ORIGINAL ARTICLE

Time of day effects on the incidence of anesthetic adverse events

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Background: We hypothesized that time of day of surgery would influence the incidence of anesthetic adverse events (AEs).

Methods: Clinical observations reported in a quality improvement database were categorized into different AEs that reflected (1) error, (2) harm, and (3) other AEs (error or harm could not be determined) and were analyzed for effects related to start hour of care.

Results: As expected, there were differences in the rate of AEs depending on start hour of care. Compared with a reference start hour of 7 am, other AEs were more frequent for cases starting during the 3 pm and 4 pm hours (p<0.0001). Post hoc inspection of data revealed that the predicted probability increased from a low of 1.0% at 9 am to a high of 4.2% at 4 pm. The two most common event types (pain management and postoperative nausea and vomiting) may be primary determinants of these effects.

Conclusions: Our results indicate that clinical outcomes may be different for patients anesthetized at the end of the work day compared with the beginning of the day. Although this may result from patient related factors, medical care delivery factors such as case load, fatigue, and care transitions may also be influencing the rate of anesthetic AEs for cases that start in the late afternoon.

ealth care is a 24 hour a day operation. Factors such as time on the job, effects of circadian rhythms, and issues related to demand, scheduling, and staffing may all have an effect on patient care over the course of a day. Research has revealed that human performance is adversely affected by sleep deficit, circadian rhythm disruption, and long work hours, leading to decrements in cognitive and psychomotor performance and increased risk of accidents.¹⁻⁶ Fatigue is believed to be a greater problem in transportation accidents than drugs and alcohol combined, contributing to 15–20% of all transportation accidents.⁶ Surveys, laboratory and simulator studies, and evaluation of clinical data have revealed damaging effects of fatigue, both for the patient and the healthcare worker.7-14 Decisions about scheduling, demand, and staffing can result in variations in workload over the course of the day that may be reflected in care. In addition, staffing and scheduling decisions may create specific times of day that are associated with potentially risky events such as care transitions.15-18

Research evaluating relationships between time of day and clinical performance, as defined by the occurrence of adverse events (AEs) or patient outcomes, is limited. In anesthesia, this type of research is partially hindered by a relatively low frequency of adverse outcomes.¹⁹ One exception is a prospective study of cases of unintended dural puncture in obstetric epidural anesthesia that identified a greater risk of unintended dural puncture for epidural placement performed at night than during daytime.²⁰ There is also little research evaluating clinical performance over multiple times of day. Several studies have compared night performance with day performance^{7 20} and sleep deprived practitioners with well rested practitioners,^{9–13 21–25} but few have considered potential time of day effects such as the early morning and afternoon circadian troughs or start and end of shift.

We suspect that clinical performance may vary throughout the day due to effects of time on the job, circadian lows, and times of transition. Periods that include circadian lows (3– 5 am, 3–5 pm) and transfers of patient care from one anesthesia team to another (7 am, 4–6 pm) are times of day that may be related to qualitative changes in operating room performance and the incidence of AEs. Identifying periods of relatively impaired operating room performance is an important step in applying human factors principles to the improvement of patient care in this environment.

The Duke University Medical Center Department of Anesthesiology maintains a perioperative database that serves as a patient record and as a tool for assessing and improving quality of care. Specific clinical and administrative events are documented in the database as "quality improvement" (QI) events. These data provide an opportunity for a retrospective analysis of the incidence of AEs with respect to time of day. The primary objective of this evaluation was to determine whether time of day affects the number of AEs that occur perioperatively. We hypothesized that time of day of surgery would influence the incidence of anesthetic adverse events (AEs).

METHODS

The Saturn Information System is a perioperative database and charting tool through which anesthesia providers and perioperative nurses electronically record and track a patient's clinical progress. The Saturn database includes patient demographic data, surgical and anesthetic plans, and patient notes, including QI event descriptors and provider entered text. The selection of QI event descriptors and the addition of comments are under the discretion of the anesthesia care team (self-reports) in the operating room and preoperative and postoperative care units.

This study is based on data from 130 912 operating room cases recorded in Saturn between 1 May 2000 and 4 August 2004. The data include all anesthetic procedures completed at Duke University Medical Center during that time, including both inpatient and ambulatory procedures for adult and pediatric patients. All data were de-identified before transfer

Abbreviations: AE, adverse event; PONV, postoperative nausea and vomiting; QI, quality improvement

Table 1 Definitions of event categories

Error	An error is defined using an adaptation of the definition posed by The Australian Council for Safety and Quality in Health Care Shared Meanings project ²⁷ (Merry, personal communication, 2004):
	"The failure to complete an action as intended or the unintentional use of a wrong plan to achieve an aim." This definition includes both errors due to a deficiency in knowledge or a failure in judgment or decision making (e.g. "mistakes" or "errors of judgment") and errors which are an incorrect execution of a correct action sequence (e.g. "slips" or "technical errors"). Errors may occur by doing the wrong thing (commission) or by failing to do the right thing (omission). ²⁷ Because it is difficult to determine the intent of a practitioner, we will assume the "standard of care" as the underlying assumption of intent. Therefore, any incident that represents a deviation from "standard of care", whether it is an error. For our purposes, "standard of care" is defined in accordance with NC statutes as care that is " in accordance with the standards of practice among members of the same health care profession with similar training and experience situated in the same or similar communities" (1975. 2 nd Sess. c 977. s 4).
Harm	Harm includes any untoward medical occurrence in the patient that is not reasonably expected or common, based on the procedure being conducted. The instance of harm may or may not have a causal relationship with treatment. Harm includes any unfavorable incident or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the procedure for which the patient is receiving an esthetic care, whether or not considered related to the procedure. This includes emotional distress, psychological trauma, invasion of privacy, embarrassment, loss of social status or employment, or any economic impact considered related to the conduct of the procedure. This category does not include delays of an administrative nature (see "Delay" below). Our definition is similar to an incident of "Harm" or "Loss" for the patient, as defined by the Shared Meanings project: ²⁷ "Harm: Death, disease, injury, suffering, and/or disability experienced by a person" (see loss)
Other AE	This category is included for other perioperative events that may have some association with error or harm but do not provide sufficient evidence of either error or harm based on the above definitions. This category includes, for example, events that are sometimes due to error or sometimes result in harm; events that sometimes occur concurrently with either error or harm; or events that may be associated with an increased risk for error or harm. This category does not include delays of an administrative nature (see "Delay" below).
Delay	This category is included to track administrative delays. These include events that delay the start of the procedure or the transfer of the patient. Examples include: late arrival of the surgeon, anesthesiologist, other care team members or the patient; readiness problems associated with equipment, operating room, or other care units; and lateness of laboratory results or other necessary information. This category is NOT intended to reflect changes in procedure length or anesthesia care associated with other perioperative events of the categories error, harm, or other AEs as defined above.

to the research team and were therefore exempt from institutional review.

The independent variable we selected to assess the effect of time of day on the incidence of AEs was the start hour of care. The following characteristics of the patient, procedure, and operating room environment were expected to affect the incidence of AEs and were included in our analyses as covariates:

- Age of patient (in months).
- Sex of patient.
- Global assessment of patient health (American Society of Anesthesiologists (ASA) physical risk classification).
- Emergency or non-emergency/scheduled procedure.
- Duration of anesthesia care (in minutes).

- Complexity of the procedure (ASA base units—a measure of case difficulty used for billing purposes).
- Activity level of the OR suite (number of operating rooms running).

Although of interest, details such as the experience level of the anesthesia provider, the case load of the attending anesthesiologist, and the makeup of the care team could not be determined from the de-identified data set.

Response variables for our analyses were anesthetic AEs. These were determined from the self-reported QI events recorded in the perioperative database. Based on Leape's definition of preventable and non-preventable AEs,²⁶ records that indicate an error or failure to adhere to a standard of care can be considered preventable AEs. We originally planned to separately analyze events which may be preventable, events which cause some harm to the patient, and non-preventable events. However, due to the nature of the database, we were not able to definitively distinguish preventable and non-preventable events. We were, however, able to separate the data into three categories of events. These included error (preventable events), harm (events which resulted in harm to patients), and other AEs. We included the category of "other AEs" to classify adverse events that could not be definitively described as preventable or causing harm based on the information available, but were likely to be associated with error, harm, or an increased risk of either error or harm. Detailed definitions of the categories used by the research team are provided in table 1.

When QI events are entered into the database at the point of care by a certified registered nurse anesthetist (CRNA), anesthesia resident, or staff anesthesiologist, the practitioner selects from a list of perioperative events and also has an opportunity to enter additional text describing the QI event. Five experienced anesthesiologists reviewed the QI event labels available in the database and came to a consensus (in a face to face meeting) regarding whether each QI event label represented error, harm, or other AE (table 2). The panel of reviewers also identified the QI events that represented administrative delays because we believed that there may be an association between delays and AEs. We validated the assignment of QI events into these categories by comparing the automated classification by event labels with manual classification by four experienced anesthesiologists (JT, JM, KG, MSS) using both the event labels chosen by the practitioner and associated text. Data from 148 cases showed that, for the largest portion of the events (83%), two or three of the reviewers made no change to the classification that would have been made based on the event label alone. In addition, the reviewers very rarely agreed to change from an adverse event category to no event or delay (four cases, 2.6%) and they never agreed to change from either the error or harm category to the less definitive other AE category. Based on these results, we concluded that an analysis of the data based on categorization by QI event labels was unlikely to attain different results than an analysis that included expert review of each case that contained text descriptions.

Analysis of data

Because of the binary nature of the AE response variables, the data were subjected to multiple logistic regression analysis.²⁸ The multiple regression model included start hour of care as an independent variable with the patient and procedural factors included as covariates. In order to minimize the degrees of freedom in the statistical model, the ASA physical status classification was reduced to two categories of low risk (ASA classification 1 or 2) and high risk (ASA classification 3, 4, or 5). Hour of day was treated as a categorical variable as were ASA status, sex, and emergency (yes or no). Age in

Table 2	QI events	assigned	to AE	categorie

Error	122 Delayed recognition	173 Wrong medication/wrong
events	esophageal infubation	dose
	1.33 Delayed recognition	assessment
	bronchial intubation	
Harm	114 Unplanned outpatient	165 Patient awareness
events	admission	(unintentional)
	115 Unplanned admission to ICU	171 Significant hyperthermia
	121 Inability to intubate	172 Significant (unintended)
	124 Trauma to airway	hyperthermia
	125 Damage to teeth	174 Drug/transtusion reaction
	131 Significant hypoxemia	1/6 Prolonged nausea/vomiting
	134 Severe bronchospasm	191 Eye injury
	136 Pulmonany aspiration	192 Skin/ son issue injury
	146 Confirmed myocardial infarction	195 Other injury/catastrophe
	147 Pulmonary edema/CHF	204 Emergency tracheotomy or
	148 Cardiac arrest	cricothyrotomy
	152 Excessive block	211 Wound infection
	153 Adverse event following block	212 Other infection/sepsis
	155 Post dural puncture headache	213 Deep vein thrombosis
	161 Prolonged sedation	214 Pulmonary thromboembolism
	162 Prolonged neuromuscular	215 Postoperative oliguria/anuria
	blockade	216 New postoperative need for
	163 Central nervous system	dialysis
	complication	417 Postoperative nausea and
	164 Peripheral neurologic deficit	vomiting
Other	123 Laryngospasm	151 Failed/inadequate block
adverse	127 Unanticipated difficult	154 Unintentional dural puncture
events	intubation	156 Other regional
	128 Other airway	166 Other neurological
	132 Significant hypercapnia	175 Problem with vascular access
	137 Other respiratory	181 Equipment problem (describe)
	141 Significant hypertension	194 Staff injury (describe)
	142 Significant hypotension	217 Other postoperative
	143 Significant lachycardia	416 Pain management
	145 Suspected myocardial	418 Failed discharge criteria
	ischemia	808 Unclassified (please describe)
	149 Other cardiovascular	
Delay	301 No/incomplete surgical consent	404 Room not ready: occupied
	302 No green sheet (no	405 Room not ready: not clean
	preoperative assessment paperwork)	406 No transporter
	303 Late arrival of patient	407 Floor nurse unavailable
	304 Waiting for results	408 PACU nurse admitting 2nd
	305 Time for regional anesthesia	patient
	306 OK not ready	409 Waiting for surgeon: orders
	307 Surgeon unavailable	410 Waiting for surgeon: MOIB
	200 Anesthesia unavailable	(waiting for surgeon to sign
	DV7 Anestnesia aetainea in	posioperative care unit patient
	310 Other region for delay	All Waiting for surgeon: PV
	(specify)	(prescription)
	401 No assigned intermediate	412 Waiting for surgeon: other
	bed	413 Waiting for anesthesiologist
	402 No assigned SD bed	414 Waiting for lab results
	103 No assigned ICLI had	415 X-ray to be taken or read
	405 NO ussigned ICO bed	

ICU, intensive care unit; CHF, congestive heart failure; OR, operating room; PACU, postoperative care unit; SD, stepdown.

Variable	Proportion	Mean (SD)
Emergency	8% emergency	
Sex	52% female	
ASA physical status	62% low risk	
	(ASA 1 and 2)	
Age		48 (23) years
Duration		2.7 (2.0) hours
Complexity		6.7 (3.9) ASA base
1 /		units
OR suite activity level		34 (7) OR rooms in
		operation

months, surgery duration in minutes, and surgery complexity in ASA base units were treated as continuous variables.

Since there were fewer night time cases, initial review of the data suggested that power would be maximized by grouping events into eight 3 hour intervals over a full 24 hour day. We also conducted a separate hour by hour comparison of the non-emergency (scheduled) procedures over the 12 hours of the regular work day (6 am to 6 pm). In the 12 hour analysis, the category of error was excluded due to an insufficient number of observations.

The response variables for four separate analyses were (1) harm, (2) error, (3) other AEs, and (4) delays. A review of the frequency of specific event types revealed a proportionally high frequency of postoperative nausea and vomiting (PONV) in the harm category (35% of harm events) and a proportionally high frequency of pain management issues in the other AEs category (49% of other AEs). Post hoc analyses therefore included analyses of the response variables PONV and pain management. We also analyzed harm with PONV events excluded and other AEs with pain management events excluded. Our goal in this analysis was to understand the degree to which these specific event types may be driving the overall results for harm and other AEs.

To further describe significant time of day effects, comparisons were made using odds ratio estimates. We selected the start hour time period with the highest frequency of starts (7 am hour or 6–9 am time period) as the reference point for all comparisons.

RESULTS

Cases with missing start or end times were excluded from the analysis dataset, reducing the sample from 130 912 to 107 620 cases. The frequency distribution and means of the covariates are shown in table 3, and the frequencies of all case start times for each start hour are shown in fig 1. The dataset was further reduced to 90 159 cases for the multiple regression analysis because of missing covariate data. From this dataset, the following frequencies were observed for the response measures:

- Error: 31
- Harm (including PONV events): 667
- Other AEs (including pain management events): 1995
- Delays: 9497
- PONV: 277
- Pain management: 1102

As expected, the multiple logistic regression analysis revealed a number of significant effects of covariates on AEs and delays in both the 24 hour analysis of all cases and the work day analysis of non-emergency cases. The results for the 24 hour analysis are shown in table 4.



Figure 1 Frequency of case starts throughout the day (daily averages assume 365 day/year operation).

Increased probability of an AE associated with:	For the following event categories	
Higher patient age	Other AEt, Delayt	
Female sex	Harmt, Other AEt	
High ASA status	Harm*, Other AEt, Delayt	
Longer case duration	Error*, Harmt, Other AEt, Delay	
Emergency cases	Delay†	
Higher complexity cases	Other AEt, Delayt	
Greater number of OR rooms	Harm**, Other AEt, Delayt	
in operation	, , , , , , , , , , , , , , , , , , , ,	

In the multiple logistic regression analysis over a 24 hour day, the incidence of other AEs was significantly influenced by the 3 hour time period in which surgery began (p<0.0001). The predicted probability of other AEs (with all covariates held constant) is shown in fig 2. Visual inspection of the graph suggests a higher probability of AEs in the late afternoon and early evening hours than in morning and early afternoon cases. Odds ratio estimates confirm the afternoon effect, indicating that cases that began between 3-6 pm had a higher probability of other AEs than cases that started during the reference time of 6–9 am (point estimate 1.48, 95% Wald confidence limit 1.19 to 1.84). Odds ratio estimates also indicate that, compared with the reference time of 6-9 am, there was a lower probability of events for cases starting later in the morning (9 am-noon) (point estimate 0.68, confidence limit 0.68 to 0.85) or in the early afternoon (noon-3 pm) (point estimate 0.88, confidence limit 0.77 to 0.99).

Analysis of hourly starts of scheduled cases over the workday (6 am-5 pm) revealed significant effects of start time for harm (p<0.01) and other AEs (p<0.0001). Considering the effects on harm, odds ratio estimates revealed significant differences from the reference start time of 7 am for the 8 am hour only (point estimate 0.62, confidence limit 0.45 to 0.85). However, visual inspection of the predicted probability of harm (fig 3) reveals trends toward an increase in events for cases that start in the late afternoon. For example, the predicted probability of harm is three times higher for cases that start at 3 pm (1.0%) than for those starting at 8 am (0.3%). Compared with the 7 am reference time, odds ratio estimates suggest trends toward a greater number of events for the 2 pm and 3 pm start hours (2 pm point estimate 1.38, confidence limits 0.97 to 1.98; 3 pm point estimate 1.53, confidence limits 0.98 to 2.40).

Considering the effects on other AEs, the predicted probability of an event indicated an increased risk for cases starting in the late afternoon (fig 3). Odds ratio estimates revealed a higher probability of other AEs for cases beginning in the 3 pm and 4 pm hours than for those beginning at the reference hour of 7 am (3 pm point estimate 1.49, confidence limit 1.15 to 1.93; 4 pm point estimate 1.68, confidence limit 1.16 to 2.42). Odds ratio estimates also revealed that cases starting in the 6 am hour and all hours between 8 am and 1 pm had a lower probability of an event than cases starting in the 7am hour (with the strongest effect seen at 9 am with a point estimate of 0.58 and confidence limits of 0.48 to 0.70). In examining specific data points for the size of the effect, the predicted probability of other AEs increased from a low of 1.0% for cases starting at 9 am to a high of 4.2% for cases starting at 4 pm.

Because of the high proportion of pain management events in the other AEs data set and PONV events in the harm dataset, we analyzed these specific events for time of day effects as post hoc analyses. The analyses revealed significant



Figure 2 Predicted probability of other AEs in 3 hour time increments throughout the day. Notes: (1) Error bars indicate upper and lower bounds of 95% confidence intervals. (2) Filled circles represent data points that are significantly different from the reference time of 6–9 am (represented by a cross). (3) Assumes covariates set to male sex, low ASA physical status rating, non-emergency, duration 143 minutes, number of OR rooms 34, ASA base units 6.



Figure 3 Predicted probability of harm and other AEs for scheduled cases over the work day (6 am–5 pm). Notes: (1) Error bars indicate upper and lower bounds of 95% confidence intervals. (2) Filled symbols represent data points that are significantly different from the reference time of 7 am (represented by a cross). (3) Assumes covariates set to male sex, low ASA physical status rating, non-emergency, duration 143 minutes, number of OR rooms 34, ASA base units 6.

effects for both pain management (p<0.0001) and PONV (p<0.0001) in both the 24 hour and work day analyses. For the most part, these effects mirrored the effects seen in the general analyses of other AEs and harm. There was an increased probability of pain management events for cases starting in the late afternoon (2, 3, and 4 pm) compared with 7 am. There was also a decreased probability of pain management for cases starting in the mid morning (8 amnoon) compared with 7 am. For PONV, there was an increased probability of events for cases starting at 2 pm compared with 7 am and a decreased probability of events in the late morning (8–10 am) compared with 7 am.

For the work day analysis, removal of pain management and PONV events from the other AEs and harm datasets reduced the strength of the time of day effects such that they were no longer significant (p = 0.13 for harm; p = 0.18 for other AEs. Time of day had a significant effect on other AEs over a 24 hour day (p<0.05). In this case, the midday probability of an event (9 am–noon and noon–3 pm) was lower than the reference time of 6–9 am. In general, the overall rates of occurrence with these high frequency events excluded were very low (around 0.2% for harm and 0.6% for other AEs) and the confidence intervals were very large (of the order of 1.5 to 2.5% with, for example, a point estimate of 1.00 and confidence limits of 0.59 to 1.71 at 6–9 pm).

In both the 24 hour analysis and the work day analysis, delays were significantly affected by hour of day (p<0.0001).



Figure 4 Predicted probability of delays by time of day. Notes: (1) Error bars indicate upper and lower bounds of 95% confidence intervals. (2) Filled symbols represent data points that are significantly different from the reference time (represented by a cross). (3) Assumes covariates set to male sex, low ASA physical status rating, non-emergency, duration 143 minutes, number of OR rooms 34, ASA base units 6.

The predicted probabilities of delays from both analyses are shown in fig 4. Delays appear to increase substantially over the work day. Predicted probability increases from just over 5% in the morning hours to approximately 30% in the late afternoon.

DISCUSSION

The results of our analyses support our hypothesis that AEs are influenced by the time of day of surgery. We identified a small but significant increase in AEs in the early morning compared with late morning and early afternoon hours. This effect was robust throughout a number of different analyses and event types. We also identified a significant and sizable increase in AEs in the late afternoon compared with early morning. Post hoc analyses revealed that this effect may have been driven primarily by the most frequent events of PONV and pain management.

In addition to the significant effects of AEs, there was a significant and sizeable increase in administrative delays in the late afternoon. This suggests that there may be a relationship between administrative delays and AEs that requires further investigation.

There are a number of reasons why AEs may occur more often at the end of the day, including (1) end of day fatigue, (2) afternoon circadian lows, (3) care transitions, (4) change in makeup of the care team, (5) changes in case load, (6) physiological changes in the patient, or (7) other unrecognized factors. Some of these same factors might also be relevant as an explanation for the increased AE rate in the early morning. These data were collected at our medical center where all anesthesia care is supervised by a faculty physician anesthesiologist and delivered primarily by either an anesthesia resident or a CRNA. The attending anesthesiologist may supervise up to four CRNAs or up to two residents in separate operating rooms. The work day generally begins between 6 and 7 am and ends between 3 and 6 pm for most attendings and residents. However, each day several attendings stay later to finish cases or remain on a late call schedule that ends between 6 and 9 pm. Both attendings and residents work a distinct night call schedule. CRNAs work 12 hour shifts of 7 am to 7 pm, 11 am to 11 pm, or 7 pm to 7 am. Scheduling details are visually depicted in fig 5.

Because of this scheduling system, times of transition in anesthesia care are most likely to occur around 6-8 am and 3–7 pm. Changes in the makeup of the care team may also occur during these times. In particular, a greater fraction of the case load may be covered by CRNAs rather than by residents during the 3-7 pm time frame. There also may be increases in case load per attending physician associated with the 3-7 pm time frame as supervision transitions to fewer late call anesthesiologists. Our finding of a substantial increase in delays in the late afternoon also suggests a potential problem of workload at this time. In contrast to the 6-8 am time of transition when well rested anesthesiologists arrive to begin the day, physicians supervising cases during the 3-7 pm transition times are usually physicians who are continuing cases, taking over new cases, and who began their work day between 6 and 7 am.

Arbous et al²⁹ identified specific issues associated with both transitions and the makeup of the patient care team that affect postoperative mortality and coma. They found an increased risk of perioperative death associated with intraoperative change of one anesthesiologist by another. In addition, the risk of severe morbidity and mortality was reduced by (1) direct availability of an anesthesiologist (via intercom rather than phone or pager), (2) the presence of a full time (versus part time) anesthetic nurse, and (3) the presence of two individuals at emergence and termination of anesthesia. While there are some relevant differences in the model for anesthesia care in the United States and Europefor example, differences in training and responsibilities of anesthesia nurses and requirements for anesthesiologists to be present at critical points such as induction and emergence-it is likely that, as case load increases, anesthesiologists may be faced with difficult choices about where their presence is most needed or when they should call for help.

This study has some limitations. Firstly, it is based on nonanonymous self-reports. Although the database is used as the official perioperative record which requires providers to be diligent in reporting significant events, they may be biased in



Figure 5 Approximate Duke University Medical Center anesthesia staff schedules over a 24 hour day. Note: Medium grey areas represent flexible start and stop boundaries as well as times of overlapping coverage and transition.

how they document events or in their decisions whether or not to report minor incidents. They may be more likely to select QI event labels that describe the event more generally or are seen as patient related events rather than labels that suggest clinician error and indicate a cause or possible blame. There also may be an increase in documentation associated with cases in which there are transitions, either for purposes of providing key information to oncoming providers or for providing a clear historical record of whether events occurred before or after the transition.

Secondly, a reduction of over 30% in our sample size due to missing data calls into question the robustness of the database for the purposes of these analyses. Although we were unable to identify specific causes of missing data, we have no reason to believe that there are any systematic biases associated with missing data that would affect the results of our study.

Lastly, we were unable to clearly determine which events were preventable. This limits our ability to determine whether or not the time of day effects have underlying causes that can be controlled. For example, circadian effects on the patient such as changes in the sensitivity to pain³⁰ or propensity for PONV could partly explain our results.

Most studies on the effects of fatigue on clinical outcomes have focused on sleep deprivation or disrupted circadian rhythms-for example, looking at post call effects^{15 21} or comparing night time with daytime performance.^{7 20} We are not aware of any other studies that have revealed decrements in clinical outcome associated with the beginning or end of the work day. This study presents evidence of a significant and sizeable increase in the incidence of anesthetic AEs in the late afternoon hours. It is unclear whether the increase in AEs was due to (1) problems related to increased case load and delays at these times, (2) effects of caregiver fatigue after many hours on the job, (3) problems that occur because of transitions, (4) increased reporting during times of transitions, or (5) other unidentified factors such as changes in the makeup of the anesthesia care team or physiological changes in the patients. Future research should focus on identifying the causes of increases in anesthetic AEs in the late afternoon. After these causes are identified, strategies to reduce or eliminate these events should be evaluated.

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