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Sex difference and intra-operative tidal volume:

Insights from the LAS VEGAS study

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Abstract

BACKGROUND—One key element of lung-protective ventilation is the use of a low tidal volume (V_T). A sex difference in use of low tidal volume ventilation (LTVV) has been described in critically ill ICU patients.

OBJECTIVES—The aim of this study was to determine whether a sex difference in use of LTVV also exists in operating room patients, and if present what factors drive this difference.

DESIGN, PATIENTS AND SETTING—This is a posthoc analysis of LAS VEGAS, a 1-week worldwide observational study in adults requiring intra-operative ventilation during general anaesthesia for surgery in 146 hospitals in 29 countries.

MAIN OUTCOME MEASURES—Women and men were compared with respect to use of LTVV, defined as V_T of 8 ml kg^{-1} or less predicted bodyweight (PBW). A V_T was deemed 'default' if the set V_T was a round number. A mediation analysis assessed which factors may explain the sex difference in use of LTVV during intra-operative ventilation.

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RESULTS—This analysis includes 9864 patients, of whom 5425 (55%) were women. A default V_T was often set, both in women and men; mode V_T was 500 ml. Median [IQR] V_T was higher in women than in men (8.6 [7.7 to 9.6] vs. 7.6 [6.8 to 8.4] ml kg^{-1} PBW, $P^{***} < 0.001$). Compared with men, women were twice as likely not to receive LTVV [68.8 vs. 36.0%; relative risk ratio 2.1 (95% CI 1.9 to 2.1), $P^{***} < 0.001$]. In the mediation analysis, patients' height and actual body weight (ABW) explained 81 and 18% of the sex difference in use of LTVV, respectively; it was not explained by the use of a default V_T.

CONCLUSION—In this worldwide cohort of patients receiving intra-operative ventilation during general anaesthesia for surgery, women received a higher V_T than men during intra-operative ventilation. The risk for a female not to receive LTVV during surgery was double that of males. Height and ABW were the two mediators of the sex difference in use of LTVV.

TRIAL REGISTRATION—The study was registered at Clinicaltrials.gov, NCT01601223

Introduction

One key element of lung-protective ventilation is the use of a low tidal volume (V_T).[1,2] Increasing and convincing evidence for benefit of low tidal volume ventilation (LTVV) in ICU patients[3] stimulated the use of a low V_T in the operating room.[4] Recent studies confirmed that intra-operative use of lung-protective ventilation, in part consisting of use of a low V_T, protects against postoperative pulmonary complications (PPCs).[2,5-7] Despite recommendations on use of a V_T of 8 ml kg^{-1} predicted body weight (PBW) or lower,[8] LTVV remains grossly underused. Large observational studies show that more than a third of surgery patients receive ventilation with a V_T more than 8 ml kg^{-1} PBW,[9] and one in five patients with a V_T more than 10 ml kg^{-1} PBW.[10,11]

A recent secondary analysis of the 'Large observational study to Understand the Global Impact of Severe Acute respiratory FailurE' (LUNG SAFE) showed that female patients with acute respiratory distress syndrome (ARDS) received LTVV less often than males.[12] It is uncertain whether a sex difference in use of LTVV also exists in the operating room. We reassessed the database of the 'Local Assessment of VEntilatory management during General Anaesthesia for Surgery' (LAS VEGAS) study to describe and compare the use of LTVV in female versus male surgery patients. In addition, we ascertained which factors are associated with this sex difference in use of LTVV. We hypothesised that women receive intra-operative LTVV less often than men, and that this difference is driven by anthropometric factors such as height and weight, and the use of a possibly sex-specific default V_T.

Materials and methods

This is a posthoc analysis of the LAS VEGAS study,[9] carried out in accordance with the recommendations of the 'STrengthening the Reporting of OBservational studies in Epidemiology' (STROBE) statement (checklist can be found at page 3 of Online Supplement, http://links.lww.com/EJA/A517) (http://www.strobe-statement.org/). LAS VEGAS was a worldwide, international, multicentre, prospective 1-week observational study describing in detail intra-operative ventilation practices in the operating rooms of 146

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centres in 29 countries.[9] Surgical patients were enrolled between 14 January and 4 March 2013. National coordinators selected the exact period during which data were collected for the study in their respective country.

The study protocol of the LAS VEGAS study was first approved on 22 August 2012 by the ethics committee of the Academic Medical Center, Amsterdam, The Netherlands (W12_190#12.17.0227, chairperson Prof. M.P.M. Burger). In all participating centres, approval was obtained from the institutional review board if needed, and depending on national or regional legislation, written informed consent was obtained from the individual patients.

The LAS VEGAS study was registered at clinicaltrial.gov (study identifier NCT01601223).

The LAS VEGAS study enrolled consecutive patients requiring invasive ventilation during general anaesthesia for surgery during a predefined calendar week. Exclusion criteria of the LAS VEGAS study were age less than 18 years, scheduled for pregnancy-related surgery and surgical procedures outside an operating room. The current posthoc analysis also excluded patients undergoing a surgical procedure involving cardiopulmonary bypass, thoracic surgery or planned use of one-lung ventilation during surgery.

Collected data included baseline characteristics and demographics, details of the surgical procedure, the 'Assess Respiratory Risk in Surgical Patients in Catalonia for postoperative pulmonary complications' (ARISCAT) score,[13] hourly collection of vital parameters and ventilation data, including V_T, positive end-expiratory pressure (PEEP) and peak pressure (Ppeak), fraction of inspired oxygen (FIO_2) and respiratory rate.

V_T was normalised for actual body weight (ABW) and for PBW, as follows:

$$V_{T,ABW} = \text{absolute } V_T \text{ / ABW in kg (Eq . 1)} \quad (1)$$

$$V_{T,PBW} = \text{absolute } V_T \text{ / PBW in kg (Eq . 2)} \quad (2)$$

PBW for women and men was calculated as follows:

$$\text{men, PBW} = 50.0 + 0.91 * (\text{height in cm} - 152.4)\ \text{(Eq.3a)} \quad (3a)$$

$$\text{women, PBW} = 45.5 + 0.91 * (\text{height in cm} - 152.4)\ \text{(Eq. 3b)} \quad (3b)$$

The primary outcome was use of LTVV, defined as having received a median $V_{T,PBW}$ of 8 ml kg^{-1} or less during intra-operative ventilation. A patient was defined as possibly having received ventilation with a default V_T when the reported absolute V_T was a rounded number, for example a V_T of 200, 250, 300, 350, 400, 450, 500, 550, 600 or 650 ml.

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Statistical analysis

A detailed description of the statistical analysis can be found in the eMethods in the Online Supplement, http://links.lww.com/EJA/A517. Descriptive statistics were reported for the study population stratified according to sex, and as number and relative proportions for categorical variables and median [IQR] for continuous variables. No assumptions were made for missing data. The anthropometric indices were compared between the sex groups using Wilcoxon rank sum test for continuous variables. For all analyses, the male sex was used as reference. The number and proportion of patients receiving LTVV was described and an unadjusted mixed-effect generalised linear model considering the centres as random effect was used to extract the risk difference. The proportion of patients receiving LTVV was also assessed according to quintiles of height and weight. In addition, the proportions of patients receiving a $V_{T,PBW}$ more than 9 ml kg^{-1} and $V_{T,PBW}$ more than 10 ml kg^{-1} were described using a χ^2 statistic. In all models, continuous variables were standardised to improve convergence.

Finally, to investigate whether the difference in the use of LTVV between female and male patients is due to differences in height, ABW or setting a 'default' possibly sex-dependent V_T, a mixed-effect multivariable mediation model was used. Mediators are variables that are affected by group assignment and that subsequently can affect the outcome. Therefore, mediators are on the causal pathway of the relationship between group and outcome, at least partly explaining the effects of the group on the outcome. In a first step, we assessed the individual impact of height, weight or use of a fixed V_T as potential mediators for the different use of low V_T according to sex in a multivariable model adjusted by all the covariates described above. For this model, quasi-Bayesian confidence intervals were estimated after 10 000 simulations. In a second step, height, weight and setting a default V_T were included at the same time in the same model to assess the impact and importance of each. In this second model, the confidence intervals were estimated with bootstrapping with 1000 samples. For the mediation models, the following estimates are described: the total effect (estimates the total effect of sex on ventilation), the average causal mediation effect (ACME, explains how much of the effect of sex on ventilation is explained by the mediator [height, weight or setting a default V_T]), the average direct effect (ADE, explains how much of the effect of sex on ventilation is still explained by sex after considering the effect of the mediator) and the proportion of mediation (estimates the proportion of the total effect that is explained by the mediator).

All analyses were conducted in R v.3.60 and a P value less than 0.05 was considered statistically significant.

Results

This analysis included 5425 (55%) women and 4439 (45%) men undergoing intra-operative ventilation not meeting the additional exclusion criteria. Patient characteristics and anthropometric indices are summarised in Table 1. Women were median 11 (95% CI 11 to 12) cm shorter ($P < 0.001$) and 12 (11 to 13) kg lighter than men ($P < 0.001$). Anaesthesia, surgery and intra-operative ventilation characteristics are shown in Supplementary eTables 1 and 2, http://links.lww.com/EJA/A517.

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V_T in women and men are shown in Fig. 1 and Supplementary eFigs. 1, 2 and 3, http://links.lww.com/EJA/A517. Mean V_T was 500 ml, and was similar for women and men. In women, median $V_{T, ABW}$, and median $V_{T,PBW}$ were higher than men 6.9 (5.9 to 7.9) vs. 6.6 (5.7 to 7.5) ml kg^{-1} ABW; median difference was 0.3 (0.2 to 0.4) ml kg^{-1} ABW ($P < 0.001$); and 8.6 (7.7 to 9.6) vs. 7.6 (6.8 to 8.4) ml kg^{-1} PBW; median difference was 1.1 (1.0 to 1.1) ml kg^{-1} PBW ($P < 0.001$). Women were less likely to receive a default V_T than men (64.3 vs. 67.9%; $P < 0.001$). In the lower quintiles of height, $V_{T,PBW}$ was higher, an effect that was stronger in women, and for every quintile in ABW, women received a higher $V_{T,PBW}$ (Supplementary eFigs. 4 and 5, http://links.lww.com/EJA/A517). Although women received a lower absolute V_T, the $V_{T,PBW}$ was always higher than in men (Supplementary eFigs. 6 and 7, http://links.lww.com/EJA/A517). The proportion of women receiving V_T more than 9 ml kg^{-1} was three times higher than in men (39.3 vs. 13.8%; $P < 0.001$); the proportion of females receiving V_T 10 ml kg^{-1} or higher was four times higher than in men (18.8 vs. 4.3%; $P < 0.001$). Intra-operative driving pressures were higher in women than in men, albeit that the difference between sexes was small.

The proportion of women receiving intra-operative LTVV was less than half of that in males (31.1 vs. 64.0%; $P < 0.001$). Women were at a higher risk of not receiving intra-operative LTVV than men (68.8 vs. 36.0%; $P < 0.001$). After adjustment for confounders, the difference in use of LTVV persisted [−5.78 (−8.12 to −3.45), $P < 0.001$] (Supplementary eFig. 8, http://links.lww.com/EJA/A517). In the lowest quintiles of height, and in all quintiles of ABW, women received LTVV less often than men (Fig. 2).

In the mediation models, mostly height and to a lesser extent ABW were the independent drivers of the effect of sex on use of intra-operative LTVV (Table 2). Use of a default V_T during intra-operative ventilation was not a driver of the sex difference in use of LTVV.

Discussion

The main findings of the current analysis of the LAS VEGAS database are that women, compared with men, received higher median $V_{T, ABW}$ and higher median $V_{T,PBW}$ during intra-operative ventilation. Consequently, women received LTVV much less often, a finding that was more pronounced in shorter women. The sex difference in use of LTVV was mostly mediated by differences in height and ABW, and not by sex or the use of a default V_T.

This study has several strengths. It used a large and robust database of a worldwide study in patients receiving intra-operative mechanical ventilation during general anaesthesia for various types of surgery. The study had a multicentre design, increasing the generalisability of the findings. $V_{T, ABW}$ and $V_{T,PBW}$ could be calculated in all patients, and the amount of missing data was very small. The analysis followed a strict analysis plan that used sophisticated statistical computations and the mediation analysis allowed us to explain the sex difference in use of LTVV.

This study is the largest investigation that shows differences in V_T titrations between women and men undergoing invasive ventilation during general anaesthesia for surgery. Its findings are in line with results from previous single-centre[10] and national investigations[11,14-16]

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that all showed women to be at risk of receiving larger $V_{T,PBW}$ compared with men. Its findings also suggest that anaesthesiologists are titrating V_T to ABW more than PBW, and foregoing the cumbersome process of measuring height and performing the PBW calculation altogether. Nevertheless, anaesthesiologists may have been interested in lung-protective ventilation, as the V_T based on ABW was less than 7 ml kg^{-1} for both women and men.

Thus far, studies performed in the operating room[10,11,14-16] as well as studies performed in the ICU[12] failed to identify the factors behind sex differences in use of LTVV. The current findings add to our knowledge by showing that the sex difference in use of LTVV is mostly driven by patients' height and ABW. The latter finding suggests that the risk of using too large a V_T can also occur in men, that the risk is larger in shorter individuals and that it also affects overweight patients. This is in line with previous investigations showing that these anthropometric indices influence the risk of receiving intra-operative ventilation with an incorrectly titrated V_T.[10,11,14-16,17] The current findings reject the hypothesis that incorrect titration of V_T is a sex-specific problem.

In settings with shorter individuals, the problem of receiving ventilation with too large a V_T could even be greater, albeit that the average differences in height between women and men is nearly 10–15 cm world-wide.[18,19] The same could be true in areas where there are more overweight or obese individuals. However, the current findings should increase the awareness of using the correct information for proper V_T titrations – patient's height, maybe patient's sex but not patient's ABW – should be considered when titrating V_T.

Our finding of sex disparity in V_T titrations mirrors the practice of ventilation in critically ill patients, for example invasive ventilation in ICUs. Indeed, not only in unselected critically ill patients,[19-22] but also in specific ICU cohorts such as organ donors,[23] patients with sepsis[24] and even in patients with ARDS,[25] women continue to receive LTVV less often than males. These findings suggest that the problem is widespread, and also needs attention beyond the operating room. Furthermore, the effect of anthropometric factors on intra-operative V_T titrations, and thus, the use of LTVV may be more important in patients undergoing more extreme procedures, for example intrathoracic procedures that require one-lung ventilation. In these patients, use of lung-protective ventilation is reported to be low[26] and every effort to improve this may result in better postoperative outcomes.

One additional finding was that patients undergoing surgery frequently receive a default V_T. This was also found in one French study.[11] Using a default V_T could be more straightforward and is probably an easier approach at the bedside than collecting or measuring patients' height, and performing a rather complex calculation. Of note, the mediation analysis showed use of a default V_T did not mediate the effect of sex on use of LTVV. One possible explanation is that a default V_T may already have been adjusted for sex, that is lower default V_T may have been use in women than in men. This could be a practical alternative for use at the bedside, albeit that a default V_T could better be based on whether the patient is 'short' or 'tall', than whether the patients is female or male.[27]

The results of our study should be seen against a background of an ongoing uncertainty regarding what is the best V_T during intra-operative ventilation. Although multiple studies

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directly[2,5,10] or indirectly[28,29] suggest benefit from a low V_T, the results of one recent study[30] suggest otherwise. In that study, intra-operative ventilation with a V_T of 6 ml kg^{-1} PBW was compared with a V_T of 10 ml kg^{-1} and resulted in a similar proportion of patients who developed PPC. Additional studies are needed to help decide what V_T to use in intra-operative ventilation during general anaesthesia for surgery.

Several limitations need to be mentioned. First, this was a posthoc analysis. However, to prevent data-driven analysis and reporting, we developed a cautious statistical model, aiming to compensate for potential confounding factors. Second, the present findings may not apply to all patient categories, such as children, patients undergoing cardiac surgery or one-lung ventilation during surgery, and pregnant women, as these patients were excluded from the original LAS VEGAS study.[9] Third, the LAS VEGAS study was performed more than 7 years ago. It is possible that changes in clinical practice over recent years resulted in a further reduction in V_T, mitigating sex differences in use of LTVV. It should be mentioned, however, that the sex differences found in the current analysis were not different from those in an earlier study in which patients received ventilation with a much higher V_T.[10] Fourth, patients' height and ABW were collected from patients' records, assuming that these were correctly reported – this may not be true for all patients – however, it seems logical that the recorded height was used to set V_T. Fifth, additional confounders such as actual practice and personal preferences of the anaesthesiologist could not be accounted for in the mediation analysis. It is possible that these and other yet unknown factors could have influenced the findings. Sixth, we conducted a complete case analysis, considering only patients for whom data needed for calculation of the outcome were available. Finally, we assumed that every rounded V_T was a default V_T. Although we cannot conclude that use of a default V_T had no mediation effect, we can state that use of a rounded V_T did not mediate the sex difference in use of LTVV.

Conclusion

During ventilation for general anaesthesia, women are less likely to receive LTVV than men. This sex difference is mostly mediated by patients' height and ABW. These findings raise the awareness of the importance of proper titration of V_T in operating rooms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements relating to this article

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PROVE Network: 'PROtective VEntilation Network'.

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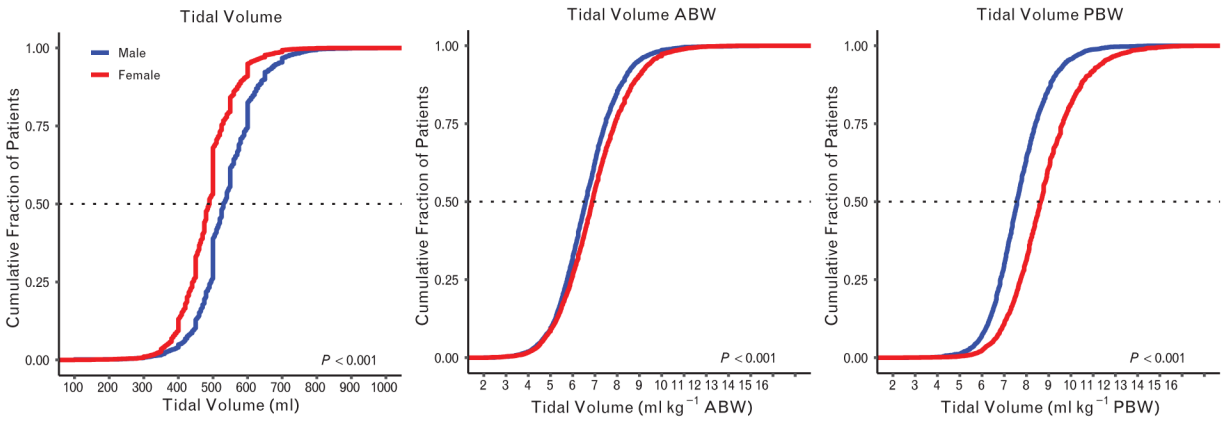


Fig. 1. Cumulative distribution plots for the median values of the ventilatory parameters during the intra-operative period stratified by sex

PBW calculated according to standard formula. *P* value from the unadjusted mixed-effect linear model with centres as random effect. ABW, actual body weight; PBW, predicted body weight.

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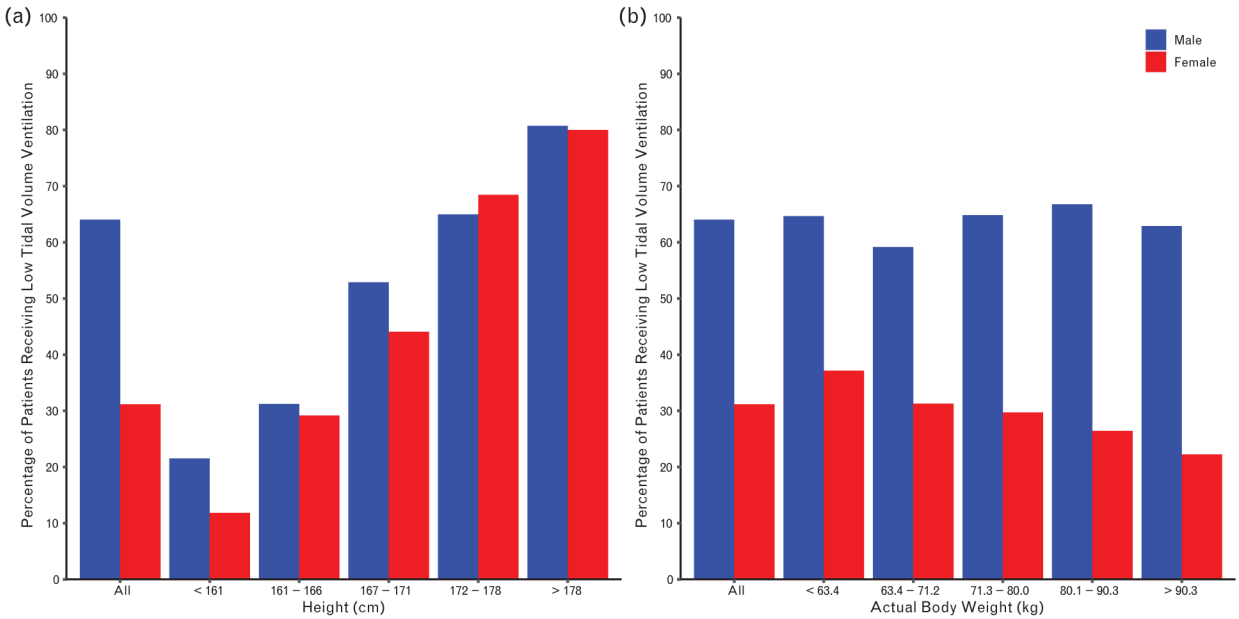


Fig. 2. Frequency of use of low tidal volume ventilation in the overall cohort stratified by sex and according to quintiles of height and weight

A low tidal volume was defined as a tidal volume ≤8 ml kg^{-1}. PBW calculated according to standard formula. ABW, actual body weight; PBW, predicted body weight.

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Table 1

Baseline characteristics of the patients

	Female (*n* = 5425)	Male (*n* = 4439)	*P*
Age (years)	52 [39 to 64]	55 [40 to 67]	<0.001
Height (cm)	164 [159 to 168]	175 [170 to 180]	<0.001
Weight (kg)	70 [60 to 81]	82 [72 to 93]	<0.001
PBW (kg)	56.1 [51.5 to 59.7]	70.6 [66.0 to 75.1]	<0.001
BMI (kg m^{-2})	25.9 [22.7 to 30.4]	26.5 [24.1 to 29.7]	<0.001
ASA physical status			<0.001
1	1720 (31.8)	1293 (29.2)	
2	2703 (50.0)	2040 (46.0)	
3	907 (16.8)	996 (22.5)	
4	75 (1.4)	98 (2.2)	
5	4 (0.1)	4 (0.1)	
ARISCAT score	15.00 [3.00 to 26.00]	16.00 [3.00 to 27.00]	0.293
Low	3806 (73.4)	2937 (69.4)	<0.001
Moderate	1148 (22.2)	1067 (25.2)	
High	228 (4.4)	227 (5.4)	
Pre-operative anaemia (Hb ≤10 g dl^{-1})	204 (4.5)	125 (3.4)	0.015
Pre-operative haemoglobin, g dl^{-1}	13.2 [12.2 to 14.0]	14.6 [13.3 to 15.5]	<0.001
Pre-operative SpO_2, %	98 [96 to 99]	97 [96 to 99]	<0.001
Respiratory infection <30 days	198 (3.6)	165 (3.7)	0.902
Blood transfusion <30 days	43 (0.8)	32 (0.7)	0.771
Pre-operative creatinine (μmol l^{-1})	64.6 [56.6 to 78.0]	80.5 [70.7 to 97.3]	<0.001
Functional status			0.265
Independent	5027 (92.7)	4078 (92.0)	
Partially dependent	331 (6.1)	290 (6.5)	
Totally dependent	65 (1.2)	67 (1.5)	
Chronic comorbidities			
Smoking	1008 (18.6)	1282 (28.9)	<0.001
Chronic obstructive pulmonary disease	263 (4.8)	333 (7.5)	<0.001

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	Female (*n* = 5425)	Male (*n* = 4439)	*P*
Cancer	190 (3.5)	202 (4.6)	0.009
Chronic kidney disease	125 (2.3)	185 (4.2)	<0.001
Heart failure	288 (5.3)	297 (6.7)	0.004
Obstructive sleep apnoea	91 (1.7)	114 (2.6)	0.003
Planned duration of surgery			<0.001
≤2 h	3899 (72.0)	2963 (66.9)	
2 to 3 h	1021 (18.9)	893 (20.1)	
>3 h	495 (9.1)	576 (13.0)	
Urgency of surgery[a]			<0.001
Elective	4888 (90.1)	3877 (87.4)	
Urgent	415 (7.7)	430 (9.7)	
Emergency	121 (2.2)	131 (3.0)	
Surgical technique[b]			
Open	933 (17.2)	840 (18.9)	0.028
Laparoscopic	1167 (21.5)	570 (12.8)	<0.001
Laparoscopic-assisted	97 (1.8)	70 (1.6)	0.465
Peripheral	964 (17.8)	863 (19.4)	0.036
Other type	2309 (42.6)	2118 (47.7)	<0.001
Surgical procedure			
Lower gastrointestinal	486 (9.0)	610 (13.7)	<0.001
Upper gastrointestinal	774 (14.3)	583 (13.1)	0.110
Vascular[c]	103 (1.9)	206 (4.6)	<0.001
Aortic	8 (0.1)	56 (1.3)	<0.001
Neurosurgery, head and neck	962 (17.7)	1044 (23.5)	<0.001
Urological and kidney	214 (3.9)	651 (14.7)	<0.001
Gynaecological	1134 (20.9)	0 (0.0)	<0.001
Endocrine	151 (2.8)	43 (1.0)	<0.001
Transplant	12 (0.2)	22 (0.5)	0.032
Plastic, cutaneous, breast	784 (14.5)	253 (5.7)	<0.001
Bone, joint, trauma spine	736 (13.6)	859 (19.4)	<0.001

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	Female (*n* = 5425)	Male (*n* = 4439)	*P*
Others	246 (4.5)	339 (7.6)	<0.001

Data are presented as median [IQR] or *n* (%). ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; ASA, American Society of Anesthesiologists; Hb, haemoglobin; PBW, predicted body weight.

[a] Urgency of surgery, elective: surgery that is scheduled in advance because it does not involve a medical emergency; urgent, surgery required within < 48 h; emergency, nonelective surgery performed when the patient's life or wellbeing is in direct jeopardy.

[b] Patient can have more than one.

[c] Vascular surgery is carotid endarterectomy, aortic surgery and peripheral vascular taken together.

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Table 2

Mediation analysis

	Adjusted absolute difference (95% CI)[a,b]	P
Low tidal volume ventilation		
Height as mediator[c]		
Total effect of sex	−32.91 (−34.99 to −31.00)	<0.001
Average causal mediation effect of height	−26.56 (−28.14 to −25.00)	<0.001
Average direct effect of female sex	−6.35 (−8.67 to −4.00)	<0.001
Proportion of mediation by height in female sex	80.70 (74.76 to 87.00)	<0.001
Actual body weight as mediator[d]		
Total effect of sex	−5.41 (−7.81 to −3.00)	<0.001
Average causal mediation effect of weight	0.95 (0.42 to 2.00)	<0.001
Average direct effect of female sex	−6.37 (−8.73 to −4.00)	<0.001
Proportion of mediation by weight in female sex	−17.65 (−39.54 to −7.00)	<0.001
Default V_T as mediator[e]		
Total effect of sex	−5.14 (−7.55 to −3.00)	<0.001
Average causal mediation effect of default V_T	−0.00 (−0.05 to 0.00)	0.730
Average direct effect of female sex	−5.13 (−7.54 to −3.00)	<0.001
Proportion of mediation by weight in female sex	0.05 (−0.60 to 1.00)	0.730
Height, weight and default V_T as mediators[f]		
Total effect of sex	−30.80 (−34.30 to −27.20)	<0.001
Average causal mediation effect of height	−31.90 (−34.10 to −29.70)	<0.001
Average causal mediation effect of weight	6.10 (5.00 to 7.20)	<0.001
Average causal mediation effect of default V_T	0.00 (−0.10 to 0.10)	0.618
Average direct effect of female sex	−5.00 (−8.80 to −1.10)	0.011

ASA, American Society of Anesthesiologists' physical status; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia for postoperative pulmonary complications' (ARISCAT) score; $etCO_2$, end-tidal carbon dioxide tension.

[a]Multilevel mediation model with quasi–Bayesian confidence intervals, with centres as random effects and adjusted for ASA, ARISCAT, presence of obstructive sleep apnoea, urgency of surgery, total fluid intake, need of intra-operative transfusion, reversal of neuromuscular blockade, duration of anaesthesia and intra-operative $etCO_2$.

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[b] All estimates generated after 10 000 simulations.

[c] Further adjusted by weight and default V_T.

[d] Further adjusted by height and default V_T.

[e] Further adjusted by height and weight.

[f] Adjusted only for the variables described in 'a' (height, weight and default V_T excluded) and confidence intervals estimated with bootstrapping with 1000 samples.

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STROBE Statement checklist

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4,5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any pre–specified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	9 - 11
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8 – 11 Supplement p. 15
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	9 - 11 Supplement p. 14
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	n.a.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10, 11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	10, 11
Bias	9	Describe any efforts to address potential sources of bias	8 – 12
Study size	10	Explain how the study size was arrived at	9

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11 – 13
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11 – 14
		(*b*) Describe any methods used to examine subgroups and interactions	10 – 11
		(*c*) Explain how missing data were addressed	-
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	13
		(*e*) Describe any sensitivity analyses	x
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	15, fig.1
		(b) Give reasons for non-participation at each stage	15, fig.1
		(c) Consider use of a flow diagram	fig.1
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	15 – 17, tab 1, eTab 3
		(b) Indicate number of participants with missing data for each variable of interest	tab 1 – 4, eTab 4, 6 – 8
		(c) *Cohort study*—Summarise follow-up time (e.g., average and total amount)	15 – 17, Fig 4
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	15 – 17, tab 2, 3, 4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	n.a.
		(*b*) Report category boundaries when continuous variables were categorized	tab 1, 2, eTab 4, 6 – 8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	x

Continued on next page

Other analyses	17	Report other analyses done - e.g. analyses of subgroups and interactions, and sensitivity analyses	n.a.
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21, 22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18 – 21
Generalisability	21	Discuss the generalisability (external validity) of the study results	18, 19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

Randomization procedure

Centres with >180 eligible patients per week are offered the option to reduce their patient cohort by randomization. These centres are identified according to the number of eligible patients per week, as reported in the LAS VEGAS Site Survey.

Distribution:

< 180 procedures per week: no randomization

180 – 360 procedures per week: randomization to include 50% of their cohort

> 360 procedures per week: randomization to include 25% of their cohort

Only eligible, planned patients are suitable for randomization. All Emergency procedures and all procedures performed outside office hours (evening/ night/weekend) must be included and therefore should not enter the randomization program.

Details on randomization:

- Randomization program: ALEA (computerized)
- Stratified per centre
- 1 inlog provided per centre
- Random blocks
- Variables collected:

*Center name

*Date of surgery

*Urgency of procedure

*Surgical Procedure (same categories as collected in CRF)

*Planned duration of surgery (in hours)

*Age patient (in years)

*ASA score (1 to 5 or not available)

- Output: INCLUDE vs EXCLUDE

eTable 1. ARISCAT risk score [1]

Independent predictors of risk for postoperative pulmonary complications identified in logistic regression model

	multivariate analysis	**ß-coefficients**	**risk score**[†]
Age (years)			
≤ 50	1		
51 – 80	1.4 (0.6 - 3.3)	0.331	3
> 80	5.1 (1.9 - 13.3)	1.619	16
Preoperative SpO_2 (%)			
≥ 96	1		
91 – 95	2.2 (1.2 - 4.2)	0.802	8
≤ 90	10.7 (4.1 - 28.1)	2.375	24
Respiratory infection in the last month	5.5 (2.6 - 11.5)	1.698	17
Preoperative anaemia (≤ 100 g/L)	3.0 (1.4 - 6.5)	1.105	11
Surgical incision			
Peripheral	1		
Upper abdominal	4.4 (2.3 - 8.5)	1.480	15
Intrathoracic	11.4 (4.9 - 26.0)	2.431	24
Duration of surgery (hours)			
≤ 2	1		
2 to 3	4.9 (2.4 - 10.1)	1.593	16
> 3	9.7 (4.7 - 19.9)	2.268	23
Emergency procedure	2.2 (1.04 - 4.5)	0.768	8

Abbreviations: CI, confidence interval; OR, odds ratio; SpO_2, oxyhaemoglobin saturation by pulse oximetry breathing air in supine position

[†] The simplified risk score was the sum of each logistic regression coefficient multiplied by 10, after rounding off its value

eTable 2. Full list of participating centres

Country	City	Institution	# Patients
Austria	Graz	LKH Graz	51
Austria	Linz	AKH Linz	40
Austria	Vienna	Medical University Vienna	34
Belgium	Brussels	UCL - Cliniques Universitaires Saint Luc Brussels	119
Belgium	Brussels	Universitary Hospital Brussels (UZ Brussel)	27
Belgium	Genk	Het ZOL (Ziekenhuis Oost Limburg)	65
Belgium	Gent	Ghent University Hospital	154
Belgium	Gent	Maria Middelares Gent	10
Bosnia and Herzegovina	Sarajevo	General Hospital "prim Dr Abdulah Nakas" Sarajevo	48
Croatia	Cakovec	General Hospital Čakovec	40
Croatia	Karlovac	General Hospital Karlovac	28
Croatia	Osijek	University Clinical Hospital Osijek	125
Croatia	RIJEKA	University Hospital Rijeka	53
Croatia	Slavonski Brod	General Hospital Dr J Bencevic	46
Croatia	Split	University Hospital Center Split	96
Croatia	Zagreb	University Hospital Merkur	48
Croatia	Zagreb	University Hospital Sveti Duh	59
Croatia	Zagreb	University Hospital, Medical school, "Sestre milosrdnice" (Sister of Charity)	85
Czech Republic	Brno	University Hospital Brno	149
Czech Republic	Hradec Kralove	University Hospital Hradec Kralove	82
Czech Republic	Ostrava	University Hospital Ostrava	102
Czech Republic	Znojmo	Nemocnice Znojmo, p.o.	62
Egypt	Cairo	El Sahel Teaching hospital	62
Egypt	Cairo	Kasr Al-Ainy Medical School, Cairo University	38
Egypt	Giza	Beni Sueif University Hospital	42
Egypt	Giza	Fayoum University Hospital	49
Egypt	Suis	Suis medical Insurance Hospital	48
Estonia	Tallinn	North Estonia Medical Center	164
Estonia	Tartu	Tartu University Hospital	80
France	Clermont-Ferrand	Estaing Hospital, University Hospital of Clermont-Ferrand	30
France	Levallois-Perret	Institut Hospitalier Franco-Britannique	21
France	Montpellier	Saint Eloi University Hospital, Montpellier	140
Germany	Coswig	Fachkrankenhaus Coswig Gmbh, centre for pneumology and thoracic surgery	10
Germany	Dresden	University Hospital Carl Gustav Carus	219
Germany	Duesseldorf	Duesseldorf University Hospital, Heinrich-Heine University	129
Germany	Hannover	Diakoniekrankenhaus Friederikenstift	133
Germany	Leipzig	University of Leipzig	71
Greece	Athens	"Alexandra" general hospital of Athens	43
Greece	Athens	251 General air force hospital	41
Greece	Athens	Aretaieion University Hospital	41
Greece	Athens	Attikon University Hospital	54
Greece	Thessaloniki	Ahepa University Hospital Thessaloniki	50

Israel	Haifa	The Lady Davis Carmel Medical Center	40
Italy	Bari	Ospedale San. Paolo Bari	35
Italy	Bari	University of Bari “Aldo Moro”	81
Italy	Candiolo (Turin)	Institute for Cancer Research and treatment	28
Italy	Catania	Azienda Ospedaliera per l’emergenza Cannizzaro	39
Italy	Cernuso (Milano)	Ospedale Melegnano	5
Italy	Ferrara	Azienda Ospedaliera – Universitaria Sant’Anna (Ferrara)	88
Italy	Foggia	Ospedali Riuniti Di Foggia - University of Foggia	85
Italy	Genoa	IRCCS San Martino AOU IST Hospital, University of Genoa	173
Italy	Milano	IRCCS San Raffaele Scientific Institute	156
Italy	Milano	Istituto europeo di oncologia - ieo	131
Italy	Milano	Ospedale Niguarda Ca'Granda Milano	19
Italy	Milano	Ospedale San Paolo - University of Milano	46
Italy	Naples	University of Naples “Federico II”	57
Italy	Palermo	Policlinico "P. Giaccone"	92
Italy	Parma	Azienda Ospedaliero-Universitaria	81
Italy	Pordenone	Santa Maria degli Angeli	18
Italy	Prato	Ospedale Misericordia e Dolce - Usl4 Prato	41
Italy	Sassari	University hospital of Sassari	54
Italy	Varese	Insubria University	125
Lithuania	Kaunas	Kaunas Medical University Hospital, Hospital of Lithuanian University of Health Sciences	160
Lithuania	Vilnius	Vilnius University Hospital - Institute of Oncology	108
Lithuania	Vilnius	Vilnius University Hospital - Santariskiu Clinics	104
Malta	Msida	Mater Dei Hospital	27
Netherlands	Amsterdam	Academic Medical Center, University of Amsterdam	183
Netherlands	Amsterdam	VU University Medical Center	104
Netherlands	Den Haag	MC Haaglanden	94
Netherlands	Hoorn	Westfriesgasthuis	104
Norway	Bergen	Haukeland University Hospital	106
Norway	Førde	Førde Central Hospital /Førde Sentral Sykehus	58
Norway	Gjettum	Martina Hansens Hospital	57
Norway	Rud	Bærum Hospital, Vestre Viken	57
Norway	Stavanger	Stavanger University Hospital	70
Panama	Panama	Hospital Santo Tomás	40
Portugal	Évora	Hospital do Espírito Santo - Évora, EPE.	55
Portugal	Lisboa	Centro Hospitalar de Lisboa Central, EPE	49
Portugal	Lisboa	Centro Hospitalar de Lisboa Ocidental, EPE	41
Portugal	Santarem	Santarem Hospital	44
Republic of Kosovo	Gjakovë	Distric hospital Gjakova	9
Republic of Kosovo	Prishtina	University Clinical Center of Kosova	92
Republic of Kosovo	Prizren	Regional Hospital ”Prim.Dr. Daut Mustafa”	39
Romania	Bolintin Vale	Spital orasenesc Bolintin Vale	8
Romania	Bucharest	Clinical Emergency Hospital of Bucharest	58
Romania	Bucharest	Elias University Emergency Hospital	53
Romania	Bucharest	Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu"	6

Romania	Bucharest	Fundeni Clinical institute - Anaesthesia and Intensive Care	43
Romania	Bucharest	Fundeni Clinical institute - Intensive Care Unit	40
Romania	Bucharest	Hospital Profesor D Gerota	21
Romania	Constanta	Constanta County Emergency Hospital	73
Romania	Targu Mures	University Emergency County Hospital Targu Mures	138
Russia	Krasnoyarsk	Krasnoyarsk State Medical University	52
Russia	Moscow	Burdenko Neurosurgery Institute	60
Russia	Moscow	Moscow Regional Research Clinical Institute	59
Russia	Moscow	Municipal Clinical Hospital 7	49
Russia	Moscow	Reanimatology Research Institute n.a. Negovskij RAMS	61
Serbia	Novisad	Clinical Center of Vojvodina, Emergency Center	42
Slovakia	Bratislava	National Cancer Institute	18
Slovakia	Banská Bystrica	F.D.Roosevelt teaching Hospital	64
Slovakia	Nové Zámky	Faculty Hospital Nove Zamky	47
Slovenia	Ljubljana	Institute of Oncology Ljubljana	64
Slovenia	Ljubljana	University Medical Centre Ljubljana	108
Spain	Barcelona	Hospital Sant Pau	73
Spain	Barcelona	Hospital Universitari Germans Trias I Pujol	103
Spain	Pamplona	University of Navarra	90
Spain	Sabadell	Corporacion Sanitaria Parc Tauli	66
Spain	Valencia	Consorcio Hospital General Universitario de Valencia	61
Spain	Valencia	Hospital Clinico Valencia	62
Spain	Valladolid	Hospital Universitario Rio Hortega	82
Sweden	Kristianstad	Central Hospital in Kristianstad	83
Turkey	Ankara	Ufuk University Hospital Ankara	30
Turkey	Antalya	Akdeniz University Hospital	165
Turkey	Istanbul	Istanbul university, Istanbul medical faculty	81
Turkey	Istanbul	Acibadem University	25
Turkey	Istanbul	Maltepe University	37
Turkey	Izmir	Dokuz Eylül Universitesi Tip Fakültesi	161
Turkey	Izmir	Şifa University Hospital / İzmir	74
Turkey	Konya	Selcuk University faculty of medicine	138
Turkey	Istanbul	Fatih Sultan Mehmet Eğitim Ve Araştirma Hastanesi	53
Ukraine	Kiev	Institute Of Surgery And Transplantology	17
Ukraine	Zaporizhzhia	Zaporizhzhia State Medical University	18
United Kingdom	Barnstaple	Northern Devon Healthcare NHS Trust	69
United Kingdom	Clydebank, Scotland	Golden Jubilee National Hospital	67
United Kingdom	Darlington	Darlington Memorial Hospital, County Durham and Darlington Foundation NHS Trust	54
United Kingdom	Derby	Royal Derby Hospital	59
United Kingdom	Dorchester	Dorset County Hospital	63
United Kingdom	Essex	The Princess Alexandra NHS Hospital Trust	71
United Kingdom	Exeter	Royal Devon and Exeter NHS Foundation Trust	123
United Kingdom	Great Yarmouth	Hospital James Paget University Hospital NHS Foundation Trust	43
United Kingdom	Guildford	Royal Surrey County Hospital NHS Foundation Trust	70
United Kingdom	Kettering	Kettering General Hospital NHS Foundation Trust	40
United Kingdom	London	Barts Health NHS Trust, Royal London Hospital	104

United Kingdom	Newcastle upon Tyne	Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton	125
United Kingdom	Plymouth	Derriford Hospital Plymouth Hospitals NHS Trust	179
United Kingdom	Sheffield	Royal Hallamshire Hospital	103
United Kingdom	Stafford	Mid Staffordshire NHS	28
United Kingdom	Taunton	Musgrove Park Hospital	50
United Kingdom	Torquay, Torbay	South Devon Healthcare NHS Foundation Trust /Torbay Hospital,	83
United Kingdom	Truro	Royal Cornwall Hospital	81
United Kingdom	Wakefield	Mid Yorkshire Hospitals NHS Trust; Pinderfields Hospital	65
United Kingdom	West Bromich	Sandwell and West Birmingham NHS Trust	127
United Kingdom	York	York Teaching Hospitals NHS Foundation Trust	81
United States	Aurora, Colorado	University of Colorado School of Medicine/University of Colorado Hospital	56
United States	Boston	Massachusetts General Hospital, Boston	120
United States	Rochester	Mayo Clinic	200

eTable 3. Hospital characteristics of participating centres

	Centres responded (N = 145)
Community hospital	33
Teaching hospital	108
Number of hospital beds	600 [400 – 960]
Number of ICU beds	20 [11 – 35]
Number of operating theatres	15 [9 -22]
Staff (anaesthesiologists)	25 [12 – 40]
Invasive mechanical ventilation for surgery per week	103 [60 – 200]
Surgical procedures	
Abdominal surgery	135 (93%)
Bariatric surgery	66 (46%)
Cardiothoracic surgery	71 (49%)
Endocrine surgery	88 (61%)
Eye surgery	97 (67%)
General surgery	132 (91%)
Gynaecological surgery	126 (87%)
Interventional neuroradiology	56 (39%)
Neurosurgery	82 (57%)
Oral and maxillofacial surgery	96 (62%)
Orthopaedic surgery	121 (83%)
Plastic surgery	91 (63%)
Surgical oncology	107 (74%)
Trauma surgery	111 (77%)
Urology	121 (83%)
Vascular surgery	109 (75%)

Data are presented as median [QR] or N (%). One participating centre did not respond; ICU: intensive care unit

eTable 4. Patient and surgical characteristics 2			
Variable	**All patients**	**Low risk of PPCs**	**Increased risk of PPCs**
Ethnicity – %			
Caucasian	90.0 (8845/9829)	89.2 (5995/6723)	92.0 (2446/2660)
Black ethnicity	1.1 (104/9829)	1.2 (83/6723)	0.6 (15/2660)
Asian	2.3 (230/9829)	2.4 (161/6723)	2.1 (56/2660)
Other	6.6 (650/9829)	7.2 (484/6723)	5.4 (143/2660)
BMI (kg/m^2)	26.2 [23.4 – 30.0]	26.0 [23.2 – 29.7]	26.8 [23.7 – 30.7]
Underweight (< 18.5) – %	2.4 (200/8460)	2.3 (140/6162)	2.6 (57/2192)
No obesity (18.5 – 24.9)	37.1 (3142/8460)	38.6 (2381/6162)	32.7 (717/2192)
Overweight (≥ 25.0 - 29.9)	35.5 (3001/8460)	35.1 (2160/6162)	36.6 (802/2192)
Obesity Class 1 (30.0 to 34.9)	16.3 (1378/8460)	16.0 (985/6162)	17.2 (376/2192)
Obesity Class 2 (35.0 to 39.9)	5.7 (479/8460)	5.4 (332/6162)	6.6 (145/2192)
Morbid obesity (≥ 40)	3.1 (260/8460)	2.7 (164/6162)	4.3 (95/2192)
Respiratory infection (< 30 days preoperatively) – %	3.7 (363/9864)	1.7 (113/6743)	9.0 (241/2670)
Blood transfusion (< 24h preoperatively) – %	0.8 (75/9864)	0.2 (13/6739)	2.3 (61/2670)
Haemoglobin – g/dL*	13.7 [12.6 – 14.8]	13.8 [12.9 – 14.9]	13.2 [11.6 – 14.5]
White blood cells ($x10^9/L$)*	7.0 [6.0 – 9.0]	7.0 [5.9 – 8.6]	7.0 [6.0 – 9.0]
< 4 (%)	2.4 (190/7772)	2.2 (118/5248)	3.0 (70/2372)
4 – 11	89.2 (6935/7772)	90.6 (4753/5248)	86.6 (2053/2372)
> 11	8.3 (647/7772)	7.2 (377/5248)	10.5 (249/2372)
Creatinine – mg/dL*	0.80 [0.70 – 0.99]	0.80 [0.70 – 0.94]	0.84 [0.70 – 1.04]
< 1.5 (%)	95.2 (6856/7204)	96.7 (4578/4733)	92.0 (2130/2314)
1.5 – 3.0	3.2 (234/7204)	2.3 (108/4733)	5.2 (121/2314)
> 3.0	1.6 (114/7204)	1.0 (47/4733)	2.7 (63/2314)
Planned duration of surgery – %			
≤ 2 hours	69.7 (6862/9847)	88.0 (5927/6735)	22.2 (593/2670)
> 2 – 3 hours	19.4 (1914/9847)	9.9 (670/6735)	43.8 (1170/2670)
> 3 hours	10.9 (1071/9847)	2.0 (138/6735)	34.0 (907/2670)
Antibiotic prophylaxis – %	69.0 (6800/9859)	62.7 (4225/6740)	85.1 (2272/2670)
Intraoperative transfusion of PRBC – %	3.3 (330/9864)	1.0 (65/6743)	9.3 (249/2670)
Units PRBC transfused intraoperatively	0.0 [0.0 – 0.0]	0.0 [0.0 – 0.0]	0.0 [0.0 – 0.0]

Data is presented as: median [QR] or proportion (n/N); Increased versus high risk for PPCs, according to the Assess Respiratory Risk in Surgical Patients in Catalonia risk (ARISCAT) score (< versus ≥ 26, respectively); *Laboratory values: haemoglobin was collected when available from collection within routine care; white blood cell count and creatinine were collected when available from collection within routine care; PRBC: packed red blood cells

eTable 5. Severe postoperative pulmonary complications

Variable	All patients	Low risk of PPCs	Increased risk of PPCs	Relative Risk (95% CI)	*P* value
Postoperative pulmonary complications					
Total PPCs[#]	10.4 (1004/9697)	7.0 (467/6675)	19.2 (505/2632)	3.16 (2.76 – 3.61)	< 0.001
Total severe PPCs[##]	2.8 (270/9697)	1.6 (104/6675)	14.5 (156/2632)	3.98 (3.09 – 5.12)	< 0.001

All data is presented as proportion, % (n/N); Comparison of differences within a subgroup is performed by using the t-test for continuous variables and Chi-square for categorical variables; CI: confidence interval; Low versus increased risk of PPCs, according to the Assess Respiratory Risk in Surgical Patients in Catalonia risk (ARISCAT) score (< versus ≥ 26, respectively); PPCs: Postoperative pulmonary complications; [#]Total PPCs: one patient could present with multiple PPCs, but was scored only once (YES or NO principle); [##]Total severe PPCs: same composite as total PPCs, without unplanned supplemental O_2

eTable 6. Patient and surgical characteristics (ARISCAT low, moderate, high)

	ARISCAT < 26 (*n* = 6743)	ARISCAT 26–44 (*n* = 2215)	ARISCAT ≥ 45 (*n* = 455)
Patient characteristics			
Male sex	2937 / 6743 (43.6)	1067 / 2215 (48.2)	227 / 455 (49.9)
Age (years)	50 (36–63)	60 (49–70)	69 (58–81)
≤ 50	3510 / 6742 (52.1)	622 / 2214 (28.1)	58 / 455 (12.7)
51 – 80	3111 / 6742 (46.1)	1459 / 2214 (65.9)	282 / 455 (62.0)
> 80	121 / 6742 (1.8)	133 / 2214 (6.0)	115 / 455 (25.3)
BMI (kg/m^2)	26.0 (23.2–29.7)	27.0 (23.9–30.8)	26.1 (23.1–29.7)
ASA	2 (1–2)	2 (2–3)	3 (2–3)
1	2445 / 6734 (36.3)	356 / 2210 (16.1)	17 / 453 (3.8)
2	3305 / 6734 (49.1)	1102 / 2210 (49.9)	150 / 453 (33.1)
3	929 / 6734 (13.8)	686 / 2210 (31.0)	233 / 453 (51.4)
4	53 / 6734 (0.8)	63 / 2210 (2.9)	52 / 453 (11.5)
5	2 / 6734 (0.0)	3 / 2210 (0.1)	1 / 453 (0.2)
Functional status			
Independent	6385 / 6739 (94.7)	1984 / 2215 (89.6)	324 / 454 (71.4)
Partially dependent	291 / 6739 (4.3)	197 / 2215 (8.9)	110 / 454 (24.2)
Totally dependent	63 / 6739 (0.9)	34 / 2215 (1.5)	20 / 454 (4.4)
Smoker		466 / 2215 (21.0)	75 / 454 (16.5)
ARISCAT score	11 (3–16)	34 (28–39)	52 (49–58)
Pre-operative SpO_2 (%)	98 (97–99)	97 (95–98)	95 (93–97)
≥ 96	5450 / 6043 (90.2)	1422 / 2002 (71.0)	187 / 438 (42.7)
91 – 95	591 / 6043 (9.8)	539 / 2002 (26.9)	182 / 438 (41.6)
≤ 90	2 / 6043 (0.0)	41 / 2002 (2.0)	69 / 438 (15.8)
Pre-operative anaemia (Hb ≤ 10 g/dl)	53 / 5573 (1.0)	142 / 2081 (6.8)	123 / 447 (27.5)
Chronic co-morbidity - *a patient can have more than one co-morbidity*			
Metastatic cancer	124 / 6743 (1.8)	179 / 2215 (8.1)	81 / 455 (17.8)
Chronic kidney dysfunction	137 / 6743 (2.0)	120 / 2215 (5.4)	42 / 455 (9.2)
COPD	322 / 6743 (4.8)	199 / 2215 (9.0)	57 / 455 (12.5)
Heart failure	313 / 6743 (4.6)	193 / 2215 (8.7)	62 / 455 (13.6)
Obstructive sleep apnoea	132 / 6743 (2.0)	57 / 2215 (2.6)	11 / 455 (2.4)
Neuromuscular disease*	66 / 6743 (1.0)	17 / 2215 (0.8)	4 / 455 (0.9)
Liver dysfunction	54 / 6743 (0.8)	28 / 2215 (1.3)	15 / 455 (3.3)
Surgical characteristics			
Surgical procedure - *a patient can have more than one type of surgical procedure*			
Lower gastro-intestinal	466 / 6743 (6.9)	405 / 2215 (18.3)	174 / 455 (38.2)
Upper GI, hepato-biliary, pancreas	753 / 6743 (11.2)	446 / 2215 (20.1)	122 / 455 (26.8)
Vascular surgery[§]	197 / 6743 (2.9)	80 / 2215 (3.6)	19 / 455 (4.2)
Aortic surgery	18 / 6743 (0.3)	39 / 2215 (1.8)	6 / 455 (1.3)
Neurosurgery, head & neck	1558 / 6743 (3.1)	318 / 2215 (14.4)	24 / 455 (5.3)
Urological and kidney	455 / 6743 (6.7)	308 / 2215 (13.9)	60 / 455 (13.2)
Gynaecological	733 / 6743 (10.9)	308 / 2215 (13.9)	37 / 455 (8.1)
Endocrine surgery	159 / 6743 (2.4)	28 / 2215 (1.3)	2 / 455 (0.4)
Transplant	5 / 6743 (0.1)	21 / 2215 (0.9)	7 / 455 (1.5)
Plastic, cutaneous, breast	885 / 6743 (13.1)	107 / 2215 (4.8)	6 / 455 (1.3)
Bone, joint, trauma, spine	1253 / 6743 (18.6)	228 / 2215 (10.3)	27 / 455 (5.9)
Other procedure	483 / 6743 (7.2)	65 / 2215 (2.9)	14 / 455 (3.1)
Surgical technique			
Open abdominal surgery	512 / 6743 (7.6)	1316 / 2215 (40.6)	296 / 455 (65.1)
Laparoscopic surgery	1082 / 6743 (16.0)	504 / 2215 (22.8)	83 / 455 (18.2)
Laparoscopic assisted surgery	73 / 6743 (1.1)	79 / 2215 (3.6)	11 / 455 (2.4)
Peripheral surgery	1500 / 6743 (22.2)	191 / 2215 (8.9)	21 / 455 (4.6)
Other	3594 / 6743 (53.3)	573 / 2215 (25.9)	55 / 455 (12.1)
Urgency of surgery[#]			
Elective	6141 / 6742 (91.1)	1921 / 2215 (86.7)	327 / 455 (71.9)
Urgency	508 / 6742 (7.5)	222 / 2215 (10.0)	66 / 455 (14.5)
Emergency	93 / 6742 (1.4)	72 / 2215 (3.3)	62 / 455 (13.6)
Duration of surgery (min)†	60 (35–95)	125 (75–193)	157 (91–220)
Duration of anaethesia (min)††	90 (60–128)	165 (105–240)	205 (130–280)

Data is presented as: median (QR) or proportion (n/N); Low, moderate, versus high risk of PPCs, according to the Assess Respiratory Risk in Surgical Patients in Catalonia risk (ARISCAT) score (< 26, 26 – 44, versus ≥ 45, respectively); BMI: Body Mass Index; ASA: American Society of Anaesthesiology; SpO_2: Peripheral Oxygen Saturation; COPD: Chronic Obstructive Pulmonary Disease; *Neuromuscular disease affecting the respiratory system; [§]Vascular surgery is carotid endarterectomy, aortic surgery and peripheral vascular taken together; [#]Urgency of surgery: elective: surgery that is scheduled in advance because it does not involve a medical emergency, urgent: surgery required within < 48 hours, emergency: non-elective surgery performed when the patient's life or well-being is in direct jeopardy; †Duration of surgery is the time between skin incision and closure of the incision. ††Duration of anaesthesia is the time between start induction and extubation or discharge from operation room if mechanical ventilation remained.

eTable 7. Intraoperative ventilation characteristics (ARISCAT low, moderate, high)

	ARISCAT < 26 (*n* = 6743)	**ARISCAT 26–44 (*n* = 2215)**	**ARISCAT ≥ 45 (*n* = 455)**	***P* value**
Ventilation mode				
Volume Control	4589 / 6649 (69.0)	1574 / 2180 (72.2)	336 / 449 (74.8)	
Pressure Control	1161 / 6649 (17.5)	301 / 2180 (13.8)	57 / 449 (12.7)	< 0.001
Pressure Support or	87 / 6649 (1.3)	126 / 2180 (5.8)	29 / 449 (6.5)	
Spontaneous	812 / 6649 (12.2)	179 / 2180 (8.2)	27 / 449 (6.0)	
Other				
Tube type				
Endotracheal tube	5194 / 6742 (77.0)	2105 / 2215 (95.0)	445 / 455 (97.8)	
Nasotracheal tube	97 / 6742 (1.4)	19 / 2215 (0.9)	2 / 455 (0.4)	< 0.001
Supra-glottic device	1386 / 6742 (20.6)	67 / 2215 (3.0)	5 / 455 (1.1)	
Other[$]	65 / 6742 (1.0)	24 / 2215 (1.1)	3 / 455 (0.7)	
Tidal volume (ml)	500 (454–553)	500 (460–567)	500 (450–550)	0.003
Tidal volume (ml/kg PBW)	8.1 (7.2–9.1)	8.2 (7.3–9.2)	8.1 (7.4–9.1)	0.003
Tidal volume (ml/kg ABW)	6.7 (5.8–7.7)	6.7 (5.8–7.6)	6.8 (5.9–7.8)	0.130
PEEP (cmH_2O)	3 (0–5)	4 (2–5)	5 (2–5)	< 0.001
Respiratory rate (bpm)	12 (12–13)	12 (12–13)	12 (12–13)	0.355
Minute ventilation (ml/min)	6000 (5185–6816)	6000 (5000–6900)	5775 (4692–6600)	< 0.001
Peak pressure (cmH_2O)	17 (14–20)	19 (16–22)	19 (16–23)	< 0.001
Plateau pressure (cmH_2O)	15 (13–18)	17 (14–20)	17 (14–20)	< 0.001
Driving pressure (cmH_2O)	12 (10–15)	13 (10–16)	13 (10–17)	< 0.001
Dynamic compliance (ml/cmH_2O)	35.4 (28.6–43.5)	33.8 (27.1–41.3)	33.1 (27.0–40.1)	< 0.001
Static compliance (ml/cmH_2O)	42.3 (34.3–52.0)	40.4 (32.3–50.0)	38.4 (30.3–48.0)	< 0.001
Recruitment manoeuvre performed	570 / 6719 (8.5)	284 / 2204 (12.9)	59 / 452 (13.1)	< 0.001
FiO_2 (%)	54 (47–72)	50 (45–60)	50 (45–60)	< 0.001
< 40	440 / 6727 (6.5)	200 / 2205 (9.1)	40 / 455 (8.8)	
40 – 60	3288 / 6727 (48.9)	1325 / 2205 (60.1)	284 / 455 (62.4)	< 0.001
60 – 80	2156 / 6727 (32.0)	504 / 2205 (22.9)	95 / 455 (20.9)	
≥ 80	843 / 6727 (12.5)	176 / 2205 (8.0)	36 / 455 (7.9)	
SpO_2 (%)	99 (98–100)	99 (98–100)	99 (98–100)	0.437
≥ 96	6571 / 6721 (97.8)	2140 / 2200 (97.3)	433 / 452 (95.8)	
90 – 96	140 / 6721 (2.1)	59 / 2200 (2.7)	18 / 452 (4.0)	0.038
≤ 90	10 / 6721 (0.1)	1 / 2200 (0.0)	1 / 452 (0.2)	
$etCO_2$ (kPa)	4.5 (4.1–4.9)	4.5 (4.1–4.8)	4.4 (4.0–4.8)	< 0.001

Data is presented as median (QR) or proportion % (n/N); Chi-square for categorical variables and Mann-Whitney for continuous variables; Low, moderate, versus high risk of PPCs, according to the Assess Respiratory Risk in Surgical Patients in Catalonia risk (ARISCAT) score (< 26, 26 – 44, versus ≥ 45, respectively); [$]Other (e.g. high frequency oscillatory ventilation, jet ventilation, synchronized intermittent mandatory ventilation (SIMV); PBW: predicted body weight, calculated as: 50 + 0.91 x (centimetres of height – 152.4) for males and 45.5 + 0.91 x (centimetres of height – 152.4) for females; ABW: actual body weight; PEEP: positive end-expiratory pressure; bpm: breaths per minute; Cdyn.calc.: calculated dynamic respiratory compliance: Cdyn = tidal volume / (peak pressure minus PEEP); Cq.stat.: static respiratory compliance; F_iO_2: fraction inspired oxygen; SpO_2: peripheral oxygen saturation; $etCO_2$: expiratory carbon dioxide.

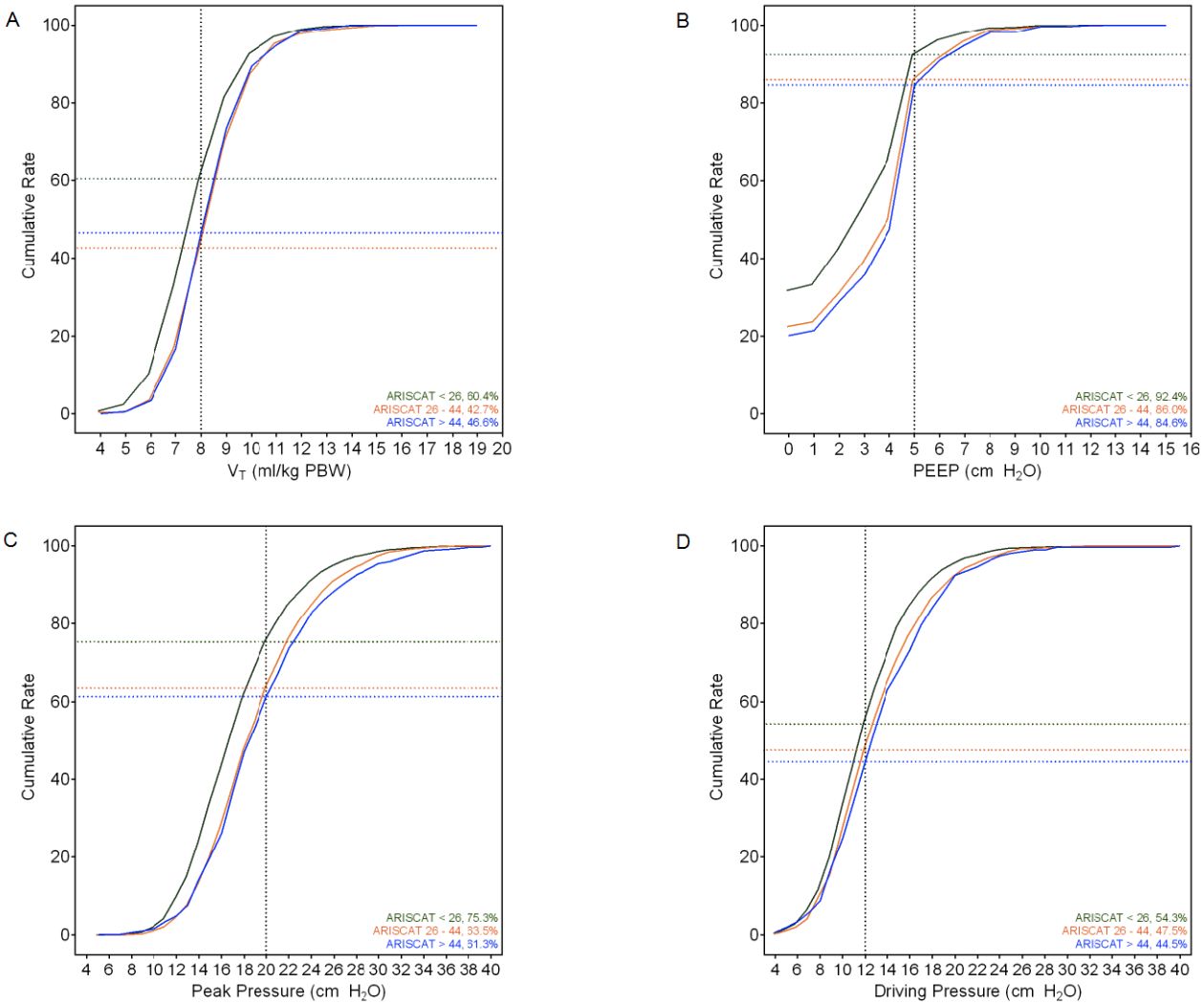
eTable 8. Patient outcomes (ARISCAT low, moderate, high)

	ARISCAT < 26 (*n* = 6743)	ARISCAT 26–44 (*n* = 2215)	ARISCAT > 44 (*n* = 455)	ARISCAT < 26 *vs.* ARISCAT 26–44		ARISCAT < 26 *vs.* ARISCAT > 44	
				Relative Risk (95% CI)	*P* value	Relative Risk (95% CI)	*P* value
Intraoperative events							
Any desaturation	219 / 6736 (3.3)	113 / 2204 (5.1)	37 / 454 (8.1)	1.61 (1.27 – 2.03)	< 0.001	2.64 (1.84 – 3.79)	< 0.001
Unplanned recruitment manoeuvre	171 / 6731 (2.5)	112 / 2204 (5.1)	36 / 453 (7.9)	2.05 (1.61 – 2.62)	< 0.001	3.31 (2.28 – 4.81)	< 0.001
Ventilatory pressure reduction	147 / 6730 (2.2)	93 / 2200 (4.2)	29 / 451 (6.4)	1.98 (1.52 – 2.57)	< 0.001	3.08 (2.04 – 4.64)	< 0.001
Expiratory flow limitation	25 / 6703 (0.4)	19 / 2186 (0.9)	5 / 449 (1.1)	2.34 (1.29 – 4.26)	0.005	3.01 (1.15 – 7.89)	0.025
Hypotension	1594 / 6737 (23.7)	748 / 2206 (33.9)	191 / 453 (42.2)	1.65 (1.49 – 1.84)	< 0.001	2.35 (1.94 – 2.86)	< 0.001
Vaso-active drugs	1246 / 6737 (18.5)	705 / 2206 (32.0)	192 / 453 (42.4)	2.07 (1.86 – 2.31)	< 0.001	3.24 (2.66 – 3.94)	< 0.001
New arrhythmias	24 / 6732 (0.4)	28 / 2204 (1.3)	4 / 453 (0.9)	3.60 (2.08 – 6.22)	< 0.001	2.49 (0.86 – 7.21)	0.092
Postoperative pulmonary complications							
Total PPCs[#]	467 / 6675 (7.0)	385 / 2184 (17.6)	120 / 448 (26.8)	2.84 (2.46 – 3.29)	< 0.001	4.86 (3.87 – 6.12)	< 0.001
Total severe PPCs[##]	104 / 6675 (1.6)	115 / 2184 (5.3)	41 / 448 (9.2)	3.51 (2.68 – 4.60)	< 0.001	6.36 (4.37 – 9.26)	< 0.001
Unplanned supplemental O_2[$]	390 / 6675 (5.8)	315 / 2184 (14.4)	93 / 448 (20.8)	2.72 (2.32 – 3.18)	< 0.001	4.22 (3.29 – 5.42)	< 0.001
Respiratory failure	60 / 6675 (0.9)	70 / 2184 (3.2)	20 / 448 (4.5)	3.65 (2.58 – 5.17)	< 0.001	5.15 (3.08 – 8.63)	< 0.001
Invasive MV	41 / 6675 (0.6)	42 / 2184 (1.9)	19 / 448 (4.2)	3.17 (2.06 – 4.89)	< 0.001	7.17 (4.12 – 12.45)	< 0.001
ARDS	1 / 6675 (0.0)	4 / 2184 (0.2)	4 / 448 (0.9)	12.25 (1.37 – 109.62)	0.025	60.13 (6.71 – 439.07)	< 0.001
Pneumonia	10 / 6675 (0.1)	17 / 2184 (0.8)	11 / 448 (2.5)	5.23 (2.39 – 11.44)	< 0.001	16.78 (7.09 – 39.72)	< 0.001
Pneumothorax	8 / 6675 (0.1)	2 / 2184 (0.1)	2 / 448 (0.4)	0.76 (0.16 – 3.60)	0.733	3.74 (0.79 – 17.65)	0.096
Postoperative outcome							
Hospital Length of Stay	1 (0–3)	4 (1–7)	5 (2–8)	---	---	---	---
In-hospital mortality	13 / 6163 (0.2)	26 / 2034 (1.3)	15 / 411 (3.6)	6.12 (3.14 – 11.94)	< 0.001	17.92 (8.47 – 37.92)	< 0.001
Hospital-free days*	26 (24–27)	23 (21–26)	22 (20–25)	---	---	---	---

All data is presented as proportion, % (n/N) or median (QR); Comparison of differences within a subgroup is performed by using the *t*-test for continuous variables and Chi-square for categorical variables; CI: confidence interval; Low, moderate, versus high risk of PPCs, according to the Assess Respiratory Risk in Surgical Patients in Catalonia risk (ARISCAT) score (< 26, 26 – 44, versus ≥ 45, respectively); Definitions intraoperative events: Any de–saturation: defined as occurrence of SpO_2 < 92%; Unplanned recruitment manoeuvre: ventilation strategies aimed to restore lung aeration; ventilation pressure reduction: ventilation strategies aimed to lower peak and/or plateau pressures; Expiratory flow limitation: defined as expiratory flow higher than zero at end-expiration as suggested by visual analysis of the flow curve; Hypotension: defined as SAP < 90mmHg for 3 min or longer; Need for vaso-active drugs: any vaso-active drug given to correct hypotension; New onset arrhythmias: defined as new onset of atrial fibrillation, sustained ventricular tachycardia, supraventricular tachycardia, and ventricular fibrillation. PPCs: Postoperative pulmonary complications; NIV: non-invasive ventilation by mask or helmet; MV: mechanical ventilation; ARDS: the acute respiratory distress syndrome; LOS: length of hospital stay; PPCs: on day 1 to 5 were scored YES as soon as the event occurred on either ward or intensive care unit; [#]Total PPCs: one patient could present with multiple PPCs, but was scored only once (YES or NO principle); [##]Total severe PPCs: same composite as total PPCs, without unplanned supplemental O_2; [$]unplanned supplementary O_2: supplemental oxygen administered due to PaO_2 < 8 kPa or SpO_2 < 90% in room air, excluding oxygen supplementation given as standard care (e.g. directly after arrival in the PACU; *Hospital-free days when discharged and alive at day 28.

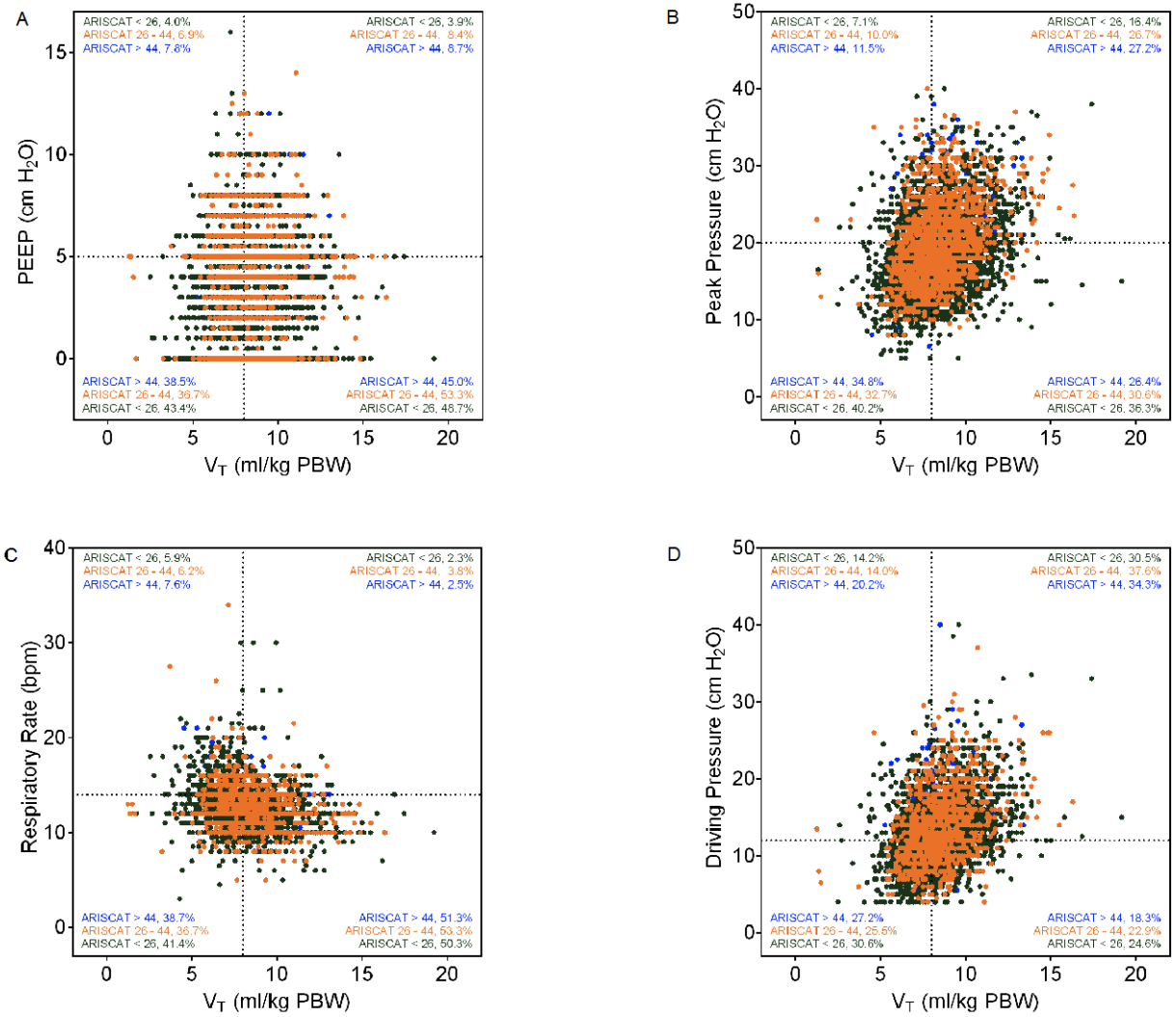
eFigure 1. Ventilation parameters in patients at low, moderate, and high risk of PPC

A) Cumulative frequency distribution of tidal volume; B) cumulative frequency distribution of positive end–expiratory pressure; C) cumulative distribution of peak pressure; D) cumulative distribution of driving pressure. Abbreviations: PPC: postoperative pulmonary complications; PEEP: positive end–expiratory pressure; PBW: predicted body weight; VT: tidal volume



eFigure 2. Scatterplots showing ventilator combinations of patients at low, moderate, high risk of PPC

Scatterplot showing distribution of: A) tidal volume– positive end–expiratory pressure combinations; B) tidal volume– peak pressure; C) tidal volume– respiratory rate; D) tidal volume– driving pressure in patients at low, moderate, and high risk of PPC.
Hourly–collected data were averaged per patient and presented as medians for tidal volume (expressed in mL/kg predicted body weight) and positive end–expiratory pressure (expressed in cm H_2O)
Abbreviations: PPC: postoperative pulmonary complications; VT, tidal volume; PBW, predicted body weight; PEEP, positive end–expiratory pressure, bpm: breaths per minute



References

1. Canet J, Gallart L, Gomar C, et al. Prediction of Postoperative Pulmonary Complications in a Population-based Surgical Cohort. *Anesthesiology* 2010; **113**: 1338-50