Association Between Night-time Surgery and Occurrence of Intraoperative Adverse Events and Postoperative Pulmonary Complications – a posthoc analysis of LAS VEGAS

Andrea Cortegiani[1], Cesare Gregoretti[1], Ary Serpa Neto[2,3], Sabrine NT Hemmes[2,4], Lorenzo Ball[5,6], Jaume Cane[7], Michael Hiesmayr[8], Markus W. Hollmann[4], Gary H Mills[9], Marcos F. Vidal Melo[10], Christian Putensen[11], Werner Schmid[8], Paolo Severgnini[12], Hermann Wrigge[13], Marcelo Gama de Abreu[14], Marcus J. Schultz[2,15], and Paolo Pelosi[5,6] for the LAS VEGAS* investigators**, the PROVE Network*** and the Clinical Trial Network of the European Society of Anaesthesiology

*'Local ASsessment of VEntilatory management during General Anaesthesia for Surgery' study

**Collaborators are listed in the online supplement

***PROtective VEntilation Network (www.provenet.eu)

Policlinico Paolo Giaccone, University of Palermo, Italy

[1]Department of Bipathology and Medical Biotechnologies (DIBIMED). Section of Anesthesia Analgesia Intensive Care and Emergency.

Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

[2]Department of Intensive Care & Laboratory of Experimental Intensive Care and Anesthesia (L·E·I·C·A)

[4]Department of Anaesthesiology

Hospital Israelita Albert Einstein, São Paulo, Brazil

[3]Department of Critical Care Medicine

[5]Dipartimento di Scienze Chirurgiche e Diagnostiche Integrate (DISC), Università degli Studi di Genova, Genova, Italy

[6]IRCCS Ospedale Policlinico San Martino, Genova, Italy

Hospital Universitari Germans Trias I Pujol, Barcelona, Spain

[7]Department of Anesthesiology and Postoperative Care

Medical University Vienna, Vienna, Austria

[8]Division Cardiac, Thoracic, Vascular Anesthesia and Intensive Care

Sheffield Teaching Hospitals, Sheffield and University of Sheffield, United Kingdom

[9]Operating Services, Critical Care and Anesthesia

Massachusetts General Hospital, Boston, U.S.A.

[10]Department of Anesthesia, Critical Care and Pain Medicine

University Hospital Bonn, Bonn, Germany
[11]Department of Anesthesiology and Intensive Care Medicine

University of Insubria, Varese, Italy
[12]Department of Biotechnology and Sciences of Life, ASST- Settelaghi Ospedale di Circolo e Fondazione Macchi

University of Leipzig, Leipzig, Germany
[13]Department of Anesthesiology and Intensive Care Medicine

University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany
[14]Department of Anaesthesiology and Intensive Care Medicine, Pulmonary Engineering Group

Mahidol University, Bangkok, Thailand
[15]Mahidol Oxford Tropical Medicine Research Unit (MORU)

*LAS VEGAS (the 'Local ASsessment of VEntilatory management during General Anesthesia for Surgery study')

**The PROVE Network; the PROtective VEntilation Network (www.provenet.eu)

Collaborators are listed in the Appendix A.

Word count - abstract: 246 words
Word count: 2742 words (excl. references)
Figures: 1
Tables: 5
Online supplement: 1

Running Title: Intraoperative adverse events during night-time surgeries

Corresponding author:
Dr. Andrea Cortegiani
Department of Biopathology and Medical Biotechnologies (DIBIMED)
Policlinico Paolo Giaccone, University of Palermo
Via del Vespro 129
90127 Palermo, Italy
Email: andrea.cortegiani@unipa.it

ABSTRACT

Background: The aim of this posthoc analysis of the LAS VEGAS cohort was to evaluate the association between night-time surgery and occurrence of intraoperative adverse events (AEs) and postoperative pulmonary complications (PPCs).

Methods: LAS VEGAS was a conveniently-sized prospective international 1-week study that enrolled adult patients undergoing mechanical ventilation during anaesthesia for surgery in 146 hospitals across 29 countries. For this analysis, time slots were defined as 'day-time' (induction of anaesthesia between 8:00 AM and 7:59 PM) or 'night-time' (between 8:00 PM and 7:59 AM).

Results: Of 9,861 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 an unmatched (43.6% *vs* 34.1%; *P*<0.001) and a propensity-matched analyses (43.7% *vs* 36.8%%; *P*=0.029). PPCs occurred more often in patients who underwent night-time surgery than patients who underwent day-time surgery (14% *vs*. 10%; *P*=0.004) in an unmatched cohort analysis, though not in a propensity-matched analysis (13.8% *vs.* 11.8%; *P*=0.39). In a multivariate regression model including patient demographics, and types of surgery and anaesthesia, night-time surgery was independently associated with a higher incidence of intraoperative AEs [OR 1.44 (95% CI 1.09-1.9); *P*=0.01], but not with a higher incidence of PPCs [OR 1.32 (95% CI 0.89-1.9); *P*=0.152].

Conclusions: Intraoperative AEs and PPCs occur more often in patients undergoing night-time surgery. Unbalances in clinical characteristics of patients, types of surgery, and intraoperative management at night-time may explain the higher incidence of PPCs, but not the higher incidence of AEs.

MESH Keywords: Intraoperative complications, Patient safety, Postoperative complications

Trial registration: LAS VEGAS study was registered at www.clinicaltrials.gov (registration number NCT01601223)

Background

The literature on the impact of timing of surgery on the occurrence of intraoperative adverse events (AEs) and patients' outcome has been conflicting.[1-6] For instance, performance of a surgical team during night-time could be affected by human factors, including mental or physical fatigues and reduced alertness that may increase the risk of adverse events and intraoperative complications.[7-11] However, also logistic factors such as lower number of available healthcare workers, lack of the most skilled colleagues and even suboptimal early postoperative care may affect night-time working. In addition, these factors may lower adherence to 'best practices' and guidelines potentially leading to an higher incidence of perioperative adverse events.[3-5,12] Postoperative pulmonary complications (PPCs) are associated with morbidity and mortality in the perioperative period.[13,14] Beyond patients' clinical characteristics, occurrence of intraoperative complications and PPCs may depend on several factors related to type of surgery and intraoperative management.[15,16]

Knowledge on the exact incidence of intraoperative AEs and PPCs according to surgery scheduled at different time-slots remains uncertain. We aimed to address the occurrence of intraoperative AEs and PPCs, and to determine the association with timing of surgery, in patients who underwent night-time *vs* day-time surgeries. Therefore, we analysed the 'Local ASsessment of VEntilatory management during General Anaesthesia for Surgery study' (LAS VEGAS) cohort.[17] We hypothesized that occurrence of intraoperative AEs and PPCs depend on timing of surgery.

Methods

This was a posthoc analysis of LAS VEGAS, a prospective observational international 1-week study aimed to describe epidemiology and ventilation practice in operating room and the incidence of intraoperative AEs and PPCs.[17]

Cohort description

LAS VEGAS enrolled adult patients requiring intraoperative ventilation (via either an endotracheal 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 years, pregnancy related surgery, surgical procedures outside the operating room, procedures involving cardiopulmonary bypass.

Timeslots

For the purpose of this posthoc analysis, we categorized patients according to start of anaesthesia registered in the LAS VEGAS-case report form (CRF). Procedures that started with induction of anaesthesia between 08:00 AM and 7:59 PM were considered 'day-time' surgeries, and those between 8:00 PM and 7:59 AM 'night-time' surgeries.

Outcomes definition and data reporting

The primary outcomes of this posthoc analysis were the incidence of collapsed composite of intraoperative AEs and incidence of collapsed composite of PPCs.

Intraoperative AEs included: 1) desaturation (SpO_2 < 92% for more than 2 minutes); 2) need for unplanned lung recruitment manoeuvres (defined as ventilator strategies aimed to restore aeration of the lungs); 3) hypotension (systolic arterial blood pressure < 90 mmHg for 3 minutes or longer); 4) use of vasoactive drugs to correct hypotension; 5) new onset of expiratory flow limitation (expiratory flow higher than zero at end expiration as suggested by visual analysis of flow curve); 6) need for ventilator pressure reduction (defined as ventilatory strategies aimed to lower peak and plateau pressure); and 7) onset of new arrhythmias (atrial fibrillation, sustained ventricular tachycardia, supraventricular tachycardia, or ventricular fibrillation).

PPCs were defined as before[17]: 1) unplanned need of supplementary oxygen (oxygen administered due to 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 post-anaesthetic care unit); 2) respiratory failure (PaO_2< 8 kPa or SpO_2< 90% despite oxygen therapy, or a need for non-invasive positive pressure ventilation); 3) unplanned new or prolonged invasive mechanical ventilation (after discharge from the operating room); 4) Acute Respiratory Distress Syndrome (ARDS) (defined according to the Berlin definition of ARDS)[18]; 5) pneumonia (presence of a new or progressive radiographic infiltrate and at least two of three clinical features; fever > 38° C or > 100.4° F, leucocytosis or leucopenia (WBC count >12000 cells/mL or <4000 cells/mL and purulent secretions); and 6) 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 of supplementary oxygen’ from the composite.

Other reported data were preoperative data as patients’ characteristics, American Society of Anesthesiologists (ASA) classification, preoperative SpO_2, relevant comorbidities, ‘type of surgery’ (i.e. laparoscopic or non-laparoscopic), duration of surgery and anaesthesia, ventilator management and ventilation parameters (e.g. tidal volume, peak and plateau pressure, compliance, respiratory rate, positive end-expiratory pressure – PEEP, and driving pressure [calculated by subtracting PEEP from plateau pressure] and intraoperative management (e.g., fluids administered, neuromuscular blockade management, transfusions, epidural anaesthesia).

Statistical analysis

Patients were stratified according to the different timeslots described above. Ventilation settings were presented for all patients and were standardized as the median during the procedure according to the number of observations. No adjustment for multiplicity was applied across the analyses. Therefore, the results do not claim confirmatory statistical evidence.

Hourly–collected variables, including tidal volume (V_T) size, PEEP level, peak and plateau pressure level *or* maximum airway pressure level (where available), respiratory rate, oxygen fraction of inspired air (FiO_2), and calculated variables including driving pressure levels and compliance, were presented as medians with their interquartile ranges. V_T size was presented as absolute volume (ml) and volume normalized for predicted body weight (ml kg^{-1} PBW). The PBW 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). As amounts of missing data were low (see Appendix B for the rate of missing data for specific variables), no assumptions were made for missing data. Proportions were compared using χ^2 or Fisher exact tests and continuous variables were compared using the Student's *t*-test or Wilcoxon rank sum test, as appropriate.

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 (demographic 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 covariate balancing propensity score (CBPS) matching was performed. The CBPS is a robust method which concurrently maximizes the covariate balance and the treatment assignment prediction. The CBPS was used to estimate the probability of being operated during day-time or during night-time considering several baseline covariates. 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' (ARISCAT) risk score for PPCs [19], ASA class, age, functional status, cancer, pre-operative red blood cell transfusion, duration of surgery, BMI (body mass index), pre-operative SpO_2, smoking, chronic obstructive pulmonary disease, chronic kidney diseases, heart failure, obstructive apnoea, respiratory infection, type of surgery, condition of surgery, duration of anaesthesia, epidural anaesthesia, antibiotic prophylaxis, fluid intake and 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.

Statistical significance was considered to be at 2–sided $p < 0.05$. All analyses were performed with R v.3.4.1 (http://www.R-project.org/).

Results

Unmatched cohort

Of 9,861 included patients, 9,306 (94.4%) underwent surgery during day-time and 555 during night-time (5.6%). Table 1 shows patients' characteristics, preoperative evaluation and data related to type of surgery presented in day and night-time groups. Night-time patients had higher ASA class scores, higher ARISCAT 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 relevant proportion (74.2%) of elective surgeries. Moreover, in the night-time the duration of both anaesthesia and surgery were significantly longer. During night-time patients received significantly more fluids, mainly crystalloid and colloid, more patients received antibiotic prophylaxis, and less patients received neuromuscular block reversal despite a similar use of neuromuscular blocking agents (NMBA). Concerning ventilation, we did not detect a clinically relevant difference in ventilator settings and parameters between day and night-time.

Intraoperative adverse events

The proportion of patients who developed intraoperative AEs was higher during night-time (n = 242 (43.6%) compared to day-time n = 3,165 (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 [OR 1.44 (95% 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=0.460).

Postoperative pulmonary complications

PPCs occurred more frequent in patients who underwent surgery during night-time (n = 77 (14%) in night-time *vs* n = 926 (10%) in day-time; *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 higher incidence of PPCs [OR 1.32 (95% CI 0.89-1.9); *P*=0.152]. Also with respect to occurrence of PPCs, there was no interaction between the time of surgery and whether or not surgery was laparoscopic (P=0.118). There was a significant difference in the cumulative incidence of PPCs between the night-time and day-time groups till day 5 (*P*=0.017; Fig. 1).

Hospital discharge and survival

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*<0.0001); Fig. S1 – Appendix B), but not for survival (*P*=0.17; Fig. S2 – Appendix B) between the night-time and day-time patients.

Matched analysis

After matching, 757 patients were included in the day-time group and 380 in the night-time group. The two groups were well balanced in terms of patients' characteristics, preoperative data, and data related to surgery in the matched cohort (supplementary material - Table S1). However, patients in the night-time group more frequently received NMBAs and less NBMA reversal (Table S2 – Appendix B). Intraoperative AEs remained significantly more frequent in the night-time. On the contrary, the proportion of patients developing PPCs was not statistically different between night and day-time (Table S3 – Appendix B). We found no difference between day and night-time in hospital length of stay and mortality (Table S3 –

Appendix B), cumulative incidence for PPCs, hospital discharge and survival in the propensity matched analysis (Fig. S3, Fig. S4, Fig. S5 – Appendix B).

Discussion

The main results of the present study are: 1) intraoperative AEs occurred significantly more frequently during night-time, even after correcting for confounding factors, i.e., patients' characteristics, type of surgery and anaesthesia characteristics; 2) PPCs occurred more frequently in patients undergoing surgery during night-time; however, 3) after adjusting, night-time surgery was not independently associated with occurrence of PPCs. To the best of our knowledge this is the first study addressing differences in occurrence of common intraoperative AEs and PPCs during night *vs.* day-time surgery in a large prospectively enrolled cohort of patients.

It can be hypothesized that human factors or logistic factors leading to loss in alertness, team-working, performance and quality of care, may have contributed 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] The authors found significantly worse task performances, such as manual tasks and monitoring tasks, and mood which may be attributable to fatigue during night work.[21] These findings were confirmed in another study demonstrating an increased reaction time due to sleep deprivation in 21 anesthesiologists.[22] In a prospective analysis of recorded cases, night-time obstetric epidural anaesthesia was associated with an higher risk of unintentional puncture of the dura.[7] The authors speculated that these findings may be explained by human factors such as fatigue, sleep interruption or deprivation.[7]

Our findings are in line with other studies reporting an association between perioperative adverse events and timing of surgery.[3-5] Interestingly, there is also a known association between late-afternoon anaesthesia start time and anaesthetic adverse events (i.e. pain and postoperative nausea and vomiting).[23] However, a recent retrospective analysis of the American College of Surgeons' National Surgical Quality Improvement Program administrative dataset evaluated intraoperative AEs during night-time.[24] The authors found that night-time surgery was not independently associated with a higher risk of intraoperative adverse events. Of note, the outcome of adverse events was generally defined as 'an injury caused by medical management rather than the underline disease'.[24]

We hypothesized that different anaesthesia and ventilator management or patients' comorbidity and surgical conditions could differentiate night and day-time working and that this may contribute to a higher incidence of PPCs. The number of patients in specific surgery categories was too low to evaluate thoroughly the effect of timing of the intervention of each surgical procedure. However, our analysis suggests there was no effect of whether or not the surgery was laparoscopic on the association between timing of surgery and occurrence of intraoperative AEs or PPCs. Of note, 'type of surgery' was a variable used in the propensity score matching.

We did not find a clinically relevant difference in ventilator management and ventilator settings between day- and night-time surgery. However, the night-time group had higher ARISCAT scores, mainly due to preoperative SpO_2, higher proportions of urgent and emergency surgery, and longer duration of surgery.[19] Moreover, the proportion of NMBA reversal was significantly less during night-time versus day-time. Residual neuromuscular blockade has been found associated with pulmonary complications in the postoperative period after use muscle relaxant agents.[25,26] We could hypothesize that lower use of NMBAs reversal could favour development of PPCs,[26] although we could not collect data on how NMBA reversal was given (i.e. adherence to guidelines in terms of drugs and dosage). These factors, along with several unbalances in patients' comorbidities between night and day working, may explain the different incidence of 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

Strengths of the study are the size and the prospective, multicentre design of the original dataset; the strict criteria used to define intraoperative complications and PPCs; the correction of the results for multiple potential confounders related to patients' characteristics, type of surgery, type of anaesthesia and intraoperative management.

The findings of this posthoc analysis should be considered in light of some limitations. First, we selected the day and night-time slots according to the time of anaesthesia induction.[1] This criterion may have resulted in strict categorization of patients who underwent surgeries during both day and night. However, the time of induction seemed to be a reasonable factor since the very early phase of the anaesthesia and surgery needs an active and focused performance by the whole operating room team, especially by the anaesthesiologist, which may be affected by factors related to night working (e.g. fatigue, lack of concentration, team members shortage, and other logistic issues). Moreover, the choice of the induction scheme and the selection of ventilatory settings at the beginning of mechanical ventilation may have an influence on the subsequent risk of developing PPCs. The time limits of 8 am - 8 pm were selected by consensus among authors to consider the day and night shifts of the majority of anaesthesiologists and surgical teams worldwide. LAS VEGAS failed to collect data regarding factors like level of training, year of training, and experience of anaesthesiologists and surgeons. Also, the hours on duty when performing anaesthesia or surgical procedures were not collected.[17] Consequently, we can only speculated on such factors, which without doubt play a role. The multicentre design of the study led to the inclusion of centres with different characteristics, experience, as well as approaches to night working. Actually, 74% of patients in the night-time group underwent elective surgery. However, LAS VEGAS failed to collect data regarding such important factors, hampering further analysis. Finally, definitive inference is not possible due to the pure observational design of LAS VEGAS. Thus, our results can only be seen as hypothesis generating, and future studies are needed to establish causal relationships, if any.

Conclusions

Intraoperative AEs and PPCs occur more frequently in patients undergoing night-time surgery. Unbalanced clinical characteristics of patients, surgery and intraoperative management between day- and night-time may explain the occurrence of PPCs, but not intraoperative AEs.

Figure legend

Fig. 1 – Kaplan-Meier estimate of cumulative incidence of PPCs in the day-time and night-time group till day 5 in the unmatched day- and night-time group.

Authors' Contributions

AC and ASN take responsibility for the integrity of data. AC, CG, ASN, SNH, MGA, LB, MJS, PP, designed this secondary analysis of the LAS VEGAS study, interpreted the results and drafted the manuscript. ASN performed the statistical analysis. SNH, ASN, JC, MH, MWH, GHM, MFVM, CP, WS, PS, HW, MGA, PP, MJS were members of the steering committee of the LAS VEGAS study, collected data, interpreted the results of this posthoc analysis and revised the manuscript critically for important intellectual content. All authors reviewed and approved the final version of this manuscript. All authors have agreed to be accountable for all aspects of the projects.

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 NIH-NHLBI grant 1R34HL123438.

Acknowledgment

None

Declaration of interest

The authors have no conflict of interest to disclose for this manuscript.

Appendix A. LAS VEGAS study Network Collaborators

<u>Austria</u>

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

AKH Linz, Linz**:** Hans Gombotz

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

<u>Belgium</u>

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

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

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

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

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

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

<u>Bosnia and Herzegovina</u>

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

<u>Croatia</u>

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

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

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

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

General Hospital Dr J Bencevic, Slavonski Brod**:** Jasminka Kopic, Ivan Mirkovic

University Hospital Center Split, Split**:** Nenad Karanovic, Mladen Carev, Natasa Dropulic

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

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

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

<u>Czech Republic</u>

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

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

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

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

<u>Egypt</u>

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

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

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

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

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

<u>Estonia</u>

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

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

France

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

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

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

Germany

Fachkrankenhaus Coswig, Coswig: Jens Krassler, Simone Merzky

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

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

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

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

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

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

Greece

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

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

Aretaieion University Hospital, Athens: Kassiani Theodorak, Georgios Gkiokas, Marios-Konstantinos Tasoulis

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

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

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

Italy

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

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

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

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

Ospedale Melegnano, Cernuso, Milano: Maurizio Solca

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

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

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

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

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

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

Ospedale San Paolo - University of Milano, Milano: Concezione Tommasino, Francesca Rapido, Paola Morelli

University of Naples "Federico II" Naples: Maria Vargas, Giuseppe Servillo

Policlinico "P. Giaccone", Palermo: Andrea Cortegiani, Santi Maurizio Raineri, Francesca Montalto, Vincenzo Russotto, Antonino Giarratano

Azienda Ospedaliero-Universitaria, Parma: Marco Baciarello, Michela Generali, Giorgia Cerati

Santa Maria degli Angeli, Pordenone: Yigal Leykin
Ospedale Misericordia e Dolce - Usl4 Prato, Prato: Filippo Bressan, Vittoria Bartolini, Lucia Zamidei
University hospital of Sassari, Sassari: Luca Brazzi, Corrado Liperi, Gabriele Sales, Laura Pistidda
Insubria University, Varese: Paolo Severgnini, Elisa Brugnoni, Giuseppe Musella, Alessandro Bacuzzi

Republic of Kosovo
Distric hospital Gjakova, Gjakove: Dalip Muhardri
University Clinical Center of Kosova, Prishtina: Agreta Gecaj-Gashi, Fatos Sada
Regional Hospital "Prim.Dr. Daut Mustafa", Prizren: Adem Bytyqi

Lithuania
Medical University Hospital, Hospital of Lithuanian University of Health Sciences, Kaunas: Aurika Karbonskiene, Ruta Aukstakalniene, Zivile Teberaite, Erika Salciute
Vilnius University Hospital - Institute of Oncology, Vilnius: Renatas Tikuisis, Povilas Miliauskas
Vilnius University Hospital - Santariskiu Clinics, Vilnius: Sipylaite Jurate, Egle Kontrimaviciute, Gabija Tomkute

Malta
Mater Dei Hospital, Msida: John Xuereb, Maureen Bezzina, Francis Joseph Borg

The Netherlands
Academic Medical Centre, University of Amsterdam: Sabrine Hemmes, Marcus Schultz, Markus Hollmann, Irene Wiersma, Jan Binnekade, Lieuwe Bos
VU University Medical Center, Amsterdam: Christa Boer, Anne Duvekot
MC Haaglanden, Den Haag: Bas in 't Veld, Alice Werger, Paul Dennesen, Charlotte Severijns
Westfriesgasthuis, Hoorn: Jasper De Jong, Jens Hering, Rienk van Beek

Norway

Haukeland University Hospital, Bergen: Stefan Ivars, Ib Jammer
Førde Central Hospital /Førde Sentral Sykehus, Førde: Alena Breidablik
Martina Hansens Hospital, Gjettum: Katharina Skirstad Hodt, Frode Fjellanger, Manuel Vico Avalos
Bærum Hospital, Vestre Viken, Rud: Jannicke Mellin-Olsen, Elisabeth Andersson
Stavanger University Hospital, Stavanger: Amir Shafi-Kabiri

<u>Panama</u>
Hospital Santo Tomás, Panama: Ruby Molina, Stanley Wutai, Erick Morais

<u>Portugal</u>
Hospital do Espírito Santo - Évora, E.P.E, Évora.: Glória Tareco, Daniel Ferreira, Joana Amaral
Centro Hospitalar de Lisboa Central, E.P.E, Lisboa.: Maria de Lurdes Goncalves Castro, Susana Cadilha, Sofia Appleton
Centro Hospitalar de Lisboa Ocidental, E.P.E. Hospital de S. Francisco Xavier, Lisboa: Suzana Parente, Mariana Correia, Diogo Martins
Santarem Hospital, Santarem: Angela Monteirosa, Ana Ricardo, Sara Rodrigues

<u>Romania</u>
Spital Orasenesc, Bolintin Vale: Lucian Horhota
Clinical Emergency Hospital of Bucharest, Bucharest: Ioana Marina Grintescu, Liliana Mirea, Ioana Cristina Grintescu
Elias University Emergency Hospital, Bucharest: Dan Corneci, Silvius Negoita, Madalina Dutu, Ioana Popescu Garotescu
Emergency Institute of Cardiovascular Diseases Inst. "Prof. C. C. Iliescu", Bucharest: Daniela Filipescu, Alexandru Bogdan Prodan
Fundeni Clinical institute - Anaesthesia and Intensive Care, Bucharest: Gabriela Droc, Ruxandra Fota, Mihai Popescu
Fundeni Clinical institute - Intensive Care Unit, Bucharest: Dana Tomescu, Ana Maria Petcu, Marian Irinel Tudoroiu
Hospital Profesor D Gerota, Bucharest: Alida Moise, Catalin-Traian Guran
Constanta County Emergency Hospital, Constanta: Iorel Gherghina, Dan Costea, Iulia Cindea

University Emergency County Hospital Targu Mures, Targu Mures: Sanda-Maria Copotoiu, Ruxandra Copotoiu, Victoria Barsan, Zsolt Tolcser, Magda Riciu, Septimiu Gheorghe Moldovan, Mihaly Veres

Russia

Krasnoyarsk State Medical University, Krasnoyarsk: Alexey Gritsan, Tatyana Kapkan, Galina Gritsan, Oleg Korolkov

Burdenko Neurosurgery Institute, Moscow: Alexander Kulikov, Andrey Lubnin

Moscow Regional Research Clinical Institute, Moscow: Alexey Ovezov, Pavel Prokoshev, Alexander Lugovoy, Natalia Anipchenko

Municipal Clinical Hospital 7, Moscow: Andrey Babayants, Irina Komissarova, Karginova Zalina

Reanimatology Research Institute n.a. Negovskij RAMS, Moscow: Valery Likhvantsev, Sergei Fedorov

Serbia

Clinical Center of Vojvodina, Emergency Center, Novisad: Aleksandra Lazukic, Jasmina Pejakovic, Dunja Mihajlovic

Slovakia

National Cancer Institute, Bratislava: Zuzana Kusnierikova, Maria Zelinkova

F.D. Roosevelt teaching Hospital, Banská Bystrica: Katarina Bruncakova, Lenka Polakovicova

Faculty Hospital Nové Zámky, Nové Zámky: Villiam Sobona

Slovenia

Institute of Oncology Ljubljana, Ljubljana: Barbka Novak-Supe, Ana Pekle-Golez, Miroljub Jovanov, Branka Strazisar

University Medical Centre Ljubljana, Ljubljana: Jasmina Markovic-Bozic, Vesna Novak-Jankovic, Minca Voje, Andriy Grynyuk, Ivan Kostadinov, Alenka Spindler-Vesel

Spain

Hospital Sant Pau, Barcelona: Victoria Moral, Mari Carmen Unzueta, Carlos Puigbo, Josep Fava

Hospital Universitari Germans Trias I Pujol, Barcelona: Jaume Canet, Enrique Moret, Mónica Rodriguez Nunez, Mar Sendra, Andrea Brunelli, Frederic Rodenas

University of Navarra, Pamplona: Pablo Monedero, Francisco Hidalgo Martinez, Maria Jose Yepes Temino, Antonio Martínez Simon, Ana de Abajo Larriba

Corporacion Sanitaria Parc Tauli, Sabadell: Alberto Lisi, Gisela Perez, Raquel Martinez

Consorcio Hospital General Universitario de Valencia, Valencia: Manuel Granell, Jose Tatay Vivo, Cristina Saiz Ruiz, Jose Antonio de Andrés Ibañez

Hospital Clinico Valencia, Valencia: Ernesto Pastor, Marina Soro, Carlos Ferrando, Mario Defez

Hospital Universitario Rio Hortega, Valladolid: Cesar Aldecoa Alvares-Santullano, Rocio Perez, Jesus Rico

Sweden

Central Hospital in Kristianstad: Monir Jawad, Yousif Saeed, Lars Gillberg

Turkey

Ufuk University Hospital Ankara, Ankara: Zuleyha Kazak Bengisun, Baturay Kansu Kazbek

Akdeniz University Hospital, Antalya: Nesil Coskunfirat, Neval Boztug, Suat Sanli, Murat Yilmaz, Necmiye Hadimioglu

Istanbul University, Istanbul medical faculty, Istanbul: Nuzhet Mert Senturk, Emre Camci, Semra Kucukgoncu, Zerrin Sungur, Nukhet Sivrikoz

Acibadem University, Istanbul: Serpil Ustalar Ozgen, Fevzi Toraman

Maltepe University, Istanbul: Onur Selvi, Ozgur Senturk, Mine Yildiz

Dokuz Eylül Universitesi Tip Fakültesi, Izmir: Bahar Kuvaki, Ferim Gunenc, Semih Kucukguclu, Şule Ozbilgin

Şifa University Hospital, İzmir: Jale Maral, Seyda Canli

Selcuk University faculty of medicine, Konya: Oguzhan Arun, Ali Saltali, Eyup Aydogan

Fatih Sultan Mehmet Eğitim Ve Araştirma Hastanesi, Istanbul: Fatma Nur Akgun, Ceren Sanlikarip, Fatma Mine Karaman

Ukraine

Institute Of Surgery And Transplantology, Kiev: Andriy Mazur

Zaporizhzhia State Medical University, Zaporizhzhia: Sergiy Vorotyntsev

United Kingdom

SWARM Research Collaborative: for full list of SWARM contributors please see www.ukswarm.com

Northern Devon Healthcare NHS Trust, Barnstaple: Guy Rousseau, Colin Barrett, Lucia Stancombe

Golden Jubilee National Hospital, Clydebank, Scotland: Ben Shelley, Helen Scholes

Darlington Memorial Hospital, County Durham and Darlington Foundation NHS Trust, Darlington: James Limb, Amir Rafi, Lisa Wayman, Jill Deane

Royal Derby Hospital, Derby: David Rogerson, John Williams, Susan Yates, Elaine Rogers

Dorset County Hospital, Dorchester: Mark Pulletz, Sarah Moreton, Stephanie Jones

The Princess Alexandra NHS Hospital Trust, Essex: Suresh Venkatesh, Maudrian Burton, Lucy Brown, Cait Goodall

Royal Devon and Exeter NHS Foundation Trust, Exeter: Matthew Rucklidge, Debbie Fuller, Maria Nadolski, Sandeep Kusre

Hospital James Paget University Hospital NHS Foundation Trust, Great Yarmouth: Michael Lundberg, Lynn Everett, Helen Nutt

Royal Surrey County Hospital NHS Foundation Trust, Guildford: Maka Zuleika, Peter Carvalho, Deborah Clements, Ben Creagh-Brown

Kettering General Hospital NHS Foundation Trust, Kettering: Philip Watt, Parizade Raymode

Barts Health NHS Trust, Royal London Hospital, London: Rupert Pearse, Otto Mohr, Ashok Raj, Thais Creary

Newcastle Upon Tyne Hospitals NHS Trust The Freeman Hospital High Heaton, Newcastle upon Tyne: Ahmed Chishti, Andrea Bell, Charley Higham, Alistair Cain, Sarah Gibb, Stephen Mowat

***Derriford Hospital Plymouth Hospitals NHS Trust, Plymouth*:** Danielle Franklin, Claire West, Gary Minto, Nicholas Boyd

***Royal Hallamshire Hospital, Sheffield*:** Gary Mills, Emily Calton, Rachel Walker, Felicity Mackenzie, Branwen Ellison, Helen Roberts

***Mid Staffordshire NHS, Stafford*:** Moses Chikungwa, Clare Jackson

***Musgrove Park Hospital, Taunton*:** Andrew Donovan, Jayne Foot, Elizabeth Homan

***South Devon Healthcare NHS Foundation Trust /Torbay Hospital, Torquay, Torbay*:** Jane Montgomery, David Portch, Pauline Mercer, Janet Palmer

***Royal Cornwall Hospital, Truro*:** Jonathan Paddle, Anna Fouracres, Amanda Datson, Alyson Andrew, Leanne Welch

***Mid Yorkshire Hospitals NHS Trust; Pinderfields Hospital, Wakefield*:** Alastair Rose, Sandeep Varma, Karen Simeson

***Sandwell and West Birmingham NHS Trust, West Bromich*:** Mrutyunjaya Rambhatla, Jaysimha Susarla, Sudhakar Marri, Krishnan Kodaganallur, Ashok Das, Shivarajan Algarsamy, Julie Colley

***York Teaching Hospitals NHS Foundation Trust, York*:** Simon Davies, Margaret Szewczyk, Thomas Smith

United States

***University of Colorado School of Medicine/University of Colorado Hospital, Aurora*:** Ana Fernandez- Bustamante, Elizabeth Luzier, Angela Almagro

***Massachusetts General Hospital, Boston*:** Marcos Vidal Melo, Luiz Fernando, Demet Sulemanji

***Mayo Clinic, Rochester*:** Juraj Sprung, Toby Weingarten, Daryl Kor, Federica Scavonetto, Yeo Tze

Appendix B. Supplementary data

Reference

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* 2017;**123**:1600–nyx485VL–IS–

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. *Continuing Education in Anaesthesia Critical 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, Abreu MG de, Pelosi P. Mechanical ventilation strategies for the surgical patient. *Curr Opin Crit Care* 2015;**21**:351–7

17. 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 Factors* 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

Table 1. Patient and surgical characteristic in the day-time and night-time unmatched groups

	Day-time (*n*=9,306)	Night-time (*n*=555)	*P* value
Female sex	5124 (55.1)	299 (53.9)	0.615
Age (years)	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 class			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)	
ARISCAT 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 anemia (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 apnea	190 (2.0)	15 (2.7)	0.364
Neuromuscolar 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			<0.001
≤ 2 hours	6522 (70.2)	339 (61.2)	
2-3 hours	1805 (19.4)	108 (19.5)	
>3 hours	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

Table 1. Patient and surgical characteristic in the day-time and night-time unmatched groups

	Day-time (*n*=9,306)	Night-time (*n*=555)	*P* value
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

Data are presented as median [25th, 75th percentile] or event (%).
BMI: body mass index; ASA: American Society of Anesthesiologists; Hb: haemoglobin; GI: gastrointestinal; SpO_2: peripheral oxygen saturation
[a]Neuromuscolar 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 hours, emergency: nonelective 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 endoarterectomy, aortic surgery and peripheral vascular surgery taken togheter. [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 the mechanical ventilation 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 day- and night-time groups

	Day-time (*n*=9,306)	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)	1000.00 [800.00, 1600.00]	1100.00 [1000.00, 2000.00]	<0.001
Crystalloid (ml)	1000.00 [620.00, 1500.00]	1000.00 [750.50, 1800.00]	0.002
Colloid (ml)	500.00 [0.00, 500.00]	500.00 [500.00, 500.00]	0.004
Transfusion during surgery	306 (3.3)	24 (4.3)	0.231
NMBA	7807 (84.0)	465 (84.1)	1.000
NMBA reversal	3152 (34.5)	142 (25.9)	<0.001
Mode of ventilation			<0.001
Volume controlled	6470 (70.6)	344 (62.9)	
Pressure controlled	1469 (16.0)	102 (18.6)	
Pressure support ventilation	99 (1.1)	5 (0.9)	
Spontaneous	503 (5.5)	35 (6.4)	
Other	626 (6.8)	61 (11.2)	
Peak pressure (cmH$_2$O)	17.50 [15.00, 21.00]	17.50 [15.00, 20.00]	0.750
Plateau pressure (cmH$_2$O)	15.50 [13.00, 18.50]	16.00 [14.00, 19.00]	0.089
Tidal volume (ml)	500.00 [456.00, 560.00]	500.00 [450.00, 550.00]	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$_2$ (%)	52.00 [46.00, 70.00]	51.25 [45.00, 70.00]	0.253
PEEP (cmH$_2$O)	3.00 [0.00, 5.00]	4.00 [2.00, 5.00]	<0.001
Driving pressure	12.00 [10.00, 15.00]	12.00 [10.00, 15.00]	0.400
Respiratory rate	12.00 [12.00, 13.00]	12.00 [12.00, 13.62]	0.002
Minute ventilation (L min^{-1})	6000.00 [5000.00, 6763.69]	6000.00 [4980.00, 6819.75]	0.920
Recruitment maneuvers	914 (9.9)	51 (9.2)	0.670
SpO$_2$ (%)	99.00 [98.00, 100.00]	99.00 [98.00, 100.00]	0.789
EtCO$_2$ (kPa)	4.50 [4.13, 4.86]	4.53 [4.19, 4.79]	0.219

Data are presented as median [25th, 75th percentile] or event (%).
NMBA: neuromuscular blocking agents; PEEP: positive end expiratory pressure; ABW: actual body weight; PBW: predicted body weight calculated as: 50 + [0.91 x (cm height - 152.4)] for males and 45.5 + [0.91 - (cm height - 152.4)] for females; Driving pressure: calculated as plateau pressure - PEEP; SpO2: peripheral oxygen saturation; EtCO$_2$: expiratory carbon dioxide

Table 3. Intraoperative adverse events (AEs), postoperative pulmonary complications (PPCs) and clinical outcomes in the unmatched day and night-time groups

	Day-time (*n*=9,306)	Night-time (*n*=555)	*P* value
Total intraoperative 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 maneuvers[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 arrhytmia[h]	56 (0.6)	4 (0.7)	0.946
Total PPCs[i]	926 (10.1)	77 (14.0)	0.004
Severe PPCs[l]	230 (2.5)	40 (7.3)	<0.001
Unplanned supplemental oxygen[m]	775 (8.5)	50 (9.1)	0.662
Respiratory failure[n]	134 (1.5)	22 (4.0)	<0.001
New use of MV during follow-up	89 (1.0)	18 (3.3)	<0.001
ARDS	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])	1.00 [0.00, 4.00]	2.00 [0.00, 5.00]	<0.001
Death[o]	48 (0.6)	8 (1.5)	0.016

[a]Total intraoperative 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]Intraoperative desaturation: SpO_2 < 92% for more than 2 minutes; [c]Intraoperative need for unplanned recruitment maneuvers: ventilator strategies aimed to lower peak and plateau pressure; [d]Intraoperative need for ventilator pressure reduction: ventilator strategies aimed to lower peak and plateau pressure; [e]Intraoperative onset of expiratory flow limitation: expiratory flow higher than zero at end-expiration as suggested by visual analysis of the flow curve; [f]Intraoperative hypotension: Systolic arterial blood pressure <90 mmHg; [g]Intraoperative need for vasopressors: any vasoactive drug given to correct hypotension as defined above; [h]Intraoperative new arrhythmia: atrial fibrillation, sustained ventricular tachycardia, supraventricular tachycardia or ventricular fibrillation.

PPCs on day 1 to 5 were score YES as soon as the event occurred on either ward or intensive care unit. [i]Total PPCs: 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). [l]Severe PPCs were defined by excluding the variable "unplanned supplemental oxygen"; [m]Unplanned supplemental oxygen: supplemental oxygen administered due to PaO2 < 8 kPa or SpO_2 < 90% in room air, excluding oxygen supplementation given as standard care: death at the end of follow-up; [n]Respiratory failure: PaO_2 < 60 mmHg or SpO_2 < 90% despite oxygen therapy, or need for non-invasive mechanical ventilation. [o]Death: on day 28.

Table 4. Logistic regression model for the occurrence of intraoperative adverse events (AEs)

	OR (95%CI)	*P* value
Age	1.02 (1.02-1.03)	<0.001
BMI	1.01 (1-1.02)	0.036
ASA class	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 ≤ 10 g/dl)	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 apnea	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
Leukocite 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 anesthesia	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 curarization	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**

BMI: body mass index; ASA: American Society of Anesthesiology; Hb: haemoglobin; FS: functional status; SpO_2: peripheral oxygen saturation; COPD: chronic obstructive pulmonary disease; RBC: red blood cells

Table 5. Logistic regression model for the occurrence of postoperative pulmonary complications (PPCs).

	OR (95%CI)	*P* value
Age	1.01 (1-1.02)	0.002
BMI	1.02 (1-1.03)	0.081
ASA	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 ≤ 10 g/dl)	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 apnea	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
Leukocite 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 curarization	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**

BMI: body mass index; ASA: American Society of Anesthesiology; Hb: haemoglobin; FS: functional status; SpO2: peripheral oxygen saturation; COPD: chronic obstructive pulmonary disease; RBC: red blood cells