ASSOCIATION BETWEEN NIGHT/AFTER-HOURS SURGERY AND MORTALITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Word count - abstract: 250 words
Word count: 3097 words (excl. references)
Figures: 2
Tables: 2
Online supplement: 1

Running Title: Night/after-hours surgery and mortality

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ABSTRACT

Background: The association between night/after-hours surgery and patients' mortality is unclear.

Methods: The protocol of this systematic review was registered in PROSPERO (CRD42019128534). We searched Medline, Pubmed and EMBASE from inception until August 29 2019 for studies examining an association between timing of surgical procedures (time of anaesthesia induction or surgery start) and mortality (within 30 day or in-hospital) in adult patients. Studies reporting patients' mortality after surgery performed during the weekend only were excluded. All analyses were done using the random-effects model.

Results: We included 40 observational studies (36 retrospective and 4 prospective) that examined a total of 2,957,065 patients. Twenty-eight studies were judged of good quality and 12 of poor quality according to Newcastle-Ottawa score (NOS), due to lack of adequate comparability between study groups. Primary analysis from adjusted estimates demonstrated as association between night/after-hours surgery and a higher risk of mortality (odds ratio [OR] 1.16, 95% confidence interval [CI] 1.06 to 1.28, p= 0.002; studies=18; I^2=67%) based on low certainty evidence. Analysis from unadjusted estimates demonstrated a consistent association (OR 1.47, 95% CI 1.19-1.83; p=0.0005; studies=38, I^2=97%; low certainty). The number of centers per study had no credible subgroup effect on the association between the time of surgery and mortality. We were unable to evaluate the subgroup effect of urgency of surgery due to high heterogeneity.

Conclusions: Night/after-hours surgery may be associated with a higher risk of mortality. Patients' and surgical characteristics seem not to completely explain this finding. However, the certainty of the evidence was low.

Keywords: anaesthesia; surgery; nighttime; patient safety; perioperative

INTRODUCTION

Over 320 million surgical procedures are performed annually in response to global health requirements [1]. Recent estimates suggest that approximately 50 million people suffer peri-operative complications annually, leading to more than 1.5 million deaths [2]. The occurrence of peri-operative complications is multifactorial, and the outcome of these complications is related to the interaction between both *patient-related* and *patient-independent factors* [3]. *Patient-related factors* include the individual comorbidities and baseline clinical condition of the patient at the time of surgery. *Patient-independent factors* include the characteristics of the specific hospital and perioperative environment (i.e. infrastructure, organization, culture of safety) as well as human-factors. Among *patient-independent factors,* the timing of surgery has been extensively studied in several surgical settings with regards to its impact on patients' outcomes.

Urgent surgery is traditionally provided at all times, regardless of office hours, for urgent surgical cases. Scheduling of elective surgery at night or after-hours in an attempt to shorten surgical waiting time and reduce overcrowding of daytime operating rooms is a more recent practice [4]. Fatigue may worsen both individual physician and team performance [5 6] potentially leading to the occurrence of medical errors. Yet fatigue is a common phenomenon among healthcare workers working at night/after-hours [7 8 9 10]. The availability of a sufficient number of skilled medical practitioners is also lower at night or after-hours. As a result there may be less adherence to best practices resulting in lower quality perioperative care at these times.

Despite the presence of these and additional factors which seemingly predispose to poorer surgical outcomes in cases performed at night or after-hours, the literature remains divided regarding the association between the timing of surgery and mortality rates. We therefore conducted a systematic review and meta-analysis with the aim of finding in adult patients undergoing elective or nonelective surgery whether interventions performed during night or after-hours compared with daytime were associated with an increased risk of 30-day or in-hospital mortality.

METHODS

The protocol of this systematic review was prospectively registered in PROSPERO (CRD42019128534).

Data sources and searches: we performed a comprehensive search of Pubmed, Medline and EMBASE from inception until August 29th 2019. We searched for studies that referred to patients undergoing surgery using the key words "surgery" OR "anesthesia" OR "anaesthesia" AND "night" OR "nighttime" OR "out-of-hour" OR "after-hour" OR "off-hour". We restricted the search to studies of humans in the English language but did not apply any a-priori quality restrictions. The full search strategy is described in the **Supplementary appendix A**.

Eligible studies (randomized and nonrandomized) reported on adult patients undergoing surgical procedures (elective, urgent or emergency) regardless of specialty, and provided data on mortality, comparing procedures performed during nighttime/after-hours versus daytime. The time of surgery was defined as either the time of anaesthesia induction or the time of surgery initiation, as reported by the authors. We used the definitions of the authors for night/after-hours surgery, provided this category included cases that began after 4pm and included hours after 8pm. In studies comparing more than two groups, the data were re-classified into two groups ('night/after-hours' vs. 'day'). This was performed through discussion of the paper among the authors in order to achieve consensus regarding the best mode of division and only for raw data of deaths and total number of patients per group. We excluded case series, studies that did not describe surgical procedures, and those that included only paediatric patients. Studies reporting patients' mortality after surgery performed during the weekend only were excluded. We also excluded any study that did not report mortality until after hospital discharge.

We performed screening in two stages; first, two authors (AC, GM) independently screened all titles and abstracts to select potentially eligible studies. In the initial screening we excluded conference proceedings, case reports and case series. We also searched the reference list ('snowballing method') of all studies selected for full text review (by authors AC, GM, GI) to identify additional eligible studies. Studies selected for full review were included if two of the reviewers (MI, GI) agreed on their eligibility. Data extraction was performed in duplicate (AC, MI) and using a standard data extraction form. Discrepancies at any stage were adjudicated by two other authors (SE, AG). We contacted the corresponding authors of any study with questions regarding eligibility or data presentation. **Supplementary appendix B, Fig. S1** describes the inclusion/exclusion process of the papers according to PRISMA [11].

Outcomes and data abstraction

The primary outcome was mortality, within 30 days of surgery, or in-hospital if the former was unavailable as the longest relevant timepoint. In case of multiple time points, we used the closest to day 30. We abstracted mortality estimates and confidence intervals (CIs) or standard errors from the multivariable models of included studies that reported adjusted effect estimates for relevant covariates (e.g. patients' severity, surgical characteristics) [12]. If more than one multivariable model was presented in a study, we selected the adjusted estimate from the model that included the greatest number of covariates. The number of events (deaths) and the number of variables included in the model was captured [13]. Studies in which the ratio of covariates per events included in the model provided was too low (i.e. less than 1:10) were excluded [13]. We also abstracted the unadjusted number of deaths and total number of patients in the included studies in the two study groups (‘night/after-hours’ vs. day’). Finally, we abstracted data from propensity score matching analyses if reported.

We collected study data including patient and surgery characteristics as well as the definitions used by the authors to describe the times of surgery using a standardized case report form. The types of surgery were classified as follows: 1) Major abdominal-urological-vascular; 2) Cholecystectomy-appendectomy; 3) Bone-joint-spine-trauma; 4) Cardiac; 5) Transplantation or 6) Mixed (if more than one type of surgery was included in the cohort). For the classification in “elective” and “nonelective” we used the definitions and information provided by the authors; for studies including both elective and nonelective surgeries without proving separated data, we used a cut-off of at least 60% of the total number of surgical procedures to categorise such studies.

We report the detailed methods and results of this systematic review and meta-analysis according to the MOOSE checklist for Meta-analysis of observational Studies in **Supplementary appendix C** [14].

Risk of bias and certainty assessment

Two authors (YH, AC) independently assessed the methodological quality of the studies using the Newcastle-Ottawa Scale (NOS) [12 15]. This scale has three main domains and assigns one point of each subset of assessment criteria within the selection and exposure domains. Studies can obtain up to two points within the comparability domain. A “good” quality score required three or four stars in selection, one or two stars in comparability, and two or three stars in outcomes. A “fair” quality score required two stars in selection, one or two stars in comparability, and two or three stars in outcomes. A “poor” quality score reflected no or one star(s) in selection, or no stars in comparability, or no or one star(s) in outcomes. We assessed certainty in overall effect estimates using Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods [16].

Statistical analysis

In accordance with Cochrane guidance, we used the generic inverse variance method to pool adjusted estimates and standard errors from included studies reporting odds ratios (ORs) and 95% CIs from multivariable models [12]. The ORs were transformed to natural log, and standard errors (SEs) were calculated from the 95% CIs using standard formulas [12]. The results are reported as ORs with 95% CI. We used the DerSimonian and Laird method to analyze mortality from raw data (events and totals for each group) [17].

All the p-values were two tailed and considered significant if <.05. We assessed for statistical heterogeneity (i.e. chance variation between studies) using the non-parametric X^2 (Cochran Q) test, the I-squared statistic and visual inspection of the forest plots. Heterogeneity was considered likely if Q>df (degrees of freedom) and considered confirmed if P ≤0.10. This p-value was adopted to adjust for possible under-powering due to low event rates. We performed all analyses using a random-effects model (DerSimonian and Laird) [17].

We performed sensitivity analyses using unadjusted data (events and totals) and data from propensity score matched populations. We stratified studies according to the type of surgery subgroups in the primary and sensitivity analyses. Formal subgroup analyses were performed according to the number of centres (single vs. multi-centre in included studies) and according to the urgency of surgery (elective vs. urgent/emergency). All the analyses were performed by AC and MI with input from SE and BR, using Revman 5.3.

RESULTS

Characteristics of included studies

Of 5731 citations, 274 were selected for full text review and 40 observational studies proved eligible (see **Supplementary appendix B, Fig. S1)** [4 18-56]. These studies included 2,957,065 patients. Thirty-six studies were retrospective, one was a post-hoc analysis and one was a secondary analysis of a prospective study. Only two studies were defined as prospective. Fourteen studies were multi-centre while 26 were single centre. We classified five studies as relating to major abdominal-urological-vascular surgery, five to cholecystectomy-appendectomy, eleven to bone-joint-spine-trauma surgery, six to cardiac surgery, five to transplant surgery and eight as mixed. **Table 1** presents the included studies, their designs, their patient and surgical characteristics and their definitions for night/after-hours.

Risk of bias

Twenty-eight studies were judged of good quality and 12 of poor quality (**Supplementary appendix B, Table S1)**. The main reason for downgrading was the lack of adequate comparability between groups.

Primary analysis: Mortality (within 30-day or in-hospital)

Analysis from adjusted estimates

Twenty studies reported adjusted analyses. However, only eighteen of the studies were included. Two studies were excluded because their event:covariates ratio was below the accepted threshold for the model provided [26 57]. One study reported adjusted analyses for emergency and nonemergency subgroups separately [35].

Among the eighteen studies, six related to bone-joint-spine-trauma surgery, four to cardiac surgery, two to major-abdominal-urological-vascular surgery, two to transplant surgery and four described a mixed surgical cohort. All of the studies were of good quality according to NOS (**Supplementary appendix B – Table S1**) and had the highest scores in the within-study "comparability" item. The confounders adjusted for in each study are listed in **Supplementary appendix B – Table S2**. Briefly, almost all the studies adjusted for patient characteristics, comorbidities and the severity of the surgical condition.

Overall, surgery performed at night/after-hours was associated with a higher adjusted risk of mortality than surgery performed during the day (OR 1.16, 95% CI 1.06 to 1.28, p= 0.002; I^2=67%; **Fig. 1**) based on low certainty evidence (**Table 2**). The adjusted association between the timing of surgery and mortality stratified by the type of surgery is shown in **Fig. 1**.

Sensitivity analysis

Analysis from unadjusted data

Thirty-eight studies reported unadjusted data, including 322,228 patients (10,300 deaths) in the night/after-hours group and 2,605,760 patients (13,293 deaths) in the daytime group. The mixed surgery group contributed for 82.6% of the total number of patients included in this analysis, followed by major abdominal-urological-vascular (7.6%), bone-joint-spine-trauma (5.3%), transplant (3.8%), cardiac (0.5%) and cholecystectomy-appendectomy (0.2%).

Overall, surgery performed during night/after-hours was associated with higher unadjusted mortality than surgery performed during the day (OR 1.47, 95% CI 1.19 to 1.83, p=0.0005; I^2=97%; low certainty) (**Fig. 2**). The unadjusted association between the timing of surgery and mortality stratified by the type of surgery is shown in **Fig. 2**.

Analysis using data from propensity score matched groups

Five studies reported data from propensity score matching analysis, for a total of 130,541 patients in the night/after-hours (134 deaths) and 1,415,453 patients in the day group (81 deaths). The list of variables used in the propensity score matching analysis is included in **Supplementary appendix B – Table S3.** Most patients included in this analysis were from studies relating mixed surgery. Using data from propensity score analyses we found no significant association between surgery performed at night/after-hours and mortality but the confidence interval was very wide (OR 2.83, 95% CI 0.64-12.52; p=0.17; I^2=95%; n studies=5 - **Supplementary appendix B – Fig. S2**).

Subgroup analyses

Number of centres

Fig. S3 in the **Supplementary appendix B** showed the results of the analyses from adjusted estimates reported in multi-centre (OR 1.22, 95% CI 1.05-1.42; p=0.009; n studies=10) and single centre studies (OR 1.26, 95% CI 0.99-1.60; p=0.007; n studies=8). There was no credible subgroup effect based on multi-centre versus single centre (P=0.84) on the adjusted association, suggesting that the number of centres per study does not modify the association of night/after-hours surgery on mortality.

Urgency of surgery

Fig. S4 in the **Supplementary appendix B** shows the forest plot from adjusted estimates reported in studies included in the elective and nonelective subgroups. We were unable to make assumptions on the subgroup effect of urgency of surgery due to both high clinical and statistical heterogeneity.

DISCUSSION

In this study data from nearly 3 million patients suggest that surgery performed at night/after-hours is associated with a higher postoperative risk of death than surgery performed during the day. This effect was consistent in both adjusted and unadjusted analysis and across subgroups of interest. The adjusted odds of death were 16% higher in nighttime/after hour surgery than in daytime surgery (true population effect between 6% and 28%). Neither the number of centers per study nor the urgency of surgery had a credible subgroup effect on this association. This finding carries important implications for both scheduling of surgery and peri-operative risk management.

To the best of our knowledge this is the largest and most updated systematic review and meta-analysis evaluating the association between the timing of surgery and mortality. A previous meta-analysis on this topic included only 10 studies examining the outcome of mortality, and a much smaller number patients (n=165,409) [58]. Although they also found increased mortality among patients undergoing surgery after-hours as compared to daytime (non-event: OR=0.71, 95% CI=0.55–0.91, p=0.008), their analysis did not examine adjusted risk estimates of death, or the risk associated with specific types of surgery.

We decided to group night and after-hours surgery together as this is how most studies reported surgical timing and it is reasonable to assume that similar factors may lead to a decrease in the quality of surgical care at these times (e.g. fatigue, number and skill of the treating healthcare practitioners, availability of equipment and services). Although surgery performed during the weekend shares several features to that performed during the night, a decision was made to exclude studies reporting the outcomes of weekend surgery only in order to reduce the heterogeneity of the reviewed intervention and because fatigue is less likely to affect outcomes during weekends.

While only one of the studies included in this analysis specifically included healthcare practitioner fatigue as a variable of interest [45] (concluding that acute care surgeons have similar outcomes in fatigued or rested state), several studies unrelated to our topic have demonstrated the effect of fatigue on healthcare workers performance [7-10 59].

In a national survey among anaesthesiologists in New Zealand (70% response rate) 80% disclosed that they had made a medical error due to fatigue [60]. Sixty percent of respondents of a national survey among trainees in anaesthesia in the UK (59% response rate) believe that fatigue impairs their ability to do their job [9]. Working at night seems the most common cause of fatigue [9]. The implementation of several measures has been suggested to ameliorate fatigue and its effect on performance. These can be applied at both personal and organizational levels. Examples include improving education on rest, sleep and circadian rhythm, improving water and calorie intake during night shifts, enforcement of strategic breaks and micro-naps, shared decision making, the use of checklists and the availability of on- and post-shift rest facilities [7 9 61]. However, whether implementation of these strategies actually improves patient outcomes remains unknown.

The strength of the association between performance of surgery during night/after-hours surgery and mortality may differ according to the type of surgery. This could be explained by the large differences in the number of included patients and the rate of events reported across the different types of surgery It remains to be seen whether additional adjustment for the type of surgery and additional comorbidities may have affected the outcome. For some types of surgery, such as transplantation, the surgical setting often remains unchanged at all hours of the day and night. Regarding the effect according to study centres, it may well be that specific centres that have chosen to study this issue are a-priori more aware of the possibility of an increased risk and have therefore already implemented institutional safety measures [62].

Strengths and Limitations

This study has a number of strengths. These include protocol preregistration, a comprehensive search, a large number of included studies, both adjusted and unadjusted analysis careful risk of bias assessment and GRADE application to assess certainty of evidence [12 16].

The main limitation is the lack of randomized controlled studies addressing this question. As no randomised trials were identified, we only included non-randomised studies. As a result, residual confounding remains an important concern. To address this, we considered only the outcome of mortality as it is less prone to bias and is described most homogeneously across studies. We used adjusted estimates and standard error from studies that employed different statistical models and this may have contributed to heterogeneity in pooled estimate of effect. High clinical heterogeneity across included studies is another limitation. Indeed, a high degree of statistical heterogeneity was encountered in all analyses. The definition of night/after-hours varied among the studies included. This difference was most notable in the hour used to define the start of the “day” and in that defining the cut-off between day- and after-hours and nighttime as no consensus exists in the literature about the definition of “after-hours” or “night” surgery. Data on “human factors” (e.g. practitioner age, experience, hours on duty, wellbeing, fatigue) were largely lacking in included studies. We were therefore unable to directly evaluate the relation between these factors and mortality. This should be seen as a limitation of available evidence rather than of our review and further research on night/after-hours perioperative care should focus on these potentially modifiable factors. The results of the subgroup analysis basing on urgency of surgery should be considered with caution due to high heterogeneity and because three studies [25,32,52] included in the adjusted analysis reported on a cohort composed of both elective and nonelective surgeries, in various proportions. We used the ratio of events per covariates included in the models to valuate the possibility of inclusion in the adjusted analysis but there is no single correct solution to this conundrum[13]. Large part of this review population came from one study [52]. However, excluding this study from the adjusted analysis did not alter conclusions (OR 1.09, 95% CI 1.01-1.19; p=0.04; I^2=54%). Lastly, we decided not to create a funnel plot to assess potential publication bias due to the high degree of heterogeneity [17].

CONCLUSIONS

Surgery performed during night/after-hours seems associated with a higher adjusted risk of death than surgery performed during the day, but the certainty of the evidence supporting this finding is low. The patient and surgical characteristics that we have studied do not completely explain this finding. Further research should focus on human and logistic factors that could potentially modify this association.

Figure legend

Fig. 1 – Forest plot from adjusted estimates and standard error (primary analysis) for the outcome of mortality.

I-V: generic inverse variance method; SE: standard error; Yaghoubian 2010a refers to reference n. 54. Kelz 2009E refers to the emergency and NE to the nonemergency subgroups of the reference n. 35.

Fig. 2 – Forrest plot from unadjusted raw data for the outcome of mortality.

M-H: Mantel-Haentsel method; Yaghoubian 2010a refers to reference n. 54; Yaghoubian 2010b refers to reference n. 55.

Authors' Contributions

AC, CG, AG, SE conceived the content of this study. AC, MI, GM, GB, GI, YH, CG performed the systematic review and/or extracted the data and/or the assessment of quality of the study. AC, MI performed the analysis with input from BR and SE. AG, YH, GB, GI, CG, AG, BR, SE gave important intellectual content for the interpretation of the data. AC, MI, BR, SE wrote the manuscript. All authors' read and approved the final version of the manuscript.

Funding

None.

Acknowledgment

None.

Declaration of interest

The authors declare that they have no conflict of interest.

Appendix A: Search strategy

Appendix B: Supplementary data including PRISMA flow chart of inclusion-exclusion process, risk of bias table, subgroup and sensitivity analyses

Appendix C: MOOSE checklist

REFERENCES

1. Rose J, Weiser TG, Hider P, Wilson L, Gruen RL, Bickler SW. Estimated need for surgery worldwide based on prevalence of diseases: a modelling strategy for the WHO Global Health Estimate. *Lancet Glob Health* 2015;**3 Suppl 2**:S13–20

2. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. *Br J Anaesth* 2016;**117**:601–9

3. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet* 2012;**380**:1059–65

4. 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

5. Saadat H, Bissonnette B, Tumin D, et al. Effects of partial sleep deprivation on reaction time in anesthesiologists. *Paediatr Anaesth* 2017;**27**:358–62

6. Banfi T, Coletto E, d'Ascanio P, et al. Effects of Sleep Deprivation on Surgeons Dexterity. *Front Neurol* Frontiers; 2019;**10**:404

7. Farquhar M. For nature cannot be fooled. Why we need to talk about fatigue. *Anaesthesia* 2017;**72**:1055–8

8. 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

9. McClelland L, Holland J, Lomas J-P, Redfern N, Plunkett E. A national survey of the effects of fatigue on trainees in anaesthesia in the UK. *Anaesthesia* 2017;**72**:1069–77

10. Bernstrøm VH, Alves DE, Ellingsen D, Ingelsrud MH. Healthy working time arrangements for healthcare personnel and patients: a systematic literature review. *BMC Health Services Research* 2019;**19**:193

11. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;**6**:e1000100

12. Reeves BC, Deeks JJ, Higgins JP. Chapter 13: Including non-randomized studies. *Cochrane handbook for systematic reviews of interventions* Wiley Online Library; 2008;**1**:391

13. Green SB. How Many Subjects Does It Take To Do A Regression Analysis. *Multivariate Behav Res* 1991;**26**:499–510

14. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;**283**:2008–12

15. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;**25**:603–5

16. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**:924–6

17. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions. John Wiley & Sons; 2011;**4**

18. Ahlsson A, Wickbom A, Geirsson A, et al. Is There a Weekend Effect in Surgery for Type A Dissection?: Results From the Nordic Consortium for Acute Type A Aortic Dissection Database. *Ann Thorac Surg* 2019;**108**:770–6

19. Becker F, Voss T, Mohr A, et al. Impact of nighttime procedures on outcomes after liver transplantation. *PLoS One* 2019;**14**:e0220124

20. Chacko AT, Ramirez MA, Ramappa AJ, Richardson LC, Appleton PT, Rodriguez EK. Does late night hip surgery affect outcome? *J Trauma* 2011;**71**:447–53–discussion453

21. Chan YM, Tang N, Chow SK. Surgical outcome of daytime and out-of-hours surgery for elderly patients with hip fracture. *Hong Kong Med J* 2018;**24**:32–7

22. Charest-Morin R, Flexman AM, Bond M, et al. 'After-hours' non-elective spine surgery is associated with increased perioperative adverse events in a quaternary center. *Eur Spine J* 2019;**28**:817–28

23. Chiu CK, Chan CYW, Chandren JR, et al. After-hours elective spine deformity corrective surgery for patients with Adolescent Idiopathic Scoliosis: Is it safe? *Journal of Orthopaedic Surgery* 2019;**27**:2309499019839023

24. Cortegiani A, Gregoretti C, Neto AS, et al. Association between night-time surgery and occurrence of intraoperative adverse events and postoperative pulmonary complications. *Br J Anaesth* 2019;**122**:361–9

25. Coumbe A, John R, Kuskowski M, Agirbasli M, McFalls EO, Adabag S. Variation of mortality after coronary artery bypass surgery in relation to hour, day and month of the procedure. *BMC Cardiovasc Disord* 2011;**11**:63

26. 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

27. Dhadwal AK, Vaynblat M, Balasubramanya S, et al. Circadian rhythm has no effect on mortality in coronary artery bypass surgery. *J Card Surg* 2007;**22**:26–31

28. 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

29. Fernandes S, Carvalho AF, Rodrigues AJ, et al. Day and night surgery: is there any influence in the patient postoperative period of urgent colorectal intervention? *Int J Colorectal Dis* 2016;**31**:525–33

30. Gabriel RA, A'Court AM, Schmidt UH, Dutton RP, Urman RD. Time of day is not associated with increased rates of mortality in emergency surgery: An analysis of 49,196 surgical procedures. *J Clin Anesth* 2018;**46**:85–90

31. George TJ, Arnaoutakis GJ, Merlo CA, et al. Association of operative time of day with outcomes after thoracic organ transplant. *JAMA* 2011;**305**:2193–9

32. Halvachizadeh S, Teuber H, Cinelli P, Allemann F, Pape H-C, Neuhaus V. Does the time of day in orthopedic trauma surgery affect mortality and complication rates? *Patient Saf Surg* 2019;**13**:8

33. Heller JA, Kothari R, Lin H-M, Levin MA, Weiner M. Surgery Start Time Does Not Impact Outcome in Elective Cardiac Surgery. *J Cardiothorac Vasc Anesth* 2017;**31**:32–6

34. Kelz RR, Freeman KM, Hosokawa PW, et al. Time of day is associated with postoperative morbidity: an analysis of the national surgical quality improvement program data. *Ann Surg* 2008;**247**:544–52

35. Kelz RR, Tran TT, Hosokawa P, et al. Time-of-day effects on surgical outcomes in the private sector: a retrospective cohort study. *J Am Coll Surg* 2009;**209**:434–445.e2

36. Koltka AK, Ilhan M, Ali A, et al. Is nighttime laparoscopic general surgery under general anesthesia safe? *Ulus Travma Acil Cerrahi Derg* 2018;**24**:20–4

37. Lindemann J, Dageforde LA, Brockmeier D, et al. Organ procurement center allows for daytime liver transplantation with less resource utilization: May address burnout, pipeline, and safety for field of transplantation. *Am J Transplant* 2019;**19**:1296–304

38. Lonze BE, Parsikia A, Feyssa EL, et al. Operative start times and complications after liver transplantation. *Am J Transplant* 2010;**10**:1842–9

39. Matsuyama T, Iranami H, Fujii K, Inoue M, Nakagawa R, Kawashima K. Risk factors for postoperative mortality and morbidities in emergency surgeries. *J Anesth* 2013;**27**:838–43

40. Orman ES, Hayashi PH, Dellon ES, Gerber DA, Barritt AS4. Impact of nighttime and weekend liver transplants on graft and patient outcomes. *Liver Transpl* 2012;**18**:558–65

41. Ou R, Ramos G, Bowles C, Juo Y-Y, Shemin RJ, Benharash P. Are nonemergent cardiac operations performed during off-time associated with worse outcome? *J Surg Res* 2017;**218**:348–52

42. Phatak UR, Chan WM, Lew DF, et al. Is nighttime the right time? Risk of complications after laparoscopic cholecystectomy at night. *J Am Coll Surg* 2014;**219**:718–24

43. Pincus D, Desai SJ, Wasserstein D, et al. Outcomes of After-Hours Hip Fracture Surgery. *J Bone Joint Surg Am* 2017;**99**:914–22

44. Rashid RH, Zubairi AJ, Slote MU, Noordin S. Hip fracture surgery: does time of the day matter? A case-controlled study. *Int J Surg* 2013;**11**:923–5

45. Schuster KM, Hazelton JP, Rattigan D, et al. Can acute care surgeons perform while fatigued? An EAST multicenter study. *J Trauma Acute Care Surg* 2018;**85**:476–84

46. Siada SS, Schaetzel SS, Chen AK, et al. Day versus night laparoscopic cholecystectomy for acute cholecystitis: A comparison of outcomes and cost. *Am J Surg* 2017;**214**:1024–7

47. Steenkamp C, Kong VY, Clarke DL, et al. The effect of systematic factors on the outcome of trauma laparotomy at a major trauma centre in South Africa. *Ann R Coll Surg Engl* 2017;**99**:540–4

48. Switzer JA, Bennett RE, Wright DM, et al. Surgical time of day does not affect outcome following hip fracture fixation. *Geriatr Orthop Surg Rehabil* 2013;**4**:109–16

49. Tan PJ, Xu M, Sessler DI, Bashour CA. Operation timing does not affect outcome after coronary artery bypass graft surgery. *Anesthesiology* 2009;**111**:785–9

50. Tessler MJ, Charland L, Wang NN, Correa JA. The association of time of emergency surgery - day, evening or night - with postoperative 30-day hospital mortality. *Anaesthesia* 2018;**73**:1368–71

51. 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

52. 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

53. Wu JX, Nguyen AT, de Virgilio C, et al. Can it wait until morning? A comparison of nighttime versus daytime cholecystectomy for acute cholecystitis. *Am J Surg* 2014;**208**:911–8–discussion917–8

54. Yaghoubian A, Kaji AH, Putnam B, de Virgilio C. Trauma surgery performed by ‘sleep deprived’ residents: are outcomes affected? *J Surg Educ* 2010;**67**:449–51

55. Yaghoubian A, Kaji AH, Ishaque B, et al. Acute care surgery performed by sleep deprived residents: are outcomes affected? *J Surg Res* 2010;**163**:192–6

56. Zafar SN, Libuit L, Hashmi ZG, et al. The sleepy surgeon: does night-time surgery for trauma affect mortality outcomes? *Am J Surg* 2015;**209**:633–9

57. Novello M, Gori D, Di Saverio S, et al. How Safe is Performing Cholecystectomy in the Oldest Old? A 15-year Retrospective Study from a Single Institution. *World J Surg* 2018;**42**:73–81

58. Yang N, Elmatite WM, Elgallad A, Gajdos C, Pourafkari L, Nader ND. Patient outcomes related to the daytime versus after-hours surgery: A meta-analysis. *J Clin Anesth* 2019;**54**:13–8

59. Landrigan CP, Rothschild JM, Cronin JW, et al. Effect of reducing interns' work hours on serious medical errors in intensive care units. *N Engl J Med* 2004;**351**:1838–48

60. Gander PH, Merry A, Millar MM, Weller J. Hours of work and fatigue-related error: a survey of New Zealand anaesthetists. *Anaesth Intensive Care* 2000;**28**:178–83

61. Wong LR, Flynn-Evans E, Ruskin KJ. Fatigue Risk Management: The Impact of Anesthesiology Residents' Work Schedules on Job Performance and a Review of Potential Countermeasures. *Anesth Analg* 2018;**126**:1340–8

62. Cortegiani A, Misseri G, Gregoretti C, Giarratano A. Outcome of after-hours surgery: Setting, skill and timing may explain the outcome. *J Orthop Surg (Hong Kong)* 2019;**27**:2309499019861264