The LAS VEGAS risk score for prediction of postoperative pulmonary complications

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The LAS VEGAS risk score for prediction of postoperative pulmonary complications

An observational study

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BACKGROUND Currently used pre-operative prediction scores for postoperative pulmonary complications (PPCs) use patient data and expected surgery characteristics exclusively. However, intra-operative events are also associated with the development of PPCs.

OBJECTIVE We aimed to develop a new prediction score for PPCs that uses both pre-operative and intra-operative data.

DESIGN This is a secondary analysis of the LAS VEGAS study, a large international, multicentre, prospective study.

SETTINGS A total of 146 hospitals across 29 countries.

PATIENTS Adult patients requiring intra-operative ventilation during general anaesthesia for surgery.

INTERVENTIONS The cohort was randomly divided into a development subsample to construct a predictive model, and a subsample for validation.

MAIN OUTCOME MEASURES Prediction performance of developed models for PPCs.

RESULTS Of the 6063 patients analysed, 10.9% developed at least one PPC. Regression modelling identified 13 independent risk factors for PPCs: six patient characteristics [higher age, higher American Society of Anesthesiology (ASA) physical score, pre-operative anaemia, pre-operative lower SpO_2 and a history of active cancer or obstructive sleep apnoea], two procedure-related features (urgent or emergency surgery and surgery lasting $\geq$ 1 h), and five intra-operative events [use of an airway other than a supraglottic device, the use of intravenous anaesthetic agents along with volatile agents (balanced anaesthesia), intra-operative desaturation, higher levels of positive end-expiratory pressures $>$ 3 cmH_2O and use of vasopressors]. The area under the receiver operating characteristic curve of the LAS VEGAS risk score for prediction of PPCs was 0.78 [95% confidence interval (95% CI), 0.76 to 0.80] for the development subsample and 0.72 (95% CI, 0.69 to 0.76) for the validation subsample.

CONCLUSION The LAS VEGAS risk score including 13 peri-operative characteristics has a moderate discriminative ability for prediction of PPCs. External validation is needed before use in clinical practice.

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

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Introduction

An estimated 230 million major surgical procedures are undertaken worldwide each year.[1] Complications after major surgery occur frequently and are an important cause of mortality and morbidity,[2,3] especially when they affect the lungs.[4] Indeed, one in every seven patients who develops a so-called postoperative pulmonary complication (PPC) dies before hospital discharge, and patients who survive often suffer from a sustained reduction in functional status.[1–3] Early identification of patients at risk of developing PPCs could enable the use of preventive measures as well as timely treatment.

The 'Assess Respiratory Risk in Surgical Patients in Catalonia' (ARISCAT) risk score[2] and the 'Surgical Lung Injury Prediction' (SLIP) model[5,6] are two prediction scores used for the identification of patients at risk of developing PPCs or the acute respiratory distress syndrome (ARDS), respectively. Both scores are composed of pre-operative patient characteristics, such as age and the presence of comorbidities, and pre-operative procedure-related features, such as type of surgery and expected duration of the surgical intervention,[2,3,5] but fail to use intra-operative events, such as those related to intra-operative ventilation,[7] and systemic circulation.[8,9] Intra-operative events have also been found to have an association with postoperative outcomes, and incorporation of these in prediction models could thus strengthen predictability.[10]

We sought to develop and validate an improved prediction score, partly based on the above-mentioned ARISCAT prediction score and SLIP model, but using both pre-operative and intra-operative data. For this, we reanalysed the database of the 'Local Assessment of Ventilatory Management During General Anesthesia for Surgery' (LAS VEGAS) study. We hypothesised that the addition of intra-operative data would enhance predictability compared with existing models.

Materials and methods

This manuscript was reported according to the TRIPOD checklist.[11]

Source of data

This is a secondary analysis of the LAS VEGAS study, an international, multicentre, prospective, cross-sectional study that took place in 146 centres worldwide.[12,13] The complete list of planned secondary analyses of LAS VEGAS is available in the Appendix, http://links.lww.com/EJA/A163 and on the PROVENet website (www.provenet.eu). LAS VEGAS was registered at Clinicaltrials.gov (NCT01601223) and was endorsed, and partly funded by the European Society of Anaesthesiology (ESA). The Clinical Trial Network of the ESA assisted in developing the electronic case record forms and hosted the electronic database, but had no influence on study design, study conduct, data analysis and interpretation, nor final reporting.

Ethics

The study protocol was first approved by the ethics committee of the Academic Medical Center, Amsterdam, the Netherlands (W12_190#12.17.0227, approved on 22 August 2012; Chair mw. Dr M.D. Trip) and subsequently in each centre, as requested by national guidelines. Surgical patients were enrolled over a period of 7 consecutive days between 14 January and 4 March 2013.

Participants

Patients who fulfilled the following inclusion criteria were included in the LAS VEGAS study: age more than 18 years, and receiving invasive ventilation during general anaesthesia for elective or nonelective surgery. Patients were excluded if they were scheduled for pregnancy-related surgery, or underwent a surgical procedure outside the operating room. For this secondary analysis, we had the following additional exclusion criteria: surgery involving cardiopulmonary bypass and thoracic surgery or surgery involving one-lung ventilation. In addition, patients who had received ventilation at any time in the previous 30 days were also excluded. Finally, for the present analysis, we considered only patients for whom there were no missing values in the variables of interest.

Data collection

As described in detail elsewhere,[12,13] baseline patient characteristics, including age, sex, weight, height, ASA physical score, functional status and comorbidities, were collected before surgery. During the intra-operative period, ventilator settings, including tidal volume, positive end-expiratory pressure (PEEP) and peak pressure, inspired fraction of oxygen (FiO_2), respiratory rate and recruitment manoeuvres, and hourly-recorded vital signs, including heart rate and blood pressure, pulse oximetry readings and administration of unplanned vasoactive drugs were recorded.

PPCs were observed and recorded daily from the day of surgery (day 0) until discharge from hospital or until postoperative day five, whichever came first. Each adverse pulmonary event was recorded daily, but only counted once in the composite score. Length of hospital stay and in-hospital mortality was determined from patient records at postoperative day 28 as determined in the original protocol, and following common practice.[12,13]

Outcome

The primary endpoint was the development of PPCs during the first five postoperative days. This endpoint was a composite of unplanned supplementary oxygen,

respiratory failure, unplanned new or prolonged invasive mechanical ventilation, ARDS, pneumonia and/or pneumothorax (eTable 1, http://links.lww.com/EJA/A162).

Definitions

The definitions for the following intra-operative events were desaturation, defined as SpO_2 less than 92% for more than 2 min; hypotension, a SBP less than 90 mmHg for 3 min or longer; arrhythmia, new-onset atrial fibrillation, ventricular tachycardia, supraventricular tachycardia or ventricular fibrillation; and vasoactive support, infusion of any unplanned vasoactive drug.

Analysis plan

We divided the sample randomly into two cohorts using a computer algorithm without the influence of the researcher (using the function 'sample' from R, https://www.R-project.org). The development subsample (65% of patients) was used to construct a model, and the validation subsample (35%) was used to confirm its discriminatory capability.

Predictors

Potential predictors of PPCs were any of those used in previous studies on PPCs.[2–6,14,15] The following predictors were considered for the initial multivariable model (after univariable selection as described below): sex, age, BMI, ASA physical score, smoker, functional status, pre-operative anaemia, respiratory infection, pre-operative SpO_2, chronic obstructive pulmonary disease, cancer, chronic kidney disease, heart failure, obstructive sleep apnoea, condition of surgery, duration of surgery, use of supraglottic device, use of epidural anaesthesia, use of antibiotic prophylaxis, total fluid infusion, need for blood transfusion, type of anaesthesia, use of neuromuscular blocking agents, intraoperative desaturation, need for unplanned lung recruitment manoeuvre, intraoperative hypotension, arrhythmia, need of vasoactive drug, use of antagonists to neuromuscular blocking agents, level of PEEP, peak pressure and FiO_2.

Sample size

The reported incidence of PPCs varies between 2.6 and 5.0%.[2,14] We anticipated that to provide a sample of at least 120 PPC-events, the inclusion of at least 4800 patients in 96 centres would be required.[12,13]

Missing

As described above, we considered only patients for whom there were no missing values in the variables of interest.

Statistical analyses

Normally distributed data were described as mean ± standard deviation (SD); non-normally distributed data were reported as median and interquartile range (lower quartile to upper quartile). Categorical variables were reported as proportions (%). According to the distribution of the variables, the continuous variables were compared using independent or paired Student's *t* tests; analysis of variance; Mann–Whitney test; or Kruskal–Wallis test. Categorical variables were compared using Chi-squared or Fisher exact tests.

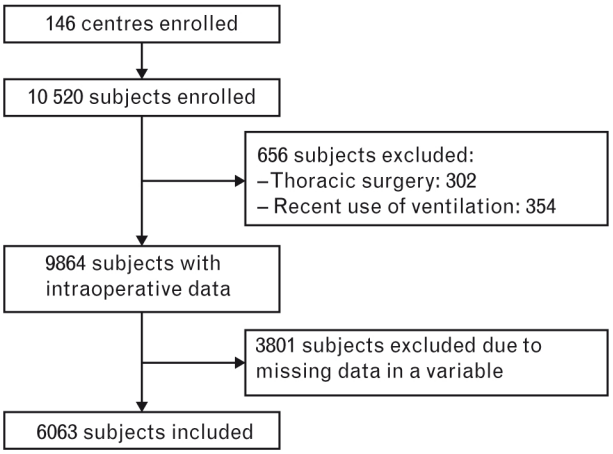
The unadjusted association between the potential predictors and development of PPCs was assessed using multilevel univariable logistic regression models. Variables with *P* value less than 0.2 in this univariable model were selected for inclusion in the multivariable model. The multilevel multivariable logistic regression model was constructed using a backward stepwise selection procedure. Potential predictors were sequentially removed if this exclusion did not result in a significant change in the log-likelihood ratio test. The cutoff for variable removal used a significance level of 0.05. Linearity for each continuous variable was assessed and transformations applied where appropriate. In all multilevel models, the participating centres were treated as a random effect.[16] We then calculated the adjusted odds ratios and the corresponding 95% confidence intervals (95% CIs) values. Calibration was formally assessed by the Hosmer–Lemeshow goodness of fit and by calibration plots.[17]

To avoid overfitting of the data for the development sample, a bootstrap method was used to find the best subset of factors. One thousand computer-generated samples were derived from the development subsample by random-selection with replacement.[18] Within each bootstrap sample, the β coefficient was calculated using all selected independent variables. The reliability of predictor variables in the final regression model was estimated by the 80% CI of the β coefficient in the bootstrap samples. Reliable predictors were expected to be retained if the 80% CI of bootstrap samples indicated statistical significance ($P < 0.05$).

A predictive risk score was then calculated according to the following formula: $P = e^{a+bX} / 1 + e^{a+bX}$, where P is the predictive probability of development of PPCs, *e* is exponential, a is the intercept of the final model, b is the β coefficient of the logistic regression and X is the value of the variable.[16] To assess the discriminative performance of this risk score in both the development and validation subsamples, we used the c-statistic, which was also displayed graphically as the area under the receiver operating characteristic (ROC) curve. An area under the ROC curve (AUC) of 0.5 indicates no discrimination, whereas an AUC of 1.0 indicates perfect discrimination. The area under the ROC of the LAS VEGAS score and the area under the ROC of the ARISCAT score were compared. A *P* value less than 0.05 means that the area under the ROC curves differ significantly.[19]

To increase the readiness of the score, we recalculated the final model with the continuous variables categorised

Fig. 1



Flowchart of inclusion.

according to their tertiles or based on previous cut-offs.[1,5,14,15] Then, a simplified predictive risk score was calculated by multiplying each logistic β coefficient of regression by 10 and rounding off its value. The simplified score for development subsample cases were added together to produce an overall PPCs risk score for each patient. To evaluate the ability of the model to predict increasing rates of PPCs, we used that score and the minimum description length principle to divide the subsample into three ranges reflecting low, medium, and high risk for PPCs, each containing a similar number of patients with a PPC.

In another posthoc analysis, we tested the ability of the score in predicting severe PPCs (i.e. excluding 'unplanned supplementary oxygen'). Finally, we also tested the predictive ability of the score after removing PEEP from it.

All analyses were conducted with R v.3.3.2 (http://www.R-project.org). For all analyses, two-sided *P* values less than 0.05 were considered significant.

Results

Participants

Of the 10 520 patients enroled in 146 centres, 6063 patients were included in the present analyses (Fig. 1 and Table 1). Patients who developed one or more PPCs had a higher in-hospital mortality (3.2 vs. 0.3%; $P < 0.001$) and longer hospital length of stay (4 [1 to 5] vs. 2 [0 to 4]; $P < 0.001$). There was no difference between the cohort of patients who entered the final analysis and the cohort of patients excluded due to missing values of interest (eTable 2, http://links.lww.com/EJA/A162). The development and validation subsample were comparable with regard to case-mix and occurrence of PPCs (eTable 3 and eTable 4, http://links.lww.com/EJA/A162).

Model development, validation, specification and performance

The results of the univariable logistic regression are summarised in eTable 5, http://links.lww.com/EJA/A162. Multivariable adjustment showed six patient characteristics [higher age, higher ASA physical score, pre-operative anaemia, pre-operative lower SpO_2 and a history of active cancer or obstructive sleep apnoea, two procedure-related features (urgent/emergency surgery and longer duration of surgery) and five intra-operative events [use of an airway other than a supraglottic device, the use of intravenous anaesthetic agents along with volatile agents (balanced anaesthesia), intra-operative desaturation, higher levels of PEEP and use of vasopressors] to have an independent association with occurrence of PPCs (Table 2). Bootstrap validation indicated that all 13 factors were present in more than 80% of bootstrap samples and thus all were kept in the final model (eTable 6, http://links.lww.com/EJA/A162). The Hosmer–Lemeshow statistic was 6.626 ($P = 0.578$). The c-statistic of the model was 0.781 (95% CI, 0.758 to 0.804; $P < 0.001$) in the development cohort (Fig. 2a). In the validation cohort, the c-statistic was 0.724 (95% CI, 0.690 to 0.757; $P < 0.001$) and Hosmer–Lemeshow was 11.388 ($P = 0.181$) (Fig. 2a). The Brier score for the model in the validation cohort is 0.093. Calibration plots are shown in Fig. 2b and c. Considering the overall cohort, the LAS VEGAS score performed better than the ARISCAT score: AUC for LAS VEGAS score was 0.757 [95% CI, 0.746 to 0.776) vs. AUC for ARISCAT score 0.700 (95% CI, 0.678 to 0.711), $P < 0.001$] (Fig. 2d).

LAS VEGAS risk score for postoperative pulmonary complications

The simplified risk score is summarised in Table 3. The ROC curves for the simplified score in the development

Table 1 Characteristics of the included patients

	Development cohort ($n = 3919$)	Validation cohort ($n = 2144$)	P
Demographic characteristics			
Age (years)	54 [41 to 67]	55 [40 to 66]	0.581
Gender, male	1778/3919 (45.4)	931/2144 (43.4)	0.145
BMI (kg m^{-2})	26.3 [23.3 to 29.9]	26.2 [23.4 to 30.0]	0.601
ASA PS	2 [1 to 2]	2 [1 to 2]	0.210
1	1058 / 3919 (27.0)	613 / 2144 (28.6)	
2	1954 / 3919 (49.9)	1046 / 2144 (48.8)	
3	826 / 3919 (21.1)	459 / 2144 (21.4)	0.087
4	80 / 3919 (2.0)	24 / 2144 (1.1)	
5	1 / 3919 (0.0)	2 / 2144 (0.1)	
Functional status			
Independent	3629 / 3919 (92.6)	1999 / 2144 (93.2)	
Partially dependent	241 / 3919 (6.1)	127 / 2144 (5.9)	0.318
Totally dependent	49 / 3919 (1.3)	18 / 2144 (0.8)	
ARISCAT score	16 [3 to 26]	15 [3 to 26]	0.818
< 26	2772 / 3919 (70.7)	1530 / 2144 (71.4)	
26–44	938 / 3919 (23.9)	510 / 2144 (23.8)	0.700
> 44	209 / 3919 (5.3)	104 / 2144 (4.9)	
Smoking	930 / 3919 (23.7)	495 / 2144 (23.1)	0.572
Preoperative SpO_2, %	98 [96 to 99]	98 [96 to 99]	0.448
Preoperative anaemia[a]	129 / 3919 (3.3)	79 / 2144 (3.7)	0.421
Respiratory infection < 30 days	157 / 3919 (4.0)	96 / 2144 (4.5)	0.380
Comorbidities			
Cancer	195 / 3919 (5.0)	92 / 2144 (4.3)	0.230
Chronic kidney failure	141 / 3919 (3.6)	71 / 2144 (3.3)	0.561
COPD	259 / 3919 (6.6)	123 / 2144 (5.7)	0.181
Heart failure	249 / 3919 (6.4)	144 / 2144 (6.7)	0.583
Obstructive sleep apnoea	76 / 3919 (1.9)	41 / 2144 (1.9)	0.941
Neuromuscular disease[b]	41 / 3919 (1.0)	15 / 2144 (0.7)	0.177
Liver dysfunction	46 / 3919 (1.2)	22 / 2144 (1.0)	0.601
Surgical characteristics			
Surgical procedure[b]			
Lower gastrointestinal	470 / 3919 (12.0)	225 / 2144 (10.5)	0.079
Upper GI, HB and pancreas	567 / 3919 (14.5)	337 / 2144 (15.7)	0.191
Vascular surgery[d]	121 / 3919 (3.1)	98 / 2144 (4.6)	0.003
Aortic surgery	27 / 3919 (0.7)	24 / 2144 (1.1)	0.079
Neurosurgery and HN	739 / 3919 (18.9)	398 / 2144 (18.6)	0.779
Urological and kidney	382 / 3919 (9.7)	177 / 2144 (8.3)	0.055
Gynaecological	435 / 3919 (11.1)	251 / 2144 (11.7)	0.475
Endocrine	99 / 3919 (2.5)	48 / 2144 (2.2)	0.486
Transplant	19 / 3919 (0.5)	9 / 2144 (0.4)	0.721
Plastic, cutaneous, breast	436 / 3919 (11.1)	227 / 2144 (10.6)	0.521
Bone, joint, trauma, spine	603 / 3919 (15.4)	336 / 2144 (15.7)	0.769
Others	204 / 3919 (5.2)	140 / 2144 (6.5)	0.033
Surgical technique[c]			
Open	765 / 3919 (19.5)	426 / 2144 (19.9)	0.743
Laparoscopic	742 / 3919 (18.9)	376 / 2144 (17.5)	0.180
Laparoscopic assisted	74 / 3919 (1.9)	40 / 2144 (1.9)	0.950
Peripheral	661 / 3919 (16.9)	402 / 2144 (18.8)	0.065
Other	1709 / 3919 (43.6)	915 / 2144 (42.7)	0.484
Condition of surgery			
Elective	3513 / 3919 (89.6)	1919 / 2144 (89.5)	
Urgent	319 / 3919 (8.1)	176 / 2144 (8.2)	0.981
Emergency	87 / 3919 (2.2)	49 / 2144 (2.3)	
Duration of surgery (min)	77 [47 to 130]	75 [45 to 130]	0.420
Duration of anaesthesia (min)	107 [74 to 169]	105 [70 to 170]	0.405
Intraoperative characteristics			
Use of supraglottic devices	507 / 3919 (12.9)	298 / 2144 (13.9)	0.291
Epidural anaesthesia	230 / 3919 (5.9)	122 / 2144 (5.7)	0.776
Fluid infused (ml)	1000 [1000 to 1900]	1000 [900 to 2000]	0.139
Blood transfusion	161 / 3919 (4.1)	79 / 2144 (3.7)	0.418
Use of opioid	3902 / 3919 (99.6)	2128 / 2144 (99.3)	0.113
Type of anaesthesia			0.889
Totally intravenous	531 / 3919 (13.5)	282 / 2144 (13.2)	
Volatile	2763 / 3919 (70.5)	1523 / 2144 (71.0)	
Balanced	625 / 3919 (15.9)	339 / 2144 (15.8)	
Use of NMBA	3431 / 3919 (87.5)	1878 / 2144 (87.6)	0.959
Desaturation	146 / 3919 (3.7)	85 / 2144 (4.0)	0.641
Unplanned recruitment manoeuvre	140 / 3919 (3.6)	68 / 2144 (3.2)	0.412

Table 1 (*continued*)

	Development cohort ($n = 3919$)	Validation cohort ($n = 2144$)	P
Hypotension	1050 / 3919 (26.8)	524 / 2144 (24.4)	0.045
Arrhythmia	26 / 3919 (0.7)	12 / 2144 (0.6)	0.624
Need of vasoactive drugs	881 / 3919 (22.5)	443 / 2144 (20.7)	0.101
Reversal of NMBA	1584 / 3919 (40.4)	851 / 2144 (39.7)	0.581
Antibiotic prophylaxis	2800 / 3919 (71.4)	1524 / 2144 (71.1)	0.764
Mechanical ventilation characteristics			
Tidal volume (ml/kg PBW)	8.2 [7.3 to 9.2]	8.2 [7.4 to 9.1]	0.426
PEEP (cmH_2O)	4 [0 to 5]	3 [0 to 5]	0.933
Peak pressure (cmH_2O)	17 [15 to 21]	17 [15 to 21]	0.610
FiO_2	0.50 [0.45 to 0.70]	0.50 [0.45 to 0.70]	0.952
Respiratory rate, bpm	12 [12 to 13]	12 [12 to 13]	0.599
Clinical outcomes			
PPC	419 / 3919 (10.7)	246 / 2144 (11.5)	0.351
Hospital length of stay (days)	2 [1 to 4]	2 [1 to 4]	0.937
In-hospital mortality	23 / 3649 (0.6)	9 / 1986 (0.5)	0.397

Data are median [interquartile range] and No./Total (%). ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia risk; ASA PS, American Society of Anaesthesiology physical score; BPM, breaths per minute; COPD, chronic obstructive pulmonary disease; FiO_2, inspired fraction of oxygen; GI, gastrointestinal; HB, hepatobiliary; HN, head and neck; LQ, lower quartile; NMBA, neuromuscular blocking agents; PBW, predicted body weight; PEEP, positive end-expiratory pressure; PPC, postoperative pulmonary complication; SpO_2, peripheral oxygen saturation; UQ, upper quartile. [a] Defined as haemoglobin $< 10\ g\ dl^{-1}$. [b] Neuromuscular disease affecting the respiratory system. [c] A patient can have more than one type of surgical procedure or technique. [d] Carotid endarterectomy, aortic surgery and peripheral vascular taken together.

and in the validation cohort is shown in Fig. 3a. In the development cohort, the c-statistic was 0.778 (95% CI, 0.755 to 0.801; $P < 0.001$), and in the validation cohort, it was 0.703 (95% CI, 0.667 to 0.739; $P < 0.001$) (Fig. 3a). Considering the overall cohort, the simplified score performed better than the ARISCAT score: AUC for LAS VEGAS score: 0.750 (95% CI, 0.731 to 0.770) vs. AUC for ARISCAT score 0.700 (95% CI, 0.678 to 0.711), $P < 0.001$ (Fig. 3b). Categorisation using cutoffs of 7 and 17 produced three groups with clearly different incidences of PPCs (Fig. 4).

Table 2 Multivariable logistic regression of risk factor for postoperative pulmonary complications in the development cohort

	β coefficient	Odds ratio (95% CI)	P
Demographic characteristics			
Age (years)	0.012	1.01 (1.00 to 1.02)	0.004
ASA PS	0.290	1.34 (1.12 to 1.59)	0.001
Preoperative anaemia	0.572	1.77 (1.10 to 2.85)	0.018
Preoperative SpO_2	−0.057	0.94 (0.90 to 0.99)	0.021
Cancer	0.544	1.72 (1.18 to 2.52)	0.005
Obstructive sleep apnoea	0.917	2.50 (1.40 to 4.47)	0.002
Surgical characteristics			
Condition of surgery			
Elective	1 (Reference)	1 (Reference)	
Urgency	0.769	2.16 (1.54 to 3.02)	< 0.001
Emergency	0.941	2.56 (1.43 to 4.59)	0.002
Duration of surgery (min)	0.005	1.00 (1.00 to 1.01)	< 0.001
Intra-operative characteristics			
Use of supraglottic device	−0.653	0.52 (0.31 to 0.86)	0.011
Type of anaesthesia			
Totally intravenous	1 (Reference)	1 (Reference)	
Volatile	0.002	1.00 (0.71 to 1.41)	0.992
Balanced	0.590	1.80 (1.20 to 2.70)	0.004
Desaturation	1.101	3.01 (1.99 to 4.54)	< 0.001
Need of vasoactive drug	0.405	1.50 (1.17 to 1.92)	0.002
Mechanical ventilation characteristics			
PEEP (cmH_2O)	0.078	1.08 (1.03 to 1.13)	0.002

c-index (95% CI): 0.781 (0.758 to 0.804) ($P < 0.001$). Hosmer–Lemeshow Chi-square test: 6.626 ($P = 0.578$). ASA PS, American Society of Anaesthesiology physical score; CI, confidence interval; PEEP, positive end-expiratory pressure; SpO_2, peripheral oxygen saturation.

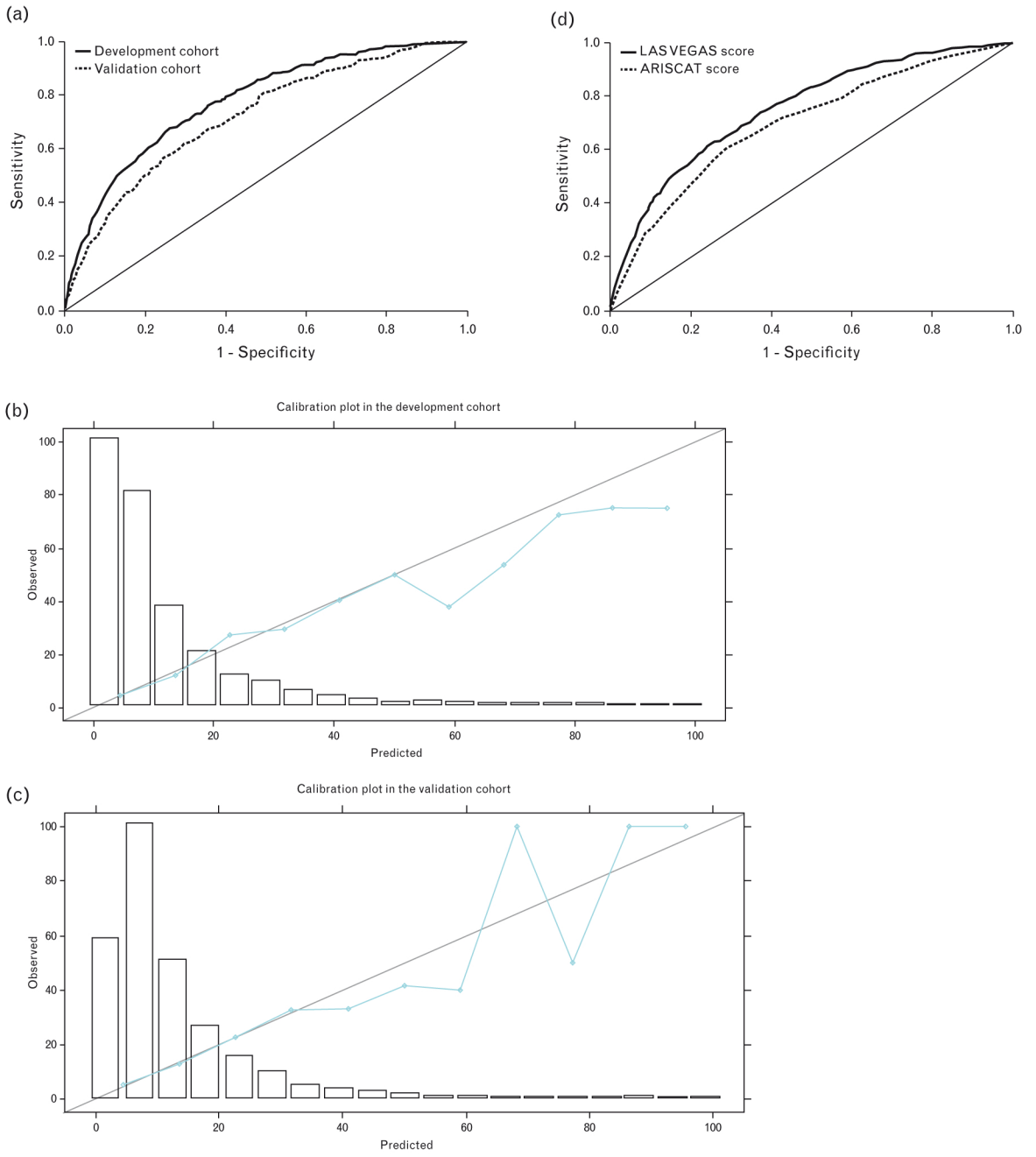
The performance of the LAS VEGAS risk score in predicting severe PPCs when using the β coefficients as well as when using the simplified score is shown in eFigure 1, http://links.lww.com/EJA/A162. Categorisation using the same cutoffs as described above again produced three groups with clearly different incidences (eFigure 2, http://links.lww.com/EJA/A162). In all these analyses, the LAS VEGAS risk score performed better than the ARISCAT score (eFigure 1, http://links.lww.com/EJA/A162). Finally, the removal of PEEP from the model did not change the c-statistics: 0.721 (95% CI, 0.688 to 0.754) without PEEP vs. 0.724 (0.690 to 0.757) with PEEP, $P = 0.530$ (eFigure 3, http://links.lww.com/EJA/A162).

Discussion

In this secondary analysis of the LAS VEGAS study, 13 easily collected peri-operative characteristics had an independent association with the development of PPCs. The combination of these peri-operative characteristics into a predictive score resulted in a score with moderate discriminative power for identifying patients at risk of a PPC, as indicated by the AUC of the ROC curve.

The finding that age was an independent predictor of PPCs is in line with the existing literature.[2,3,20–22] The ASA physical score was also a predictor of PPCs. In fact, the ASA physical score reflects comorbidity and functional capacity of patients and PPCs are related to target organ dysfunctions and the general health of patients.[2,14,15] However, in a recent study, the ASA physical score by itself did not perform well in predicting PPCs after renal transplant.[23] The association between pre-operative anaemia and the development of PPCs was previously shown in the ARISCAT score, as the

Fig. 2



(a) Receiver operating characteristic (ROC) curve using β coefficients; (b) calibration plot in the development cohort; (c) calibration plot in the validation cohort; (d) comparison of the ROC curves of LAS VEGAS score and ARISCAT score in the overall cohort.

association between pre-operative low SpO_2 measurements and PPCs.[2,3] A low SpO_2 in room air may reflect a poor baseline cardiopulmonary status.[2,3,5] Finally, the association between duration of surgery and the development of PPCs was also in accordance with the findings from ARISCAT.[2] In the present analysis, unlike ARISCAT, the actual and not the predicted duration of surgery was used as a risk factor.

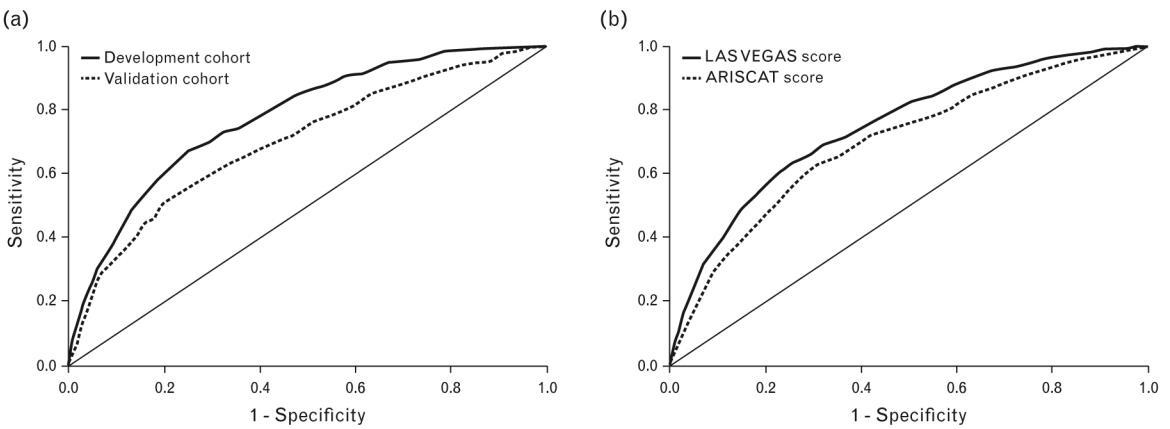
Obstructive sleep apnoea showed an important risk association with PPCs, which has not been shown before, but a recent investigation suggested that postoperative complications occurred at a higher rate in obstructive sleep apnoea patients who underwent hip or knee replacement.[24] Such a finding could be explained partially by the combined effects of anaesthetic agents, sedatives and narcotics, which relax upper airway muscles and increase

Table 3 Multivariable logistic regression of risk factor for postoperative pulmonary complications in the development cohort (simplified risk score)

	β coefficient	Odds ratio (95% CI)	Risk score[a]
Demographic characteristics			
Age (years)			
≤ 46	1 (Reference)	1 (Reference)	
47–67	0.291	1.34 (0.99 to 1.81)	3
≥ 68	0.407	1.50 (1.07 to 2.11)	4
ASA PS			
< 3	1 (Reference)	1 (Reference)	
≥ 3	0.644	1.90 (1.49 to 2.44)	6
Preoperative anaemia	0.483	1.62 (1.01 to 2.59)	5
Preoperative SpO_2			
> 96	1 (Reference)	1 (Reference)	
≤ 96	0.249	1.28 (1.01 to 1.62)	2
Cancer	0.538	1.71 (1.17 to 2.50)	5
Obstructive sleep apnoea	0.900	2.46 (1.38 to 4.39)	9
Surgical characteristics			
Condition of surgery			
Elective	1 (Reference)	1 (Reference)	
Urgency	0.760	2.14 (1.53 to 2.98)	8
Emergency	0.943	2.57 (1.45 to 4.55)	9
Duration of surgery (min)			
≤ 55	1 (Reference)	1 (Reference)	
56–134	0.390	1.48 (1.08 to 2.01)	4
≥ 135	1.121	3.07 (2.23 to 4.21)	11
Intra-operative characteristics			
Use of supraglottic device	−0.644	0.525 (0.31 to 0.87)	−6
Type of anaesthesia			
Totally intravenous	1 (Reference)	1 (Reference)	
Volatile	−0.010	0.99 (0.70 to 1.40)	0
Balanced	0.535	1.71 (1.14 to 2.56)	5
Desaturation	1.229	3.42 (2.29 to 5.10)	12
Need of vasoactive drug	0.473	1.60 (1.25 to 2.05)	5
Mechanical ventilation characteristics			
PEEP (cmH_2O)			
≤ 2	1 (Reference)	1 (Reference)	
3–4	0.358	1.43 (1.05 to 1.95)	3
≥ 5	0.400	1.49 (1.14 to 1.96)	4

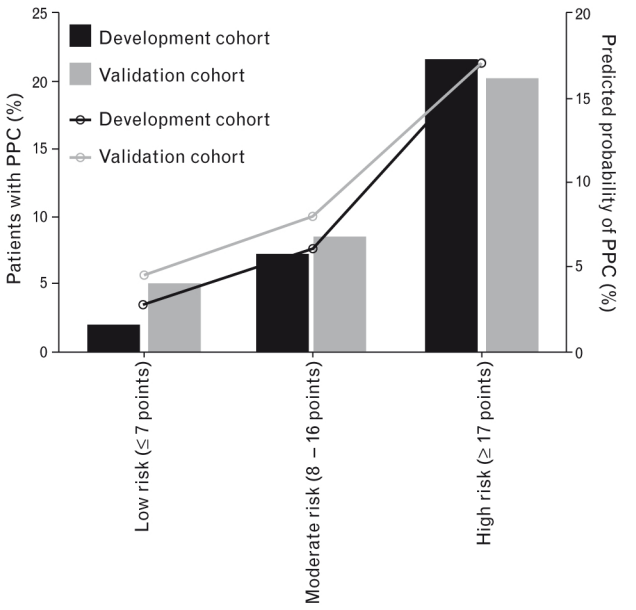
ASA PS, American Society of Anaesthesiology physical score; CI, confidence interval; PEEP, positive end-expiratory pressure; SpO_2, peripheral oxygen saturation. [a]The simplified risk score was the sum of each β logistic regression coefficient multiplied by 10, after rounding off its value.c-index (95% CI): 0.778 (0.755 to 0.801) ($P < 0.001$).Hosmer–Lemeshow Chi-square test: 15.414 ($P = 0.052$).

Fig. 3



(a) Receiver operating characteristic (ROC) curve using the simplified score; (b) comparison of the ROC curves of simplified LAS VEGAS score and ARISCAT score in the overall cohort.

Fig. 4



Incidence and predicted probability of PPCs according to cut-offs of simplified LAS VEGAS risk score. Low risk, ≤ 7; moderate risk, 8–16; and high risk, ≥ 17. PPCs, postoperative pulmonary complications.

upper airway resistance, thus aggravating the effects of obstructive sleep apnoea.[25] Also of interest, a history of active cancer increased the risk of PPCs. The reasons for this are not entirely clear. It may be the result of some disease process that is more frequent in cancer patients, such as pulmonary dysfunction due to mass effects, pleural effusions or metastasis, immunosuppression or general frailty.[26]

The association between intra-operative desaturations and development of PPCs could reflect higher pulmonary instability during intra-operative ventilation, most likely the occurrence of atelectasis and airway closure, and a consequent decrease in functional residual capacity. The association between intra-operative use of vasoactive drugs and development of PPCs could be the effect of more intensive mechanical ventilation strategies, for example the use of higher PEEP and recruitment manoeuvres, leading to a reduction in venous return, low cardiac output and hypotension.[27,28] Another possible explanation is systemic inflammation leading to hypotension with subsequent organ dysfunction, including pulmonary dysfunction.[29]

The association between the use of supraglottic devices and PPCs may be due to the fact that these devices are used more frequently for patients who are considered to be more stable during surgery with a lower risk of perioperative complications,[13,30] and for less complex or shorter-lasting surgical procedures.[30] The same is true for PEEP, where its impact could be explained by the use of higher levels in more severely ill patients and in more complex situations. In addition, the relatively small range of PEEP used here may not reflect substantial physiological effects. Taken together, the data do not support the idea that a prospective general use of lower PEEP, especially in patients with the potential to benefit from it, will reduce the incidence of PPCs. Also, it should be noted that the level of PEEP used may not be a matter of perceived clinical risk or problems in gas exchange, but rather it is a general concept within a specific department. In line with this, the addition of the PEEP level to the model had no effect. Indeed, the area under the ROC-curves are close to identical. It is important to emphasise that some studies suggest a beneficial impact of PEEP in patients undergoing abdominal surgery[31,32]; nevertheless, more evidence is needed to confirm the impact of PEEP in this group of patients.

Notably, the LAS VEGAS risk score performed better than the highly regarded ARISCAT risk score. But it is important to understand the possible reasons for the lower predictive performance of the ARISCAT score in the present study compared with the original description and validation. Previous evaluations suggested that the score performs better in Western compared with Eastern countries, and better in Spain than in the rest of Europe.[2,3] We speculate that as several centres in the LAS VEGAS were outside Europe, average surgical and anaesthetic practice may have differed slightly from the very first cohort. Also, the ARISCAT score seems to have a better predictive value for higher risk patients, but in the LAS VEGAS study, patients at lower risk of complications formed the majority. However, the moderate performance of our score suggests it is useful for screening in this heterogeneous patient population, independent from geographic distributions. Although several factors included in the ARISCAT risk score were also included in the LAS VEGAS risk score, the addition of some important factors, including intra-operative complications and obstructive sleep apnoea, had a significant impact on the final score and this could explain its better performance. Moreover, for the development of the LAS VEGAS risk score, a larger number of patients, and consequently a larger number of events, was used than for the development of the ARISCAT risk score. Overfitting the model was thus less likely, decreasing the chance of underestimation in the probability of events in low-risk patients, and overestimation in high risk patients.[33] However, it is important to note that the ARISCAT risk score is a pre-operative score, while the LAS VEGAS risk score also considered intra-operative variables. Indeed, the ability of a score to predict an event is higher when you are closer to the event.[34] Other available pre-operative scores, such as the 'Predictors of Respiratory Insufficiency and Mortality (PRIM)' and the 'Score for Prediction of Postoperative Respiratory Complications (SPORC)',[35,36] were not addressed in the

present article. Nevertheless, the PRIM score has a good discriminative ability to predict the need for mechanical ventilation and in-hospital mortality in patients with acute cervical spine injury,[35] and the SPORC also has a good discriminative power to predict PPCs in patients undergoing surgery.[36]

It is important to emphasise that the LAS VEGAS risk score should always be used in its total form and not be used to consider the impact of only one or two variables. For example, one should not focus on PEEP as a predictor of PPCs, once it is included in an analysis involving several other factors. The weight and relative importance of each factor in the final score was calculated in the presence of other factors, so it is of importance always to consider the whole score and not individual components.

The strengths of this analysis lie in the use of data from a broad surgical population in a prospective, international multicentre study. A fully representative target population extract was used, and a robust multivariable logistic regression method was applied allowing an appropriate validation in the present cohort.

Nevertheless, the present study has a number of limitations. First, the willingness of participating centres to join the study may have caused a selection bias. Second, any prospective observational study can interfere with daily practice. Third, there is always a possibility of unknown confounding factors. Fourth, we had no restriction on the number of centres per country, and this resulted in overrepresentation of some countries. Fifth, it is possible that additional variables that improve the prediction may be identified in future studies and need to be added to the LAS VEGAS risk score. Sixth, it is important to note that our definition of PPCs differs from that used in other studies.[2,3,23] We chose to follow the approach of most PPCs studies to date, in which risk is established for a composite outcome, and that composite outcome can be attained by the presence of one or several of the list of complications. Seventh, the discriminative power was moderate. Finally, despite the use of advanced statistical methods, observational data typically cannot elicit complex aetiological relationships.

Conclusion

The LAS VEGAS score is a simple risk score, with moderate discriminative performance, for predicting PPCs and is based on 13 easy to capture peri-operative characteristics. It could be useful for identifying individual patients at a high risk of PPCs, and in the design of future trials to assess interventions to prevent these complications. However, external validation is still needed to confirm the accuracy of the score.

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The LAS VEGAS study collaborators are listed in the Supplemental digital content, http://links.lww.com/EJA/A163.

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