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RESEARCH ARTICLE

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# Intraoperative ventilator settings and their association with postoperative pulmonary complications in neurosurgical patients: post-hoc analysis of LAS VEGAS study

Chiara Robba<sup>1\*</sup>, Sabine N. T. Hemmes<sup>2,3</sup>, Ary Serpa Neto<sup>2,4</sup>, Thomas Bluth<sup>5</sup>, Jaime Canet<sup>6</sup>, Michael Hiesmayr<sup>7</sup>, M. Wiersma Hollmann<sup>3</sup>, Gary H. Mills<sup>8</sup>, Marcos F. Vidal Melo<sup>9</sup>, Christian Putensen<sup>10</sup>, Samir Jaber<sup>11</sup>, Werner Schmid<sup>7</sup>, Paolo Severgnini<sup>12</sup>, Hermann Wrigge<sup>13</sup>, Denise Battaglini<sup>1,14</sup>, Lorenzo Ball<sup>1,14</sup>, Marcelo Gama de Abreu<sup>5</sup>, Marcus J. Schultz<sup>2,15</sup>, Paolo Pelosi<sup>1,14</sup>, FERS for the LAS VEGAS investigators and the PROtective VEntilation Network and the Clinical Trial Network of the European Society of Anaesthesiology

## Abstract

**Background:** Limited information is available regarding intraoperative ventilator settings and the incidence of postoperative pulmonary complications (PPCs) in patients undergoing neurosurgical procedures. The aim of this post-hoc analysis of the 'Multicentre Local ASsessment of VEntilatory management during General Anaesthesia for Surgery' (LAS VEGAS) study was to examine the ventilator settings of patients undergoing neurosurgical procedures, and to explore the association between perioperative variables and the development of PPCs in neurosurgical patients.

**Methods:** Post-hoc analysis of LAS VEGAS study, restricted to patients undergoing neurosurgery. Patients were stratified into groups based on the type of surgery (brain and spine), the occurrence of PPCs and the assess respiratory risk in surgical patients in Catalonia (ARISCAT) score risk for PPCs.

**Results:** Seven hundred eighty-four patients were included in the analysis; 408 patients (52%) underwent spine surgery and 376 patients (48%) brain surgery. Median tidal volume ( $V_T$ ) was 8 ml [Interquartile Range, IQR = 7.3–9] per predicted body weight; median positive end–expiratory pressure (PEEP) was 5 [3 to 5] cmH<sub>2</sub>O. Planned recruitment manoeuvres were used in the 6.9% of patients. No differences in ventilator settings were found among the sub-groups. PPCs occurred in 81 patients (10.3%). Duration of anaesthesia (odds ratio, 1.295 [95% confidence interval 1.067 to 1.572];  $p = 0.009$ ) and higher age for the brain group (odds ratio, 0.000 [0.000 to 0.189];  $p = 0.031$ ), but not intraoperative ventilator settings were independently associated with development of PPCs.

**Conclusions:** Neurosurgical patients are ventilated with low  $V_T$  and low PEEP, while recruitment manoeuvres are seldom applied. Intraoperative ventilator settings are not associated with PPCs.

**Keywords:** LAS VEGAS, Mechanical ventilation, Postoperative pulmonary complications, Neurosurgery

\* Correspondence: [kiarobba@gmail.com](mailto:kiarobba@gmail.com)

<sup>1</sup>Anaesthesia and Intensive Care, San Martino Policlinico Hospital, IRCCS for Oncology and Neurosciences, Largo Rosanna Benzi 8, 16131 Genoa, Italy  
Full list of author information is available at the end of the article



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## Background

Lung-protective ventilation strategies are increasingly used in surgical patients [1, 2]. Typical lung-protective strategies include the use of a low tidal volume ( $V_T$ ) and a low plateau pressure (Pplat), with moderate positive end-expiratory pressure (PEEP) and use of recruitment manoeuvres (RM) if needed [1, 2]. Among these settings, a low  $V_T$  seems to have the most protective effects compared with moderate or high PEEP [3, 4].

However, lung-protective ventilation is rarely used in brain injured patients, in whom median  $V_T$  is generally 9 ml/kg of predicted body weight (PBW) [5]. The role of intraoperative ventilator settings and their potential impacts on the development of postoperative complications (PPCs) has been scarcely evaluated in neurological patients [6]. Typically, patients with neurosurgical pathologies have been excluded from most trials on protective intraoperative ventilation. This may be because lung-protective strategies could have detrimental effects on cerebrovascular physiology, and thus might be potentially contraindicated in acute neurosurgical patients [7]. Moreover, just few and inconclusive data exist regarding the ventilator settings applied in patients undergoing spinal surgery and the incidence of PPCs in this population [8, 9].

We therefore conducted a post-hoc analysis of the 'Local ASsessment of Ventilatory management during General Anaesthesia for Surgery-study' (LAS VEGAS), a conveniently sized international observational study in the operating rooms of patients receiving mechanical ventilation [10]. We focused on neurosurgical patients, including patients undergoing brain or spine surgery. The aims of this analysis were to assess which ventilator strategies were used in neurosurgical patients during general anaesthesia, and to assess the incidence of PPCs and risk factors (including type of surgery, ventilator settings, risk for PPCs) associated with the development of PPCs. The main hypothesis tested was that neurosurgical patients are ventilated with high tidal volume and low positive end expiratory pressure, and that intraoperative ventilator settings can have an effect on PPCs development.

## Methods

### LAS VEGAS study

This article is reported as per Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines ([www.strobe-statement.org](http://www.strobe-statement.org)) (Electronic supplementary material ESM Table S1).

LAS VEGAS [8] was an international multicentre observational prospective study (registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (study identifier NCT01601223)), endorsed and supported by the European Society of Anaesthesiology and the Amsterdam University Medical Centres,

location AMC, Amsterdam, The Netherlands. Details about the LAS VEGAS study collaborators, participating centres and hospital characteristics of participating centres are reported in ESM Tables S2a, b and S3.

All adult patients requiring invasive ventilation for surgical procedures in a time window of 7 days were included. Exclusion criteria were: age under 18 years, obstetric procedures, recent ventilation before surgery (< 28 days), surgical procedures not performed in the operating room, and interventions requiring cardiopulmonary bypass.

For this study, we restricted the analysis to patients receiving intraoperative ventilation for neurosurgical procedures (brain or spine surgery) (ESM Flow Chart).

### Data collection

After inclusion, the following data were collected: patients' baseline and demographic characteristics; the assess respiratory risk in surgical patients in Catalonia (ARISCAT) score [11]; American Society of Anaesthesiologists (ASA) scale; details on the surgical procedure including intraoperative hourly vital parameters and ventilation data (mode of ventilation, fraction of inspired oxygen ( $FiO_2$ ),  $V_T$ , PEEP, peak pressure (Ppeak), respiratory rate (RR)), end-tidal  $CO_2$  (ETCO<sub>2</sub>), oxygen saturation (SpO<sub>2</sub>), number and type of recruitment manoeuvres, and intraoperative complications.

Recruitment manoeuvres were defined as 'rescue' when the recruitment manoeuvre was not part of the planned ventilation strategy and defined as 'planned' if it was part of routine ventilation practice (ESM Table S4). Mechanical power (MP) was calculated according to the following formula [12]:  $0.098 \times V_T \times RR \times [P_{peak} \times (P_{plat} - PEEP)/2]$ . Hourly data were collected starting at the induction of anaesthesia (T1/40) and then hourly until the end of anaesthesia, up to the 7th hour of surgery (T1/47).

### Endpoints

The primary endpoint was to describe the current practice and ventilator strategies in patients undergoing neurosurgical interventions, in particular ventilator mode,  $V_T$ , PEEP, driving pressure, Ppeak and Pplat and RR, as well as mechanical power.

The secondary outcome was to assess the prevalence of PPCs and the association with preoperative and intraoperative variables including mechanical ventilator settings, type of surgery, ARISCAT score. Detailed definitions of the composites of PPCs and severe PPCs are provided in ESM Table S5. Intraoperative complications included desaturation, rescue recruitment manoeuvres, need for airway pressure reduction, expiratory flow limitation, hypotension and use of vasoactive drugs, onset of a new cardiac arrhythmia (ESM Table S6). The

occurrence of each type of PPC was monitored until hospital discharge, but maximum up to postoperative day 5.

Other secondary endpoints included the occurrence of severe PPCs, intraoperative complications, in-hospital mortality and length of hospital stay.

### Statistical analysis

Patients were stratified into groups based on type of surgery (brain and spine), the occurrence of PPCs and risk for PPC according to ARISCAT (low risk [ARISCAT < 26] vs. moderate-to-high risk [ARISCAT  $\geq$ 26]). Continuous variables are expressed as mean  $\pm$  standard deviation (SD) or median (interquartile range [IQR]) per variable distribution. Discrete variables are presented as percentages. Baseline characteristics among type of neurosurgery were compared by either t-test, Wilcoxon rank-sum test, or chi-squared tests, as appropriate. The effect of type of neurosurgery on the incidence (per 10 P-days) of in-hospital PPC, severe PPC, and discharged alive was evaluated using log-rank test (stratified by centre); differences in survival probabilities and hospital discharge were depicted with an outcome-specific Kaplan-Meier plot.

A multivariable regression model was built, with PPC as dependent variables. Because this outcome is binary (0/1), a logistic regression analysis was applied. Candidate covariates were chosen based on previous medical knowledge, independent of their *p*-value. From this preliminary selection, those variables with *P* < 0.20 in the univariate analysis were preferentially chosen for the stepwise procedure. Then, a reduced and parsimonious model was derived using backward stepwise selection. During this selection process, the linearity assumption for continuous variables was tested and transformed, if appropriate, with fractional polynomials (14). In all regression models, the Huber/White/sandwich estimator of variance correction was applied to account for any clustering effect due to centre sampling.

We set a two-sided *p* value of < 0.05 as the threshold for statistical significance. Stata 15.1 (Stata Statistical Software, release 15 [2017] (Stata Corp LP, College Station, TX, USA), and R (Version 3.5.3; R Foundation for Statistical Computing, Vienna, Austria) were used.

### Results

A total of 784 patients were included in the analysis. Of these, 408 (52%) underwent spine surgery and 376 (48%) brain surgery. The characteristics of the patients according to subgroups are described in Table 1. Patients with moderate-to-high risk for PPCs- compared to those at low risk were older, with a higher incidence of co-morbidities (in particular chronic kidney failure), worse ASA physical status, and worse pre-hospital functional

status and preoperative conditions (as for laboratory tests and vital signs) (Table 1). Patients who developed PPCs were older, with more frequent co-morbidities (in particular respiratory and cardiological), worse ASA and preoperative functional status (Table 1).

### Ventilation variables and intraoperative characteristics

Most of the patients underwent elective surgical procedure (72%), with a median surgical duration of 95 min (1st-3rd interquartile range IQR = 60–160) and median anaesthetic time of 126 min (IQR = 90–192.8 min). The most common ventilation mode was volume-controlled ventilation (VCV) (Table 2). VCV was more commonly used in patients undergoing brain surgery. Median  $V_T$  was 510 ml (Interquartile range, IQR 475–575), thus resulting in 8 ml/kg predicted body weight (IQR = 7.3–9). Median PEEP level was 5 cmH<sub>2</sub>O (IQR 3–5), Ppeak was 18 cmH<sub>2</sub>O (IQR = 15–21) and driving pressure was 12 (IQR = 11–15) cmH<sub>2</sub>O (Table 2).

Routine RMs were performed in 54 patients (6.9%). Unplanned RMs occurred in 1.4% of cases. No statistical difference was found between the spine and brain surgery group or regarding the ventilator settings (Table 2, ESM Figure S1). EtCO<sub>2</sub> values were significantly lower in the brain surgery group compared with the spine surgery group (*p* = 0.001). Patients who developed PPCs received a higher amount of fluids compared to those with no PPCs (Table 2), but no differences were found in the ventilator settings between the two groups (Fig. 1).

Scatter plots showing the combinations of  $V_T$  with PEEP, driving pressure, Ppeak, and respiratory rate in patients who developed versus patients who did not develop PPCs, between the spine and brain group, and in patients with low risk [ARISCAT < 26] vs. moderate-to-high risk [ARISCAT  $\geq$ 26] are shown in Fig. 2, ESM Figures S2, S3.

### Occurrence of PPCs, intraoperative complications and outcomes

Among the 784 patients included in the analysis, 81 (10.4%) developed PPCs (Table 2). PPCs occurred mainly on day 3. No differences between the surgical groups were found as for probability of PPCs occurrence and hospital length of stay (ESM Figure S4).

Patients with ARISCAT  $\geq$ 26 showed an increased probability of PPCs occurrence compared to patients at lower risk (HR 2.50; 95% CI 1.61–3.58, *p* < 0.000), and of longer hospital length of stay (HR 0.81; 95% CI 0.69.0.97, *p* = 0.019) (ESM Figure S4).

Intraoperative episodes of hypotension and the need for vasoactive drugs during the procedure were frequent, especially in the spine group compared to the brain group (38.7% vs 31.2% for hypotension; *p* = 0.028 and 34.6% vs 27.7% for vasoactive drugs, *p* = 0.04,

**Table 1** Pre-Operative Characteristics of the Patients According to Subgroups

|                                      | All Patients | Brain      | Spine      | <i>p</i> value | All patients | PPC         | No PPC     | <i>p</i> value | All patients | ARISCAT < 26 | ARISCAT ≥ 26 | <i>p</i> value |
|--------------------------------------|--------------|------------|------------|----------------|--------------|-------------|------------|----------------|--------------|--------------|--------------|----------------|
| <b><i>n</i> (%)</b>                  | 784 (100)    | 376 (48)   | 408 (52)   |                | 777 (100.0)  | 81 (10.4)   | 696 (89.6) |                | 548 (73.3)   | 200 (26.7)   | 748 (100.0)  |                |
| <b>Demographics</b>                  |              |            |            |                |              |             |            |                |              |              |              |                |
| Age, years, mean (SD)                | 53 (16)      | 52 (16)    | 54 (15)    | 0.104          | 53 (16)      | 59 (15)     | 52 (16)    | 0.000          | 50 (15)      | 51 (15)      | 63 (16)      | 0.000          |
| Gender, n (%)                        |              |            |            |                |              |             |            |                |              |              |              |                |
| Male                                 | 392 (50)     | 183 (48.7) | 209 (51.2) | 0.060          | 392 (50.5)   | 37 (45.7)   | 355 (51.0) | 0.072          | 285 (52.0)   | 97 (48.5)    | 382 (51.1)   | 0.065          |
| Ethnicity, n (%)                     |              |            |            |                |              |             |            |                |              |              |              |                |
| Black                                | 2 (0.3)      | 0 (0.0)    | 2 (0.5)    |                | 2 (0.3)      | 2 (2.5)     | 0 (0.0)    |                | 1 (0.2)      | 1 (0.5)      | 2 (0.3)      | 0.663          |
| Caucasian                            | 709 (90.4)   | 340 (90.4) | 369 (90.4) |                | 704 (90.6)   | 71 (87.7)   | 633 (90.9) |                | 493 (90.0)   | 183 (91.5)   | 676 (90.4)   |                |
| Asian                                | 4 (0.5)      | 1 (0.3)    | 3 (0.7)    |                | 4 (0.5)      | 1 (1.2)     | 3 (0.4)    |                | 4 (0.7)      | 0 (0.0)      | 4 (0.5)      |                |
| Other                                | 33 (4.2)     | 13 (3.5)   | 20 (4.9)   |                | 33 (4.2)     | 2 (2.5)     | 31 (4.5)   |                | 26 (4.7)     | 6 (3.0)      | 32 (4.3)     |                |
| <b>Anthropometry</b>                 |              |            |            |                |              |             |            |                |              |              |              |                |
| Height, cm, mean (SD)                | 170 (10)     | 170 (10)   | 170 (9)    | 0.416          | 170 (10)     | 169 (10)    | 170 (10)   | 0.421          | 170 (10)     | 169 (10)     | 170 (10)     | 0.243          |
| Weight, kg, mean (SD)                | 79 (17)      | 80 (18)    | 78 (16)    | 0.309          | 79 (17)      | 80 (18)     | 79 (17)    | 0.597          | 79 (17)      | 79 (17)      | 79 (17)      | 0.677          |
| BMI, kg/m <sup>2</sup> , mean (SD)   | 27.3 (5.8)   | 27.7 (6.6) | 27.0 (4.9) | 0.148          | 27.3 (5.8)   | 28.3 (6.5)  | 27.2 (5.7) | 0.141          | 27.3 (6.0)   | 27.4 (5.0)   | 27.3 (5.8)   | 0.874          |
| Co-morbidities, n (%)                |              |            |            |                |              |             |            |                |              |              |              |                |
| Co-morbidities                       | 161 (20.5)   | 84 (22.3)  | 77 (18.9)  | 0.230          | 160 (20.6)   | 30 (37.0)   | 130 (18.7) | 0.000          | 98 (17.9)    | 59 (29.5)    | 157 (21.0)   | 0.001          |
| COPD                                 | 47 (6.0)     | 21 (5.6)   | 26 (6.4)   | 0.643          | 47 (6.0)     | 8 (9.9)     | 39 (5.6)   | 0.127          | 32 (5.8)     | 15 (7.5)     | 47 (6.3)     | 0.407          |
| Respiratory                          | 19 (2.4)     | 8 (2.1)    | 11 (2.7)   | 0.605          | 19 (2.4)     | 5 (6.2)     | 14 (2.0)   | 0.022          | 12 (2.2)     | 7 (3.5)      | 19 (2.5)     | 0.313          |
| Liver cirrhosis                      | 4 (0.5)      | 2 (0.5)    | 2 (0.5)    | 0.935          | 4 (0.5)      | 0 (0.0)     | 4 (0.6)    | 0.494          | 3 (0.5)      | 1 (0.5)      | 4 (0.5)      | 0.937          |
| Chronic kidney failure               | 16 (2.0)     | 4 (1.1)    | 12 (2.9)   | 0.063          | 16 (2.1)     | 4 (4.9)     | 12 (1.7)   | 0.054          | 6 (1.1)      | 9 (4.5)      | 15 (2.0)     | 0.003          |
| Heart failure                        | 45 (5.7)     | 27 (7.2)   | 18 (4.4)   | 0.096          | 45 (5.8)     | 10 (12.3)   | 35 (5.0)   | 0.008          | 29 (5.3)     | 14 (7.0)     | 43 (5.7)     | 0.374          |
| Neuro disease                        | 12 (1.5)     | 8 (2.1)    | 4 (1.0)    | 0.191          | 12 (1.5)     | 2 (2.5)     | 10 (1.4)   | 0.476          | 11 (2.0)     | 1 (0.5)      | 12 (1.6)     | 0.146          |
| <b>Pre-operative medical history</b> |              |            |            |                |              |             |            |                |              |              |              |                |
| ASA physical status, n (%)           | 214 (27.4)   | 96 (25.5)  | 118 (29.1) | 0.007          | 208 (26.8)   | 14 (17.5)   | 194 (27.9) | 0.000          | 165 (30.1)   | 29 (14.6)    | 194 (26.0)   | 0.000          |
| ASA I                                | 395 (50.5)   | 178 (47.3) | 217 (53.4) |                | 395 (51.0)   | 33 (41.3)   | 362 (52.1) |                | 292 (53.3)   | 90 (45.2)    | 382 (51.1)   |                |
| ASA II                               | 395 (50.5)   | 178 (47.3) | 217 (53.4) |                | 153 (19.7)   | 28 (35.0)   | 125 (18.0) |                | 85 (15.5)    | 68 (34.2)    | 153 (20.5)   |                |
| ASA III                              | 154 (19.7)   | 87 (23.1)  | 67 (16.5)  |                | 18 (2.3)     | 5 (6.3)     | 13 (1.9)   |                | 6 (1.1)      | 11 (5.5)     | 17 (2.3)     |                |
| ASA IV                               | 18 (2.3)     | 14 (3.7)   | 4 (1.0)    |                | 1 (0.1)      | 0 (0.0)     | 1 (0.1)    |                | 0 (0.0)      | 1 (0.5)      | 1 (0.1)      |                |
| ASA V                                | 1 (0.1)      | 1 (0.3)    | 0 (0.0)    |                | 208 (26.8)   | 14 (17.5)   | 194 (27.9) |                | 165 (30.1)   | 29 (14.6)    | 194 (26.0)   |                |
| Functional status, n (%)             |              |            |            | 0.004          |              |             |            | 0.000          |              |              |              | 0.006          |
| Independent                          | 708 (90.3)   | 327 (87.0) | 381 (93.4) |                | 702 (90.3)   | 67 (82.7)   | 635 (91.2) |                | 506 (92.3)   | 168 (84.0)   | 674 (90.1)   |                |
| Partially dependent                  | 62 (7.9)     | 38 (10.1)  | 24 (5.9)   |                | 62 (8.0)     | 12 (14.8)   | 50 (7.2)   |                | 33 (6.0)     | 27 (13.5)    | 60 (8.0)     |                |
| Totally dependent                    | 13 (1.7)     | 11 (2.9)   | 2 (0.5)    |                | 12 (1.5)     | 2 (2.5)     | 10 (1.4)   |                | 8 (1.5)      | 5 (2.5)      | 13 (1.7)     |                |
| ARISCAT score, median (IQR)          | 215 (27.4)   | 102 (27.1) | 113 (27.7) | 0.000          | 16 (3; 26)   | 23 (11; 32) | 16 (3; 24) | 0.002          | 8 (3; 18)    | 31 (26; 37)  | 16 (3; 26)   | 0.000          |
| Smoking, n (%)                       | 40 (5.1)     | 23 (6.1)   | 17 (4.2)   | 0.859          | 214 (27.5)   | 22 (27.2)   | 192 (27.6) | 0.442          | 165 (30.1)   | 44 (22.0)    | 209 (27.9)   | 0.029          |
| Transfusion (< 24 h), n (%)          | 5 (0.6)      | 3 (0.8)    | 2 (0.5)    | 0.215          | 39 (5.0)     | 6 (7.4)     | 33 (4.7)   | 0.000          | 16 (2.9)     | 22 (11.0)    | 38 (5.1)     | 0.000          |

**Table 1** Pre-Operative Characteristics of the Patients According to Subgroups (Continued)

|   | All Patients | Brain       | Spine       | <i>p</i> value | All patients | PPC         | No PPC      | <i>p</i> value | All patients | ARISCAT < 26 | ARISCAT ≥ 26 | <i>p</i> value |
|---|--------------|-------------|-------------|----------------|--------------|-------------|-------------|----------------|--------------|--------------|--------------|----------------|
| RBC transfusion (< 24 h)                | 28 (3.6)     | 16 (4.3)    | 12 (2.9)    | 0.589          | 5 (0.6)      | 1 (1.2)     | 4 (0.6)     | 0.722          | 1 (0.2)      | 4 (2.0)      | 5 (0.7)      | 0.007          |
| Respiratory infection (< 30d), n (%)    | 1 (0.1)      | 0 (0.0)     | 1 (0.2)     | 0.322          | 28 (3.6)     | 3 (3.7)     | 25 (3.6)    | 0.002          | 7 (1.3)      | 19 (9.5)     | 26 (3.5)     | 0.000          |
| <b>Laboratory tests and vital signs</b> |              |             |             |                |              |             |             |                |              |              |              |                |
| Pre-operative values                    |              |             |             |                |              |             |             |                |              |              |              |                |
| SpO <sub>2</sub> , %, median (IQR)      | 97 (96; 99)  | 97 (96; 98) | 97 (96; 99) | 0.230          | 97 (96; 99)  | 97 (95; 98) | 98 (96; 99) | 0.002          | 98 (96; 99)  | 96 (94; 98)  | 97 (96; 99)  | 0.000          |
| Hb, (g/dL), mean (SD)                   | 13.8 (1.8)   | 13.8 (1.8)  | 13.9 (1.8)  | 0.540          | 13.8 (1.8)   | 13.7 (2.0)  | 13.8 (1.8)  | 0.442          | 14.0 (1.6)   | 13.3 (2.1)   | 13.8 (1.8)   | 0.000          |
| WBC, (cell/mm <sup>3</sup> ), mean (SD) | 7879 (3497)  | 8199 (3097) | 7568 (3825) | 0.019          | 7891 (3503)  | 9261 (6168) | 7721 (2978) | 0.000          | 7696 (3362)  | 8438 (3845)  | 7905 (3518)  | 0.015          |
| Creatinine, (mg/dL), mean (SD)          | 0.89 (0.69)  | 0.90 (0.86) | 0.88 (0.49) | 0.758          | 0.89 (0.69)  | 0.87 (0.28) | 0.90 (0.73) | 0.722          | 0.87 (0.59)  | 0.95 (0.91)  | 0.89 (0.70)  | 0.192          |
| <b>Surgical characteristics</b>         |              |             |             |                |              |             |             |                |              |              |              |                |
| Condition, n (%)                        |              |             |             | 0.318          |              |             |             | 0.140          |              |              |              | 0.000          |
| Elective                                | 717 (91.5)   | 338 (89.9)  | 379 (92.9)  |                | 712 (91.6)   | 73 (90.1)   | 639 (91.8)  |                | 513 (93.6)   | 172 (86.0)   | 685 (91.6)   |                |
| Urgency                                 | 50 (6.4)     | 28 (7.4)    | 22 (5.4)    |                | 49 (6.3)     | 4 (4.9)     | 45 (6.5)    |                | 31 (5.7)     | 16 (8.0)     | 47 (6.3)     |                |
| Emergency                               | 17 (2.2)     | 10 (2.7)    | 7 (1.7)     |                | 16 (2.1)     | 4 (4.9)     | 12 (1.7)    |                | 4 (0.7)      | 12 (6.0)     | 16 (2.1)     |                |
| Planned duration, hours, n (%)          |              |             |             | 0.000          |              |             |             | 0.000          |              |              |              | 0.000          |
| 0                                       | 1 (0.1)      | 1 (0.3)     | 0 (0.0)     |                | 1 (0.1)      | 0 (0.0)     | 1 (0.1)     |                |              |              |              |                |
| ≤ 2                                     | 432 (55.1)   | 186 (49.5)  | 246 (60.3)  |                | 426 (54.8)   | 36 (44.4)   | 390 (56.0)  |                | 378 (69.0)   | 25 (12.5)    | 403 (53.9)   |                |
| 2–3                                     | 201 (25.6)   | 90 (23.9)   | 111 (27.2)  |                | 201 (25.9)   | 15 (18.5)   | 186 (26.7)  |                | 124 (22.6)   | 73 (36.5)    | 197 (26.3)   |                |
| > 3                                     | 150 (19.1)   | 99 (26.3)   | 51 (12.5)   |                | 149 (19.2)   | 30 (37.0)   | 119 (17.1)  |                | 46 (8.4)     | 102 (51.0)   | 148 (19.8)   |                |
| Antibiotic prophylaxis, n (%)           | 711 (90.9)   | 338 (90.1)  | 373 (91.6)  | 0.462          | 705 (91.0)   | 74 (91.4)   | 631 (90.9)  | 0.897          | 500 (91.4)   | 184 (92.0)   | 684 (91.6)   | 0.796          |

*P* value refers to the between-groups with Fisher-Freeman-Halton Exact test, Mann Whitney u-test, or Kruskal Wallis test, as appropriate. *N* Number, *IQR* Interquartile range, *SD* Standard deviation, *h* Hours, *d* Days, *PPC* Postoperative pulmonary complications, *COPD* Chronic obstructive pulmonary disease, *ASA* American society of anesthesiologists, *RBC* Blood red cells, *SpO<sub>2</sub>* Blood oxygen saturation, *Hb* Hemoglobin, *WBC* White blood cells

respectively) (Table 3). The incidence of desaturation was less frequent than hypotension or need of vasoactive drugs. No differences were found in terms of mortality or hospital length of stay in patients who developed and did not develop PPCs or the type of surgery. Patients with ARISCAT ≥ 26 compared to those with ARISCAT < 26, had longer LOS and higher hospital mortality (Table 3).

#### Risk factors for PPCs

Multivariable logistic regression was used to identify the predictors of PPCs. Duration of anaesthesia was independently associated for the development of PPCs. Analysing the predictors for type of neurosurgery, for age we found a significantly effect in the brain group (the omnibus *p*-value for the neurosurgery-age interaction was *p* = 0.031), but not in the spine group. (Table ESM S7, ESM Figure S5, Fig. 3). The effect of age on PPC in the

brain group was significant at age above 62 (ESM Figure S5).

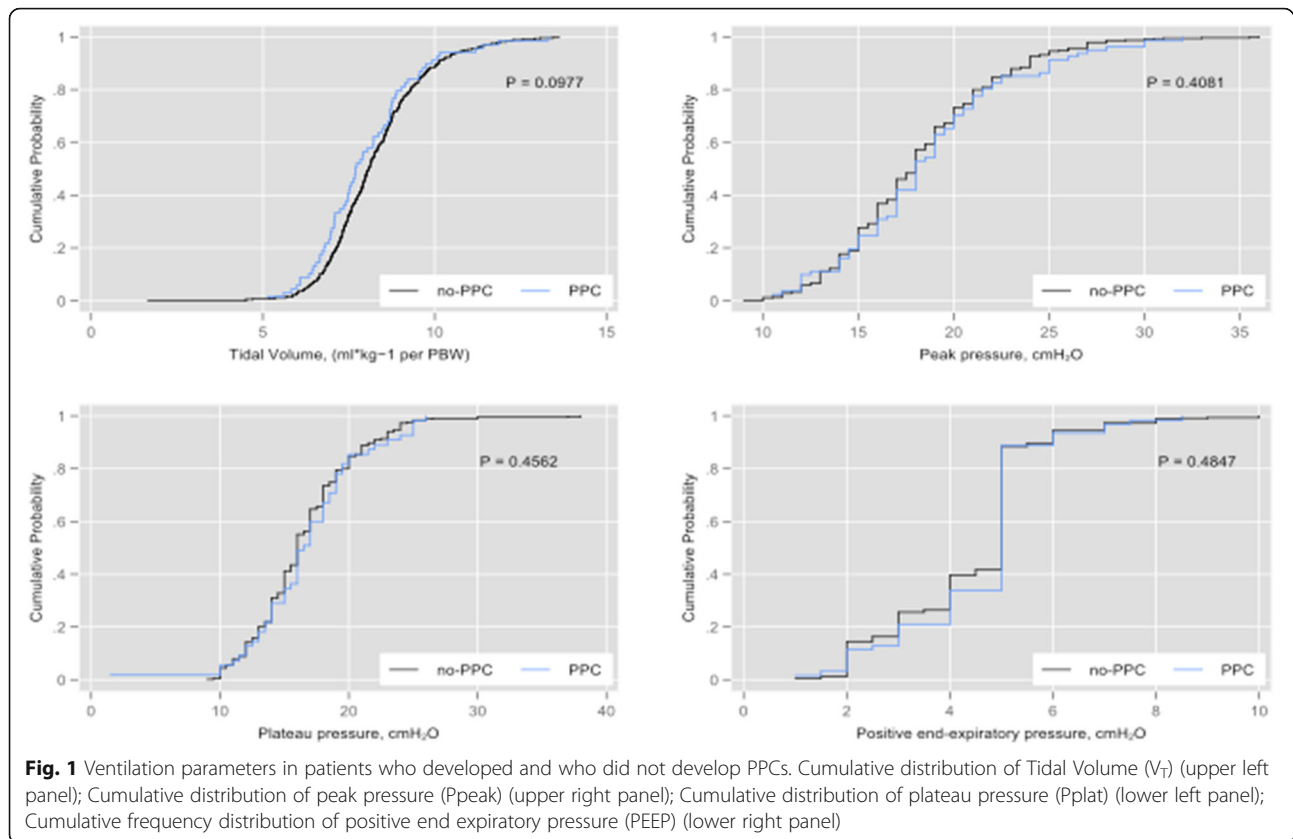
#### Discussion

Our results show that: 1) Neurosurgical patients are ventilated with low V<sub>T</sub> and low PEEP levels, while recruitment manoeuvres are seldom applied. No clinically significant differences exist between the intraoperative ventilator settings and the incidence of PPCs between the subgroups analysed, and in patients undergoing brain and spine surgery. ETCO<sub>2</sub> levels are generally medium-low, especially in the brain surgery group; 2) PPCs are common, with similar incidence in the spine- and the brain surgical groups; 3) Intraoperative complications occur in a large number of patients (44% of the total population); of these, hypotension and the need for vasopressors are common; 4) Increasing age (for the brain group) and long surgical procedures are independently associated with development of PPCs.

**Table 2** Intra-Operative Characteristics of the Patients According to Subgroups

|   | All Patients      | Brain             | Spine             | <i>p</i> value | All patients      | PPC               | No PPC            | <i>p</i> value | All patients      | ARISCAT < 26      | ARISCAT ≥ 26      | <i>p</i> value |
|---|-------------------|-------------------|-------------------|----------------|-------------------|-------------------|-------------------|----------------|-------------------|-------------------|-------------------|----------------|
| <b>n (%)</b>  | 784 (100.0)       | 376 (48.0)        | 408 (52.0)        |                | 777 (100.0)       | 81 (10.4)         | 696 (89.6)        |                | 748 (100.0)       | 548 (73.3)        | 200 (26.7)        |                |
| <b>Ventilation and vital signs</b>                      |                   |                   |                   |                |                   |                   |                   |                |                   |                   |                   |                |
| Ventilatory mode, n (%)                                 |                   |                   |                   | 0.000          |                   |                   |                   | 0.376          |                   |                   |                   | 0.452          |
| Volume controlled                                       | 494 (63.8)        | 259 (70.2)        | 235 (58.0)        |                | 488 (63.5)        | 50 (64.1)         | 438 (63.5)        |                | 467 (63.2)        | 341 (62.9)        | 126 (64.0)        |                |
| Pressure controlled                                     | 149 (19.3)        | 42 (11.4)         | 107 (26.4)        |                | 149 (19.4)        | 20 (25.6)         | 129 (18.7)        |                | 146 (19.8)        | 112 (20.7)        | 34 (17.3)         |                |
| Pressure support  | 3 (0.4)           | 2 (0.5)           | 1 (0.2)           |                | 3 (0.4)           | 0 (0.0)           | 3 (0.4)           |                | 3 (0.4)           | 1 (0.2)           | 2 (1.0)           |                |
| Spontaneous   | 64 (8.3)          | 21 (5.7)          | 43 (10.6)         |                | 64 (8.3)          | 4 (5.1)           | 60 (8.7)          |                | 60 (8.1)          | 42 (7.7)          | 18 (9.1)          |                |
| Other   | 64 (8.3)          | 45 (12.2)         | 19 (4.7)          |                | 64 (8.3)          | 4 (5.1)           | 60 (8.7)          |                | 63 (8.5)          | 46 (8.5)          | 17 (8.6)          |                |
| V <sub>T</sub> , ml, median (IQR)                       | 510 (475; 575)    | 511 (475; 584)    | 506 (471; 562)    | 0.183          | 510 (475; 575)    | 500 (458; 560)    | 513 (475; 575)    | 0.096          | 510 (475; 572)    | 506 (475; 565)    | 525 (480; 590)    | 0.142          |
| V <sub>T</sub> , (ml/kg PBW), median (IQR)              | 8.0 (7.3; 9.0)    | 8.2 (7.3; 9.1)    | 8.0 (7.2; 8.9)    | 0.150          | 8.0 (7.3; 9.0)    | 7.7 (7.0; 8.8)    | 8.1 (7.3; 9.0)    | 0.060          | 8.0 (7.3; 9.0)    | 8.0 (7.3; 9.0)    | 8.0 (7.3; 9.1)    | 0.420          |
| P <sub>Peak</sub> , cmH <sub>2</sub> O, median (IQR)    | 18 (15; 21)       | 18 (15; 21)       | 18 (16; 21)       | 0.225          | 18 (15; 21)       | 18 (16; 21)       | 18 (15; 21)       | 0.183          | 18 (15; 21)       | 18 (15; 21)       | 18 (16; 21)       | 0.061          |
| P <sub>Plateau</sub> , cmH <sub>2</sub> O, median (IQR) | 16 (14; 19)       | 16 (14; 19)       | 16 (14; 18)       | 0.201          | 16 (14; 19)       | 17 (14; 19)       | 16 (14; 19)       | 0.150          | 16 (14; 19)       | 16 (14; 18)       | 17 (15; 19)       | 0.012          |
| PEEP, cmH <sub>2</sub> O, median (IQR)                  | 5.0 (3.0; 5.0)    | 5.0 (4.0; 5.0)    | 5.0 (3.0; 5.0)    | 0.669          | 5.0 (3.0; 5.0)    | 5.0 (4.0; 5.0)    | 5.0 (3.0; 5.0)    | 0.225          | 5.0 (3.0; 5.0)    | 5.0 (3.0; 5.0)    | 5.0 (3.3; 5.0)    | 0.156          |
| DP, cmH <sub>2</sub> O, median (IQR)                    | 12 (11; 15)       | 13 (11; 15)       | 12 (10; 16)       | 0.585          | 12 (11; 15)       | 13 (11; 15)       | 12 (11; 15)       | 0.201          | 12 (11; 15)       | 12 (11; 15)       | 14 (11; 17)       | 0.009          |
| RR, bpm, mean (SD)                                      | 12.0 (1.5)        | 12.1 (1.5)        | 12.0 (1.4)        | 0.237          | 12.0 (1.5)        | 12.1 (1.7)        | 12.0 (1.4)        | 0.669          | 12.0 (1.4)        | 12.1 (1.3)        | 11.9 (1.7)        | 0.188          |
| FiO <sub>2</sub> , %, median (IQR)                      | 50 (43; 65)       | 50 (40; 60)       | 50 (44; 68)       | 0.021          | 50 (43; 64)       | 50 (46; 65)       | 50 (42; 63)       | 0.585          | 50 (43; 65)       | 50 (43; 70)       | 50 (45; 60)       | 0.143          |
| SpO <sub>2</sub> , %, median (IQR)                      | 99 (98; 100)      | 99 (99; 100)      | 99 (98; 100)      | 0.169          | 99 (98; 100)      | 99 (98; 100)      | 99 (98; 100)      | 0.237          | 99 (98; 100)      | 99 (99; 100)      | 99 (98; 100)      | 0.069          |
| ETCO <sub>2</sub> , mmHg, mean (SD)                     | 33 (4)            | 32 (4)            | 33 (5)            | 0.001          | 33 (4)            | 33 (4)            | 33 (5)            | 0.554          | 33 (4)            | 33 (4)            | 33 (5)            | 0.549          |
| MP, J/min, median (IQR)                                 | 6.6 (4.9; 9.2)    | 6.9 (5.0; 10.3)   | 6.2 (4.8; 7.8)    | 0.058          | 6.6 (4.9; 9.2)    | 6.1 (4.8; 10.5)   | 6.6 (4.9; 9.1)    | 0.856          | 6.6 (4.9; 9.3)    | 6.6 (4.9; 8.6)    | 6.7 (5.1; 10.8)   | 0.230          |
| MAP, mmHg, mean (SD)                                    | 80 (12)           | 79 (12)           | 80 (13)           | 0.083          | 79 (12)           | 78 (11)           | 80 (13)           | 0.021          | 79 (12)           | 79 (12)           | 80 (13)           | 0.212          |
| Heart rate, bpm, mean (SD)                              | 71 (12)           | 69 (12)           | 72 (12)           | 0.004          | 71 (12)           | 68 (12)           | 71 (12)           | 0.169          | 70 (12)           | 71 (12)           | 70 (13)           | 0.355          |
| RM, n (%)   | 54 (6.9)          | 29 (7.8)          | 25 (6.1)          | 0.365          | 54 (6.9)          | 29 (7.8)          | 25 (6.1)          | 0.365          | 51 (6.8)          | 36 (6.6)          | 15 (7.5)          | 0.664          |
| <b>Anesthesia characteristics</b>                       |                   |                   |                   |                |                   |                   |                   |                |                   |                   |                   |                |
| Opioids, n (%)  |                   |                   |                   |                |                   |                   |                   |                |                   |                   |                   |                |
| No  | 2 (0.3)           | 0 (0.0)           | 2 (0.5)           |                | 2 (0.3)           | 0 (0.0)           | 2 (0.5)           |                | 90 (12.0)         | 65 (11.9)         | 25 (12.5)         |                |
| Yes   | 782 (99.7)        | 376 (100.0)       | 406 (99.5)        | 0.174          | 782 (99.7)        | 376 (100.0)       | 406 (99.5)        | 0.629          | 746 (99.7)        | 546 (99.6)        | 200 (100.0)       | 0.392          |
| Opioids type, n (%)                                     |                   |                   |                   | 0.000          |                   |                   |                   | 0.055          |                   |                   |                   | 0.836          |
| Short acting  | 221 (28.2)        | 137 (36.4)        | 84 (20.6)         |                | 220 (28.3)        | 20 (24.7)         | 200 (28.7)        |                | 2 (0.3)           | 2 (0.4)           | 0 (0.0)           |                |
| Long acting   | 466 (59.4)        | 189 (50.3)        | 277 (67.9)        |                | 460 (59.2)        | 43 (53.1)         | 417 (59.9)        |                | 212 (28.3)        | 154 (28.1)        | 58 (29.0)         |                |
| Total fluids, ml, median (IQR)                          | 1500 (1000; 2000) | 1500 (1000; 2000) | 1500 (1000; 2000) | 0.022          | 1500 (1000; 2000) | 1800 (1200; 2125) | 1500 (1000; 2000) | 0.001          | 1500 (1000; 2000) | 1300 (1000; 2000) | 2000 (1100; 3000) | 0.000          |
| Cristalloids  | 1175 (1000; 2000) | 1200 (1000; 2000) | 1000 (1000; 1500) | 0.012          | 1200 (1000; 2000) | 1500 (1000; 2050) | 1000 (1000; 2000) | 0.000          | 1200 (1000; 2000) | 1000 (1000; 1500) | 1725 (1000; 2475) | 0.000          |
| Colloids  | 0.0 (0.0; 500.0)  | 0.0 (0.0; 500.0)  | 0.0 (0.0; 500.0)  | 0.649          | 0.0 (0.0; 500.0)  | 0.0 (0.0; 500.0)  | 0.0 (0.0; 500.0)  | 0.719          | 0.0 (0.0; 500.0)  | 0.0 (0.0; 125.0)  | 0.0 (0.0; 500.0)  | 0.649          |

*P*-value refers to the between-groups difference with Fisher-Freeman-Halton Exact test, Mann Whitney u-test, or Kruskal Wallis test, as appropriate. *N* Number; *IQR* Interquartile range, *SD* Standard deviation, *PPC* Postoperative pulmonary complications, *PBW* Predicted body weight, *V<sub>T</sub>* Tidal volume, *P<sub>Peak</sub>* Peak pressure, *P<sub>Plateau</sub>* Plateau pressure, *PEEP* Positive end-expiratory pressure, *DP* Driving pressure, *RR* Respiratory rate, *FiO<sub>2</sub>* Fraction of inspired oxygen, *SpO<sub>2</sub>* Blood oxygen saturation, *ETCO<sub>2</sub>* End-tidal carbon dioxide, *MP* Mechanical power, *MAP* Mean arterial pressure, *HR* Heart rate, *RM* Recruitment maneuvers



To our knowledge, this is the first prospective observational study in neurosurgical patients specifically focusing on the prevalence of PPCs and the effects of intraoperative mechanical ventilation settings on PPCs development. Our study is a sub-analysis of the LAS VEGAS study [10], a large international observational study describing the ventilator settings and PPCs occurrence in the perioperative period across different countries, and can therefore be considered representative for the current clinical practice in this population.

#### Ventilator strategies in patients undergoing neurosurgical interventions

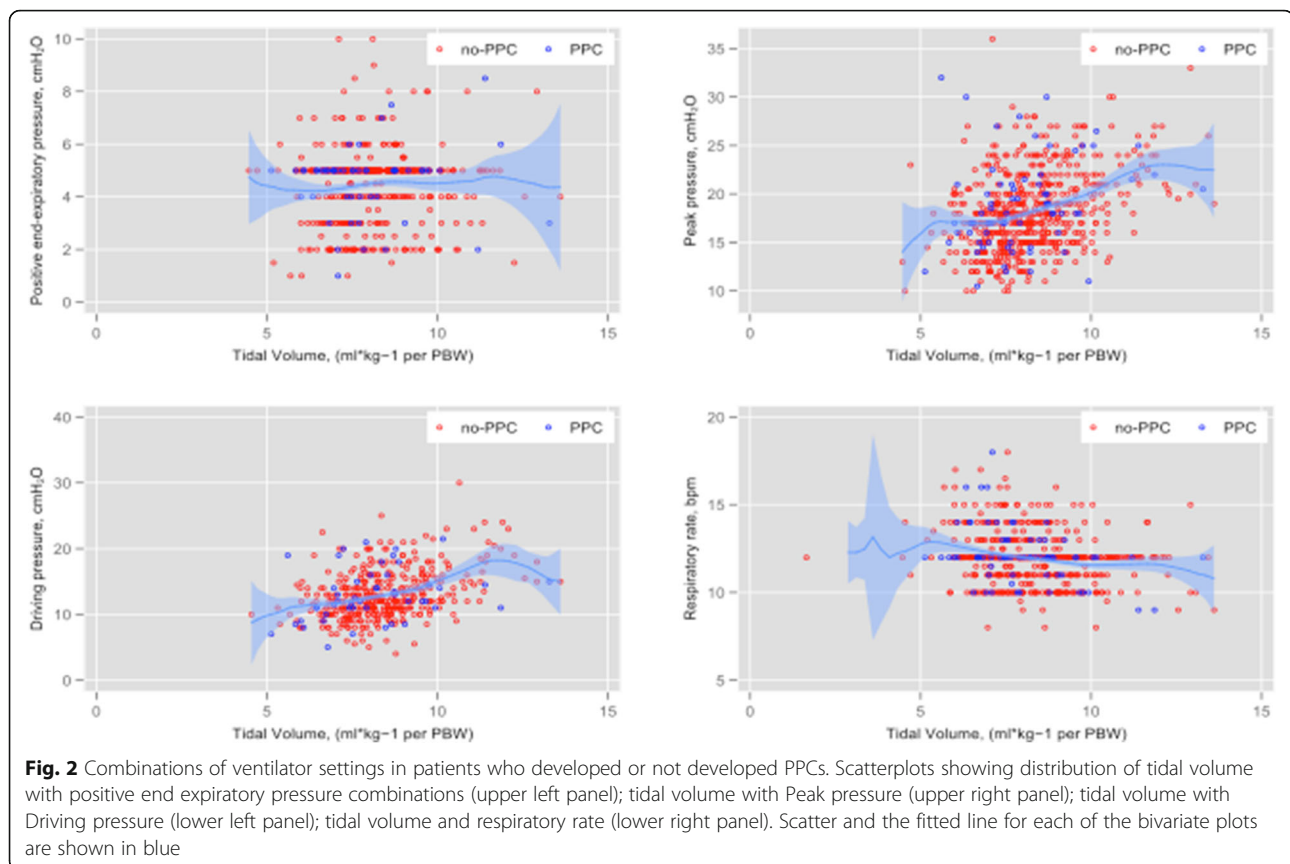
Currently applied lung-protective ventilation strategies have shown to reduce PPCs [13, 14]. In patients undergoing spine surgery, the prone position has various effects on pulmonary function, including a decreased dynamic lung compliance and increased peak inspiratory pressure [13]; however, no large observational studies or randomized controlled trials are available regarding protective ventilator settings and their effect on PPCs in the prone position in non-ARDS patients.

In brain injured patients, lung-protective ventilation could be deleterious [7]; in particular, possible high intra-thoracic pressures when using high PEEP levels and permissive hypercapnia can have detrimental effects

on cerebral perfusion pressure (CPP) and intracranial pressure (ICP). Therefore, brain injury patients are traditionally ventilated with tidal volumes approximating 9 ml/kg of PBW [5]. However, recent studies suggest that high  $V_T$  is a risk factor for acute lung injury even in patients with neurological disorders [4]. Indeed, our results suggest that the use of low  $V_T$  is increasingly applied also in neurosurgical patients. Similarly, the application of PEEP in brain injured patients has been traditionally considered detrimental for ICP, by reducing venous outflow [15]. However, recent evidence demonstrates that PEEP application might not compromise ICP, provided that arterial blood pressure is preserved [16, 17].

In our cohort, neurosurgical patients were ventilated with low PEEP levels and no differences in PEEP levels were detected between the brain and spine groups. No data is available on the effects of RM in neurosurgical patients and their role within the intraoperative protective ventilation bundle remains unclear. In brain injured patients, RMs can have a dangerous effect on ICP by impairment of jugular blood outflow, and increase of intra-thoracic pressure with impediment of cerebral venous return to the right atrium [8]. Although pressure-control recruitment manoeuvres improve oxygenation without impairing ICP or CPP, there is still concern regarding their application in neurosurgical patients, and therefore





are rarely performed [8]. Indeed, our results show that recruitment manoeuvres are seldom applied in neurosurgical patients.

To date, no clinical studies comparing pressure-controlled ventilation (PCV) and VCV in brain injured patients are published. In obese [18], ARDS [19], and thoracic patients [20], research suggests no difference in outcome between the modes of ventilation (PCV and VCV). In a trial [21] including patients undergoing spinal surgery, PCV decreased intraoperative surgical bleeding compared with the VCV group ( $p < 0.001$ ), possibly by lowering peak inspiratory pressures. A recent randomized controlled trial during lumbar spine surgery demonstrated that hemodynamic variables and arterial blood gas results did not differ significantly between the VCV and PCV with volume guaranteed (PCV-VG) mode groups [13]. Also, a recent large observational study suggested that PCV is associated with increase of PPC compared to VCV [22]. This association is not confirmed by our results. In our cohort, patients undergoing spinal surgery were more frequently ventilated with VCV than the brain injured group. However, despite the pathophysiological differences of prone vs supine ventilation, we did not find any other differences in the ventilator settings between the two groups.

In our cohort,  $\text{ETCO}_2$  levels were generally medium-low, with significantly lower values in the brain surgery group compared to the spinal surgery group. This result suggests that patients undergoing brain surgery are more likely to be hyperventilated. This is most likely out of concern for potential increased intracranial pressure.

Although the subgroup with  $\text{ARISCAT} \geq 26$  shows higher values of driving pressure and plateau pressure (plateau pressure (17 vs 16  $\text{cmH}_2\text{O}$ ,  $p = 0.012$ ), and higher driving pressure (14 vs 12  $\text{cmH}_2\text{O}$ ;  $p = 0.009$ ), these values still remain within the recommended ranges for protective ventilation [22, 23]. In general, in the whole population, a low total energy was applied to the respiratory system [23] (median mechanical power (6.2 J/min)), with values which remain far from the threshold of 12 J/min suggested as increased risk of lung injury [23].

#### Post-operative pulmonary complications

Clinical studies suggest that the application of protective ventilation can reduce PPCs [24, 25], with high  $V_T$  identified as an independent predictor of PPCs development [26, 27]. Trials in obese [27] and non-obese [28] patients undergoing abdominal surgery demonstrated that the intraoperative application of high level of PEEP and RMs

**Table 3** Outcomes According to Subgroups

|                                  | All Patients | Brain      | Spine      | <i>p</i> value | All patients | PPC        | No PPC     | <i>p</i> value | All patients | ARISCAT < 26 | ARISCAT ≥ 26 | <i>p</i> value |
|----------------------------------|--------------|------------|------------|----------------|--------------|------------|------------|----------------|--------------|--------------|--------------|----------------|
| <b>n (%)</b>                     | 784 (100.0)  | 376 (48.0) | 408 (52.0) |                | 777 (100.0)  | 81 (10.4)  | 696 (89.6) |                | 748 (100.0)  | 548 (73.3)   | 200 (26.7)   |                |
| <b>PPCs, n (%)</b>               |              |            |            |                |              |            |            |                |              |              |              |                |
| PPCs                             | 81 (10.4)    | 46 (12.4)  | 35 (8.6)   | 0.085          | 777 (100.0)  | 81 (10.4)  | 696 (89.6) | 0.000          | 80 (10.8)    | 43 (7.9)     | 37 (18.6)    | 0.000          |
| Need of oxygen                   | 69 (8.9)     | 38 (10.2)  | 31 (7.6)   | 0.202          | 81 (10.4)    | 81 (100.0) | 0 (0.0)    | 0.000          | 68 (9.2)     | 39 (7.2)     | 29 (14.6)    | 0.002          |
| Respiratory failure              | 14 (1.8)     | 8 (2.2)    | 6 (1.5)    | 0.478          | 69 (8.9)     | 69 (85.2)  | 0 (0.0)    | 0.000          | 14 (1.9)     | 6 (1.1)      | 8 (4.0)      | 0.010          |
| NIV                              | 9 (1.2)      | 4 (1.2)    | 5 (1.2)    | 0.963          | 14 (1.8)     | 14 (17.3)  | 0 (0.0)    | 0.000          | 9 (1.3)      | 7 (1.3)      | 2 (1.1)      | 0.801          |
| ARDS                             | 1 (0.1)      | 1 (0.3)    | 0 (0.0)    | 0.295          | 9 (1.2)      | 5 (6.3)    | 4 (0.6)    | 0.003          | 1 (0.1)      | 0 (0.0)      | 1 (0.5)      | 0.098          |
| Pneumothorax                     | 1 (0.1)      | 1 (0.3)    | 0 (0.0)    | 0.295          | 1 (0.1)      | 1 (1.2)    | 0 (0.0)    | 0.003          | 1 (0.1)      | 0 (0.0)      | 1 (0.5)      | 0.098          |
| <b>Secondary outcomes, n (%)</b> |              |            |            |                |              |            |            |                |              |              |              |                |
| Severe PPCs                      | 19 (2.4)     | 13 (3.5)   | 6 (1.5)    | 0.068          | 19 (2.4)     | 19 (23.5)  | 0 (0.0)    | 0.000          | 19 (2.6)     | 6 (1.1)      | 13 (6.5)     | 0.000          |
| Intra-operative complications    | 344 (43.9)   | 154 (41.1) | 190 (46.6) | 0.121          | 342 (44.1)   | 46 (56.8)  | 296 (42.6) | 0.015          | 336 (44.9)   | 237 (43.2)   | 99 (49.5)    | 0.128          |
| Desaturation                     | 38 (4.9)     | 23 (6.1)   | 15 (3.7)   | 0.110          | 37 (4.8)     | 11 (13.6)  | 26 (3.7)   | 0.000          | 36 (4.8)     | 21 (3.8)     | 15 (7.5)     | 0.038          |
| Unplanned RMs                    | 25 (3.2)     | 15 (4.0)   | 10 (2.5)   | 0.220          | 24 (3.1)     | 5 (6.2)    | 19 (2.7)   | 0.091          | 22 (2.9)     | 12 (2.2)     | 10 (5.0)     | 0.043          |
| Pressure reduction               | 25 (3.2)     | 11 (2.9)   | 14 (3.4)   | 0.692          | 25 (3.2)     | 3 (3.7)    | 22 (3.2)   | 0.795          | 22 (2.9)     | 17 (3.1)     | 5 (2.5)      | 0.666          |
| Flow limitation                  | 5 (0.6)      | 3 (0.8)    | 2 (0.5)    | 0.590          | 4 (0.5)      | 1 (1.3)    | 3 (0.4)    | 0.322          | 4 (0.5)      | 2 (0.4)      | 2 (1.0)      | 0.289          |
| Hypotension                      | 275 (35.1)   | 117 (31.2) | 158 (38.7) | 0.028          | 274 (35.3)   | 34 (42.0)  | 240 (34.5) | 0.185          | 270 (36.1)   | 197 (35.9)   | 73 (36.5)    | 0.890          |
| Vasopressors                     | 245 (31.3)   | 104 (27.7) | 141 (34.6) | 0.040          | 244 (31.4)   | 37 (45.7)  | 207 (29.8) | 0.004          | 242 (32.4)   | 168 (30.7)   | 74 (37.0)    | 0.101          |
| New arrhythmias                  | 9 (1.1)      | 6 (1.6)    | 3 (0.7)    | 0.257          | 9 (1.2)      | 0 (0.0)    | 9 (1.3)    | 0.303          | 9 (1.2)      | 5 (0.9)      | 4 (2.0)      | 0.227          |
| Hospital LOS, days, median (IQR) | 2 (1; 5)     | 2 (1; 5)   | 2 (1; 5)   | 0.993          | 2 (1; 5)     | 3 (1; 5)   | 2 (1; 5)   | 0.447          | 2 (1; 5)     | 2 (1; 5)     | 3 (1; 5)     | 0.033          |
| Hospital mortality               | 5 (0.7)      | 4 (1.2)    | 1 (0.3)    | 0.145          | 5 (0.7)      | 1 (1.3)    | 4 (0.6)    | 0.500          | 5 (0.7)      | 1 (0.2)      | 4 (2.2)      | 0.006          |

*n* Number, *IQR* Interquartile range, *PPCs* Postoperative pulmonary complications, *NIV* Non-invasive ventilation, *ARDS* Acute respiratory distress syndrome, *LOS* Length of hospital stay, *RMs* Recruitment maneuvers, *ARISCAT* Assess respiratory risk in surgical patients in Catalonia

did not reduce PPCs, when compared with lower PEEP level without RMs.

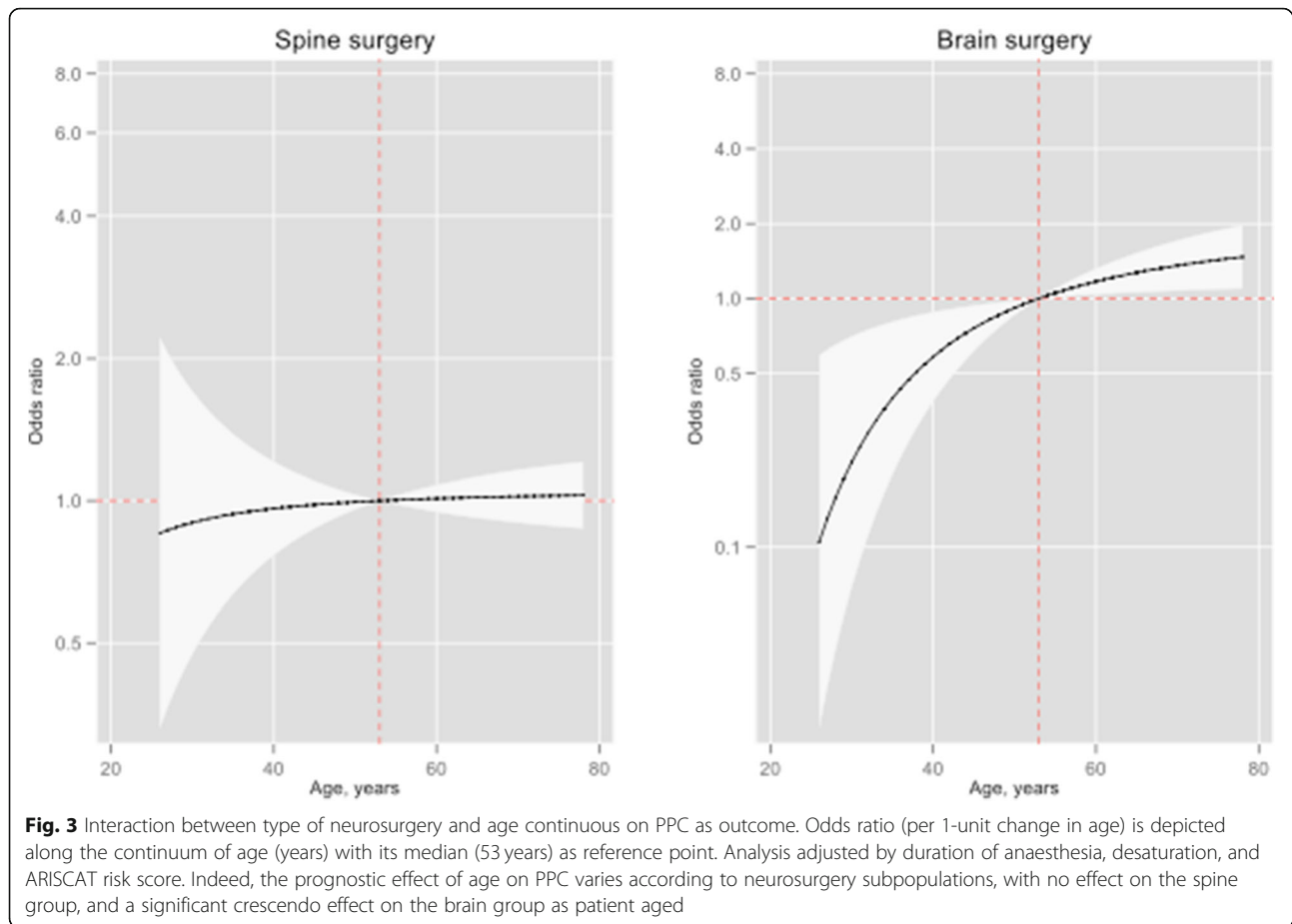
In our neurosurgical population, 10.3% of patients developed PPCs, similar to the results from the whole population of the LAS VEGAS [8]. No clinically significant differences exist in the incidence of PPCs when comparing the different intraoperative ventilator settings in the subgroups analysed.

Patients who developed PPCs had worse preoperative conditions (age, ARISCAT score, ASA status), longer duration of anaesthesia (thus suggesting a more complicated surgical procedure), intraoperative complications (in particular hypotension) and the administration of higher volumes of fluid. This latter point is of extreme importance as cerebral and spinal perfusion pressures are generally maintained by the administration of vasopressors and a large

amount of fluids; however, a positive fluid balance can increase the risk for pulmonary damage and complications [28]. Finally, increasing age in the brain surgical group was associated with PPCs occurrence, thus making preoperative assessment extremely important in the management of this group of patients in order to optimize hospital resources and empathetically begin discussions with patients and their carers.

#### **Intraoperative complications and outcomes**

In our cohort, intraoperative complications occurred in a large number of patients (44% of our total population). Moreover, we found an increased prevalence of intraoperative hemodynamic deterioration as compared to respiratory impairment in the intraoperative settings. According to our results, patients undergoing



spine surgery have commonly episodes of intraoperative hypotension requiring the use of vasoactive drugs, probably related to the effects of prone position on cardiac function, including a decreased cardiac index [13].

Our results suggest that in neurosurgical patients, the most common intraoperative complications are related to hemodynamic rather than respiratory function. The fact that hypotension and hemodynamic impairment are common might suggest that limited levels of PEEP could be beneficial in this type of patients by having less negative impact on hemodynamic. These results are in accordance with recently published literature [24, 29], suggesting that the use of high PEEP can negatively impact the hemodynamic system, thus challenging the traditional concept of “open lung approach”, and avoiding repeated alveolar collapse and expansion and keeping the lung partially at rest [30].

#### Limitations

Several limitations need to be mentioned. First, the manuscript derives from a secondary analysis from the LAS VEGAS study. Thus, the results represent

an observation of associations and do not allow to draw causality conclusions, considering that there exist unaccounted confounding factors.

Second, this is an unplanned secondary analysis from the main study, and even though we built a meticulous statistical model, there could still be confounding factors affecting our results.

Third, as the design of the original study focused on intraoperative settings and variables in the general population, limited information was available regarding specific perioperative data in neurosurgical patients, in particular on the use neuro-monitoring and type of brain and spine surgery.

#### Conclusions

The main findings of this study are that MV settings in neurosurgical patients are characterized by low  $V_T$  and low PEEP with seldom use of RMs. PPCs are frequent in this population and not associated with intraoperative ventilator setting. Further studies are warranted to assess the effect of ventilation strategies on the outcome of this cohort of patients.

## Supplementary information

Supplementary information accompanies this paper at <https://doi.org/10.1186/s12871-020-00988-x>.

### Additional file 1.

#### Abbreviations

V<sub>T</sub>: Tidal volume; Pplat: Plateau pressure; PEEP: Positive end-expiratory pressure; RM: Recruitment manoeuvres; PBW: Predicted body weight; PPCs: Post-operative pulmonary complications; ESM: Electronic supplemental material; Ppeak: Peak pressure; RR: Respiratory rate; FiO<sub>2</sub>: Fraction of inspired oxygen; ETCO<sub>2</sub>: End-tidal carbon dioxide; SpO<sub>2</sub>: Peripheral saturation of oxygen; MP: Mechanical power; ASA: American Society of Anaesthesiologists; ARISCAT: Assess Respiratory Risk in Surgical Patients in Catalonia; VCV: Volume-controlled ventilation; IQR: Interquartile range; SD: Standard deviation; PCV: Pressure-controlled ventilation; LOS: Length of stay; CPP: Cerebral perfusion pressure; ICP: Intracranial pressure

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#### Contributors

##### Las Vegas Investigators:

Austria

**LKH Graz, Graz:** Wolfgang Kroell, Helfried Metzler, Gerd Struber, Thomas Wegscheider

**AKH Linz, Linz:** Hans Gombotz

**Medical University Vienna:** Michael Hiesmayr, Werner Schmid, Bernhard Urbanek

Belgium

**UCL - Cliniques Universitaires Saint Luc Brussels:** David Kahn, Mona Momeni, Audrey Pospiech, Fernande Lois, Patrice Forget, Irina Grosu

**University Hospital Brussels (UZ Brussel):** Jan Poelaert, Veerle van Mossevelde, Marie-Claire van Malderen

**Het Ziekenhuis Oost Limburg (ZOL), Genk:** Dimitri Dylst, Jeroen van Melkebeek, Maud Beran

**Ghent University Hospital, Gent:** Stefan de Hert, Luc De Baerdemaeker, Bjorn Heyse, Jurgan Van Limmen, Piet Wyffels, Tom Jacobs, Nathalie Roels, Ann De Bruyne

**Maria Middelaers, Gent:** Stijn van de Velde

**European Society of Anaesthesiology, Brussels:** Brigitte Leva, Sandrine Damster, Benoit Plichon

Bosnia and Herzegovina

**General Hospital "prim Dr Abdulah Nakas" Sarajevo:** Marina Juros-Zovko, Dejana Djonović- Omanović

Croatia

**General Hospital Cakovec, Cakovec:** Selma Pernar

**General Hospital Karlovac, Karlovac:** Josip Zunic, Petar Miskovic, Antonio Zilic

**University Clinical Hospital Osijek, Osijek:** Slavica Kvolik, Dubravka Ivic, Darija Azenic-Venzera, Sonja Skiljic, Hrvoje Vinkovic, Ivana Oputric

**University Hospital Rijeka, Rijeka:** Kazimir Juricic, Vedran Frkovic

**General Hospital Dr J Benčević, SlavonSKI Brod:** Jasminka Kopic, Ivan Mirkovic  
**University Hospital Center Split, Split:** Nenad Karanovic, Mladen Carev, Natasa Dropulic

**University Hospital Merkur, Zagreb:** Jadranka Pavicic Saric, Gorjana Erceg, Matea Bogdanovic Dvorscak

**University Hospital Sveti Duh, Zagreb:** Branka Mazul-Sunko, Anna Marija Pavicic, Tanja Goranovic

**University Hospital, Medical school, "Sestre milosrdnice" (Sister of Charity), Zagreb:** Branka Maldini, Tomislav Radocaj, Zeljka Gavranovic, Inga Mladic-Batinica, Mirna Sehovic

Czech Republic

**University Hospital Brno, Brno:** Petr Stourac, Hana Harazim, Olga Smekalova, Martina Kosinova, Tomas Kolacek, Kamil Hudacek, Michal Drab

**University Hospital Hradec Kralove, Hradec Kralove:** Jan Brujevic, Katerina Vitkova, Katerina Jirmanova

**University Hospital Ostrava, Ostrava:** Ivana Volfova, Paula Dzurakovska, Katarina Liskova

**Nemocnice Znojmo, Znojmo:** Radovan Dudas, Radek Filipisky

Egypt

**El Sahel Teaching hospital, Cairo:** Samir el Kafrawy

**Kasr Al-Ainy Medical School, Cairo University:** Hisham Hosny Abdelwahab, Tarek Metwally, Ahmed Abdel-Razek

**Beni Sueif University Hospital, Giza:** Ahmed Mostafa El-Shaarawy, Wael Fathy Hasan, Ahmed Gouda Ahmed

**Fayoum University Hospital, Giza:** Hany Yassin, Mohamed Magdy, Mahdy Abdelhady

**Suis medical Insurance Hospital, Suis:** Mohamed Mahran

Estonia

**North Estonia Medical Center, Tallinn:** Eiko Herodes, Peeter Kivik, Juri Oganjan, Annika Aun

**Tartu University Hospital, Tartu:** Alar Sormus, Kaili Sarapuu, Merilin Mall, Juri Karjagin

France

**University Hospital of Clermont-Ferrand, Clermont-Ferrand:** Emmanuel Futier, Antoine Petit, Adeline Gerard

**Institut Hospitalier Franco-Britannique, Levallois-Perret:** Emmanuel Marret, Marc Solier

**Saint Eloi University Hospital, Montpellier:** Samir Jaber, Albert Prades

Germany

**Fachkrankenhaus Coswig, Coswig:** Jens Krassler, Simone Merzky

**University Hospital Carl Gustav Carus, Dresden:** Marcel Gama de Abreu, Christopher Uhlig,

Thomas Kiss, Anette Bundy, Thomas Bluth, Andreas Gueldner, Peter Spieth, Martin Scharffenberg, Denny Tran Thiem, Thea Koch

**Duesseldorf University Hospital, Heinrich-Heine University:** Tanja Treschan, Maximilian Schaefer,

Bea Bastin, Johann Geib, Martin Weiss, Peter Kienbaum, Benedikt Pannen

**Diakoniekrankenhaus Friederikenstift, Hannover:** Andre Gottschalk, Mirja Konrad, Diana Westerheide, Ben Schwerdtfeger

**University of Leipzig, Leipzig:** Hermann Wrigge, Philipp Simon, Andreas Reske, Christian Nestler

Greece

**"Alexandra" general hospital of Athens, Athens:** Dimitrios Valsamidis, Konstantinos Stroumpoulis

**General air force hospital, Athens:** Georgios Antholopoulos, Antonis Andreou, Dimitris Karapanos

**Areataieion University Hospital, Athens:** Kassiani Theodoraki, Georgios Gkiokas, Marios-Konstantinos Tasoulis

**Attikon University Hospital, Athens:** Tatiana Sidiropoulou, Foteini Zafeiropoulou, Panagiota Florou, Aggeliki Pandazi

**Ahepa University Hospital Thessaloniki, Thessaloniki:** Georgia Tsaousi, Christos Nouris, Chryssa Pourzitaki,

Israel

**The Lady Davis Carmel Medical Center, Haifa:** Dmitri Bystritski, Reuven Pizov, Arieh Eden

Italy

**Ospedale San. Paolo Bari, Bari:** Caterina Valeria Pesce, Annamaria Campanile, Antonella Marrella

**University of Bari "Aldo Moro", Bari:** Salvatore Grasso, Michele De Michele

**Institute for Cancer Research and treatment, Candiolo, Turin:** Francesco Bona, Gianmarco Giacoletto, Elena Sardo

**Azienda Ospedaliera per l'emergenza Cannizzaro, Catania:** Luigi Giancarlo, Vicari Sottosanti

**Ospedale Melegnano, Cernusco, Milano:** Maurizio Solca

**Azienda Ospedaliera - Universitaria Sant'Anna, Ferrara:** Carlo Alberto Volta, Savino Spadaro, Marco Verri, Riccardo Ragazzi, Roberto Zoppellari

**Ospedali Riuniti Di Foggia - University of Foggia, Foggia:** Gilda Cinnella, Pasquale Raimondo, Daniela La Bella, Lucia Mirabella, Davide D'antini

**IRCCS AOU San Martino IST Hospital, University of Genoa, Genoa:** Paolo Pelosi, Alexandre Molin, Iole Brunetti, Angelo Gratarola, Giulia Pellerano, Rosanna Sileo, Stefano Pezzatto, Luca Montagnani

**IRCCS San Raffaele Scientific Institute, Milano:** Laura Pasin, Giovanni Landoni, Alberto Zangrillo, Luigi Beretta, Ambra Licia Di Parma, Valentina Tarzia, Roberto Dossi, Marta Eugenia Sassone

**Istituto europeo di oncologia - ieo, Milano:** Daniele Sances, Stefano Tredici, Gianluca Spano, Gianluca Castellani, Luigi Delunas, Sopio Peradze, Marco Venturino

**Ospedale Niguarda Ca'Granda Milano, Milano:** Ines Arpino, Sara Sher

- Ospedale San Paolo - University of Milano, Milano:** Concezione Tommasino, Francesca Rapido, Paola Morelli
- University of Naples "Federico II" Naples:** Maria Vargas, Giuseppe Servillo
- Policlinico "P. Giaccone", Palermo:** Andrea Cortegiani, Santi Maurizio Raineri, Francesca Montalto, Vincenzo Russotto, Antonino Giarratano
- Azienda Ospedaliero-Universitaria, Parma:** Marco Baciarello, Michela Generali, Giorgia Cerati
- Santa Maria degli Angeli, Pordenone:** Yigal Leykin
- Ospedale Misericordia e Dolce - Usl4 Prato, Prato:** Filippo Bressan, Vittoria Bartolini, Lucia Zamidei
- University hospital of Sassari, Sassari:** Luca Brazzi, Corrado Liperi, Gabriele Sales, Laura Pistidda
- Insubria University, Varese:** Paolo Severgnini, Elisa Brugnioni, Giuseppe Musella, Alessandro Bacuzzi
- Republic of Kosovo
- Distric hospital Gjakova, Gjakove:** Dalip Muhardri
- University Clinical Center of Kosovo, Prishtina:** Agreta Gecaj-Gashi, Fatos Sada
- Regional Hospital" Prim.Dr. Daut Mustafa", Prizren:** Adem Bytyqi
- Lithuania
- Medical University Hospital, Hospital of Lithuanian University of Health Sciences, Kaunas:** Aurika Karbonskiene, Ruta Aukstakalniene, Zivile Teberaite, Erika Salciute
- Vilnius University Hospital - Institute of Oncology, Vilnius:** Renatas Tikuisis, Povilas Miliauskas
- Vilnius University Hospital - Santariskiu Clinics, Vilnius:** Sipylyte Jurate, Egle Kontrimaviciute, Gabija Tomkute
- Malta
- Mater Dei Hospital, Msida:** John Xuereb, Maureen Bezzina, Francis Joseph Borg
- Netherlands
- Academic Medical Centre, University of Amsterdam:** Sabrine Hemmes, Marcus Schultz, Markus Hollmann, Irene Wiersma, Jan Binnekade, Lieuwe Bos
- VU University Medical Center, Amsterdam:** Christa Boer, Anne Duvekot
- MC Haaglanden, Den Haag:** Bas in 't Veld, Alice Werger, Paul Dennesen, Charlotte Severijns
- Westfriesgasthuis, Hoorn:** Jasper De Jong, Jens Hering, Rien van Beek
- Norway
- Haukeland University Hospital, Bergen:** Stefan Ivars, Ib Jammer
- Førde Central Hospital /Førde Sentral Sykehus, Førde:** Alena Breidablik
- Martina Hansens Hospital, Gjettem:** Katharina Skirstad Hodt, Frode Fjellanger, Manuel Vico Avalos
- Bærum Hospital, Vestre Viken, Rud:** Jannicke Mellin-Olsen, Elisabeth Andersson
- Stavanger University Hospital, Stavanger:** Amir Shafi-Kabiri
- Panama
- Hospital Santo Tomás, Panama:** Ruby Molina, Stanley Wutai, Erick Morais
- Portugal
- Hospital do Espírito Santo - Évora, E.P.E, Évora:** Glória Tareco, Daniel Ferreira, Joana Amaral
- Centro Hospitalar de Lisboa Central, E.P.E, Lisboa:** Maria de Lurdes Goncalves Castro, Susana Cadilha, Sofia Appleton
- Centro Hospitalar de Lisboa Ocidental, E.P.E. Hospital de S. Francisco Xavier, Lisboa:** Suzana Parente, Mariana Correia, Diogo Martins
- Santarem Hospital, Santarem:** Angela Monteiroa, Ana Ricardo, Sara Rodrigues
- Romania
- Spital Orasenesc, Bolintin Vale:** Lucian Horhota
- Clinical Emergency Hospital of Bucharest, Bucharest:** Ioana Marina Grintescu, Liliانا Mirea, Ioana Cristina Grintescu
- Elias University Emergency Hospital, Bucharest:** Dan Corneci, Silvius Negoita, Madalina Dutu, Ioana Popescu Garotescu
- Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu", Bucharest:** Daniela Filipescu, Alexandru Bogdan Prodan
- Fundeni Clinical institute - Anaesthesia and Intensive Care, Bucharest:** Gabriela Droc, Ruxandra Fota, Mihai Popescu
- Fundeni Clinical institute - Intensive Care Unit, Bucharest:** Dana Tomescu, Ana Maria Petcu, Marian Irinel Tudoroiu
- Hospital Profesor D Gerota, Bucharest:** Alida Moise, Catalin-Traian Guran
- Constanta County Emergency Hospital, Constanta:** Iorel Gherghina, Dan Costea, Iulia Cindea
- University Emergency County Hospital Targu Mures, Targu Mures:** Sanda-Maria Copotou, Ruxandra Copotou, Victoria Barsan, Zsolt Tolcser, Magda Riciu, Septimiu Gheorghe Moldovan, Mihaly Veres
- Russia
- Krasnoyarsk State Medical University, Krasnoyarsk:** Alexey Gritsan, Tatyana Kapkan, Galina Gritsan, Oleg Korolkov
- Burdenko Neurosurgery Institute, Moscow:** Alexander Kulikov, Andrey Lubnin
- Moscow Regional Research Clinical Institute, Moscow:** Alexey Ovezov, Pavel Prokoshchev, Alexander Lugovoy, Natalia Anipchenko
- Municipal Clinical Hospital 7, Moscow:** Andrey Babayants, Irina Komissarova, Karginova Zalina
- Reanimatology Research Institute n.a. Negovskij RAMS, Moscow:** Valery Likhvantsev, Sergei Fedorov
- Serbia
- Clinical Center of Vojvodina, Emergency Center, Novisad:** Aleksandra Lazukic, Jasmina Pejakovic, Dunja Mihajlovic
- Slovakia
- National Cancer Institute, Bratislava:** Zuzana Kusnierikova, Maria Zelinkova
- F.D. Roosevelt teaching Hospital, Banská Bystrica:** Katarina Bruncakova, Lenka Polakovicova
- Faculty Hospital Nové Zámky, Nové Zámky:** William Sobona
- Slovenia
- Institute of Oncology Ljubljana, Ljubljana:** Barbka Novak-Supe, Ana Pekle-Golez, Mirosljub Jovanov, Branka Strazisar
- University Medical Centre Ljubljana, Ljubljana:** Jasmina Markovic-Bozic, Vesna Novak-Jankovic, Minca Voje, Andriy Grynyuk, Ivan Kostadinov, Alenka Spindler-Vesel
- Spain
- Hospital Sant Pau, Barcelona:** Victoria Moral, Mari Carmen Unzueta, Carlos Puigbo, Josep Fava
- Hospital Universitari Germans Trias I Pujol, Barcelona:** Jaume Canet, Enrique Moret, Mónica Rodriguez Nunez, Mar Sendra, Andrea Brunelli, Frederic Rodenas
- University of Navarra, Pamplona:** Pablo Monedero, Francisco Hidalgo Martinez, Maria Jose Yepes Temino, Antonio Martínez Simon, Ana de Abajo Larriba
- Corporacion Sanitaria Parc Tauli, Sabadell:** Alberto Lisi, Gisela Perez, Raquel Martinez
- Consorcio Hospital General Universitario de Valencia, Valencia:** Manuel Granell, Jose Tatay Vivo, Cristina Saiz Ruiz, Jose Antonio de Andrés Ibañez
- Hospital Clinico Valencia, Valencia:** Ernesto Pastor, Marina Soro, Carlos Ferrando, Mario Defez
- Hospital Universitario Rio Hortega, Valladolid:** Cesar Aldecoa Alvares-Santullano, Rocio Perez, Jesus Rico
- Sweden
- Central Hospital in Kristianstad:** Monir Jawad, Yousif Saeed, Lars Gillberg
- Turkey
- Ufuk University Hospital Ankara, Ankara:** Zuleyha Kazak Bengisun, Baturay Kansu Kazbek
- Akdeniz University Hospital, Antalya:** Nesli Coskunfirat, Neval Boztug, Suat Sanli, Murat Yilmaz, Necmiye Hadimioglu
- Istanbul University, Istanbul medical faculty, Istanbul:** Nuzhet Mert Senturk, Emre Camci, Semra Kucukgoncu, Zerrin Sungur, Nukhet Sivrikoz
- Acibadem University, Istanbul:** Serpil Ustalar Ozgen, Fevzi Toraman
- Maltepe University, Istanbul:** Onur Selvi, Ozgur Senturk, Mine Yildiz
- Dokuz Eylul Universitesi Tip Fakültesi, Izmir:** Bahar Kuvaki, Ferim Gunenc, Semih Kucukguclu, Şule Ozbilgin
- Şifa University Hospital, Izmir:** Jale Maral, Seyda Canli
- Selcuk University faculty of medicine, Konya:** Oguzhan Arun, Ali Saltali, Eyup Aydogan
- Fatih Sultan Mehmet Eğitim Ve Araştırma Hastanesi, Istanbul:** Fatma Nur Akgun, Ceren Sanlikarip, Fatma Mine Karaman
- Ukraine
- Institute Of Surgery And Transplantology, Kiev:** Andriy Mazur
- Zaporizhzhia State Medical University, Zaporizhzhia:** Sergiy Vorotyntsev
- United Kingdom
- SWARM Research Collaborative: for full list of SWARM contributors please see [www.ukswarm.com](http://www.ukswarm.com)
- Northern Devon Healthcare NHS Trust, Barnstaple:** Guy Rousseau, Colin Barrett, Lucia Stancombe

**Golden Jubilee National Hospital, Clydebank, Scotland:** Ben Shelley, Helen Scholes  
**Darlington Memorial Hospital, County Durham and Darlington Foundation NHS Trust, Darlington:** James Limb, Amir Rafi, Lisa Wayman, Jill Deane  
**Royal Derby Hospital, Derby:** David Rogerson, John Williams, Susan Yates, Elaine Rogers  
**Dorset County Hospital, Dorchester:** Mark Pullett, Sarah Moreton, Stephanie Jones  
**The Princess Alexandra NHS Hospital Trust, Essex:** Suresh Venkatesh, Maudrian Burton, Lucy Brown, Cait Goodall  
**Royal Devon and Exeter NHS Foundation Trust, Exeter:** Matthew Rucklidge, Debbie Fuller, Maria Nadolski, Sandeep Kusre  
**Hospital James Paget University Hospital NHS Foundation Trust, Great Yarmouth:** Michael Lundberg, Lynn Everett, Helen Nutt  
**Royal Surrey County Hospital NHS Foundation Trust, Guildford:** Maka Zuleika, Peter Carvalho, Deborah Clements, Ben Creagh-Brown  
**Kettering General Hospital NHS Foundation Trust, Kettering:** Philip Watt, Parizade Raymode  
**Barts Health NHS Trust, Royal London Hospital, London:** Rupert Pearse, Otto Mohr, Ashok Raj, Thais Creary  
**Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton, Newcastle upon Tyne:** Ahmed Chishti, Andrea Bell, Charley Higham, Alistair Cain, Sarah Gibb, Stephen Mowat  
**Derriford Hospital Plymouth Hospitals NHS Trust, Plymouth:** Danielle Franklin, Claire West, Gary Minto, Nicholas Boyd  
**Royal Hallamshire Hospital, Sheffield:** Gary Mills, Emily Calton, Rachel Walker, Felicity Mackenzie, Branwen Ellison, Helen Roberts  
**Mid Staffordshire NHS, Stafford:** Moses Chikungwa, Clare Jackson  
**Musgrove Park Hospital, Taunton:** Andrew Donovan, Jayne Foot, Elizabeth Homan  
**South Devon Healthcare NHS Foundation Trust /Torbay Hospital, Torquay, Torbay:** Jane Montgomery, David Portch, Pauline Mercer, Janet Palmer  
**Royal Cornwall Hospital, Truro:** Jonathan Paddle, Anna Fouracres, Amanda Datson, Alyson Andrew, Leanne Welch  
**Mid Yorkshire Hospitals NHS Trust; Pinderfields Hospital, Wakefield:** Alastair Rose, Sandeep Varma, Karen Simeson  
**Sandwell and West Birmingham NHS Trust, West Bromich:** Mrutyunjaya Rambhatla, Jaysimha Susarla, Sudhakar Marri, Krishnan Kodaganallur, Ashok Das, Shivarajan Algarsamy, Julie Colley  
**York Teaching Hospitals NHS Foundation Trust, York:** Simon Davies, Margaret Szewczyk, Thomas Smith  
**United States**  
**University of Colorado School of Medicine/University of Colorado Hospital, Aurora:** Ana Fernandez- Bustamante, Elizabeth Luzier, Angela Almagro  
**Massachusetts General Hospital, Boston:** Marcos Vidal Melo, Luiz Fernando, Demet Sulemanji  
**Mayo Clinic, Rochester:** Juraj Sprung, Toby Weingarten, Daryl Kor, Federica Scavonetto, Yeo Tze

#### Authors' contributions

CR wrote the first draft of the manuscript, performed the statistical analysis and contributed to conception and design, acquisition of data, or analysis and interpretation of data, to the final drafting the article and revised it critically for important intellectual content; PP wrote the first draft of the manuscript; DB helped CR and PP to write the first draft of the manuscript; SNTH, ASN, TB, JC, MH, MHW, GHM, MFVM, CP, SJ, WS, PS, HW, LB, MGA, MJS, PP, DB contributed to conception and design, acquisition of data, or analysis and interpretation of data, to the final drafting the article and revised it critically for important intellectual content; all authors have read and approved the submitted manuscript; and agreed that the article is accountable for all aspects of the work thereby ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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#### Availability of data and materials

The dataset used and analysed during the current study are available from the corresponding author on reasonable request.

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#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

#### Author details

<sup>1</sup>Anaesthesia and Intensive Care, San Martino Policlinico Hospital, IRCCS for Oncology and Neurosciences, Largo Rosanna Benzi 8, 16131 Genoa, Italy. <sup>2</sup>Department of Intensive Care, Amsterdam University Medical Centers, location 'AMC', Amsterdam, The Netherlands. <sup>3</sup>Department of Anaesthesiology, Amsterdam University Medical Centers, location 'AMC', Amsterdam, The Netherlands. <sup>4</sup>Department of Critical Care Medicine, Hospital Israelita Albert Einstein, Sao Paulo, Brazil. <sup>5</sup>Department of Anaesthesiology and Intensive Care Medicine, Pulmonary engineering group, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany. <sup>6</sup>Department of Anaesthesiology and Postoperative Care, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain. <sup>7</sup>Division Cardiac, Thoracic, Vascular Anesthesia and Intensive Care, Medical University Vienna, Vienna, Austria. <sup>8</sup>Operating Services, Critical Care and Anaesthesia, Sheffield Teaching Hospitals and University of Sheffield, Sheffield, UK. <sup>9</sup>Department of Anaesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, USA. <sup>10</sup>Department of Anaesthesiology and Intensive Care Medicine, University Hospital Bonn, Bonn, Germany. <sup>11</sup>Department of Anaesthesia and Intensive Care, Saint Eloi Montpellier University Hospital, and PhyMedExp, University of Montpellier, Montpellier, France. <sup>12</sup>Department of Biotechnology and Sciences of Life, ASST-Setteleghi Ospedale di circolo e Fondazione Macchi, University of Insubria, Varese, Italy. <sup>13</sup>Department of Anaesthesiology and Intensive Care Medicine, University of Leipzig, Leipzig, Germany. <sup>14</sup>Department of Surgical Sciences and Integrated Diagnostics, University of Genoa, Genoa, Italy. <sup>15</sup>Mahidol-Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand.

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#### References

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