

# Nonelective surgery at night and in-hospital mortality - Prospective observational data from the European Surgical Outcomes Study

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Goranović, Tatjana; Mazul-Sunko, Branka; Oremuš, Krešimir; Bešlić, Gabrijela; Đuzel, Viktor; Hauptman, Ada; Peremin, Sanja; Šribar, Andrej; Župčić, Miroslav; Benčević, Josip; ...

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## ORIGINAL ARTICLE

**Nonelective surgery at night and in-hospital mortality***Prospective observational data from the European Surgical Outcomes Study*

Bas van Zaane, Wilton A. van Klei, Wolfgang F. Buhre, Peter Bauer, E. Christiaan Boerma, Andreas Hoeft, Philipp Metnitz, Rui P. Moreno, Rupert Pearse, Paolo Pelosi, Michael Sander, Benoit Vallet, Ville Pettilä, Jean-Louis Vincent and Andrew Rhodes, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology\*

**BACKGROUND** Evidence suggests that sleep deprivation associated with night-time working may adversely affect performance resulting in a reduction in the safety of surgery and anaesthesia.

**OBJECTIVE** Our primary objective was to evaluate an association between nonelective night-time surgery and in-hospital mortality. We hypothesised that urgent surgery performed during the night was associated with higher in-hospital mortality and also an increase in the duration of hospital stay and the number of admissions to critical care.

**DESIGN** A prospective cohort study. This is a secondary analysis of a large database related to perioperative care and outcome (European Surgical Outcome Study).

**SETTING** Four hundred and ninety-eight hospitals in 28 European countries.

**PATIENTS** Men and women older than 16 years who underwent nonelective, noncardiac surgery were included according to time of the procedure.

**INTERVENTION** None.

**MAIN OUTCOME MEASURES** Primary outcome was in-hospital mortality; the secondary outcome was the duration of hospital stay and critical care admission.

**RESULTS** Eleven thousand two hundred and ninety patients undergoing urgent surgery were included in the analysis with 636 in-hospital deaths (5.6%). Crude mortality odds ratios (ORs) increased sequentially from daytime [426 deaths (5.3%)] to evening [150 deaths (6.0%), OR 1.14; 95% confidence interval 0.94 to 1.38] to night-time [60 deaths (8.3%), OR 1.62; 95% confidence interval 1.22 to 2.14]. Following adjustment for confounding factors, surgery during the evening (OR 1.09; 95% confidence interval 0.91 to 1.31) and night (OR 1.20; 95% confidence interval 0.9 to 1.6) was not associated with an increased risk of postoperative death. Admittance rate to an ICU increased sequentially from daytime [891 (11.1%)], to evening [347 (13.8%)] to night time [149 (20.6%)].

**CONCLUSION** In patients undergoing nonelective urgent noncardiac surgery, in-hospital mortality was associated with well known risk factors related to patients and surgery, but we did not identify any relationship with the time of day at which the procedure was performed.

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From the Department of Anaesthesiology, University Medical Centre Utrecht, Utrecht (BVZ,WAVK), Department of Anaesthesiology, Maastricht University Medical Centre, Maastricht, the Netherlands (WFB), Section of Medical Statistics, Medical University of Vienna, Vienna, Austria (PB), Department of Intensive Care, Medical Centre Leeuwarden, Leeuwarden, the Netherlands (ECB), Department of Anaesthesiology, University of Bonn, Bonn, Germany (AH), Department of General Anaesthesiology, Emergency and Intensive Care Medicine, Medical University of Graz, Graz, Austria (PM), UCINC, Hospital de São José, Centro Hospitalar de Lisboa Central, EPE, Lisbon, Portugal (RPM), Barts and The London School of Medicine and Dentistry, Queen Mary University of London, Department of intensive care, London, UK (RP), IRCCS AOU San Martino-IST (RP), Department of Surgical Sciences and Integrated Diagnostics, University of Genoa, Genova, Italy (PP), Charité-Universitätsmedizin, Department of Anaesthesiology (MS), Anaesthesiology and Critical Care, University Hospital Lille, Lille, France (BV), Intensive Care Units, Helsinki University Hospital, Helsinki, Finland (VP), Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium (J-LV), and St George's Healthcare NHS Trust, London, UK (AR)

Correspondence to Bas van Zaane, Department of Anesthesiology, University Medical Centre Utrecht, Mailstop: Q.04.2.313, P.O. Box 85500, Utrecht 3508 GA, the Netherlands

Tel: +31 88 75 55555; e-mail: b.vanzaane@umcutrecht.nl

\*Members listed in appendix I, <http://links.lww.com/EJA/A68>.

## Introduction

Over 230 million surgical procedures are performed worldwide each year with an estimated mortality between 1 and 4%.<sup>1,2</sup> Mortality following noncardiac surgery may be higher than previously thought and may partly relate to high mortality rates following emergency surgery.<sup>2–5</sup> The factors contributing to mortality following surgery are complex and may include the urgency of surgery, the availability and performance of personnel and the time of day.

The findings of several studies investigating various medical procedures have suggested an association between medical care administered at night and increased morbidity and mortality.<sup>6–8</sup> Patients requiring emergency surgery are at an increased risk compared with elective surgery, even when the procedure is performed under ideal circumstances.<sup>9,10</sup> If such procedures are performed during the evening or night, the outcome may be adversely affected, as the most skilled professionals are not always immediately available or their performance may be influenced by physical or mental fatigue. It is known that fatigue increases the incidence of medical error,<sup>11</sup> making it one of the reasons why it is thought safer to undertake surgery during the day-time whenever possible.<sup>12–14</sup>

As far as we know, this possible association between time point of operation and mortality following emergency surgery has not been studied before. Therefore, the aim of this study was to investigate, in the European Surgical Outcomes Study (EuSOS) database, the association between the time of the day (daytime, evening, night-time) at which urgent surgery is performed, and in-hospital mortality after surgery.<sup>2</sup> We hypothesised that urgent surgery performed during the night was associated with higher in-hospital mortality and also longer hospital stays and more critical care admissions.

## Materials and methods

Data were taken from the European Surgical Outcomes Study (EuSOS) database, the methods of which are described in detail elsewhere.<sup>2,15</sup> In brief, the European cohort study was performed between 09:00 (local time) on 4 April 2011, and 08:59 on 11 April 2011. All patients older than 16 years admitted to participating centres for elective or nonelective inpatient surgery commencing during the 7-day period were eligible for inclusion. Patients undergoing planned day-case surgery, cardiac surgery, neurosurgery, radiological or obstetric procedures were excluded. Participating hospitals were a voluntary convenience sample, identified through membership of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology and by direct approach from national study coordinators.

## Ethics

Ethical approval for this study (Ethical Committee Number 10/H0605/72) was primarily provided by the ethical committee of Southampton University Hospitals NHS trust, Southampton, United Kingdom, on the 15 November 2010. Subsequently, each of the 498 participating centres applied for ethical approval. The requirements differed by country. In Denmark, centres were exempt from ethics approval because this study was technically a clinical audit. In all other nations, formal ethics approval was applied for and given. In Finland, we were required to obtain written informed consent from individual patients.

## Cohort description

For this secondary analysis, all patients within the EuSOS database who had urgent or emergency surgery were included. Exclusion criteria were any site enrolling fewer than 10 patients in the study week, any site having an in-hospital mortality rate either above or below the 95th centile, any patient with missing data for in-hospital mortality, any patient with missing data for the urgency of surgery and any patient presenting for an elective surgical procedure. In EuSOS, the definition of emergency surgery was immediately, without delay, ideally within 24 h. The definition of urgent surgery was planned surgery within hours or days of the decision to operate. The severity of surgery indicated a combination of complexity and amount of tissue injury. Minor surgery would include procedures that would often involve extremities or the body surface lasting less than 30 min performed in a dedicated operating room, brief diagnostic and therapeutic procedures such as arthroscopy without intervention and removal of small cutaneous tumours. Intermediate procedures were more prolonged or complex with the risk of significant complication or tissue injury. Examples might include laparoscopic cholecystectomy, arthroscopy with intervention and fixation of a mandibular fracture. Major surgical procedures were expected to last more than 90 min and included major gut resection, major joint replacement, mastectomy, extensive head and neck tumour resection, abdominal aortic aneurysm repair and major vascular bypass procedure.

## Timing of surgery

Patients within the cohort were stratified by the time of surgery using time of induction of anaesthesia as the starting time of the procedure. A dummy variable 'time of day' was constructed that was defined as 'daytime' if between 08:01 and 17:00, 'evening' if between 17:01 and 24:00, and 'night-time' if between 00:01 and 08:00.

## Outcomes

The primary outcome was in-hospital mortality; the secondary outcome was the number of critical care admissions.

## Statistical analysis

We used SPSS (version 19.0) for data analysis. Categorical variables are presented as number (%) and continuous variables as mean (SD) when normally distributed or median (interquartile range, IQR) when not. We used  $\chi^2$  and Fisher's exact tests to compare categorical variables and the *t*-test or the Mann–Whitney *U* test to compare continuous variables. For categorical variables describing differences in hospital characteristics across time, a logistic regression analysis was used with the site being entered as a random factor. Significance was set at a *P* value less than 0.05. As the rate of missing values was very low (<0.05%), no imputation procedures were performed.

Logistic multilevel regression analysis was used to determine whether or not in-hospital mortality was different depending on the time of day the procedure occurred, as depicted by the hour of day anaesthesia commenced, and to adjust for identified confounding factors affecting outcome. The first step was to identify factors that were independently related to in-hospital mortality from univariable analysis. The following factors were entered into the model on the basis of their univariable relationship to outcome: age, American Society of Anesthesiologists (ASA) status as recorded just prior to induction<sup>16</sup> (reference category ASA I), urgency of surgery (reference urgent), severity of surgery (reference minor) and the presence of cirrhosis. Due to the multiplicity of tests performed and in order to avoid spurious associations and overfitting, only *P* values of less than 0.01 were considered as significant and therefore included in the model in order to allow for a consistent result. All factors entered were selected according to their scientific plausibility, and a low rate of missing data across the whole sample. The results of the model were reported as odds ratios (ORs) with 95% confidence interval (95% CI). We assessed the models through sensitivity analyses with four random (disjoint) subsamples of the cohort. The findings from the multivariable analysis were validated in a number of predefined subgroups, that is university hospital status, age less than 80 years, emergency procedures, intra-abdominal procedure and nonconsultant anaesthetist/surgeon performing procedure.

The second step was to evaluate the effects of time of day for the procedure. This was performed by constructing a subsequent model using the same inference factors as above, but including the time of day as a covariable to investigate a potential trend using daytime as the reference. The individual hospital was entered into each analysis as a random factor in order to adjust for the clustering effect with the consequent breaking of the

assumption that all observations are independent of one another. The analysis was repeated with time included per hour. Finally, we repeated the analysis with all hospitals, and patients.

## Sample size

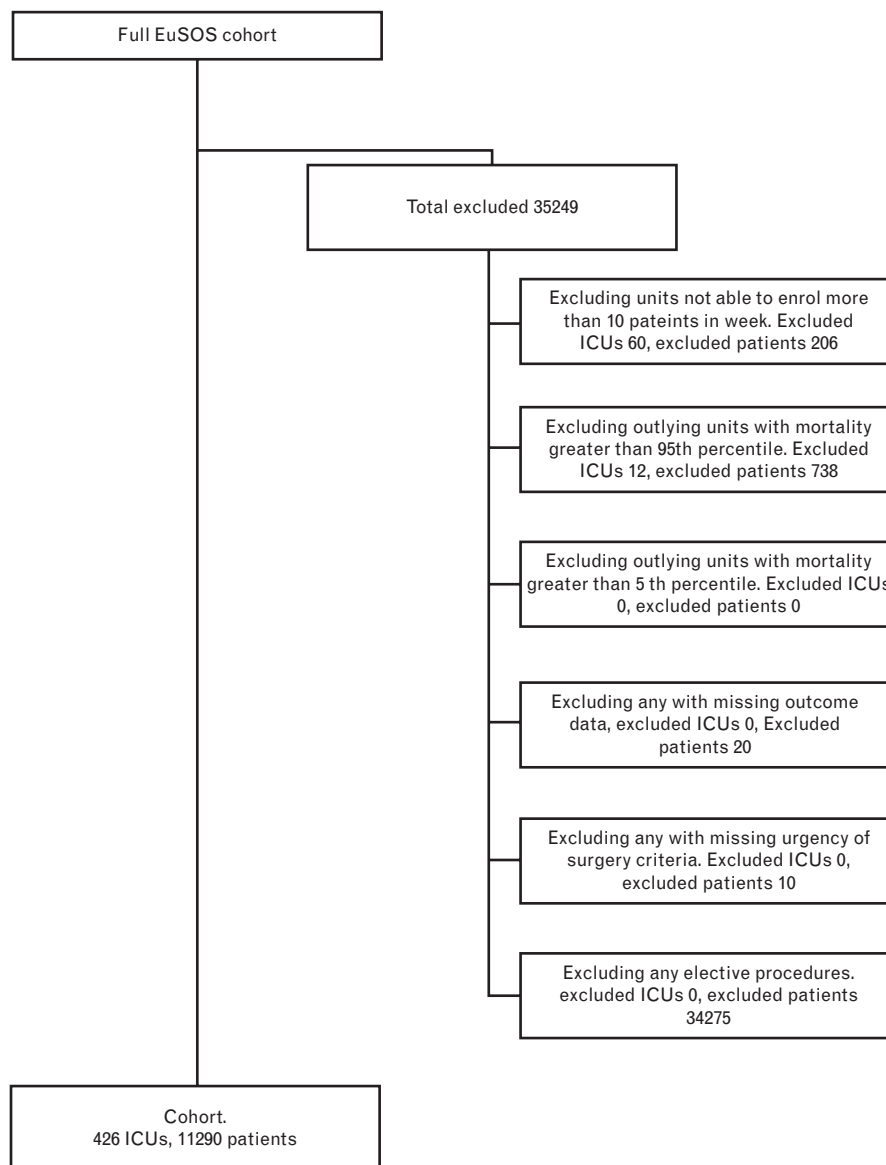
As the current study was a retrospective secondary analysis on the EuSOS database, we did not perform a formal sample size calculation in advance. In general, it is considered that one can include one confounder (or variable) for every 10 cases in a multivariable regression model.<sup>17</sup> With a total of 636 deaths in our database, we were able to adjust for all relevant confounders.

## Results

Of the 46 539 unique patients included in the original EuSOS database, 11 290 (24.3%) patients fulfilled the cohort criteria and were included in this study (Fig. 1). Characteristics of enrolling hospitals are presented in Table 1. Of the 11 290 patients, 8055 (71%), 2510 (22%) and 725 (6%) underwent urgent or emergency surgery during either the day, evening or night, respectively. Baseline characteristics of the patients are presented in Table 2 divided according to the time of day the procedure was performed. The majority underwent orthopaedic surgery or surgery of the lower gastro-intestinal tract. Patients having surgery at night were younger, more frequently received general anaesthesia and were more frequently graded ASA III, IV or V. Unadjusted 30-day in-hospital mortality for patients who underwent urgent or emergency surgery was 5.6%. The overall in-hospital mortality in patients who underwent emergency or urgent surgery was 9.1 and 4.2%, respectively.

In-hospital mortality after emergency or urgent surgery was 426 (5.3%), 150 (6.0%) and 60 (8.3%) during the day, the evening or the night, respectively. Night-time surgery was associated with a significantly higher in-hospital mortality rate than day-time surgery with an unadjusted OR of 1.62 (95% CI 1.22 to 2.14, *P* = 0.001). Other associations with in-hospital mortality included higher ASA grades, upper gastrointestinal surgical procedures, major emergency surgery and the presence of comorbid diseases. The highest in-hospital mortality was found in patients who underwent urgent or emergency surgery between 4:00 and 6:59, with a peak incidence of 19.1%, and an OR of 6.37 (95% CI 2.72 to 14.95) between 4:00 and 4:59 (Fig. 2). Patients who underwent urgent or emergency surgery during the night had a higher probability of being admitted to a critical care unit. Eight hundred and ninety-one (11.1%), 347 (13.8%) and 149 (20.6%) patients were admitted to an ICU after day, evening and night procedures, respectively. Admittance to an ICU was planned for 483 (54.3%) patients during the day, for 137 (39.7%) patients during the evening and for 54 (36.2%) patients during the night.

Fig. 1



Description of cohort.

Table 1 Hospital characteristics and overall outcomes according to the time of operative procedure

	Day 08:01 to 17:00	Evening 17:01 to 24:00	Night 00:01 to 08:00	P
No. (%) from University centre	5292/7992 (66.2)	1707/2494 (68.4)	547/720 (76.0)	0.001
No. of operating theatres	14 (9 to 21)	15 (9 to 22)	17 (10 to 25)	<0.001
No. high dependency beds	6 (0 to 11)	6 (0 to 12)	6 (0 to 12)	0.21
No. of intensive care beds	12 (8 to 24)	14 (9 to 28)	18 (10 to 32)	<0.001
No. (%) admitted to critical care	891/8053 (11.1)	347/2510 (13.8)	149/725 (20.6)	<0.001
Length hospital of stay (days)	4 (2 to 10)	4 (2 to 10)	4 (1 to 10)	0.01
In-hospital mortality (%)	426/8055 (5.3)	150/2510 (6.0)	60/725 (8.3)	0.003
Duration of surgery (min)	90 (60 to 135)	80 (52–120)	90 (58 to 130)	<0.001

Figures are given as median (IQR) except where indicated (%).

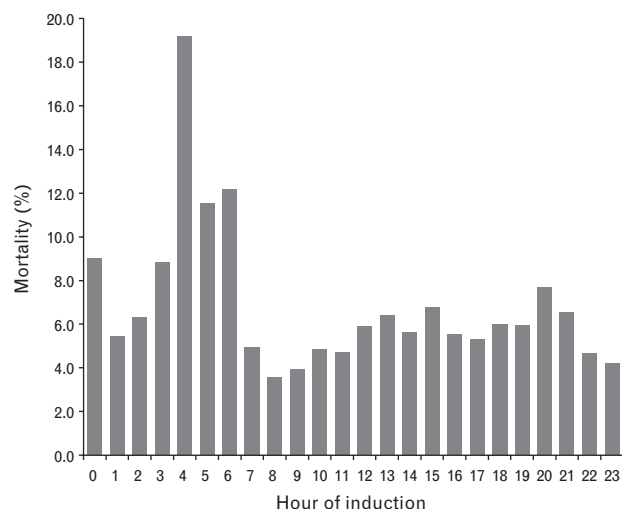
Table 2 Baseline characteristics according to the time of operative procedure

	8:01 to 17:00 n = 8055 Day	Evening 17:01 to 24:00 n = 2510	Night 00:01 to 08:00 n = 725	P
Male sex (%)	5292 (66.2)	1285 (51.2)	406 (56.0)	0.07
Mean age in years (SD)	57 (22)	53 (22)	51 (21)	<0.001
Anaesthetic technique (%)				
General anaesthesia	6264 (77.8)	1983 (79.0)	640 (88.3)	<0.001
Spinal anaesthesia	1353 (16.8)	373 (14.9)	49 (6.8)	<0.001
Epidural anaesthesia	249 (3.1)	62 (2.5)	23 (3.2)	0.26
ASA classification (%)				<0.001
I	2086 (26.0)	807 (32.2)	236 (32.6)	
II	2768 (34.4)	879 (35.1)	223 (30.8)	
III	2501 (31.1)	596 (23.8)	175 (24.1)	
IV	642 (8.0)	199 (7.9)	73 (10.1)	
V	39 (0.5)	24 (1.0)	18 (2.5)	
Surgical specialty (%)				<0.001
Orthopaedics	3125 (38.9)	687 (27.5)	105 (14.5)	
Breast	88 (1.1)	11 (0.4)	3 (0.4)	
Gynaecology	379 (4.7)	153 (6.1)	46 (6.4)	
Vascular	503 (6.3)	116 (4.6)	42 (5.8)	
Upper gastrointestinal	463 (5.8)	181 (7.3)	64 (8.9)	
Lower gastrointestinal	1284 (16.0)	730 (29.3)	269 (37.2)	
Hepato-biliary	288 (3.6)	87 (3.5)	38 (5.3)	
Plastic/cutaneous	430 (5.4)	155 (6.2)	39 (5.4)	
Urology	460 (5.7)	97 (3.9)	31 (4.3)	
Kidney	68 (0.8)	21 (0.8)	10 (1.4)	
Head and neck	471 (5.9)	104 (4.2)	30 (4.1)	
Other	467 (5.8)	153 (6.1)	46 (6.4)	
Comorbidities (%)				
Cirrhosis	116 (1.4)	38 (1.5)	27 (3.7)	<0.001
Congestive heart failure	547 (6.8)	143 (5.7)	37 (5.1)	0.047
COPD	967 (12.0)	233 (9.3)	77 (10.7)	0.001
Coronary artery disease	1,293 (16.1)	318 (12.7)	75 (10.4)	<0.001
Diabetes mellitus (insulin dependent)	483 (6.0)	125 (5.0)	38 (5.3)	0.137
Diabetes mellitus (noninsulin dependent)	602 (7.5)	154 (6.2)	41 (5.7)	0.023
Metastatic cancer	429 (5.3)	89 (3.6)	23 (3.2)	<0.001
Stroke	496 (6.2)	96 (3.8)	31 (4.3)	<0.001

Data are absolute numbers (%) unless otherwise specified.

The following variables were independently associated with in-hospital death and were thus used to adjust the univariable estimates of mortality: age, ASA status,

Fig. 2



In-hospital mortality (%) on operated patients by hour of induction.

severity of surgical procedure, urgency of surgical procedure and the presence of cirrhosis (Table 3). These variables were entered into a two-level hierarchical multivariable model with hospital as a random factor at the second level. After adjustment for factors associated with mortality in the univariable analysis, neither evening (OR 1.09; 95% CI 0.91 to 1.31;  $P=0.35$ ) nor night-time surgery (OR 1.20; 95% CI 0.90 to 1.60;  $P=0.36$ ) was significantly associated with increased in-hospital mortality (Table 4). The findings from the multivariable analysis were then validated in a number of predefined subgroups, none of which suggested any association between increased in-hospital mortality rates and surgery taking place during the evening and night-time. The sensitivity analysis showed good internal validity of the fitted model. In the per hour multivariable analysis, all univariable significant results were no longer significant (Fig. 3). Repeating the analysis with all hospitals included in the analysis did not change the results.

## Discussion

The principal finding of this study was that despite a higher in-hospital mortality rate for patients who underwent urgent or emergency noncardiac surgery at night,

**Table 3** Univariable binary logistic regression analysis (using hospital mortality as the dependent factor) presented as an odds ratio together with its 95% confidence interval

	Odds ratio (95% CI)	P
Time of surgery		
Day	Reference	
Evening	1.14 (0.94 to 1.38)	0.19
Night	1.62 (1.22 to 2.14)	0.001
ASA		
1	Reference	
2	1.62 (1.14 to 2.29)	0.007
3	4.76 (3.47 to 6.53)	<0.0001
4	20.71 (15.00 to 28.60)	<0.0001
5	76.30 (45.30 to 128.60)	<0.0001
Surgical procedure		
Orthopaedics	0.56 (0.39 to 0.79)	0.001
Breast	0.93 (0.38 to 2.24)	0.87
Gynaecology	0.45 (0.25 to 0.80)	0.007
Vascular	1.76 (1.18 to 2.62)	0.005
Upper gastrointestinal	2.05 (1.40 to 3.02)	<0.0001
Lower gastrointestinal	1.10 (0.78 to 1.57)	0.58
Hepato-biliary	1.42 (0.89 to 2.25)	0.14
Plastic/cutaneous	0.65 (0.39 to 1.07)	0.09
Urology	0.69 (0.42 to 1.14)	0.14
Kidney	0.31 (0.07 to 1.29)	0.11
Head and neck	0.59 (0.35 to 0.99)	0.05
Other	Reference	
Urgency of surgery		
Urgent	Reference	
Emergency	2.08 (1.76 to 2.46)	<0.0001
Severity of surgery		
Minor	Reference	
Intermediate	1.02 (0.80 to 1.31)	0.88
Major	3.36 (2.66 to 4.25)	<0.0001
Comorbidities		
Cirrhosis	4.83 (3.36 to 6.95)	<0.0001
Chronic obstructive pulmonary disease	1.68 (1.35 to 2.08)	<0.0001
Coronary artery disease	2.50 (2.09 to 2.99)	<0.0001
Diabetes mellitus (insulin dependent)	1.86 (1.41 to 2.45)	<0.0001
Metastatic cancer	2.72 (2.09 to 3.54)	<0.0001
Stroke	2.14 (1.63 to 2.79)	<0.0001
Congestive cardiac failure	3.53 (2.83 to 4.89)	<0.0001
Age (per year)	1.03 (1.03 to 1.04)	<0.0001

this association was no longer observed following adjustment for other known patient and surgery-related risk factors. Our analysis of the EuSOS dataset did not confirm a relationship between the time of day urgent or emergency surgery was performed and postoperative in-hospital death. Patients who were operated on during the night had a higher probability of being admitted to an ICU. The main strengths of this study are that we used a large prospective, multicentre and multinational database, which gave us the opportunity to explore different types of surgery and possible risk factors.

Our findings are comparable to the results of a study on thoracic organ transplant procedures, reporting no significant association between time of day and in-hospital mortality.<sup>18</sup> The authors of this study hypothesised that personnel involved in transplant surgery had developed alternative systems to cope with the limitations of night-time work. For example, they suggest that all personnel

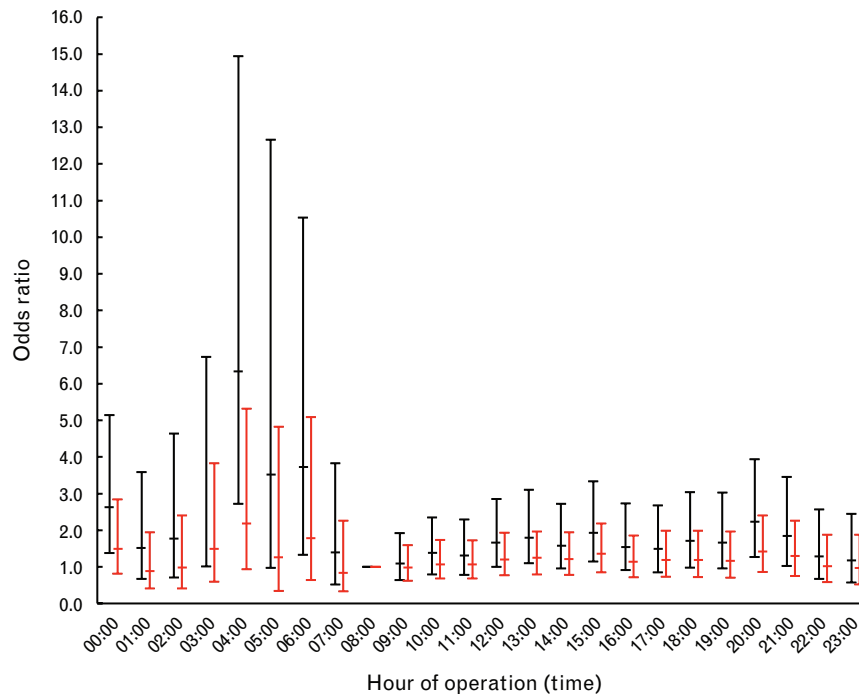
**Table 4** Hierarchical two-level binary logistic regression model (hospital as a random factor at the second level) assessing preoperative factors relating to in-hospital mortality (probability of death = 1) using a two-level model (patient/hospital) with hospital as a random factor

Variable	OR (95% CI)	P
Time of surgery		
08:00 to 17:00	1	
17:00 to 24:00	1.09 (0.91 to 1.31)	0.35
24:00 to 08:00	1.20 (0.90 to 1.60)	0.22
ASA		
1	1	
2	0.89 (0.69 to 1.17)	0.42
3	1.37 (1.03 to 1.82)	0.03
4	4.74 (3.51 to 6.40)	<0.0001
5	14.61 (8.71 to 24.49)	<0.0001
Urgency of surgery		
Urgent	1	
Emergency	1.33 (1.08 to 1.67)	0.001
Severity of surgery		
Minor	1	
Intermediate	0.91 (0.74 to 1.13)	0.4
Major	1.34 (1.08 to 1.67)	0.001
Comorbidities		
Cirrhosis	2.10 (1.41 to 3.13)	<0.0001
Age (per year)	1.01 (1.01 to 1.020)	<0.0001

Included 11 206; excluded 84; Total 11 290. ASA, American Society of Anesthesiologist's Physical Status Class; OR (95% CI) odds ratio (95% confidence interval).

have extensive experience in these procedures and are less prone to make mistakes even when the procedures are performed during the night. This suggestion should be regarded cautiously. If true, only the most experienced staff (surgeons, anaesthesiologists, operating room staff) should be available during the night, and not the less experienced senior resident or fellow with direct or indirect supervision. In contrast, a number of studies suggest that older doctors are more likely to struggle with the demands of night-time working.<sup>19,20</sup> There is more evident from a recent study of elective daytime cholecystectomy that compared the rate of conversion with open cholecystectomy, iatrogenic complications and death, according to whether the surgeon had worked the night before or not; no association was found.<sup>21</sup> Our findings are in contrast with previous studies examining medical care at night. These show that patients undergoing percutaneous coronary interventions for myocardial infarction had a higher incidence of myocardial infarction and death,<sup>6</sup> emergency orthopaedic surgery was associated with a higher rate of re-exploration,<sup>7</sup> night-time kidney transplant was associated with an increased risk of graft failure<sup>22</sup> and end-of-day procedures had more anaesthetic adverse events.<sup>23</sup> A correction for confounding factors was performed in all above-mentioned studies. These studies probably did not include the same confounders as we did, and therefore, it is difficult to make a direct comparison with our own. Inclusion of confounders merely depends on clinical and scientific reasoning, and is thus based on the researcher's individual considerations. There are a variety of possible explanations for the findings in these studies that include fatigue of the team members,

Fig. 3



Odds ratios with 95% confidence interval for in-hospital mortality on operated patients by hour of induction (black, Univariable results; red, multivariable results).

information loss due to shift changes, technical lapses, inappropriate staffing in the recovery and ward areas, and greater reliance on residents.<sup>8,13,14,24</sup>

It is interesting to note that in our study, the highest crude in-hospital mortality was found in patients who underwent urgent or emergency surgery between 04:00 and 06:59, with a peak incidence between 04:00 and 04:59. This observation could relate to the fact that surgery commenced at 4.00 is driven by urgency and therefore risk; sicker patients are unable to wait. However, this could also be explained by unintentional overestimation of the risk of out of hours surgery by doctors, perhaps concealing an increase in risk-adjusted in-hospital mortality.

We did find that during the night, more patients who underwent emergency or urgent surgery were admitted to the ICU. In our opinion, this could be an indication that those patients are sicker and that the procedure they underwent could not be postponed until day-time. An alternative explanation for this finding is that there was no alternative to ICU admission because a suitable alternative care facility was unavailable. If so, it is not surprising that ICU admittance during the night was higher. Unfortunately, we do not have data available to study this alternative hypothesis. It could be that admission to an ICU during the night improved the outcome of those patients. If so, then perhaps the higher mortality due to nocturnal surgery is counterbalanced by an

improved outcome for those admitted to the ICU during the night.

#### Clinical implications

Emergency surgery in sick patients need not wait until day-time, as mortality seems to be determined by factors related to the patient and surgical risk only, and not the time of day or seniority of the surgeon and anaesthesiologist performing the procedure. The impact of late night surgery falls on institutional resources. Staff who work at night need to rest the next day, possibly leading to cancelled cases or increased costs. This retrospective study is not designed to answer questions of this nature, but in future, studies with related outcomes are required. Our data indicate that the risk of being admitted to the ICU during the night after emergency and urgent noncardiac surgery is higher than during the day. This suggests that some organisation is required to have at least one bed available during the night.

#### Limitations

The present study has some obvious limitations. First, we retrospectively compared in-hospital mortality rates of patients undergoing emergency procedures during different time points of the day. Second, the parent study was not designed specifically to test this hypothesis. Without a biologically plausible and sound scientific rationale for the relationship between the variables (potential confounders) under study, the mortality and time of day, and



having forced them into the model, some over fitting could have occurred. This could hide a true increased risk of mortality after procedures performed during the night. Third, we excluded all patients who underwent planned day-case surgery, cardiac surgery, neurosurgery, radiological or obstetric procedures. It could be that mortality is not evenly distributed across all patient groups and that by excluding certain patient groups, we also excluded evidence of a difference between times of surgery. Fourth, the assumption that the start time of the procedure is a proxy for team fatigue is only reasonable if the evening and night teams worked all day before their evening or night shifts. If those teams did not work in the day shift, then start time would be not the most valid measure. Our data did not include the daytime activities of the night shift, and therefore, we are unable to explore the exact role of fatigue in a potentially increased nocturnal mortality.

Fifth, the nature of the data collection could have introduced bias. Those patients undergoing high-risk surgery might have assumed a higher profile than those undergoing more mundane urgent and emergency procedures, and may have been overrepresented in data collection. Although we planned to enrol every eligible patient undergoing surgery during the study period, we cannot be sure of the exact proportion of eligible patients included. Sixth, there could be residual confounding, as 30-day mortality is not only influenced by the procedure or the time of the day on which the procedure took place but also by numerous known or unknown events or factors that took place between the procedure and the death of the patient. In our study, we do not have the details of what happened in this period, and are thus unable to study those factors. It may be that these aspects affected all three groups of patients in a similar fashion and did not interfere with our analysis. Finally, our study was underpowered to detect a marginal increase in risk-adjusted mortality. A 20% increase in mortality would be clinically very important, but would not have achieved statistical significance in the present analysis. A posthoc sample size calculation based on our results (daytime incidence 5.3%, significance level 0.05, power 0.80) shows that one would need about 17 500 patients to reach statistical significance for the difference we have found. To overcome this limitation, a larger prospective study designed to address this specific question would be required. If this was a traditional cohort study, many centres and a considerable time would be needed to complete it. Our suggestion is to perform a case-control study in which patients who are operated on during the night (the cases) are compared with a sample of the patients operated on during the day (the controls). By using a case-control design, the number needed is reduced, and the study becomes more efficient.

## Conclusion

We failed to find a relationship between in-hospital mortality and the time of day a procedure was performed

in patients undergoing nonelective urgent or emergency surgery. This analysis would not have detected a small, in the region of 20%, but nevertheless a clinically significant increase in mortality, and a larger prospective study is required.

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