BJA

British Journal of Anaesthesia, 122 (3): 361–369 (2019)

doi: 10.1016/j.bja.2018.10.063
Advance Access Publication Date: 8 February 2019
Quality and Patient Safety

QUALITY AND PATIENT SAFETY

Association between night-time surgery and occurrence of intraoperative adverse events and postoperative pulmonary complications

A. Cortegiani[1,*], C. Gregoretti[1], A. S. Neto[2,3], S. N. T. Hemmes[2,4], L. Ball[5,6], J. Canet[7], M. Hiesmayr[8], M. W. Hollmann[4], G. H. Mills[9], M. F. V. Melo[10], C. Putensen[11], W. Schmid[8], P. Severgnini[12], H. Wrigge[13], M. Gama de Abreu[14], M. J. Schultz[2,15], P. Pelosi[5,6] for the LAS VEGAS Investigators, the PROVE Network, and the Clinical Trial Network of the European Society of Anaesthesiology[†,‡,¶]

[1]Department of Surgical, Oncological and Oral Science, Section of Anesthesia, Analgesia, Intensive Care and Emergency, Policlinico Paolo Giaccone, University of Palermo, Palermo, Italy, [2]Department of Intensive Care and Laboratory of Experimental Intensive Care and Anesthesia, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands, [3]Department of Critical Care Medicine, Hospital Israelita Albert Einstein, São Paulo, Brazil, [4]Department of Anaesthesiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands, [5]Dipartimento di Scienze Chirurgiche e Diagnostiche Integrate, Università degli Studi di Genova, Genova, Italy, [6]IRCCS Ospedale Policlinico San Martino, Genova, Italy, [7]Department of Anesthesiology and Postoperative Care, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, [8]Division of Cardiac, Thoracic, Vascular Anesthesia and Intensive Care, Medical University of Vienna, Vienna, Austria, [9]Operating Services, Critical Care and Anesthesia, Sheffield Teaching Hospitals, Sheffield and University of Sheffield, Sheffield, UK, [10]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, USA, [11]Department of Anesthesiology and Intensive Care Medicine, University Hospital Bonn, Bonn, Germany, [12]Department of Biotechnology and Sciences of Life, ASST Sette Laghi Ospedale di Circolo e Fondazione Macchi, University of Insubria, Varese, Italy, [13]Department of Anesthesiology and Intensive Care Medicine, University of Leipzig, Leipzig, Germany, [14]Department of Anaesthesiology and Intensive Care Medicine, Pulmonary Engineering Group, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany and [15]Mahidol Oxford Tropical Medicine Research Unit, Mahidol University, Bangkok, Thailand

*Corresponding author. E-mail: andrea.cortegiani@unipa.it

[†]'Local ASsessment of VEntilatory management during General Anaesthesia for Surgery' study.
[‡]Collaborators are listed in the online Supplementary material.
[¶]PROtective VEntilation Network (www.provenet.eu).

Editorial decision:; **Accepted:** 28 October 2018

Abstract

Background: The aim of this *post hoc* analysis of a large cohort study was to evaluate the association between night-time surgery and the occurrence of intraoperative adverse events (AEs) and postoperative pulmonary complications (PPCs).
Methods: LAS VEGAS (Local Assessment of Ventilatory Management During General Anesthesia for Surgery) was a prospective international 1-week study that enrolled adult patients undergoing surgical procedures with general anaesthesia and mechanical ventilation in 146 hospitals across 29 countries. Surgeries were defined as occurring during 'daytime' when induction of anaesthesia was between 8:00 AM and 7:59 PM, and as 'night-time' when induction was between 8:00 PM and 7:59 AM.
Results: Of 9861 included patients, 555 (5.6%) underwent surgery during night-time. The proportion of patients who developed intraoperative AEs was higher during night-time surgery in unmatched (43.6% *vs* 34.1%; $P<0.001$) and propensity-matched analyses (43.7% *vs* 36.8%; $P=0.029$). PPCs also occurred more often in patients who underwent night-time surgery (14% *vs* 10%; $P=0.004$) in an unmatched cohort analysis, although not in a propensity-matched analysis (13.8% *vs* 11.8%; $P=0.39$). In a multivariable regression model, including patient characteristics and types of surgery and anaesthesia, night-time surgery was independently associated with a higher incidence of intraoperative AEs (odds ratio: 1.44; 95% confidence interval: 1.09–1.90; $P=0.01$), but not with a higher incidence of PPCs (odds ratio: 1.32; 95% confidence interval: 0.89–1.90; $P=0.15$).
Conclusions: Intraoperative adverse events and postoperative pulmonary complications occurred more often in patients undergoing night-time surgery. Imbalances in patients' clinical characteristics, types of surgery, and intraoperative management at night-time partially explained the higher incidence of postoperative pulmonary complications, but not the higher incidence of adverse events.
Clinical trial registration: NCT01601223.

Keywords: general anaesthesia; intraoperative complications; patient safety; postoperative complications; pulmonary

Editor's key points

- There is concern that adverse events and complications occur more frequently with night-time surgery. This is relevant because elective surgeries are often undertaken at night.
- This secondary analysis of a multicentre international cohort study evaluated whether intraoperative adverse events and postoperative pulmonary complications were more common with night-time surgery.
- Without adjusting for confounders, there were significantly more intraoperative adverse events and postoperative pulmonary complications with night-time surgery. With adjustment, the significant risk for intraoperative adverse events remained.
- This study provides suggestive evidence that surgery at night is associated with intraoperative adverse events, and weak evidence regarding postoperative pulmonary complications.

The evidence is conflicting regarding the potential effect of the timing of surgery during a 24-h day on the occurrence of intraoperative adverse events (AEs) and postoperative outcomes.[1–6] For instance, the performance of a surgical team during night-time could be affected by human factors, including mental or physical fatigue, and reduced alertness. These factors may increase the risk of AEs and complications.[7–11] Furthermore, fewer healthcare workers, clinicians with less experience, and worse early postoperative care might all compromise quality with night-time surgeries. At night, there may be lower adherence to 'best practices' and guidelines, potentially leading to a higher incidence of perioperative AEs.[3–5,12] Postoperative pulmonary complications (PPCs) are common, and are associated with subsequent morbidity and mortality.[13,14] The occurrence of intraoperative AEs and PPCs is likely to be determined by patients' characteristics, type of surgery, and intraoperative events.[15,16]

It is currently unknown whether or not the timing of surgery during the 24-h day has an effect on the incidence of intraoperative AEs and PPCs. This study aimed to provide descriptive statistics on intraoperative AEs and PPCs, and to assess the association between these and the timing of surgery. We analysed data from the Local Assessment of Ventilatory Management During General Anesthesia for Surgery (LAS VEGAS) study cohort.[17] (The LAS VEGAS study network collaborators are listed in Supplementary Appendix A.) We hypothesised that the occurrence of intraoperative AEs and PPCs is increased with night-time surgery.

Methods

This was a *post hoc* analysis of data from the LAS VEGAS study, a prospective observational international 1 week study designed to describe ventilation practices in operating rooms, and the incidence of intraoperative AEs and PPCs.[17]

Cohort description

The study enrolled adult patients requiring intraoperative ventilation (via either a tracheal tube or supraglottic device) during general anaesthesia for either elective or non-elective surgery (excluding thoracic surgery) in 146 hospitals across 29 countries over a period of 7 days. Exclusion criteria were age less than 18 yr, pregnancy-related surgery, surgical procedures outside the operating room, and procedures involving cardiopulmonary bypass.

Coding of surgery timing

For the purpose of this *post hoc* analysis, we categorised the timing of surgery according to the start of anaesthesia registered in the LAS VEGAS case report form. Procedures with induction of anaesthesia between 8:00 AM and 7:59 PM were coded as 'daytime' surgeries, and those with induction between 8:00 PM and 7:59 AM were coded as 'night-time' surgeries.

Outcomes definition and data reporting

The primary outcomes of this *post hoc* analysis were the incidence of a composite of intraoperative AEs and the incidence of a composite of PPCs.

Intraoperative AEs included (i) desaturation (SpO_2 <92% for more than 2 min); (ii) need for unplanned lung recruitment manoeuvres (defined as ventilator strategies aimed to restore aeration of the lungs); (iii) hypotension (systolic arterial blood pressure <90 mm Hg for 3 min or longer); (iv) use of vasoactive drugs to correct hypotension; (v) new onset of expiratory flow limitation (expiratory flow higher than zero at end expiration, as suggested by visual analysis of flow curve); (vi) need for ventilator pressure reduction (defined as ventilatory strategies aimed to lower the peak and plateau pressures); and (vii) onset of new arrhythmias (atrial fibrillation, sustained ventricular tachycardia, supraventricular tachycardia, or ventricular fibrillation).

Postoperative pulmonary complications were defined as before[17]: (i) unplanned need for supplementary oxygen (oxygen administered as a result of PaO_2 <8 kPa or SpO_2 <90% in room air, but excluding oxygen supplementation given as standard care, e.g. directly after arrival in the PACU); (ii) respiratory failure (PaO_2 <8 kPa or SpO_2 <90% despite oxygen therapy, or a need for non-invasive positive pressure ventilation); (iii) unplanned new or prolonged invasive mechanical ventilation (after discharge from the operating room); (iv) acute respiratory distress syndrome (defined according to the Berlin definition)[18]; (v) pneumonia [presence of a new or progressive radiographic infiltrate, and at least two of three clinical features: fever >38°C, leucocytosis or leucopenia (white blood cell count >12 000 cells ml^{-1} or <4000 cells ml^{-1}), and purulent secretions]; and (vi) pneumothorax (air in the pleural space with no vascular bed surrounding in the visceral pleura on the chest radiograph). Severe PPCs were defined by excluding the variable 'unplanned need for supplementary oxygen' from the composite.

Other information reported included patient characteristics, ASA physical classification, preoperative oxygen saturation, co-morbidities, type of surgery (i.e. laparoscopic or non-laparoscopic), duration of surgery and anaesthesia, ventilation parameters [e.g. tidal volume, peak and plateau pressures, compliance, ventilatory frequency, PEEP, and driving pressure (calculated by subtracting PEEP from the plateau pressure)], and anaesthetic management choices (e.g. type and amount of fluids administered, neuromuscular block management, transfusions, and epidural anaesthesia).

Statistical analysis

Patients were stratified by daytime or night-time surgery. Variables collected hourly [including tidal volume V_T, PEEP, peak and plateau pressures (or maximum airway pressure, where available), ventilatory frequency, inspired oxygen fraction (FiO_2), and calculated variables (e.g. driving pressure and compliance)] were presented as median values with interquartile ranges. V_T was presented as absolute volume (ml) and volume normalised for predicted body weight (ml kg^{-1}). The predicted body weight of male patients was calculated as equal to 50+0·91* (centimetres of height − 152·4); that of female patients was calculated as equal to 45·5+0·91* (centimetres of height − 152·4). No assumptions were made for missing data (see Supplementary Appendix B for details on missing data for specific variables). Proportions were compared using χ^2 or Fisher's exact tests, and continuous variables were compared using Student's *t*-test or Wilcoxon rank sum test.

We performed a logistic regression analysis to detect whether the risk of intraoperative AEs and PPCs was different according to the time of surgery (night *vs* day), and to adjust for potential confounding factors (patient characteristics and perioperative data). Variables were selected to be included in the multivariable model according to clinical relevance and when a $P<0.2$ was found in the univariable analysis. We also tested the interaction between the time of surgery and whether or not surgery was laparoscopic (type of surgery).

To check the consistency of the findings, a co-variate balancing propensity score matching was performed. The co-variate balancing propensity score is a robust method, which concurrently maximises the co-variate balance and the treatment assignment prediction. The co-variate balancing propensity score was used to estimate the probability of being operated during daytime or during night-time, considering several baseline co-variates. One-to-two near-neighbour matching without replacement was performed. A caliper of 0.1 was specified to constrain the difference between pairs. The following variables were used to construct the propensity score: Assess Respiratory Risk in Surgical Patients in Catalonia risk score for PPCs[19]; ASA physical status; age; functional status; cancer; preoperative red blood cell transfusion; duration of surgery; BMI; preoperative SpO_2; smoking; chronic obstructive pulmonary disease; chronic kidney diseases; heart failure; obstructive sleep apnoea; respiratory infection; type of surgery; elective, urgent, or emergency surgery; duration of anaesthesia; epidural anaesthesia; antibiotic prophylaxis; and fluid administration and blood component transfusion during surgery. Kaplan−Meier curves were used to estimate the cumulative incidence of PPCs until Day 5, hospital discharge, and survival at Day 28.

By convention, two-sided statistical significance was assumed with $P<0.05$. No adjustment for multiple testing was applied; therefore, all outcomes in this study are exploratory. As a sensitivity analysis, we did correct for multiplicity using the Benjamini−Hochberg procedure. All analyses were performed with R version 3.4.1 (The R Foundation for Statistical Computing, http://www.R-project.org/).

Results

Unmatched cohort

Of 9861 included patients, 9306 (94.4%) underwent surgery during daytime and 555 during night-time (5.6%). Table 1 shows the patients' characteristics, preoperative evaluation, and data related to type of surgery presented in daytime and night-time groups. Night-time patients had higher ASA physical status scores, higher Assess Respiratory Risk in Surgical Patients in Catalonia scores, were more partially dependent, and more frequently suffered from heart failure. Table 2 shows surgery characteristics and intraoperative management. Night-time surgeries more often involved urgent and emergency surgeries, even though there was also a large

Table 1 Patient and surgical characteristics in the 'daytime' and 'night-time' unmatched groups. Data are presented as median (25th, 75th percentile) or event (%). GI, gastrointestinal; Hb, haemoglobin; SpO_2, peripheral oxygen saturation

	Daytime (n=9306)	Night-time (n=555)	P-value
Female sex	5124 (55.1)	299 (53.9)	0.615
Age (yr)	53.00 (39.00, 66.00)	53.00 (38.25, 66.00)	0.676
BMI (kg m^{-2})	26.26 (23.38, 30.03)	25.69 (22.78, 29.44)	0.046
ASA physical status			0.001
1	2861 (30.8)	152 (27.5)	
2	4490 (48.4)	250 (45.2)	
3	1770 (19.1)	133 (24.1)	
4	155 (1.7)	18 (3.3)	
5	8 (0.1)	0 (0.0)	
'Assess Respiratory Risk in Surgical Patients in Catalonia' score	16.00 (3.00, 31.00)	18.00 (3.00, 34.00)	<0.001
Functional status			0.051
Non-dependent	8604 (92.5)	498 (89.7)	
Partially dependent	575 (6.2)	46 (8.3)	
Totally dependent	121 (1.3)	11 (2.0)	
Preoperative SpO_2 (%)	98.00 (96.00, 99.00)	98.00 (96.00, 99.00)	0.002
Preoperative anaemia (Hb ≤10 g dl^{-1})	305 (3.9)	24 (5.1)	0.268
Smoking	2158 (23.2)	132 (23.8)	0.794
Chronic obstructive pulmonary disease	563 (6.0)	33 (5.9)	0.994
Cirrhosis	93 (1.0)	9 (1.6)	0.233
Cancer	365 (3.9)	27 (4.9)	0.321
Chronic kidney dysfunction	292 (3.1)	18 (3.2)	0.990
Heart failure	538 (5.8)	47 (8.5)	0.012
Obstructive sleep apnoea	190 (2.0)	15 (2.7)	0.364
Neuromuscular disease[a]	83 (0.9)	5 (0.9)	1.000
Respiratory infection <30 days	336 (3.6)	27 (4.9)	0.159
Red blood cell transfusion <30 days	70 (0.8)	5 (0.9)	0.888
Preoperative Hb (g dl^{-1})	13.70 (12.60, 14.80)	13.54 (12.40, 14.80)	0.234
Preoperative creatinine (mg dl^{-1})	0.80 (0.70, 0.99)	0.81 (0.70, 0.98)	0.248
Urgency of surgery[b]			<0.001
Elective	8350 (89.7)	412 (74.2)	
Urgent	749 (8.1)	96 (17.3)	
Emergency	205 (2.2)	47 (8.5)	
Duration of surgery (h)			<0.001
≤2	6522 (70.2)	339 (61.2)	
2–3	1805 (19.4)	108 (19.5)	
>3	963 (10.4)	107 (19.3)	
Surgical procedure[c] Lower GI	1018 (10.9)	77 (13.9)	0.039
Upper GI	1277 (13.7)	80 (14.4)	0.692
Vascular surgery[d]	293 (3.1)	16 (2.9)	0.823
Aortic surgery	62 (0.7)	2 (0.4)	0.549
Neurosurgery, head and neck	1887 (20.3)	119 (21.4)	0.543
Urological and kidney	817 (8.8)	41 (7.4)	0.292
Gynaecological	1097 (11.8)	43 (7.7)	0.005
Endocrine surgery	187 (2.0)	7 (1.3)	0.282
Transplant	29 (0.3)	5 (0.9)	0.054
Plastic, cutaneous, breast	996 (10.7)	41 (7.4)	0.016
Bone, joint, trauma spine	1467 (15.8)	127 (22.9)	<0.001
Other procedures	553 (5.9)	32 (5.8)	0.937
Surgical technique[e] Open abdominal surgery	1661 (17.8)	112 (20.2)	0.183
Laparoscopic surgery	1644 (17.7)	91 (16.4)	0.480
Laparoscopic-assisted surgery	159 (1.7)	8 (1.4)	0.761
Peripheral surgery	1690 (18.2)	137 (24.7)	<0.001
Other	4212 (45.3)	214 (38.6)	0.002
Duration of anaesthesia[f] (min)	101.00 (65.00, 160.00)	118.00 (75.00, 200.75)	<0.001
Duration of surgery[g] (min)	72.00 (40.00, 122.00)	80.00 (50.00, 150.00)	<0.001

[a] Neuromuscular disease affecting the respiratory system.
[b] 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, non-elective surgery performed when the patient's life or well-being is in direct jeopardy.
[c] Surgical procedure: a patient can have more than one surgical procedure.
[d] Vascular surgery is carotid endarterectomy, aortic surgery, and peripheral vascular surgery taken together.
[e] Surgical technique: surgical approach to the procedure. A patient can have more than one type of surgical technique.
[f] Duration of anaesthesia is the time between start of induction and tracheal extubation or discharge from operation room if mechanical ventilation is continued.
[g] Duration of surgery is the time between skin incision and closure of the incision.

Table 2 Intraoperative variables and ventilator parameters and settings in the unmatched 'daytime' and 'night-time' groups. Data are presented as median (25th, 75th percentile) or event (%). ABW, actual body weight; NMBA, neuromuscular blocking agent; PBW, predicted body weight calculated as 50+[0.91×(cm height−152.4)] for males and 45.5+[0.91−(cm height−152.4)] for females; driving pressure: calculated as plateau pressure−PEEP; SpO_2, peripheral oxygen saturation; $EtCO_2$, expiratory carbon dioxide

	Daytime (n=9306)	Night-time (n=555)	P-value
Epidural	458 (4.9)	18 (3.2)	0.091
Antibiotic prophylaxis	6369 (68.5)	429 (77.3)	<0.001
Train-of-four monitoring	1658 (17.8)	127 (23.0)	0.002
Total fluid amount (ml)	1000 (800, 1600)	1100 (1000, 2000)	<0.001
Crystalloid (ml)	1000 (620, 1500)	1000 (750, 1800)	0.002
Colloid (ml)	500 (0, 500)	500 (500, 500)	0.004
Transfusion during surgery	306 (3)	24 (4.3)	0.231
NMBA	7807 (84)	465 (84)	1.000
NMBA reversal	3152 (34)	142 (26)	<0.001
Mode of ventilation			<0.001
Volume controlled	6470 (71)	344 (63)	
Pressure controlled	1469 (16)	102 (19)	
Pressure support ventilation	99 (1)	5 (1)	
Spontaneous	503 (6)	35 (6.4)	
Other	626 (7)	61 (11)	
Peak pressure (cm H_2O)	17.5 (15.0, 21.0)	17.5 (15.0, 20.0)	0.750
Plateau pressure (cm H_2O)	15.5 (13.0, 18.5)	16.0 (14.0, 19.0)	0.089
Tidal volume (ml)	500 (456, 560)	500 (450, 550)	0.028
Tidal volume ml kg^{-1} ABW	6.76 (5.86, 7.69)	6.67 (5.76, 7.69)	0.287
Tidal volume ml kg^{-1} PBW	8.13 (7.23, 9.13)	7.91 (7.15, 8.72)	<0.001
FiO_2 (%)	52 (46, 70)	51 (45, 70)	0.253
PEEP (cm H_2O)	3.0 (0, 5.0)	4.0 (2.0, 5.0)	<0.001
Driving pressure	12.0 (10.0, 15.0)	12.0 (10.0, 15.0)	0.400
Ventilatory frequency	12 (12, 13)	12 (12, 14)	0.002
Minute ventilation (L min^{-1})	6000 (5000, 6764)	6000 (4980, 6820)	0.920
Recruitment manoeuvres	914 (10)	51 (9)	0.670
SpO_2 (%)	99 (98, 100)	99 (98, 100)	0.789
$EtCO_2$ (kPa)	4.5 (4.1, 4.9)	4.5 (4.2, 4.8)	0.219

proportion (74.2%) of elective surgeries. Moreover, in the night-time, the durations of both anaesthesia and surgery were longer. During night-time, patients received more i.v. fluids, more patients received antibiotic prophylaxis, and fewer patients received neuromuscular block antagonism, despite a similar use of neuromuscular blocking agents (NMBAs). Concerning ventilation, we did not detect a clinically relevant difference in ventilator settings and parameters between daytime and night-time.

Intraoperative adverse event

The proportion of patients who developed intraoperative AEs was higher during night-time [n=242 (43.6%)] compared with daytime [n=3165 (34.1%); P<0.001] (Table 3). Table 4 shows the results of the logistic regression analysis for occurrence of intraoperative complications. Night-time surgery was independently associated with a higher incidence of intraoperative AEs [odds ratio (OR): 1.44; 95% confidence interval (CI): 1.09−1.9; P=0.01]. There was no interaction between time of surgery and whether or not surgery was laparoscopic in the occurrence of intraoperative AEs (P=0.46). The association between time of surgery and intraoperative AEs remained significant after the multiplicity correction (P=0.029).

Postoperative pulmonary complications

Postoperative pulmonary complications occurred more frequently in patients who underwent surgery during night-time [n=77 (14%)] compared with daytime [n=926 (10%); P=0.004] (Table 3). Table 5 shows the results of the logistic regression analysis for occurrence of PPCs. Night-time surgery was not associated with a significantly higher incidence of PPCs (OR: 1.32; 95% CI: 0.89−1.9; P=0.152). Also, with respect to the occurrence of PPCs, there was no interaction between the time of surgery and whether or not surgery was laparoscopic (P=0.12). There was a significant difference in the cumulative incidence of PPCs between the night-time and daytime groups until Day 5 (P=0.017; Fig. 1).

Hospital discharge and survival

The hospital length of stay was longer and mortality at 28 days was higher in patients who underwent surgery at night-time (Table 3). There was also a significant difference in the cumulative incidence for hospital discharge at 28 days (P<0.001); Supplementary Appendix B, Fig. S1), but not for survival (P=0.17; Supplementary Appendix B, Fig. S2) between the night-time and daytime patients. After the multiplicity correction, the association between hospital length of stay and time of surgery remained significant (P<0.001).

Matched analysis

After matching, 757 patients were included in the daytime group and 380 in the night-time group. The two groups were well balanced in terms of patients' characteristics,

Table 3 Intraoperative adverse events, postoperative pulmonary complications, and clinical outcomes in the unmatched ‘daytime’ and ‘night-time’ groups

	Daytime (n=9306)	Night-time (n=555)	P-value
Total intraoperative adverse events (AEs)[a]	3165 (34.1)	242 (43.6)	<0.001
Intraoperative desaturation[b]	353 (3.8)	34 (6.1)	0.008
Intraoperative need for unplanned recruitment manoeuvres[c]	315 (4)	17 (3.1)	0.765
Intraoperative need for ventilatory pressure reduction[d]	263 (2.8)	19 (3.4)	0.501
Intraoperative onset of expiratory flow limitation[e]	51 (0.6)	1 (0.2)	0.403
Intraoperative hypotension[f]	2432 (26.2)	185 (33.3)	<0.001
Intraoperative need for vasopressors[g]	2032 (21.9)	176 (31.8)	<0.001
Intraoperative new arrhythmia[h]	56 (0.6)	4 (0.7)	0.946
Total postoperative pulmonary complications[i]	926 (10.1)	77 (14.0)	0.004
Severe postoperative pulmonary complications [j]	230 (2.5)	40 (7.3)	<0.001
Unplanned supplemental oxygen[k]	775 (8.5)	50 (9.1)	0.662
Respiratory failure[l]	134 (1.5)	22 (4.0)	<0.001
New use of mechanical ventilation (MV) during follow-up	89 (1.0)	18 (3.3)	<0.001
Acute respiratory distress syndrome	6 (0.1)	3 (0.5)	0.004
Pneumonia	37 (0.4)	3 (0.5)	0.872
Barotrauma	12 (0.1)	1 (0.2)	1.000
Hospital length of stay (day) [median (25th, 75th percentile)]	1.0 (0, 4.0)	2.0 (0, 5.0)	<0.001
Death[m]	48 (0.6)	8 (1.5)	0.016

[a] Total intropertive AEs: number (and proportion) of patients who developed at least one intraoperative AE. One patient could present with multiple intraoperative AEs, but was scored only one (yes-or-no principle).

[b] Intraoperaive desaturation: SpO_2 <92% for more than 2 min.

[c] Intraoperaive need for unplanned recruitment manoeuvres: ventilator strategies aimed to lower peak and plateau pressures.

[d] Intraoperaive need for ventilator pressure reduction: ventilator strategies aimed to lower peak and plateau pressures.

[e] Intraoperaive onset of expiratory flow limitation: expiratory flow higher than zero at end-expiration, as suggested by visual analysis of the flow curve.

[f] Intraoperive hypotension: systolic arterial blood pressure <90 mm Hg.

[g] Intraoperaive need for vasopressors: any vasoactive drug given to correct hypotension as defined previously.

[h] Intraoperive new arrhythmia: atrial fibrillation, sustained ventricular tachycardia, supraventricular tachycardia, or ventricular fibrillation. PPCs on Days 1–5 were score ‘yes’ as soon as the event occurred on either ward or ICU.

[i] Total PPC number (and proportion) of patients who developed at least one PPC. One patient could present with multiple PPCs, but was scored only one (yes-or-no principle).

[j] Severe PPCs were defined by excluding the variable ‘unplanned supplemental oxygen’.

[k] Unplannedupplemental oxygen: supplemental oxygen administered as a result of PaO_2 <8 kPa or SpO_2 <90% in room air, excluding oxygen supplementation given as standard care: death at the end of follow-up.

[l] Respirato failure: PaO_2 <60 mm Hg or SpO_2 <90% despite oxygen therapy, or need for non-invasive mechanical ventilation.

[m] Death: on Day 28.

preoperative data, and data related to surgery (Supplementary Appendix B, Table S1). However, patients in the night-time group more frequently received NMBAs and less frequently received NBMA antagonism (Supplementary Appendix B, Table S2). Intraoperative AEs remained significantly more frequent in the night-time. In contrast, the proportion of patients developing PPCs was not significantly different between night-time and daytime (Supplementary Appendix B, Table S3). We found no difference in the propensity-matched analysis between the daytime and night-time groups in hospital length of stay and mortality (Supplementary Appendix B, Table S3), cumulative incidence for PPCs, and hospital discharge and survival (Supplementary Appendix B, Figs S3–S5).

Discussion

The main results of the present study were (i) intraoperative AEs occurred more frequently during night-time surgeries, even after correcting for potentially confounding factors, and (ii) PPCs occurred more frequently after night-time surgeries; however, this association was not significant after adjusting for potential confounders.

Human or situational factors leading to decreased alertness, teamwork, performance, and quality of care might all contribute to the higher occurrence of intraoperative AEs during night-time.[8,9,11,20,21] One study evaluated 13 pairs of day–night matched anaesthesia cases performed by anaesthesiologists in training.[21] That study found that, at night, there was worse mood and task performance on manual and monitoring tasks. The investigators speculated that fatigue might have contributed.[21] These findings were reinforced in another study including 21 anaesthesiologists, demonstrating worse reaction times with sleep deprivation.[22] Also consistent with this interpretation, in a study including women in labour, night-time epidural insertion was associated with a higher risk of dural puncture.[7]

The findings of the current study recapitulate the results of other studies reporting an association between perioperative AEs and timing of surgery.[3–5] Interestingly, there is also a reported association between late-afternoon anaesthesia start time and anaesthetic-related AEs (e.g. pain and postoperative nausea and vomiting).[23] However, a recent retrospective analysis of the American College of Surgeons National Surgical Quality Improvement Program administrative data set evaluated intraoperative AEs during night-time.[24] The authors

Table 4 Logistic regression model for the occurrence of intraoperative adverse events. CI, confidence interval; COPD, chronic obstructive pulmonary disease; FS, functional status; Hb, haemoglobin; OR, odds ratio; RBC, red blood cell; SpO_2, peripheral oxygen saturation

	Or (95% CI)	P-value
Age	1.02 (1.02–1.03)	<0.001
BMI	1.01 (1–1.02)	0.036
ASA physical status	1.18 (1.05–1.32)	0.005
ARISCAT score	0.99 (0.99–1.01)	0.726
Partially dependent (FS)	1.33 (1.02–1.74)	0.037
Totally dependent (FS)	2 (1.07–3.78)	0.030
Preoperative SpO_2	0.93 (0.9–0.96)	<0.001
Preoperative (Hb $\leq$10 g dl^{-1})	1 (0.65–1.51)	0.987
Smoker	0.98 (0.84–1.15)	0.839
COPD	0.86 (0.66–1.11)	0.246
Cancer	1.01 (0.74–1.37)	0.950
Chronic kidney disease	1.3 (0.92–1.83)	0.129
Heart failure	0.89 (0.68–1.15)	0.370
Sleep apnoea	1.74 (1.12–2.7)	0.014
Respiratory infection <30 days	1.61 (1.16–2.23)	0.005
RBC transfusion <30 days	0.77 (0.31–1.85)	0.557
Preoperative Hb	1.02 (0.98–1.06)	0.435
Leucocyte count	1 (1–1)	0.023
Preoperative creatinine	1.03 (1–1.09)	0.136
Urgent surgery	0.81 (0.62–1.04)	0.104
Emergency surgery	1.52 (0.88–2.64)	0.133
Duration of anaesthesia	1 (1–1)	<0.001
Epidural	1.96 (1.47–2.64)	<0.001
Antibiotic prophylaxis	1.25 (1.07–1.47)	0.004
Total fluid amount	1 (1–1)	0.022
Transfusion of RBC during surgery	1.44 (1–2.09)	0.053
Residual curarisation	1.34 (0.68–2.69)	0.402
Surgery during the weekends	0.81 (0.49–1.32)	0.413
Laparoscopic surgery	0.74 (0.61–0.89)	0.002
'Night-time' surgery	1.44 (1.09–1.9)	0.010

Table 5 Logistic regression model for the occurrence of postoperative pulmonary complications. CI, confidence interval; COPD, chronic obstructive pulmonary disease; FS, functional status; Hb, haemoglobin; OR, odds ratio; RBC, red blood cell; SpO_2, peripheral oxygen saturation

	Or (95% CI)	P-value
Age	1.01 (1–1.02)	0.002
BMI	1.02 (1–1.03)	0.081
ASA physical status	1.33 (1.12–1.58)	0.001
ARISCAT score	1.01 (1–1.02)	0.070
Partially dependent (FS)	1.03 (0.72–1.43)	0.886
Totally dependent (FS)	0.78 (0.3–1.78)	0.576
Preoperative SpO_2	0.94 (0.9–0.99)	0.010
Preoperative (Hb $\leq$10 g dl^{-1})	1.19 (0.7–1.99)	0.508
Smoker	0.84 (0.64–1.08)	0.179
COPD	1.29 (0.91–1.81)	0.143
Cancer	1.64 (1.13–2.34)	0.008
Chronic kidney disease	1.37 (0.91–2.03)	0.131
Heart failure	0.97 (0.67–1.38)	0.866
Sleep apnoea	2.05 (1.17–3.49)	0.010
Respiratory infection <30 days	1.46 (0.95–2.22)	0.080
RBC transfusion <30 days	0.79 (0.25–2.17)	0.665
Preoperative Hb	0.98 (0.92–1.04)	0.514
Leucocyte count	1 (1–1)	0.012
Preoperative creatinine	1.01 (0.97–1.04)	0.670
Urgent surgery	1.4 (0.99–1.96)	0.053
Emergency surgery	2.63 (1.38–4.87)	0.003
Duration of anaesthesia	1 (1–1)	<0.001
Epidural	1.18 (0.82–1.67)	0.358
Antibiotic prophylaxis	1.07 (0.83–1.39)	0.605
Total fluid amount	1 (1–1)	0.752
Transfusion of RBC during surgery	1.49 (0.99–2.22)	0.051
Intraoperative adverse events	1.46 (1.19–1.8)	<0.001
Residual curarisation	3.85 (1.9–7.68)	<0.001
Surgery during weekend	1.62 (0.87–2.9)	0.113
Laparoscopic surgery	0.95 (0.71–1.26)	0.745
'Night-time' surgery	1.32 (0.89–1.9)	0.152

found that night-time surgery was not independently associated with a higher risk of intraoperative AEs. However, the definition of AEs[24] was different from the definition used in the current study.

In the current study, there was no clinically relevant difference in ventilator management between daytime and night-time surgeries. However, the night-time group had higher Assess Respiratory Risk in Surgical Patients in Catalonia scores, mainly as a result of preoperative SpO_2, higher proportions of urgent and emergency surgery, and longer durations of surgery.[19] Moreover, the proportion receiving NMBA antagonism was lower during night-time *vs* daytime. Residual neuromuscular block has been found associated with PPCs after the use of NMBAs.[25,26] Lower use of NMBA antagonism with night-time surgeries might have partially explained the increase in PPCs.[26] Several imbalances in patients' comorbidities between the night-time and daytime groups might also have contributed to differences in PPCs.

Since the result of this posthoc analysis suggests that timing of surgery impacts outcome of patients, it seems imperative to make the balance between risks and benefits case by case. It could be argued that surgery outside working hours should only be done if this is normal practice, meaning that the teams responsible are incorporated and prepared to perform these surgeries during these time-slots. Otherwise, risk scores, alike the ARISCAT[19] or the LAS VEGAS[27] risk scores for PPCs, could be useful in predicting which patients run the highest risk of developing PPCs, even when performed during night-time, to help to determine the balance between risks and benefits. Future studies should focus on human and logistic factors related to nigh-time surgeries.

Strengths and limitations

The strengths of the study are (i) the size and the prospective multicentre design of the original data set; (ii) the strict criteria used to define intraoperative complications and PPCs; and (iii) the correction of the results for multiple potential confounders related to patients' characteristics, type of surgery, type of anaesthesia, and intraoperative management.

There are also limitations. First, the daytime and night-time groups were defined according to the time of anaesthesia induction.[1] Many of the surgeries started in the daytime might have extended into the night-time, and vice versa. Second, the LAS VEGAS study did not include data on level of training, year of training, and experience of anaesthesiologists and surgeons. Third, information on the hours on duty when performing anaesthesia or surgical procedures

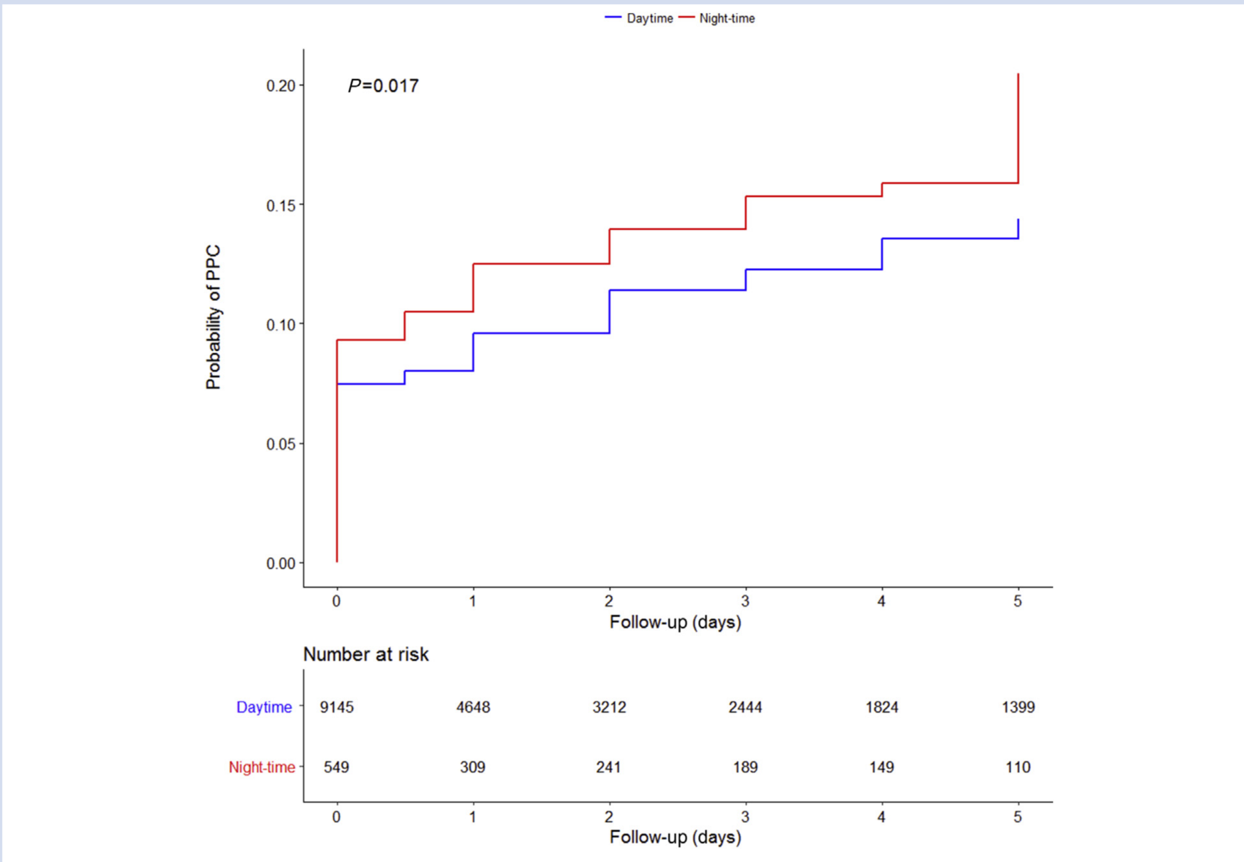

Fig 1. Kaplan–Meier estimate of cumulative incidence of postoperative pulmonary complication (PPCs) in the daytime and night-time group until Day 5 in the unmatched daytime and night-time groups.

was not recorded.[17] Consequently, we can only speculate on such factors. Fourth, the multicentre design of the study led to the inclusion of centres with different characteristics, experiences, and approaches to night working. This is reflected by the fact that 74% of patients in the night-time group underwent elective surgery. Finally, LAS VEGAS was an observational study, and the results are hypothesis generating.

Intraoperative AEs and PPCs occurred more frequently in patients undergoing night-time surgery. Imbalances in patients' clinical characteristics, types of surgery, and intraoperative management at night-time partially explained the higher incidence of PPCs, but not the higher incidence of AEs.

Authors' contributions

Study design: AC, CG, ASN, SNTH, MGA, LB, MJS, PP.
Data collection: SNTH, ASN, JC, MH, MWH, GHM, MFVM, CP, WS, PS, HW, MGA, PP, MJS.
Statistical analysis: ASN.
Interpretation of results: all authors.
Drafting of manuscript: AC, CG, ASN, SNTH, MGA, LB, MJS, PP.
Critical revision of manuscript for important intellectual content: SNTH, ASN, JC, MH, MWH, GHM, MFVM, CP, WS, PS, HW, MGA, PP, MJS.
AC and ASN take responsibility for the integrity of data. SNTH, ASN, JC, MH, MWH, GHM, MFVM, CP, WS, PS, HW, MGA, PP, MJS. were members of the steering committee of the LAS VEGAS study. All authors reviewed and approved the final version of the manuscript, and have agreed to be accountable for all aspects of the projects.

Declaration of interest

The authors declare that they have no conflicts of interest.

Funding

The LAS VEGAS study was co-funded and endorsed by the European Society of Anaesthesiology, which had no role in the study design nor data analysis and interpretation. MFVM was supported by NIHeNHLBI (1R34HL123438).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2018.10.063.

References

1. van Zaane B, van Klei WA, Buhre WF, et al. Nonelective surgery at night and in-hospital mortality: prospective observational data from the European Surgical Outcomes Study. *Eur J Anaesthesiol* 2015; **32**: 477–85

2. Turrentine FE, Wang H, Young JS, Calland JF. What is the safety of nonemergent operative procedures performed at night? A study of 10,426 operations at an academic tertiary care hospital using the American College of Surgeons national surgical quality program improvement database. *J Trauma* 2010; **69**: 313–9
3. Dalton MK, McDonald E, Bhatia P, Davis KA, Schuster KM. Outcomes of acute care surgical cases performed at night. *Am J Surg* 2016; **212**: 831–6
4. Whitlock EL, Feiner JR, Chen L-L. Perioperative mortality, 2010 to 2014: a retrospective cohort study using the national anesthesia clinical outcomes registry. *Anesthesiology* 2015; **123**: 1312–21
5. Linzey JR, Burke JF, Sabbagh MA, et al. The effect of surgical start time on complications associated with neurological surgeries. *Neurosurgery* 2018; **83**: 501–7
6. Komen N, Dijk J-W, Lalmahomed Z, et al. After-hours colorectal surgery: a risk factor for anastomotic leakage. *Int J Colorectal Dis* 2009; **24**: 789–95
7. Aya AG, Mangin R, Robert C, Ferrer JM, Eledjam JJ. Increased risk of unintentional dural puncture in night-time obstetric epidural anesthesia. *Can J Anaesth* 1999; **46**: 665–9
8. Howard SK, Rosekind MR, Katz JD, Berry AJ. Fatigue in anesthesia: implications and strategies for patient and provider safety. *Anesthesiology* 2002; **97**: 1281–94
9. Gander P, Millar M, Webster C, Merry A. Sleep loss and performance of anaesthesia trainees and specialists. *Chronobiol Int* 2008; **25**: 1077–91
10. Mansukhani MP, Kolla BP, Surani S, Varon J, Ramar K. Sleep deprivation in resident physicians, work hour limitations, and related outcomes: a systematic review of the literature. *Postgrad Med* 2012; **124**: 241–9
11. Gregory P, Edsell M. Fatigue and the anaesthetist. *Cont Educ Anaesth Crit Care Pain* 2014; **14**: 18–22
12. Peberdy MA, Ornato JP, Larkin GL, et al. Survival from in-hospital cardiac arrest during nights and weekends. *JAMA* 2008; **299**: 785–92
13. Miskovic A, Lumb AB. Postoperative pulmonary complications. *Br J Anaesth* 2017; **118**: 317–34
14. Serpa Neto A, Hemmes SNT, Barbas CSV, et al. Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis. *Lancet Respir Med* 2014; **2**: 1007–15
15. Guldner A, Kiss T, Serpa Neto A, et al. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. *Anesthesiology* 2015; **123**: 692–713
16. Schultz MJ, de Abreu MG, Pelosi P. Mechanical ventilation strategies for the surgical patient. *Curr Opin Crit Care* 2015; **21**: 351–7
17. LAS VEGAS Investigators. Epidemiology, practice of ventilation and outcome for patients at increased risk of postoperative pulmonary complications: LAS VEGAS—an observational study in 29 countries. *Eur J Anaesthesiol* 2017; **34**: 492–507
18. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA* 2012; **307**: 2526–33
19. Mazo V, Sabate S, Canet J, et al. Prospective external validation of a predictive score for postoperative pulmonary complications. *Anesthesiology* 2014; **121**: 219–31
20. Taffinder NJ, McManus IC, Gul Y, Russell RC, Darzi A. Effect of sleep deprivation on surgeons' dexterity on laparoscopy simulator. *Lancet* 1998; **352**: 1191
21. Cao CGL, Weinger MB, Slagle J, et al. Differences in day and night shift clinical performance in anesthesiology. *Hum Factor*. 2008; **50**: 276–90
22. Saadat H, Bissonnette B, Tumin D, et al. Effects of partial sleep deprivation on reaction time in anesthesiologists. *Paediatr Anaesth* 2017; **27**: 358–62
23. Wright MC, Phillips-Bute B, Mark JB, et al. Time of day effects on the incidence of anesthetic adverse events. *Qual Saf Health Care* 2006; **15**: 258–63
24. Eskesen TG, Peponis T, Saillant N, et al. Operating at night does not increase the risk of intraoperative adverse events. *Am J Surg* 2018; **216**: 19–24
25. Sauer M, Stahn A, Soltesz S, Noeldge-Schomburg G, Mencke T. The influence of residual neuromuscular block on the incidence of critical respiratory events. A randomised, prospective, placebo-controlled trial. *Eur J Anaesthesiol* 2011; **28**: 842–8
26. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesth Analg* 2008; **107**: 130–7
27. Neto AS, da Costa LGV, Hemmes SNT, et al. The LAS VEGAS risk score for prediction of postoperative pulmonary complications: an observational study. *Eur J Anaesthesiol* 2018; **35**: 691–701

Handling editor: M. Avidan