

Behavioral Modification of Intraoperative Hyperglycemia Management with a Novel Real-time Audiovisual Monitor

Subramanian Sathishkumar, M.B.B.S., Manda Lai, M.D., M.B.A.,
Paul Picton, M.B.B.Ch., F.R.C.A., Sachin Kheterpal, M.D., M.B.A.,
Michelle Morris, M.S., Amy Shanks, Ph.D., Satya Krishna Ramachandran, M.D., F.R.C.A.

ABSTRACT

Background: Hyperglycemia, defined as blood glucose (BG) levels above 200 mg/dl (11.1 mM), is associated with increased postoperative morbidity. Yet, the treatment standard for intraoperative glycemic control is poorly defined for noncardiac surgery. Little is known of the interindividual treatment variability or methods to modify intraoperative glycemic management behaviors. AlertWatch (AlertWatch, USA) is a novel audiovisual alert system that serves as a secondary patient monitor for use in operating rooms. The authors evaluated the influence of use of AlertWatch on intraoperative glycemic management behavior.

Methods: AlertWatch displays historical patient data (risk factors and laboratory results) from multiple networked information systems, combined with the patient's live physiologic data. The authors extracted intraoperative data for 19 months to evaluate the relationship between AlertWatch usage and initiation of insulin treatment for hyperglycemia. Outcome associations were adjusted for physical status, case duration, procedural complexity, emergent procedure, fasting BG value, home insulin therapy, patient age, and primary anesthetist.

Results: Overall, 2,341 patients had documented intraoperative hyperglycemia. Use of AlertWatch (791 of 2,341; 33.5%) was associated with 55% increase in insulin treatment (496 of 791 [62.7%] with and 817 of 1,550 [52.7%] without AlertWatch; adjusted odds ratio [95% CI], 1.55 [1.23 to 1.95]; $P < 0.001$) and 44% increase in BG recheck after insulin administration (407 of 791 [51.5%] with AlertWatch and 655 of 1,550 [42.3%] in controls; adjusted odds ratio [95% CI], 1.44 [1.14 to 1.81]; $P = 0.002$).

Conclusion: AlertWatch is associated with a significant increase in desirable intraoperative glycemic management behavior and may help achieve tighter intraoperative glycemic control. (**ANESTHESIOLOGY 2015; 123:29-37**)

HYPERGLYCEMIA is associated with poor outcomes in critically ill patients,^{1,2} and tighter control of blood glucose (BG) is an established tenet of clinical management.³ Perioperative hyperglycemia is associated with increased hospital length of stay,⁴ morbidity,^{5,6} and mortality after noncardiac general surgery.⁷ There is accumulating evidence that postoperative outcomes are influenced by perioperative hyperglycemia in patients with undiagnosed type 2 diabetes, calling attention on the need for appropriate glycemic control irrespective of diabetic status.⁸⁻¹¹ However, treatment thresholds for intraoperative hyperglycemia have not been defined as a standard of care, and little is known of the interindividual variability of intraoperative management of hyperglycemia. Recent reviews suggest that treatment of a moderate BG target between 150 and 200 mg/dl (8.3 to 10 mM) is associated with decreased postoperative morbidity and mortality.^{2,12} The overall effectiveness of tight glucose control is still debatable, with several studies showing lack of benefit in critically ill patients.¹³⁻¹⁵ On the other end of the therapeutic margin,

What We Already Know about This Topic

- Previous studies have demonstrated that hyperglycemia is associated with poor outcomes in critically ill patients, including increased hospital length of stay, morbidity, and mortality after noncardiac general surgery
- This study tested the hypothesis that real-time audiovisual notification of recent blood glucose values would modify therapeutic thresholds for treatment of intraoperative hyperglycemia

What This Article Tells Us That Is New

- Real-time audiovisual notification is associated with a significant increase in desirable intraoperative glycemic management behavior and may help achieve tighter intraoperative glycemic control

intraoperative insulin treatment of hyperglycemia needs vigilant monitoring to avoid fatal hypoglycemia.¹⁶ Additionally, tight glucose control was associated with a significant increase in the incidence of severe hypoglycemia (13.2% *vs.* 6.2%).¹⁷

Corresponding article on page 10.

Submitted for publication August 5, 2014. Accepted for publication February 23, 2015. From the Department of Anesthesiology, University of Michigan, Ann Arbor, Michigan.

Copyright © 2015, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. All Rights Reserved. Anesthesiology 2015; 123:29-37

Thus, desirable intraoperative BG management includes treatment of hyperglycemia and rechecking BG values after treatment to ascertain treatment response.

Previous studies looking at computerized decision support systems did not show a change in nurse behavior of treatment of hyperglycemia in the intensive care unit.¹⁷ As there are no prior studies of intraoperative behavioral change of insulin treatment with decision support, we intended to perform this as an exploratory study. We tested the hypothesis that real-time visual notification of recent BG values would modify therapeutic thresholds for treatment of intraoperative hyperglycemia.

Materials and Methods

After obtaining approval from the University of Michigan Medical School Institution Review Board (Ann Arbor,

Michigan), we conducted a retrospective analysis of our database between November 1, 2010, and February 26, 2014. The study involved a single site: the University of Michigan Health System. The inclusion criterion was BG at least 200 mg/dl (11.1 mM). Exclusion criteria were procedure less than 1 h and American Society of Anesthesiologists (ASA) physical status 5 and 6.

AlertWatch (AlertWatch Inc., USA) is a Food and Drug Administration–cleared secondary patient monitor for use in operating rooms.¹⁸ AlertWatch pulls historical patient data (risk factors and laboratory results) from multiple networked information systems and combines it with patients' live physiologic data in a real-time audiovisual display (fig. 1). At our institution, our primary intraoperative automated anesthesia information management system (AIMS) (Centricity, USA) is linked to the AlertWatch system. The AlertWatch

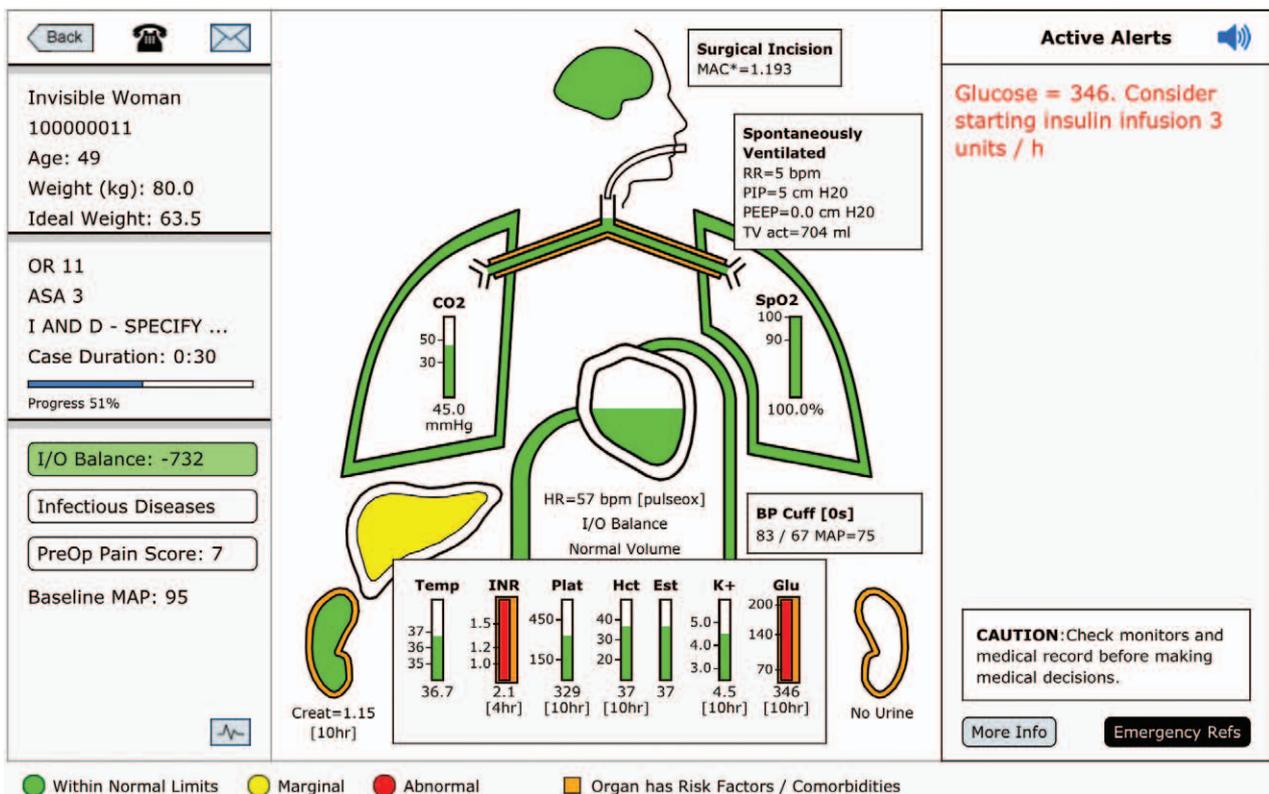


Fig. 1. AlertWatch (AlertWatch Inc., USA) display with high blood glucose highlighted in real time. The AlertWatch display integrates data from multiple sources including the anesthesia information system and the laboratory system. The display is presented in three parts: patient demographic data on the left, organ system icon display in the middle, and alerts on the right. The organs are displayed in green, yellow, or red depending on the level of alert for each organ system. If an organ (or laboratory) is outlined in orange, it designates a comorbidity of that organ. Note that the glucose bar in the lower right is highlighted in orange noting the patient has diabetes mellitus and the bar is red noting that the glucose is in a high range with the last glucose measurement 10h ago. The red alert in the upper right signifies an out-of-range/very high glucose level. Once insulin is documented in the electronic record, the alert disappears and a timer is started checking for a repeat glucose measurement. If a glucose measurement is not noted within 90min of the initiation of insulin, an alert reminding the provider to recheck glucose appears. ASA = American Society of Anesthesiologists' Physical Status; BP = blood pressure; bpm [pulseox] = beats per minute derived from the pulse oximeter monitor; CO₂ = carbon dioxide; Creat = creatinine; Est = estimated hematocrit; Glu = blood glucose; Hct = hematocrit; HR = heart rate; I and D = incision and drainage; I/O = input/output; INR = international normalized ratio; K+ = potassium; MAC = minimum alveolar concentration; MAP = mean arterial pressure; OR = operating room; PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure; Plat = platelets; Refs = references; RR = respiratory rate; SpO₂ = peripheral oxyhemoglobin saturation; Temp = temperature; TV act = actual tidal volume; Units/h = units per hour. * Link for MAC calculation.

display is presented in three parts: patient demographic data on the left, organ system icon display in the middle, and alerts on the right. The organs are displayed in green, yellow, or red depending on the level of alert for each organ system. If an organ (or laboratory value) is outlined in orange, it designates a comorbidity of that organ. The visual alerts of interest in this study are the BG bar in the lower right and a red text alert in the upper right, notifying an out of range/very high BG value. The BG bar is highlighted in orange when the patient has diabetes mellitus, and the bar is filled with red if the BG is in a high range, along with a time stamp of the last BG measurement. Once insulin is documented in the AIMS, the alert disappears and a timer is started to remind providers to check a postinsulin glucose measurement. If a glucose measurement is not noted within 90 min of the documentation of insulin, an alert reminding the provider to recheck glucose appears.

Data Collection and Management

We extracted data from the AIMS to evaluate the usage of AlertWatch in BG monitoring and initiation of appropriate treatment. AlertWatch usage was captured by intraoperative access of AlertWatch, which requires secure login by the clinician. The key study exposure variable was intraoperative access of AlertWatch. AlertWatch was installed in all operating rooms evaluated in this study in a staggered fashion. We assumed, based on initial clinical observations using the census and administrative views of the system, that AlertWatch was accessed during ~50% of all anesthetics during contemporaneous anesthetics between May 1, 2012, and October 31, 2013.

In addition, the data on the following variables were collected from the AIMS: patient age, gender, body mass index, preoperative diabetes diagnosis, home insulin therapy, fasting BG, highest intraoperative BG, and ASA class. Body mass index was categorized based on the World Health Organization's classification.¹⁹ ASA class was handled as a dichotomous variable for presence or absence of class 3 or 4. Procedural variables included emergent procedure, surgical service, primary anesthetist (resident *vs.* nurse anesthetist with de-identified unique provider numbers), attending anesthesiologist (with deidentified unique provider numbers), case duration, and procedural complexity measured by the Current Procedural Terminology (CPT) base unit value. To relate this measure in clinical terms, arthroscopy carries a CPT base unit of 3 points, radical neck dissection carries 5 points, and aortic fenestration carries 10 points. In order to evaluate systematic bias in the usage of the system, we graphed a histogram by operating room use of the device

to exclude cases from rooms that exclusively used or did not use AlertWatch. Further, we classified major groups of surgical services along the lines of existing groups of operating rooms and included them in the adjusted models. Surgical specialties were collapsed into six categories including general surgery, head–neck, hepatobiliary–transplant surgery, trauma–acute care, orthopedic–plastics, and gynecology–urology. This was performed to also adjust for service-line-specific biases in treatment of hyperglycemia. Anesthesia staff members (attending anesthesiologists) have core responsibilities along these surgical service groupings, but together with anesthesiologists (residents and Certified Registered Nurse Anesthetists) work randomly across all possible inclusion rooms during various times of the day or week.

The quality of the data was verified by confirming the accuracy against the independent query output of two different programmers. The data fields chosen for this study were either binary electronic chart entries or laboratory results. Specific continuous variables were converted to categories to increase clinical utility and improve the ability to match cases. Case duration and CPT base values were classified into quartiles, with the lowest quartile serving as the baseline in analyses. These variable transformations were performed to highlight differences in treatment behavior at either low or high case duration or complexity.

Preoperative fasting BG is collected from diabetic patients per protocol, and intraoperative BG is collected as part of an arterial blood gas in diabetic or nondiabetic patients and isolated BG analysis in diabetic patients. Arterial blood gas analysis is performed using the Gem Premier 3000 ABG analyzer (Instrumentation Laboratory, USA) located within the same patient care unit. Point-of-care glucometry is performed using Accu-Chek Inform II (Roche Diagnostics, USA). Standard maintenance and calibration of the devices are performed by quality control processes as specified by the manufacturers.

The treatment threshold for hyperglycemia was defined as any intraoperative point-of-care BG measurement or laboratory BG value at least 200 mg/dl (11.1 mM) as this is the device threshold for issuing an audiovisual alert. Since departmental protocols predating the study period*†‡ specify treatment of BG more than 180 mg/dl (10 mM), we anticipated that all patients included in the study would be treated with insulin intraoperatively. Treatment was identified by searching the AIMS for use of insulin as a bolus or infusion. A previous study of computerized decision support in the intensive care unit reported a higher incidence of hypoglycemia in the tight glucose control group.¹⁷ Device safety was evaluated by comparing the incidence of severe hypoglycemia between the study groups, defined as BG value up to 70 mg/dl (3.9 mM).

Statistical Analysis

The study outcome was defined as documentation of insulin use in response to preoperative (day of surgery) or

* Available at: <http://anes.med.umich.edu/vault/1000353-Presurg.pdf#pagemode=bookmarks>. Accessed July 19, 2014.

† Available at: <http://anes.med.umich.edu/vault/1000357-PlanI.pdf#pagemode=bookmarks>. Accessed July 19, 2014.

‡ Available at: http://anes.med.umich.edu/vault/1000354-Plan_II_III.pdf#pagemode=bookmarks. Accessed July 19, 2014.

intraoperative hyperglycemia. The secondary outcome of the study was the frequency of postinsulin BG checks in patients who were treated with insulin. The unit of analysis was set at the level of the operative case, with one or more instances of hyperglycemia or treatment permissible during the case, but counting as a single denominator and numerator, respectively.

Differences in study outcomes between the AlertWatch and no-AlertWatch groups were analyzed using Pearson chi-square tests, and *P* value of less than 0.05 was considered significant. The continuous variables' data distributions were tested for normality and data presented as mean and SD for parametric or median with interquartile ranges for nonparametric data. We used a backward Wald logistic regression model to adjust for preoperative patient or procedural characteristics, with insulin treatment of intraoperative hyperglycemia as the dependent variable. Some of the major confounders of studies of behavioral change relate to inherent biases in clinical decision-making around treatment thresholds for hyperglycemia. These biases may be influenced by the following factors that were included as independent variables in the models: AlertWatch usage, preoperative diabetic diagnosis, age, body mass index, ASA class, preoperative insulin treatment, fasting BG value, CPT base unit categories, case duration, emergent procedure, male gender, resident anesthetist, surgical service, and highest intraoperative glucose value. Missing data were handled by first quantifying magnitude of missingness. For variables with more than 5% missing data, initial unadjusted 2 × 2 analyses were performed to evaluate the relationship between missingness and the primary study outcome. Consideration for data imputation was predicated on finding significant unadjusted differences in outcome in patients with more than 5% missing data.

Model Diagnostics

The models were assessed for multicollinearity using condition index threshold of 30 and calibration using the Omnibus test for goodness-of-fit.^{20,21} Model discrimination was estimated using the *c*-statistic.²² The size of independent associations between study variables and study outcome was evaluated by adjusted odds ratios with 95% CIs.²³ Model validation was planned given the small sample size related potential for confounding.²⁴ In order to establish the feasibility of performing a propensity score-based matched analysis, we initially estimated the discrimination of a model predicting the use or nonuse of AlertWatch, as this was the study exposure of interest. If the resulting model discrimination was average or good (*c*-statistic > 0.75), we intended to perform a matched analysis. If the model discrimination was poor, we intended to perform internal validation with bootstrapping to validate model performance. Somers Dxy estimates of 0 suggest that the model's predictions are random and Dxy of 1 indicates perfect discrimination. Overestimation of model discrimination was evaluated by examining

the optimism estimates, and values less than 0.05 were indicative of excellent validation. Bias adjusted *c*-statistics were calculated using the formula $(1 + \text{index-corrected Dxy})/2$.²⁵

Provider-level Variance in Intraoperative Insulin Treatment of Hyperglycemia

All providers involved in the intraoperative care of study patients have a unique protected numeric identifier within the local information database. This is different from the hospital provider identity number or the pager number of these providers. Since intraoperative treatment behaviors possibly have significant variance at the individual provider level, additional analyses using generalized estimating equation modeling with exchangeable correlation matrix were performed to control for clustering either at primary anesthetist or attending anesthesiologist level. Tests of collinearity were performed on all model variables to assess for independence in addition to examination of the magnitudes of the standard errors. Model overfitting was limited by ensuring that more than 10 subjects per independent variable were included in the model. Estimates of adjusted odds ratios obtained by this method were compared with the primary logistic regression model estimates for the key study exposure variable, AlertWatch usage. Next, treatment variance at the primary anesthetist and attending anesthesiologist level was quantified in two separate hierarchical random effects mixed models using the primary model covariates described in the Statistical Analysis section above. Resulting variances were back transformed into the median odds ratio, which is reported as a value from 1 (no variance) to above 1 (increasing variance).^{26,27}

Results

Of 31,595 instances of unique patient care during the study period, the AlertWatch system was noted to have been accessed during intraoperative anesthetic care of 16,271 patients (51%). Overall, 2,341 patients (7.4%) had BG at least 200 mg/dl (11.1 mM), of whom 791 (33.5%) had AlertWatch and 1,550 were controls (fig. 2).

The frequency of insulin treatment of BG at least 200 mg/dl (11.1 mM) was 496 of 791 (62.7%) with and 817 of 1,550 (52.7%) without AlertWatch, respectively. The frequency of BG recheck after insulin treatment was 407 of 791 (51.5%) with AlertWatch and 655 of 1,550 (42.3%)

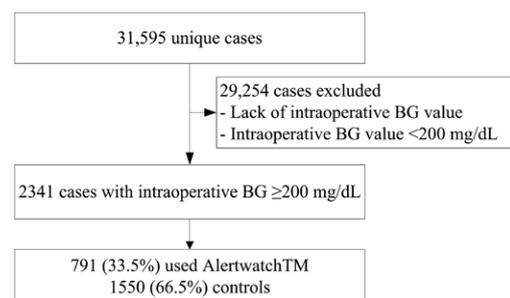


Fig. 2. Study flow. BG = blood glucose.

in controls. Device safety as defined by the frequency of hypoglycemia was 3.3% (95% CI, 2.2 to 4.8%) with AlertWatch and 3.1% (95% CI, 3.1 to 5.0%) in controls. Table 1 describes the demographic and management variables with and without use of the AlertWatch system. There were no differences between groups for distribution of age, sex, body mass index, preoperative diabetes diagnosis, home insulin therapy, ASA class 3 or 4, and preoperative fasting BG. Emergent surgery was less frequent, and intraoperative BG

values were lower in the AlertWatch group. Figure 3 displays the frequency of use or nonuse of AlertWatch across all operating rooms included in the study. Since all operating rooms had varying use of the device, no location-specific case exclusions were deemed necessary. Missing values of more than 5% were present for only one of the independent variables, preoperative fasting BG with 15% missing data, possibly reflecting patients without a preoperative diagnosis of diabetes mellitus. No differences in outcomes were noted in

Table 1. Preoperative and Intraoperative Study Characteristics

Study Variables	Control	AlertWatch	n	% Complete	P Value
Male sex	861 (56)	415 (53)	2,341	100	0.157
Age categories			2,341	100	0.111
18–30 yr	65 (4)	30 (4)			
31–40 yr	11 (7)	51 (6)			
41–50 yr	247 (16)	145 (18)			
51–60 yr	418 (27)	204 (26)			
61–70 yr	456 (30)	212 (27)			
71–80 yr	186 (12)	123 (16)			
Above 80 yr	67 (4)	26 (3)			
Body mass index, kg/m ²			2,242	95.8	0.053
18.5–24.99	280 (19)	130 (17)			
Below 18.5	25 (2)	9 (1)			
25–29.99	369 (25)	167 (22)			
Above 29.99	799 (54)	463 (60)			
Preoperative diabetes diagnosis	1034 (67)	557 (70)	2,341	100	0.069
Home insulin therapy	614 (40)	335 (42)	2,341	100	0.202
ASA class 3 or 4	1,269 (85)	655 (84)	2,281	97.4	0.647
Emergent procedure	284 (18)	99 (13)	2,341	100	<0.001
Primary anesthetist (resident)	1,101 (71)	630 (80)	2,337	99.8	<0.001
Case duration, min			2,341	100	<0.001
Quartile 1 (below 120)	166 (11)	50 (6)			
Quartile 2 (120–179)	274 (18)	103 (13)			
Quartile 3 (180–239)	239 (15)	139 (18)			
Quartile 4 (above 239)	871 (56)	499 (63)			
Case complexity—CPT base unit	1,426 (66)	737 (34)	2,163	100	0.204
Quartile 1 (below 6)	871 (40)	312 (42)			
Quartile 2 (6)	510 (23)	160 (21)			
Quartile 3 (7–9)	179 (8)	68 (9)			
Quartile 4 (above 9)	603 (28)	197(27)			
Surgical service	1,546 (100)	789 (100)	2,335	99.7	0.041
General surgery	238 (15)	97 (12)			
Head and neck	286 (18)	159 (20)			
Hepatobiliary and transplant	355 (23)	185 (23)			
Trauma and acute care surgery	183 (11)	69 (9)			
Plastics and orthopedic surgery	236 (15)	135 (17)			
Gynecology and urology	248 (16)	144 (18)			
Glycemic control, median (25th–75th percentile)					
Fasting BG value	203 (141–242)	190 (142–232)	1,952	83.4	0.063
Intraoperative BG value	226 (211–256)	224 (209–247)	2,341	100	0.011
Intraoperative glycemic management					
Insulin administered	817 (53)	496 (63)	2,341		<0.001
BG rechecked after insulin	655 (42)	407 (52)	2,341		<0.001
Device safety					
BG below 70mg/dl (3.9mM)	61 (4)	26 (3)	2,341		0.43
BG below 60mg/dl (3.3mM)	36 (2)	17 (2)	2,341		0.52

ASA = American Society of Anesthesiologists' physical status; BG = blood glucose; CPT = Current Procedural Terminology.

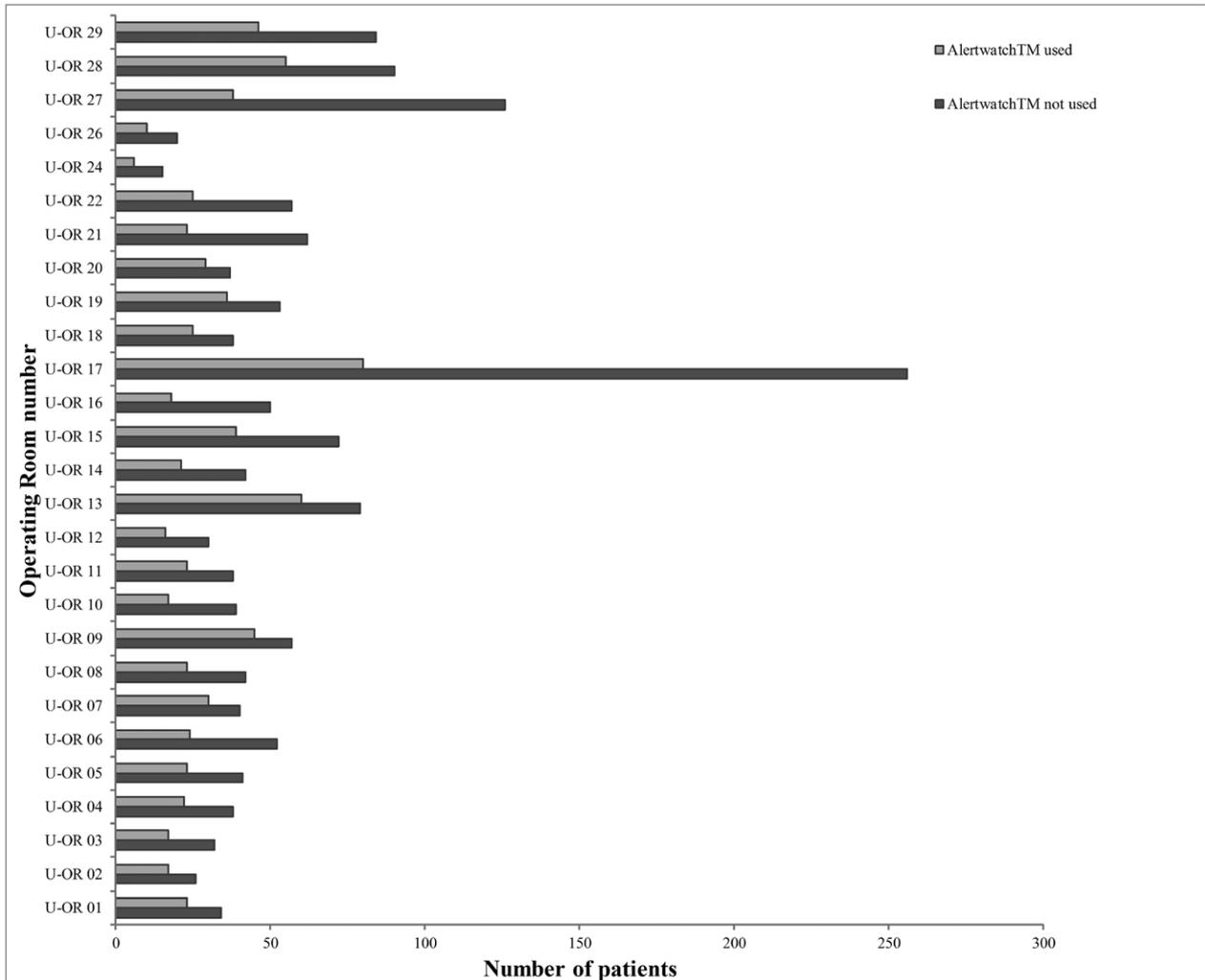


Fig. 3. Histogram of use or nonuse of AlertWatch (AlertWatch Inc., USA) by operating room in study hospital. Since all operating rooms had varying but nonexclusive usage patterns, no location-specific case exclusions were deemed necessary. U-OR = University Hospital operating room number.

patients with missing values ($P = 0.37$ for insulin treatment and $P = 0.613$ for recheck of BG after insulin).

After adjusted analyses, use of AlertWatch was associated with a 55% increase in odds of insulin treatment (adjusted odds ratio [95% CI], 1.55 [1.23 to 1.95]; $P < 0.001$) (table 2). The other significant independent associations of insulin treatment were case duration, procedural complexity, fasting BG value, and home insulin therapy. Preoperative diagnosis of diabetes, ASA physical status, emergent procedure, patient age, surgical service, and primary anesthesiologist were not associated with variance in insulin treatment. The median CPT base value was 7 (with the lower and higher quartiles at 6 and 10). The c -statistic (95% CI) for the primary outcome model was 0.74 (0.72, 0.76) with good calibration (Hosmer–Lemeshow test $P = 0.571$) and no evidence of multicollinearity. We were unable to model the use or nonuse of AlertWatch using the variables available with adequate discrimination (c -statistic, 0.6), and therefore, propensity score matched analysis was not performed.

Bootstrapping was performed using 1,000 replacements with Somers Dxy optimism estimate of 0.038, suggesting excellent model validation. The bootstrapped bias adjusted c -statistic for the primary outcome model using the index corrected Dxy was 0.73. We addressed the provider level variance by adjusting for provider level clustering in a generalized estimating equation model. The relationship between AlertWatch and study outcome was unaffected by individual provider-level case clustering (adjusted odds ratio, 1.47 [1.21, 1.8]). On random effects mixed modeling, the median odds ratio for anesthesiologist was 1.04 and attending anesthesiologist was 1.10, reflecting a 4% variance in insulin treatment of hyperglycemia at the anesthesiologist level and a 10% variance at the level of the attending anesthesiologist in an adjusted model that included the use or nonuse of AlertWatch. Anesthesia providers were also more likely to recheck intraoperative BG values after insulin treatment with AlertWatch (table 3; adjusted odds ratio [95% CI], 1.44 [1.14 to 1.81]; $P = 0.002$).

Table 2. Adjusted Associations of Treatment of Intraoperative Hyperglycemia

Study Variables	Adjusted Odds Ratio (95% CI)	P Value
AlertWatch usage	1.55 (1.23–1.95)	<0.001
Male sex	1.06 (0.85–1.32)	0.603
Age categories		
18–30 yr	Baseline	
31–40 yr	0.8 (0.4–1.61)	0.525
41–50 yr	0.96 (0.51–1.81)	0.894
51–60 yr	0.9 (0.48–1.67)	0.736
61–70 yr	1.09 (0.59–2.02)	0.788
71–80 yr	0.84 (0.44–1.62)	0.609
Above 80 yr	0.69 (0.32–1.53)	0.365
Body mass index, kg/m ²		
18.5–24.99	Baseline	
Below 18.5	0.65 (0.25–1.72)	0.386
25–29.99	0.96 (0.67–1.36)	0.8
Above 29.99	1.04 (0.76–1.41)	0.828
Preoperative diabetes diagnosis	1.16 (0.86–1.57)	0.338
Preoperative insulin therapy	1.44 (1.14–1.83)	0.002
ASA status 3 or 4	0.75 (0.55–1.03)	0.074
Emergent procedure	1.30 (0.92–1.83)	0.134
Resident anesthetist	1.13 (0.88–1.45)	0.329
Case duration, min		
Quartile 1 (below 120)	Baseline	
Quartile 2 (120–179)	1.49 (0.96–2.32)	0.075
Quartile 3 (180–239)	2.96 (1.89–4.64)	<0.001
Quartile 4 (above 239)	8.02 (5.19–12.40)	<0.001
Case complexity—CPT base unit		
Quartile 1 (below 6)	Baseline	
Quartile 2 (6)	1.39 (1.04–1.86)	0.028
Quartile 3 (7–9)	1.91 (1.22–2.99)	0.005
Quartile 4 (above 9)	1.43 (1.03–1.99)	0.034
Surgical service		
General surgery	Baseline	
Head and neck	0.72 (0.49–1.07)	0.103
Hepatobiliary and transplant	1.41 (0.95–2.11)	0.091
Trauma and acute care surgery	1.05 (0.68–1.65)	0.816
Plastics and orthopedic surgery	0.74 (0.51–1.09)	0.131
Gynecology and urology	0.90 (0.61–1.32)	0.595
Glycemic control		
Fasting blood glucose	1.01 (1.01–1.01)	0.001
Intraoperative blood glucose	1.0 (1.0–1.0)	0.175

ASA = American Society of Anesthesiologists' physical status; CPT = Current Procedural Terminology.

Discussion

In this large retrospective study of intraoperative BG management, we found a clinically relevant change in individual provider response to significant hyperglycemia with use of the AlertWatch system.

Despite controversies in perioperative BG management,¹ there is a large body of evidence suggesting that high BG is associated with poor outcomes after cardiac and noncardiac surgery.^{8,10,28} Recent studies showed improved outcomes in treating BG above 150 mg/dl (8.3 mM) during or after surgery.²⁹ The literature on perioperative BG management is

Table 3. Adjusted Associations of Postinsulin Intraoperative Recheck of Blood Glucose

Study Variables	Adjusted Odds Ratio (95% CI)	P Value
AlertWatch usage	1.44 (1.14–1.81)	0.002
Male sex	1.01 (0.81–1.26)	0.918
Age categories		
18–30 yr	Baseline	
31–40 yr	0.80 (0.39–1.64)	0.538
41–50 yr	0.99 (0.52–1.90)	0.98
51–60 yr	0.93 (0.49–1.75)	0.819
61–70 yr	0.95 (0.51–1.78)	0.871
71–80 yr	0.99 (0.51–1.93)	0.969
Above 80 yr	0.57 (0.25–1.32)	0.188
BMI (kg/m ²) categories		
18.5–24.99	Baseline	
Below 18.5	1.12 (0.41–3.03)	0.83
25–29.99	1.32 (0.92–1.88)	0.134
Above 29.99	1.31 (0.96–1.80)	0.093
Preoperative diabetes diagnosis	1.18 (0.86–1.61)	0.305
Preoperative insulin therapy	1.43 (1.13–1.81)	0.003
ASA status 3 or 4	0.74 (0.54–1.02)	0.062
Emergent procedure	1.28 (0.90–1.81)	0.168
Resident anesthetist	1.04 (0.81–1.34)	0.771
Case duration, min		
Quartile 1 (below 120)	Baseline	
Quartile 2 (120–179)	2.12 (1.26–3.58)	0.005
Quartile 3 (180–239)	4.86 (2.88–8.21)	<0.001
Quartile 4 (above 239)	12.65 (7.57–21.12)	<0.001
Case complexity—CPT base unit		
Quartile 1 (below 6)	Baseline	
Quartile 2 (6)	1.18 (0.87–1.59)	0.281
Quartile 3 (7–9)	2.06 (1.33–3.20)	0.001
Quartile 4 (above 9)	1.50 (1.08–2.10)	0.017
Surgical service		
General surgery	Baseline	
Head and neck	0.66 (0.44–0.98)	0.04
Hepatobiliary and transplant	1.26 (0.85–1.88)	0.255
Trauma and acute care surgery	0.93 (0.58–1.47)	0.741
Plastics and orthopedic surgery	0.73 (0.49–1.08)	0.117
Gynecology and urology	0.93 (0.63–1.38)	0.729
Glycemic control		
Fasting blood glucose	1.01 (1.01–1.01)	0.001
Intraoperative blood glucose	0.99 (0.99–1.0)	0.109

ASA = American Society of Anesthesiologists' physical status; BMI = body mass index; CPT = Current Procedural Terminology.

evolving, likely reflecting the overall variance in insulin treatment rates seen here.

One of the challenges in patient monitoring is the task of assimilating the large amount of real-time data and integrating this information, a process that largely relies on the operator's alertness. Continuous data tend to quickly overwhelm human alertness and effectiveness in recognizing critical events. Some monitoring data are considerably slower to change over time and are likely to be missed in complex environments. An effective strategy to prioritize clinical decisions in real time is to create clinically relevant thresholds for generation of audiovisual alerts.^{18,30} This

“human-in-the-loop” type of process monitoring has been compared to an iceberg, where only a small proportion is visible to the operator. The response of the human body to anesthesia is complex and appropriate decision support with “human-in-the-loop” monitoring relies on effectively refining those variables available to make the right clinical decision.^{31,32} This is very critical in an operating room environment, as the distractors and time available for effective clinical decision-making and treatment are often limited.³³ Automated real-time alert systems have been shown to be effective when used for therapeutic decision-making, monitoring adequacy, billing, and documentation compliance in addition to other uses.^{30,34,35} For instance, automated alert systems have been successfully used in following protective lung ventilation strategies and have been shown to improve behavioral changes in clinical decision-making.³⁴

In this study, we report that using an integrated real-time audiovisual alert system reduces variability in management of hyperglycemia. The AlertWatch system influenced glycemic management behavior to a greater extent than individual provider-level treatment variance in this study population. We also quantified the provider-level insulin treatment variance at 4% at the anesthetist level and 10% at the level of the attending anesthesiologist in an adjusted model that included the use or nonuse of AlertWatch. This suggests that despite use of AlertWatch, there is still a clinically important difference in the behavioral responses of anesthesiologists to a hyperglycemic episode. This may reflect significant variance in case complexity and duration, with more complex lengthy procedures carrying greater likelihood of occurrence and treatment of hyperglycemia, as seen in this study. Alternatively, this finding offers opportunities for exploring other novel methods to reduce the variability of intraoperative glycemic therapy.

Despite being a relatively large retrospective study, it is important to highlight some of the limitations of this study. This was undertaken at a single center, and the positive behavioral response may not be generalizable to other settings. We cannot attest to functionality of the AlertWatch system in all instances when the Web site was accessed and cannot confirm that the Web site was actually utilized throughout care. AlertWatch use may be different in different levels of training, as these data are not available. The AlertWatch development site was University of Michigan, so study estimates may not be generalizable to other centers implementing this technology. In addition to these limitations, clinical databases research has inherent challenges related to the use of retrospective data, as the quality of the data cannot be verified directly against independent patient report. We attempted to address these issues by two independent queries of the database and by verifying differences using a manual check process. The statistical methods are limited by the absence of a provider-level change in behavior with and without exposure to the AlertWatch system, owing to sample size limitations. In the absence of this direct comparison of individual provider behavior, the use of median

odds ratios quantifies the variance at the level of the providers, independent of the use or nonuse of AlertWatch. The models had modest discrimination and therefore reflect the presence of unmeasured factors that influence treatment behavior. The study was not randomized in design, a weakness that is counterbalanced by the fact that we were unable to model usage of AlertWatch. This suggests either that there are unmeasured factors dictating the choice of use or that the choice is more random than initially assumed. Finally, this is not a patient outcome study as the sample size numbers are limited for a meaningful outcome analysis. However, the sample size is of sufficient magnitude to test behavioral change, with reliable effect over concurrent and historical controls during a 2-yr study period. Despite limitations, this study demonstrates the clinical value of a novel audiovisual alert system that helps providers correct a missed treatment opportunity in real time.

In conclusion, we have demonstrated that AlertWatch is associated with a significant increase in intraoperative treatment and rechecking of hyperglycemia. This treatment behavior modification is independent of preoperative patient factors, provider-level factors, and case complexity. These findings support the hypothesis that lack of real-time awareness of abnormal BG values largely contributes to their undertreatment.

Acknowledgment

Support was provided solely from institutional and/or departmental sources.

Competing Interests

The University of Michigan (Ann Arbor, Michigan) developed the AlertWatch and has equity interest in it. Dr. Ramachandran has received honoraria for scientific consulting with Galleon Pharmaceuticals, Horsham, Pennsylvania, and Merck Sharp and Dohme, Whitehouse Station, New Jersey, and has active research funding from Merck Sharp and Dohme. The other authors declare no competing interests.

Correspondence

Address correspondence to Dr. Ramachandran: Department of Anesthesiology, University of Michigan Medical School, 1 H427 University Hospital Box 0048, 1500 E Medical Center Drive, Ann Arbor, Michigan 48109. rsatyak@med.umich.edu. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

References

1. Duncan AE: Hyperglycemia and perioperative glucose management. *Curr Pharm Des* 2012; 18:6195–203
2. Lipshutz AK, Gropper MA: Perioperative glycemic control: An evidence-based review. *ANESTHESIOLOGY* 2009; 110:408–21
3. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R: Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001; 345:1359–67

4. Underwood P, Askari R, Hurwitz S, Chamarthi B, Garg R: Preoperative A1C and clinical outcomes in patients with diabetes undergoing major noncardiac surgical procedures. *Diabetes Care* 2014; 37:611–6
5. Biteker M, Dayan A, Can MM, İlhan E, Biteker FS, Tekkeşin A, Duman D: Impaired fasting glucose is associated with increased perioperative cardiovascular event rates in patients undergoing major non-cardiothoracic surgery. *Cardiovasc Diabetol* 2011; 10:63
6. King JT Jr, Goulet JL, Perkal MF, Rosenthal RA: Glycemic control and infections in patients with diabetes undergoing noncardiac surgery. *Ann Surg* 2011; 253:158–65
7. Bolliger D, Seeberger MD, Lurati Buse G, Christen P, Seeberger E, Ruppen W, Filipovic M: The influence of pre-admission hypoglycaemic therapy on cardiac morbidity and mortality in type 2 diabetic patients undergoing major non-cardiac surgery: A prospective observational study. *Anaesthesia* 2012; 67:149–57
8. Sebranek JJ, Lugli AK, Coursin DB: Glycaemic control in the perioperative period. *Br J Anaesth* 2013; 111(Suppl 1):i18–34
9. Abdelmalak B, Abdelmalak JB, Knittel J, Christiansen E, Mascha E, Zimmerman R, Argalious M, Foss J: The prevalence of undiagnosed diabetes in non-cardiac surgery patients, an observational study. *Can J Anaesth* 2010; 57:1058–64
10. Maamoun HA, Soliman AR, Fathy A, Elkhatib M, Shaheen N: Diabetes mellitus as predictor of patient and graft survival after kidney transplantation. *Transplant Proc* 2013; 45:3245–8
11. Janis JE: Discussion: The role of chronic and perioperative glucose management in high-risk surgical closures: A case for tighter glycemic control. *Plast Reconstr Surg* 2013; 132:1005–7
12. Lena D, Kalfon P, Preiser JC, Ichai C: Glycemic control in the intensive care unit and during the postoperative period. *ANESTHESIOLOGY* 2011; 114:438–44
13. Arabi YM, Dabbagh OC, Tamim HM, Al-Shimemeri AA, Memish ZA, Haddad SH, Syed SJ, Giridhar HR, Rishu AH, Al-Daker MO, Kahoul SH, Britts RJ, Sakkijha MH: Intensive versus conventional insulin therapy: A randomized controlled trial in medical and surgical critically ill patients. *Crit Care Med* 2008; 36:3190–7
14. Preiser JC, Devos P, Ruiz-Santana S, Mélot C, Annane D, Groeneveld J, Iapichino G, Lerverve X, Nitenberg G, Singer P, Wernerman J, Joannidis M, Stecher A, Chioléro R: A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: The Glucontrol study. *Intensive Care Med* 2009; 35:1738–48
15. Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, Van Wijngaerden E, Bobbaers H, Bouillon R: Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006; 354:449–61
16. Russo N: Perioperative glycemic control. *Anesthesiol Clin* 2012; 30:445–66
17. Kalfon P, Giraudeau B, Ichai C, Guerrini A, Brechot N, Cinotti R, Dequin PF, Riu-Poulenc B, Montravers P, Annane D, Dupont H, Sorine M, Riou B, CGAO-REA Study Group: Tight computerized versus conventional glucose control in the ICU: A randomized controlled trial. *Intensive Care Med* 2014; 40:171–81
18. Kruger GH, Tremper KK: Advanced integrated real-time clinical displays. *Anesthesiol Clin* 2011; 29:487–504
19. Stewart ST, Cutler DM, Rosen AB: Forecasting the effects of obesity and smoking on U.S. life expectancy. *N Engl J Med* 2009; 361:2252–60
20. Faraway J: *Linear Models with R*. Boca Raton, Florida, Chapman & Hall/CRC, 2005
21. Bewick V, Cheek L, Ball J: Statistics review 14: Logistic regression. *Crit Care* 2005; 9:112–8
22. Hanley JA, McNeil BJ: The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982; 143:29–36
23. Houle TT: Importance of effect sizes for the accumulation of knowledge. *ANESTHESIOLOGY* 2007; 106:415–7
24. Cepeda MS, Boston R, Farrar JT, Strom BL: Comparison of logistic regression versus propensity score when the number of events is low and there are multiple confounders. *Am J Epidemiol* 2003; 158:280–7
25. Harrell F Jr: Resampling, validating, describing, and simplifying the model, *Regression Modeling Strategies*. New York, Springer, 2001, pp 87–103
26. Larsen K, Petersen JH, Budtz-Jørgensen E, Endahl L: Interpreting parameters in the logistic regression model with random effects. *Biometrics* 2000; 56:909–14
27. Larsen K, Merlo J: Appropriate assessment of neighborhood effects on individual health: Integrating random and fixed effects in multilevel logistic regression. *Am J Epidemiol* 2005; 161:81–8
28. Avitsian R, Abdelmalak B, Saad S, Xu M, O'Hara J Jr: Upper extremity arteriovenous fistula does not affect pulse oximetry readings. *Nephrology (Carlton)* 2006; 11:410–2
29. Sathya B, Davis R, Taveira T, Whitlatch H, Wu WC: Intensity of peri-operative glycemic control and postoperative outcomes in patients with diabetes: A meta-analysis. *Diabetes Res Clin Pract* 2013; 102:8–15
30. Lowe A, Jones RW, Harrison MJ: The graphical presentation of decision support information in an intelligent anaesthesia monitor. *Artif Intell Med* 2001; 22:173–91
31. Imhoff M, Kuhls S, Gather U, Fried R: Smart alarms from medical devices in the OR and ICU. *Best Pract Res Clin Anaesthesiol* 2009; 23:39–50
32. Blum JM, Tremper KK: Alarms in the intensive care unit: Too much of a good thing is dangerous: Is it time to add some intelligence to alarms? *Crit Care Med* 2010; 38:702–3
33. McIntyre JW: Ergonomics: Anaesthetists' use of auditory alarms in the operating room. *Int J Clin Monit Comput* 1985; 2:47–55
34. Blum JM, Stentz MJ, Maile MD, Jewell E, Raghavendran K, Engoren M, Ehrenfeld JM: Automated alerting and recommendations for the management of patients with preexisting hypoxia and potential acute lung injury: A pilot study. *ANESTHESIOLOGY* 2013; 119:295–302
35. Ehrenfeld JM, Epstein RH, Bader S, Kheterpal S, Sandberg WS: Automatic notifications mediated by anesthesia information management systems reduce the frequency of prolonged gaps in blood pressure documentation. *Anesth Analg* 2011; 113:356–63