clinical signs of deteriorating condition, and thus neither PCV, VCV, or PRVC ventilation modes used under sedation appeared to be harmful to the lungs in patients with normal lung function. We have noted that there is inter-individual variation in PFR values, which could be integrated into the assessment of each individual patient. Further studies could include a longitudinal observation following an individual's change in PFR over longer surgical procedures or longer ICU stays where a patient may be on mechanical ventilation for a prolonged period.

The PExA device measures particles in the size range of 0.41 μm to 4.55 μm, which are then divided into 8 different size groups by the OPC (17). The distribution regarding particle count between the bin sizes 1-8 differed between the different ventilation modes in the present study. A significantly higher number of particles was seen using PSV for all particle size groups, compared to the other ventilation modes studied. When comparing PRVC, VCV and PCV, significant differences were seen between bin sizes 1-4, which established different particle patterns in these different modes. This could imply that particle patterns have the potential to act as fingerprint of distinct change or pathology. Further study will include the use of PFR in different lung pathologies to establish if the phenomena of distinctive patterns, as noted in this study, holds true for disease states. Characterization of the composition of EBPs during different ventilation modes and clinical circumstances could provide new insight into physiology and pathology of the lung.

Our hypothesis regarding high PFR during PSV ventilation follows that while initiating their own breath in this mode, patients use a breathing pattern similar to that of spontaneously breathing patients. As seen in a previous study, PFR in spontaneously breathing patients is significantly higher than that found in patients placed on mechanical ventilation (21). The use of the diaphragm, as in spontaneous breathing, promotes the opening and closing of the distal airways and may thus influence the production of EBPs (12). While under PRVC ventilation, the machine uses positive pressure to administer air. In PSV ventilation, however, the patient initiates breathing by generating negative pressure using the diaphragm and respiratory muscles. The ventilator then supports the patient's efforts by using positive pressure to ensure each breath constitutes complete tidal breathing. PEEP is applied in any ventilatory mode as it prevents the collapse of the small distal airways.

The recruitment manoeuvre implemented in this study has been previously published in both a pre-clinical porcine study of abdominal surgery and in a clinical study of lung transplant patients. These publications showed a significantly higher PFR after the RM when using VCV (18, 19). This provided the rationale for using the same RM here but we did not see any differences in PFR between the

different ventilation modes within this patient population. This result should be considered in the light of the use of patients without lung pathology. In the study conducted by Broberg et al, (19) patients had undergone lung transplantation. Lung transplant recipients experience pulmonary inflammatory reactions postoperatively and tissue trauma in the lungs from the surgery itself which might explain the response to the RM as seen by the PFR. When considering the preclinical study on PFR following RMs in porcine, there are several potential explanations as to why the results of that study differs: anatomic differences could be considered and the length of time on mechanical ventilation. (18). There might be several explanations as to why we did not observe a higher PFR after RM in the present study. Before leaving the operating room, all patients underwent a RM according to local clinical practice. The measurements for the present study started in the ICU approximately one hour after leaving the operating room.

In considering the results and conclusions which can be drawn from the present study, we must also take note of the limitations. The scope of this study was focused on the analysis of particle rate and patterns of distribution, as this research aimed to demonstrate the utility of PFR measurement as a bedside clinical tool. As particles were collected onto a membrane, future analysis could include investigation of specific biomarkers to develop a more mechanistic view of EPBs in pathological conditions. Additionally, the RM used in the ICU was noted to be a gentler manoeuvre compared to that in the OR. As the patients have already undergone a more vigorous RM in the OR while surgeons can monitor an open chest, the RM used in the ICU is gentler in light of the risk of bleeding and possible rupture of anastomoses in the immediate postoperative phase. Future study of PFR in relation to RMs would need to be conducted in a different patient population, as we would not subject the patients in this study to an RM more aggressive than that which we implemented. Furthermore, as previously discussed, the patients included here are those who underwent routine cardiac surgery and therefore had briefer stays in the ICU. Resultantly, the time spent on ventilation was relatively short. In future, we would consider including a broader spectrum of patients with lung and other types of pathology who stay in the ICU longer. This could be achieved by extending the study to other centres through collaboration. This would allow us to both study a less homogenous population as well as conduct analyses of PFR over a greater period of time.

This study reiterates the finding that measurement of PFR using the PExA device is safe in conjunction with mechanical ventilation (18, 19, 21). This was concluded as there were no signs of significant air leakage, haemodynamic impact or increased peak pressures which could be harmful to the patients.

Conclusions

PFR can be used to monitor mechanical ventilation with the future aim of personalising ventilator settings to each individual. The results suggest further research should investigate PRVC relative to VCV and PCV as the lower PFR could indicate that this is a gentler method of ventilation in a fully sedated patient where the goal is to avoid mechanical stress on the lung. Furthermore, the various ventilator settings explored in this study resulted in different distributions of exhaled particles binned by size. This could serve as the basis for studying PFR in terms of distinctive distribution patterns as a fingerprint of lung and ventilatory condition. We further concluded that a higher PFR was measured when ventilating in PSV mode compared to PRVC, which may reflect the added contribution of the work of breathing initiated by the patient. The findings of this study support the further investigation of PFR in terms of both rate and particle distribution as a promising clinical tool by which to assess the contribution of ventilatory mode to patient care.

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Tables

Table 1

PARAMETERS	BASELINE	BEFORE RM	AFTER RM	ENDING
SBP (MMHG)	104.9 ± 3.1	116.4 ± 3.1	118.2 ± 2.4	127.6 ± 3.5
DBP (MMHG)	54.5 ± 1.8	60.2 ± 2.2	60.9 ± 2.0	62.7 ± 2.1
MAP (MMHG)	69.8 ± 2.1	77.3 ± 2.3	77.7 ± 2.0	81.2 ± 2.2
CVP (MMHG)	1.3 ± 0.8	3.4 ± 0.7	3.4 ± 0.8	6.6 ± 0.9
HR (BEATS/MIN)	76.9 ± 1.9	75.8 ± 1.9	74.1 ± 2.2	80.4 ± 2.2
SAT (%)	98.5 ± 0.4	98.8 ± 0.4	99.5 ± 0.2	97.8 ± 0.4
TOF (%)	92.9 ± 5.3	-	-	-
PH	7.38 ± 0	-	-	7.35 ± 0
PCO$_2$ (MMHG)	38.7 ± 0.8	-	-	43.2 ± 1.1
PO$_2$ (MMHG)	132.8 ± 5.7	-	-	98.3 ± 3.3

Table 1. Haemodynamic parameters, TOF and blood gases during measurement at arrival in the ICU (baseline), before and after recruitment manoeuvre (RM), and before extubation. Presented as mean and SEM. Systolic blood pressure (SBP). Diastolic blood pressure (DBP). Mean arterial pressure (MAP). Central venous pressure (CVP). Heart rate (HR). Saturation (Sat). Train of four (TOF). Partial pressure of carbon dioxide (pCO$_2$). Partial pressure of oxygen (pO$_2$).

Table 2

PARAMETERS	BASELINE	BEFORE RM	AFTER RM	ENDING
VENTILATION MODE	VCV : PCV (1:1)	VCV : PCV (1:1)	PRVC	PSV
PEEP (CMH$_2$O)	5.2 ± 0.1	5.2 ± 0.1	5.1 ± 0.1	2.4 ± 0.2
PIP (CMH$_2$O)	17.0 ± 0.9	17.0 ± 0.5	14.6 ± 0.4	12.8 ± 0.2
P$_{MEAN}$ (CMH$_2$O)	8.9 ± 0.2	9.0 ± 0.3	8.7 ± 0.2	5.1 ± 0.2
PS (CMH$_2$O), IN PCV AND PSV	11.0 ± 0.6	10.9 ± 0.6	-	10.0 ± 0.1
RR (BREATHS/MIN)	14.4 ± 0.2	14.4 ± 0.3	14.3 ± 0.2	16.2 ± 1.0
V$_T$ INSP (ML)	509.0 ± 15.6	518.5 ± 16.2	506.6 ± 11.2	586.5 ± 37.8
V$_T$ EXP (ML)	501.7 ± 15.8	507.0 ± 15.9	496.1 ± 10.7	580.7 ± 41.5
MV (L/MIN)	7.3 ± 0.3	7.2 ± 0.2	7.1 ± 0.2	8.6 ± 0.3
CDYN (ML/CMH2O)	51.5 ± 2.8	53.3 ± 2.7	54.4 ± 2.0	52.8 ± 4.4
FIO$_2$ (%)	42.0 ± 1.0	40.7 ± 0.8	40.0 ± 0.9	32.2 ± 0.6
I:E	1:2	1:2	1:2	-

Table 2. Ventilator settings and respiratory parameters at arrival in the ICU (baseline), before and after recruitment manoeuvre (RM), and before extubation. Presented as mean and SEM. Positive end expiratory pressure (PEEP). Peak inspiratory pressure (PIP). Mean pressure (P$_{mean}$). Pressure support (PS). Respiratory rate (RR). Tidal volume (V$_t$). Minute ventilation (MV). Dynamic compliance (Cdyn). Fraction of inspired oxygen (FiO$_2$). Inspiratory-expiratory ratio (I:E). Volume controlled ventilation (VCV). Pressure controlled ventilation (PCV). Pressure regulated volume control (PRVC). Pressure support ventilation (PSV).

Table 3

	VOLUME CONTROLLED VENTILATION (VCV)	PRESSURE CONTROLLED VENTILATION (PCV)	TOTAL
PATIENTS	N = 15	N = 15	N = 30
SEX M/F N (%)	10 / 5	12 / 3	22 (73) / 8 (27)
TYPE OF SURGERY			
CABG	N = 7	N = 8	N = 15
AVR	N = 4	N = 5	N = 10
CABG AND AVR	N = 3	N = 2	N = 5
AGE (YEAR)	67 (2)	69 (1)	69 (2)
SMOKING	No	No	No
NORMAL CHEST X-RAY	Yes	Yes	Yes
NORMAL RENAL FUNCTION	Yes	Yes	Yes
EF > 55%	Yes	Yes	Yes

Table 3. Patient demographics. Coronary artery bypass grafting (CABG). Aortic valve replacement (AVR).
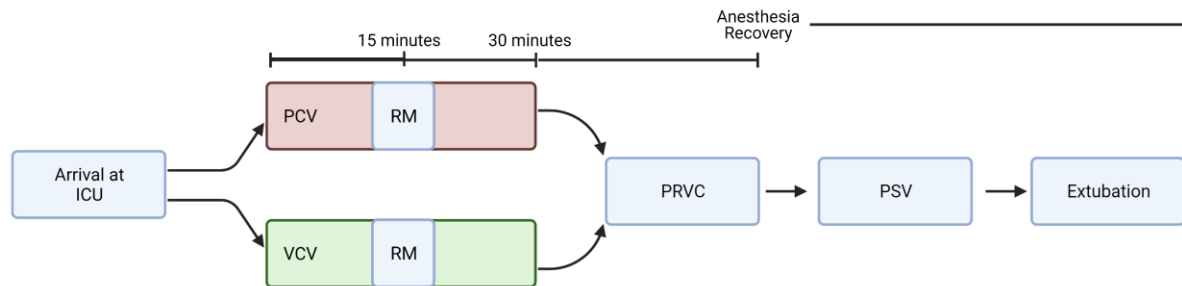
Figure legends

Figure 1. Flowchart after arrival at the ICU. The patients were randomized to either volume-controlled ventilation (VCV) or pressure-controlled ventilation (PCV) including a recruitment manoeuvre (RM) as the first line of treatment. The mechanical ventilation was thereafter set to pressure regulated volume control (PRVC) in all patients until recovery from anesthesia when the ventilator was switched to pressure support ventilation (PSV) to facilitate spontaneous breathing. Created with BioRender.com
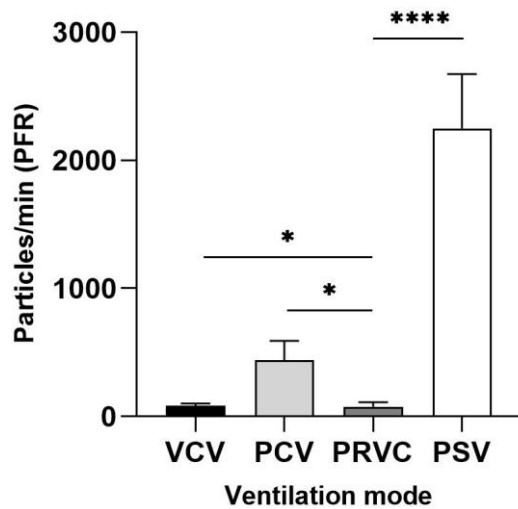
Figure 2. There was a significantly lower particle flow rate (PFR) when using pressure regulated volume control (PRVC) compared to volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV). Ventilation with pressure support ventilation (PSV) resulted in significantly higher particle flow rate (PFR) compared to pressure regulated volume control (PRVC). Statistical tests were conducted using the Mann Whitney test. Statistical significance was defined as $p < 0.0001$ (****), $p < 0.001$ (***), $p < 0.01$ (**), $p < 0.05$ (*) and $p > 0.05$ (not significant, ns).
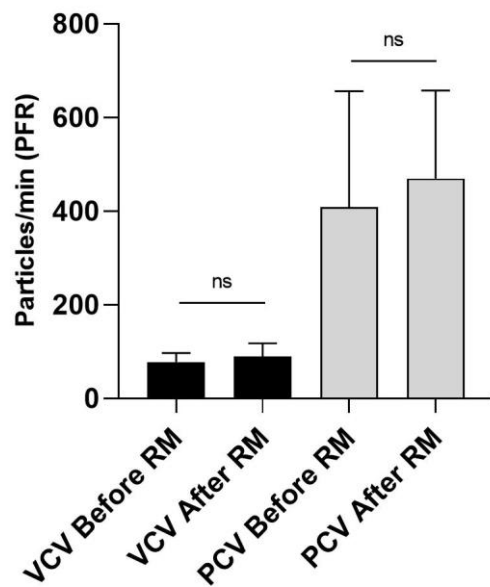
Figure 3. No significant difference was found in either ventilator mode when comparing particle flow rate (PFR) before and after the recruitment manoeuvre (RM). There was no significant difference between volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV) before and after the RM. Statistical significance was defined as $p < 0.0001$ (****), $p < 0.001$ (***), $p < 0.01$ (**), $p < 0.05$ (*) and $p > 0.05$ (not significant, ns).
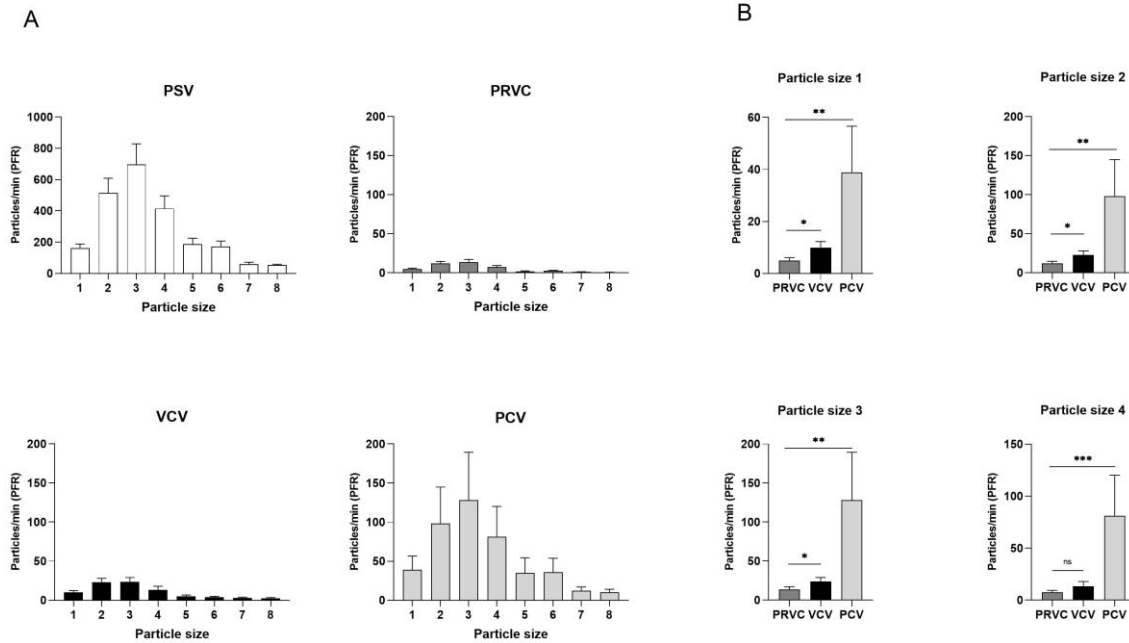
Figure 4A. Distribution of particles according to size in the different ventilation modes.

When looking at particle flow rate (PRF) according to the different particle size bins (1-8) we can distinguish distinct patterns linked to different ventilation modes. In pressure support ventilation (PSV), there was a significantly higher PFR for all particle sizes (1-8) compared to the other ventilation modes. Statistical tests were conducted using the Kruskal-Wallis test.

Figure 4B. Particle flow rate (PFR) for particle sizes 1-4 in the different ventilation modes. A significant difference was found between pressure regulated volume control (PRVC) and pressure-controlled ventilation (PCV) for particle sizes 1-4. A significant difference between PRVC and volume-controlled ventilation (VCV) was found for particle sizes 1-3. No difference was found when comparing VCV to PCV for particle sizes 1-4. Statistical significance was defined as $p < 0.0001$ (****), $p < 0.001$ (***), $p < 0.01$ (**), $p < 0.05$ (*) and $p > 0.05$ (not significant, ns).