

Advanced Monitoring Is Associated with Fewer Alarm Events During Planned Moderate Procedure-Related Sedation: A 2-Part Pilot Trial

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BACKGROUND: Diagnostic and interventional procedures are often facilitated by moderate procedure-related sedation. Many studies support the overall safety of this sedation; however, adverse cardiovascular and respiratory events are reported in up to 70% of these procedures, more frequently in very young, very old, or sicker patients. Monitoring with pulse oximetry may underreport hypoventilation during sedation, particularly if supplemental oxygen is provided. Capnometry may result in false alarms during sedation when patients mouth breathe or displace sampling devices. Advanced monitor use during sedation may allow event detection before complications develop. This 2-part pilot study used advanced monitors during planned moderate sedation to (1) determine incidences of desaturation, low respiratory rate, and deeper than intended sedation alarm events; and (2) determine whether advanced monitor use is associated with fewer alarm events.

METHODS: Adult patients undergoing scheduled gastroenterology or interventional radiology procedures with planned moderate sedation given by dedicated sedation nurses under the direction of procedural physicians (procedural sedation team) were monitored per standard protocols (electrocardiography blood pressure, pulse oximetry, and capnometry) and advanced monitors (acoustic respiratory monitoring and processed electroencephalography). Data were collected to computers for analysis. Advanced monitor parameters were not visible to teams in part 1 (standard) but were visible to teams in part 2 (advanced). Alarm events were defined as desaturation— $\text{SpO}_2 \leq 92\%$; respiratory depression, acoustic respiratory rate ≤ 8 breaths per minute, and deeper than intended sedation, indicated by processed electroencephalography. The number of alarm events was compared.

RESULTS: Of 100 patients enrolled, 10 were excluded for data collection computer malfunction or consent withdrawal. Data were analyzed from 90 patients (44 standard and 46 advanced). Advanced had fewer total alarms than standard (Wilcoxon-Mann-Whitney = 2.073, $P = 0.038$; Wilcoxon-Mann-Whitney odds, 1.67; 95% confidence interval [CI], 1.04–2.88). Similar numbers of standard and advanced had ≥ 1 alarm event (Wald difference, -10.2% ; 95% CI, -26.4% to 7.0% ; $P = 0.237$). Fewer advanced patients had ≥ 1 respiratory depression event (Wald difference, -22.1% ; 95% CI, -40.9% to -2.4% ; $P = 0.036$) or ≥ 1 desaturation event (Wald difference, -24.2% ; 95% CI, -42.8% to -3.6% ; $P = 0.021$); but there was no significant difference in deeper than intended sedation events (Wald difference, -1.38% ; 95% CI, -20.21% to 17.49% ; $P = 0.887$).

CONCLUSIONS: Use of advanced monitoring parameters during planned moderate sedation was associated with fewer alarm events, patients experiencing desaturation, and patients experiencing respiratory depression alarm events. This pilot study suggests that further study into the safety and outcome impacts of advanced monitoring during procedure-related sedation is warranted. (Anesth Analg 2016;122:1070–8)

Diagnostic and interventional procedures are often facilitated by moderate procedure-related sedation (PRS) administered by a variety of practitioners, often without the direct involvement of an anesthesiologist

at the time of the procedure. Although many studies support the overall safety of PRS,¹ concern remains regarding the potential for serious complications. The incidence of cardiovascular and respiratory adverse events during

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tion by a research clinician of monitor detection of respiratory rates from 0 to 4 breaths per minute events. Additional support was provided by Loma Linda University School of Medicine, Department of Anesthesiology Research funds.

Conflict of Interest: See Disclosures at the end of the article.

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Reprints will not be available from the authors.

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moderate PRS in adults has been reported to be anywhere from <1%^{2,3} to >70%.⁴⁻⁶ Similar adverse events are reported during PRS in pediatric patients.^{7,8} Patients with greater ASA physical status and very young or very old patients appear to be at greater risk for cardiovascular and respiratory adverse events during PRS.⁹⁻¹³

Events during PRS, such as respiratory depression, apnea, airway obstruction, or oxygen desaturation, have been reported in adult and pediatric patients and can result in significant morbidity.^{8,9,13-15} Closed-claim analysis suggests that better monitoring during PRS could decrease the number of liability cases related to these events.¹⁶ Pulse oximetry may not alert procedural teams to hypoventilation during PRS, particularly if supplemental oxygen is provided to the patient during procedures.^{3,17,18} End-tidal carbon dioxide (EtCO₂) monitoring by capnometry provides both waveform and numeric displays of respiratory rate and EtCO₂. Its use during moderate PRS allows for detection of respiratory depression and apnea¹⁹⁻²¹ and is reported to decrease the incidence of desaturation events during colonoscopy.²² The use of capnometry is recommended as a standard for moderate or deep sedation by the American Society of Anesthesiologists⁴ and for deep sedation by the Canadian Anesthesiologists' Society.²³ Other professional societies conclude that there is inadequate evidence to mandate capnometry but suggest that it may be used during PRS.^{6,24}

Continuous patient monitoring using devices that have high sensitivity for detection of critical events is valuable. However, excessive false alarms have been shown to distract providers.²⁵⁻³⁰ Several factors may result in erroneous capnometry alarms, including poor patient tolerance of a nasal cannula for oxygen delivery and capnometry,³¹ mouth breathing,^{32,33} and obstruction by secretions.³⁴⁻³⁶ Advanced monitoring not widely available in procedural areas where moderate PRS is administered could allow detection of events before complications develop.³⁷ An acoustic monitor of respiratory rate has been found to have acceptable agreement with EtCO₂ in nonintubated patients.^{31,38-40} Processed electroencephalography has been used to assess drug-induced cerebral suppression⁴¹ and could have a role in monitoring depth of sedation.⁴²

This 2-part pilot study used advanced monitoring during planned moderate PRS to (1) determine the incidences of alarm events (total number of desaturation, hypoventilation, and deeper than intended sedation events); and (2) determine whether advanced monitor use is associated with fewer alarm events.

METHODS

This study was approved by the IRB of Loma Linda University, OSR# 5110234. Patients scheduled for elective

gastrointestinal endoscopy (GI) or interventional radiology (IR) procedures with planned moderate PRS were approached regarding study participation. Those who agreed provided written informed consent to participate.

Sedation Protocol

The planned moderate sedation protocol in place defines moderate sedation as a drug-induced state in which the patient will respond to voice alone or with light touch.⁴³ Presedation assessment is done to screen for medical conditions for which anesthesiology consultation is suggested, including previous sedation-related complications, continuous positive airway pressure-dependent sleep apnea, and conditions likely to have airway abnormalities, such as advanced rheumatoid arthritis, severe cervical spine motion limitation, small mouth opening, or neuromuscular disorders that may increase respiratory depression following administration of sedative medications. Other conditions that preclude moderate PRS are a need for intubation and ventilatory support, hemodynamic instability, or depressed mental status inconsistent with determining whether a moderate depth of sedation is present. Patients who have such factors are scheduled for sedation administered by critical care sedation and transport team nurses or referred for anesthesiology care. Patients who meet institutional criteria are scheduled for planned moderate PRS administered by sedation teams. These teams include a dedicated sedation nurse under the direction of the physician performing the procedure per their usual care protocols. The sedation nurses involved in this study had a minimum of 10 years prior experience administering and monitoring moderate PRS.

Patients had IV access established before transfer to the procedure room. No oral premedication was administered. After transfer to the procedure room, standard and advanced monitors were placed, and an immediate reassessment of the patient's condition and vital signs was performed before administration of sedative medications. When sedation was assessed to be adequate, the procedure was started. Intraprocedural sedation level was assessed by sedation nurses using standard scores^{44,45} and recorded at 5-minute intervals. The sedation scores were entered into the database after completion of the procedure. In addition to clinical observation by a sedation team nurse, all patients were monitored using standard monitors that include pulse oximetry (SpO₂), electrocardiogram, and noninvasive blood pressure.

Patient and procedure characteristics, sedative medication amounts, and the number of sedative doses given were recorded. As most patients received fentanyl during the procedures, opioids were converted to fentanyl equivalents using published equivalencies^{46,47} to facilitate comparison.

Nasal cannula capnometry (EtCO₂; Capnostream 20; Covidien, Bedford, MA) was obtained using an oxygen supply cannula that samples EtCO₂ via a separate path from oxygen delivery, as these provide better EtCO₂ measurement when greater oxygen flow rates are used.⁴⁸ In addition to standard monitors, we applied advanced monitors to patients using the latest versions of sensors and software for this pilot trial. These were pulse oximetry with acoustic respiratory monitor (Pulse CO-Oximeter with Rainbow Acoustic Monitoring; Masimo Corp., Irvine, CA) and processed electroencephalography (SEDLine brain function monitor; Masimo Corp.). Data from the study monitors were captured automatically to a research

⁴American Society of Anesthesiologists. Standards for Basic Anesthetic Monitoring. Available at: <http://www.asahq.org/resources/standards-and-guidelines>. Accessed March 9, 2015.

⁵American Society for Gastrointestinal Endoscopy, American College of Gastroenterology, The American Gastroenterological Association. Statement: Universal adoption of capnography for moderate sedation in adults undergoing upper endoscopy and colonoscopy has not been shown to improve patient safety or clinical outcomes and significantly increases costs for moderate sedation. Available at: http://www.gastro.org/practice/resource-library/guidelines/Capnography_for_Moderate_Sedation.pdf. Accessed March 12, 2015.

computer, including the sound files from the acoustic respiratory monitor. Patients with skin conditions that prevent the use of the adhesive sensors for SpO₂, acoustic monitor respiratory rate (RRa) or Patient State Index (PSI) would have been excluded. Patients were excluded from the analysis if automated data capture malfunction occurred. Advanced monitors were removed after procedure completion before transfer to the recovery area. Patients were discharged upon satisfactory recovery from sedation or if transfer to another care area in the facility was needed. The time interval from procedure end to discharge from recovery was recorded.

The pilot trial was divided into 2 parts based on whether the procedural sedation team had access to information from the advanced monitors. In part 1 of the study (standard), the procedural sedation teams were blinded to advanced monitor parameters. In part 2 of the study (advanced), procedural sedation teams were able to see the advanced monitor parameters. During the interval between parts 1 and 2, the procedural sedation teams were taught how to interpret alarms from the advanced monitors, how to implement respiratory acoustic monitoring as part of their care protocol, and how to interpret alarms from the advanced monitors. No clinical interventions or medication administrations were specified in the study protocol. Alarm conditions defined for study purposes were (1) SpO₂ ≤92% (desaturation event); (2) RRa ≤8 breaths per minute (BPM; respiratory depression); and (3) PSI ≤50 (deeper than intended sedation, usually indicating general anesthesia).

To investigate the reliability of very low respiratory rates reported by either RRa or EtCO₂, an analysis of events identified by review of the collected data when respiratory rate was ≤4 BPM in the standard group was done. Capnography waveform and respiratory acoustic monitoring sound files for each event when either monitor reported respiratory rate ≤4 BPM were reviewed by a research clinician. The presence of breath sounds in the respiratory acoustic monitoring sound file was considered to indicate respiration. An interval between breaths ≥15 seconds was considered as validation of the respiratory rate ≤4 BPM event reported by either monitor. The number of events reported by each device and verified by retrospective analysis as true positive or false positive was determined.

Statistical Analysis

As a pilot trial, the enrollment number was chosen to allow determination of effect size from which the sample size for future prospective studies could be calculated. The primary outcome measure was the intergroup difference in total alarm events during PRS (SpO₂ ≤92% events + RRa ≤8 BPM events + PSI ≤50 events). Secondary outcome measures included intergroup comparisons of patient and procedure characteristics, comparison of patients who experienced the 3 types of alarm events, medications given during PRS, and time to postprocedure discharge. Continuous data were analyzed for normal distribution by Shapiro-Wilk, with $P < 0.05$ indicating data were not normally distributed. Data that were normally distributed were expressed as mean; 95% confidence interval (CI) and analyzed by t test. Data that were not normally distributed were expressed as median; smoothed empirical likelihood quantile 95% CI and analyzed by Wilcoxon rank sum test and Wilcoxon-Mann-Whitney (WMW) odds (reported as odds; 95% CI).^{49,50} Categorical data were compared using χ^2 or Fisher exact test. Differences in proportions were analyzed by using the Wald 2-sample test for proportions (reported as %; 95% CI). Repeated-measures logistic regression was performed with the Genmod procedure to evaluate nurse assigned sedation scores. The positive predictive values for detecting respiratory rate ≤4 BPM events by EtCO₂ and RRa were calculated. Statistical analyses were performed using JMP 10.0.0 or SAS/STAT 9.4 (SAS Institute, Cary, NC) with $P < 0.05$ considered significant.

RESULTS

We enrolled 50 patients in the standard group between February and May 2012, with an additional 50 patients enrolled in the advanced group between October and December 2013. Two advanced patients withdrew consent before procedure start. Data collection computer failure prevented data collection in 6 standard and 2 advanced patients. Data from 44 standard and 46 advanced patients were available for analysis. Other than sex distribution, patient and procedure characteristics were similar (Table 1). The sedation teams involved included 27 sedation nurses and 28 procedural physicians, none of whom provided care to >10%

Table 1. Patient and Procedure Characteristics

	Standard, n = 44	Advanced, n = 46	P
Sex, F; M, n	28; 16	19; 27	0.034
Age, yr ^a	57.2 (53.2–61.2)	59.1 (54.0–64.1)	0.558
ASA physical status I; II; III; IV	2; 24; 17; 1	1; 21; 18; 6	0.252
Weight, kg ^a	80.2 (74.6–85.8)	80.5 (75.0–85.9)	0.955
Body mass index, kg/m ²	27.7 (25.6–30.3)	26.9 (24.8–28.9)	0.355
Procedure type, gastrointestinal endoscopy; interventional radiology, n	27; 17	27; 19	0.796
Procedure duration, min	31.1 (26.0–36.8)	30.7 (26.2–37.0)	0.859
Procedural sedation medications			
Fentanyl, µg/kg	1.02 (0.80–1.29)	0.92 (0.79–1.10)	0.684
Midazolam, mg/kg	0.05 (0.03–0.06)	0.05 (0.04–0.05)	0.984
Number of sedation medication doses			
Opioids	3.2 (2.5–4.1)	2.4 (2.0–2.9)	0.016
Midazolam	2.8 (2.2–3.4)	2.5 (2.2–3.0)	0.684

Gender and procedure type are shown as count. Continuous data are presented as median (95% confidence interval) and analyzed by Wilcoxon rank-order test. Other than gender distribution, there were no significant differences between groups.

^aAge and weight are given as mean (95% confidence interval) and analyzed by t test.

of patients in both groups. Four of the 27 sedation nurses cared for >4 standard or advanced patients, but these were not the same sedation nurses. The largest number of standard patients cared for by 1 sedation nurse was 6 (13.64% of standard) and of advanced was 8 (17.39% of advanced). Seven of the 28 procedural physicians cared for >4 standard patients, whereas 2 of the 28 procedural physicians cared for >4 advanced patients. The largest number of standard patients cared for by 1 procedural physician was 9 (20.45% of standard) and of advanced was 6 (13.04% of advanced). The number of patients with any alarm event was not significantly different between sedation nurses providing care to more than compared with up to 4 standard (difference, 4.55%; -16.43% to 21.82%; $P = 0.782$) or advanced patients (difference, -16.15%; -36.95% to 4.08%; $P = 0.117$). The number of patients with any alarm event was not significantly different between procedural physicians providing care to more than, compared with up to 4, standard (difference, 12.33%; -27.22 to 8.57%; $P = 0.307$) or advanced patients (difference, -5.52%; -16.95% to 33.59%; $P = 0.519$). The sedations were the only case of the day for a sedation nurse and procedural physician team working together on the day of a procedure in 81 (91.0%) and the second case of the day for a sedation nurse and procedural physician team working together on the day of a procedure in 8 (9.0%) studied patients.

We found fewer alarm events in advanced patients (median, 2.5; 95% CI, 1.3–4.2) compared with standard patients (median, 5.5; 95% CI, 2.8–9.0; Fig. 1). The WMW test indicated a significant difference in the median number of alarmed events between the groups ($z = 2.073$, $P = 0.038$) and statistically significantly more alarm events in standard compared with advanced patients (WMW odds, 1.67; 95% CI, 1.04–2.88). At least 1 alarm event occurred in 71 patients (78.9%), more frequently in patients undergoing GI (50 of 54; 92.6%) compared with IR (21 of 36; 58.3%) procedures (difference, 34.26%; 18.57%–49.95%; $P = 0.0002$).

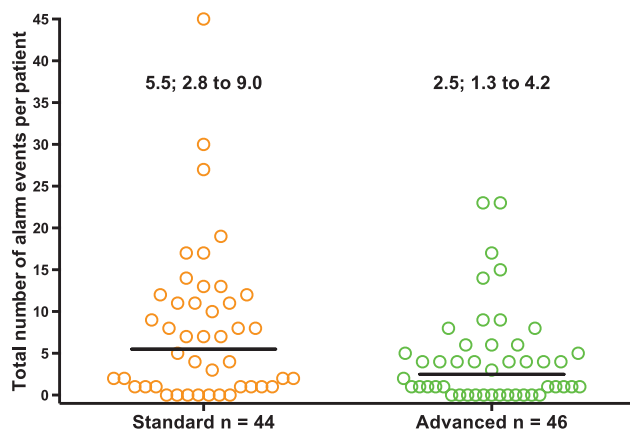


Figure 1. Total alarm events (respiratory rate ≤ 8 breaths per minute + pulse oximetry saturation $\leq 92\%$ + deeper than intended sedation indicated by processed electroencephalography) recorded in patients undergoing planned moderate procedure-related sedation. The number of alarm events per patient (median; 95% confidence interval) during planned moderate procedure-related sedation was greater when procedural sedation teams were not able to see parameters (standard) from advanced monitors including acoustic respiratory monitor and processed electroencephalography than when they were able to see those values (advanced) during the procedures ($P = 0.038$).

We evaluated for a possible effect of trend over time and found no evidence of a trend effect on the number of alarms by date of procedure, day of the week, or first versus second half of either standard or advanced patients. The total number of alarm events was subjected to a 2-way analysis of variance having 2 levels of sex (male and female) and 2 levels of monitoring groups (standard and advanced). Sex was significantly associated neither with the total number of alarm events (2-way analysis of variance; $P = 0.6764$) nor with the prevalence of ≥ 1 alarm event ($P = 0.203$). Similar numbers of patients in standard (37; 84.1%) and advanced (34; 73.9%; difference, -10.2%; -26.4 to 7.0%; $P = 0.255$) had ≥ 1 alarm event. More than 1 type of alarm event occurred in 20 standard compared with 11 advanced (difference, -21.54%; -39.55% to -1.75%; $P = 0.032$), and only 1 advanced patient had ≥ 1 episode of each type of alarm event compared with 8 standard (difference, -16.01%; -28.18% to -2.62%; $P = 0.018$). As shown in Figure 2, fewer advanced patients had ≥ 1 respiratory depression event (17 vs 26; difference, -22.1%; -40.9 to -2.4%; $P = 0.035$) or ≥ 1 desaturation event (15 vs 25; difference, -24.2%; -42.8 to -3.6%; $P = 0.020$). Overall 31.1% of patients had ≥ 1 PSI ≤ 50 event indicating deeper than intended sedation was produced, but we did not find a significant intergroup difference (14 in each group, difference, -1.38%; -20.21% to 17.49%; $P = 0.888$). The nurse-assessed sedation score indicated that a deeper than intended level of sedation was present in 4 (1.0%) of 406 recorded scores from advanced patients and in 8 (2.0%) of 393 recorded scores from standard patients (difference, -1.05%; -2.87 to 0.77%; $P = 0.222$). We were not able to run a repeated-measures analysis to account for correlated measurements of deeper than intended sedation scores from repeated nurses, as very few nurses worked in multiple procedures on a given day, and no sedation nurse provided care to >10% of both standard and advanced patients. Repeated-measures logistic regression of sedation

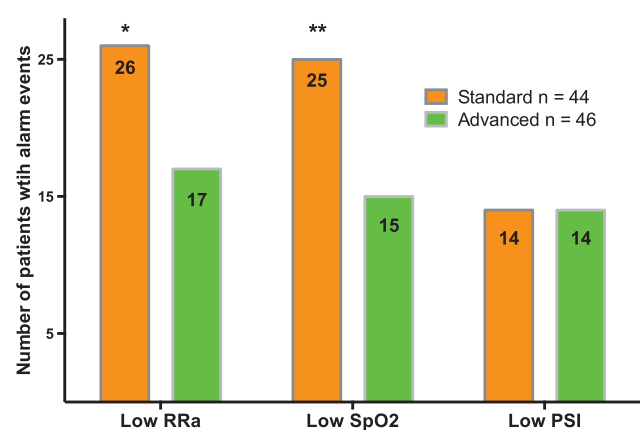


Figure 2. Comparison of the number of patients with alarm events recorded during planned moderate procedure-related sedation. During the procedures, the procedural sedation teams were either not able to see parameters (standard) from advanced monitors including acoustic monitor respiratory rate (RRa) and processed electroencephalography (PSI) or were able to see those values (advanced). More standard than advanced patients had respiratory rate ≤ 8 breaths per minute (RRa; $*P = 0.035$) or pulse oximetry saturation $\leq 92\%$ (SpO_2 ; $**P = 0.020$) alarm events. Deeper than intended sedation indicated by processed electroencephalography was not different between groups (PSI ≤ 50 ; $P = 0.89$).

scores within a patient using the Genmod procedure with a repeated statement and logit link showed no significant difference between standard or advanced in the odds of having a deeper than intended sedation score ($P = 0.504$). These deeper than intended sedation scores were recorded from 1 (2.2%) advanced and 6 (13.6%) standard patients (difference, -11.41 ; -22.84% to 0.91% ; $P = 0.046$). More detail regarding statistical modeling issues and decisions made in these analyses is provided as Supplemental Digital Content, Response to Statistical Editor Review (<http://links.lww.com/AA/B357>).

Medication administration is shown in Table 1. Patients in standard received more doses of opioid (WMW: $z = 2.4128$, $P = 0.0158$; WMW odds, 1.82; 95% CI, 1.14–3.13; $P = 0.016$) and were more likely to receive >3 doses of opioid (difference, 25.89%; 6.40%–43.24%; $P = 0.009$). We evaluated for a possible effect of trend over time and found no evidence of a trend effect on opioid or midazolam total dose or number of dose administration over time or compared with day of the week. On the basis of our data, we were not able to model the influence of specific sedation nurse or procedural physician.

Medication administration was compared in patients who had alarm events to those who did not, regardless of standard or advanced groups (Table 2). As shown in Table 2, patients who had any alarm events received more opioid doses and greater total amounts of opioid and midazolam. We attempted a multivariate analysis with the dependent variables of total opioid amount, opioid doses, total midazolam amount, and total midazolam doses and independent variables as alarm events. However, the models failed to meet assumptions of normality and homogeneity of variance. On the basis of our data, we were not able to model the influence of specific sedation nurse or procedural physician. Of the 90 patients studied, 11 standard patients were transferred to another care area early after completion of the procedure based on findings from the planned procedure. Analysis excluding these 11 patients similarly showed that

patients who had any alarm events received more opioid doses and greater total amounts of opioid and midazolam compared with those who did not have any alarm events (Supplemental Digital Content, Supplemental Table, <http://links.lww.com/AA/B357>). As we were not able to perform a multivariate analysis, tests of the 4 dependent variables in Table 2 (opioid dose, number of opioid doses, midazolam dose, and number of midazolam doses) were conducted using Bonferroni-adjusted alpha levels of 0.0125 for each alarm type. Patients who experienced ≥ 2 types of alarm events received a greater total amount of opioid ($P = 0.012$) and midazolam ($P = 0.0015$) as well as more doses of opioid ($P < 0.001$) and midazolam ($P = 0.0073$).

The time interval from procedure end to discharge from recovery was longer for advanced (median, 111; 95% CI, 92–150 minutes) than for standard (median, 65; 95% CI, 47–77 minutes). The WMW test indicated a significant difference in the median time to discharge between the groups ($z = -4.336$, $P < 0.0001$) with a statistically significantly longer time to discharge in advanced compared with standard (WMW odds, 3.33; 95% CI, 2.04–6.50). This comparison was confounded, since 11 (25.0%) patients in the standard group but no patients in the advanced group were transferred to other procedural or care areas early after study participation. Of note, patients were enrolled only if they were planned to undergo elective outpatient procedures under moderate sedation. The decision to transfer to another area for further studies or care was made based on findings of the originally planned procedure, so the sedation teams did not have advance knowledge of such transfer. Therefore, it is unlikely that these transfer decisions affected sedation administration during the procedure. Time to discharge increased in standard (median, 77; 95% CI, 67–93) when patients who were transferred to other procedural or care areas early after study participation were excluded from analysis; but the difference remained significant (WMW: $z = -2.7632$; WMW odds, 2.19; 95% CI, 1.31–4.17; $P = 0.0057$; Supplemental Table 2 (Supplemental Digital Content,

Table 2. Comparison of Medication Administration During Planned Moderate Procedure-Related Sedation in Patients With and Without Alarm Events

	Yes, $n = 71$ (78.9%)	No, $n = 19$ (21.1%)	P
Any alarm events			
Opioid dose fentanyl equivalents, $\mu\text{g}/\text{kg}$	1.07 (0.89–1.26)	0.75 (0.58–0.89)	0.015
Number of opioid doses	2.9 (2.4–3.3)	1.8 (1.4–2.5)	0.006
Midazolam dose, mg/kg	0.05 (0.04–0.06)	0.03 (0.02–0.04)	<0.001
Number of midazolam doses	2.9 (2.3–3.2)	2.0 (1.8–2.4)	0.050
Respiratory alarm event	Yes, $n = 43$ (47.8%)	No, $n = 47$ (52.2%)	
Opioid dose fentanyl equivalents, $\mu\text{g}/\text{kg}$	1.15 (0.91–1.40)	0.83 (0.72–0.99)	0.032
Number of opioid doses	3.3 (2.7–4.0)	2.1 (1.8–2.6)	<0.001
Midazolam dose, mg/kg	0.06 (0.05–0.07)	0.04 (0.03–0.05)	0.026
Number of midazolam doses	3.0 (2.5–3.6)	2.4 (2.0–2.9)	0.046
Desaturation events	Yes, $n = 40$ (44.4%)	No, $n = 50$ (55.6%)	
Opioid dose fentanyl equivalents, $\mu\text{g}/\text{kg}$	1.12 (0.89–1.33)	0.86 (0.74–1.02)	0.113
Number of opioid doses	3.2 (2.5–4.0)	2.5 (2.0–2.9)	0.035
Midazolam dose, mg/kg	0.06 (0.05–0.07)	0.04 (0.03–0.05)	0.007
Number of midazolam doses	2.9 (2.3–3.8)	2.3 (2.0–2.9)	0.050
Deeper than intended sedation events	Yes, $n = 28$ (31.1%)	No, $n = 62$ (68.9%)	
Opioid dose fentanyl equivalents, $\mu\text{g}/\text{kg}$	1.17 (0.94–1.52)	0.86 (0.73–1.06)	0.033
Number of opioid doses	3.3 (2.6–4.1)	2.3 (2.0–2.9)	0.025
Midazolam dose, mg/kg	0.05 (0.04–0.07)	0.05 (0.03–0.06)	0.100
Number of midazolam doses	3.1 (2.5–4.1)	2.3 (2.1–2.9)	0.026

These continuous data were not normally distributed, so are presented as median (95% confidence interval) and were analyzed by Wilcoxon rank-order test. Patients who had any alarm events received more opioid doses and greater total amounts of opioid and midazolam.

http://links.lww.com/AA/B357) shows comparison of medication administration excluding patients who were transferred to other procedural or care areas early after study participation).

During a total of 2029.7 monitored minutes in standard patients, 225 respiratory rate ≤ 4 BPM events were reported by either or both EtCO₂ and RRA in 25 (56.8%) standard patients. The number of verified true-positive or false-positive respiratory rate ≤ 4 BPM events reported by each method is shown in Table 3. The proportion of true-positive respiratory rate ≤ 4 BPM alarm events was greater for RRA compared with EtCO₂ ($P < 0.0001$).

DISCUSSION

At least 1 alarm event occurred in nearly 80% of patients receiving planned moderate sedation to facilitate GI or IR procedures. These events included respiratory depression or desaturation events in nearly half of the patients. Providing additional patient monitoring parameters to procedural sedation teams during planned moderate PRS was associated with >50% reduction in the total number of alarm events and a 35% to 40% reduction in the number of patients with respiratory depression or desaturation events. We did not find a difference in the number of patients who experienced deeper than intended sedation events, which were recorded in nearly one-third of these patients undergoing planned moderate sedation.

It is likely that the alarm events recorded were related to the sedative medications administered. As reported in 123 adults undergoing GI endoscopy with planned moderate sedation, 7% of sedative medication administrations were followed by desaturation, many within 5 minutes.⁵¹ Analysis of medication administration to our patients is interesting. Although we found a similar total opioid dose, advanced patients received fewer dose administrations than standard. This may reflect a change in procedural sedation team assessment of drug effects based on parameters from the advanced monitors. The observational design of this study limits our ability to draw conclusions from this finding. However, the fewer dose administrations to advanced, coupled with the findings of greater medication dosage and administration number to patients who had alarm events regardless of study group, suggests that the use of advanced monitors could allow more careful titration of sedation medications to patients undergoing planned moderate PRS. Future research could be designed to test specific algorithms of medication administration based on the parameters provided by the monitors.

Nearly one-third of our patients had episodes of deeper than intended sedation detected by PSI, despite the planned moderate sedation. This is less than reported in patients who received bolus propofol⁵² or midazolam with opioid

administration during GI procedures⁵³ but suggests that procedural sedation teams may not accurately detect deeper than intended sedation during procedures. We did not find a difference between groups, which may be related to muscle activity impacting PSI during PRS. Since PSI is falsely elevated by muscle activity,⁵⁴ a patient may be at a deeper level of sedation than indicated by PSI. This could potentially decrease the sensitivity of PSI to detect deepening sedation until the patient approaches general anesthesia. It appears that algorithms used to process electroencephalography may not filter muscle activity effectively. Improved filtering or correction for muscle activity may be needed for use of these monitors during PRS. Although this study was not designed to investigate the correlation of PSI to sedation scores, the recorded scores based on clinical assessment indicated that fewer patients had deeper than intended sedation compared with the number indicated by PSI.

Our findings show interesting differences between capnometry and respiratory acoustic monitoring. Prior studies comparing these monitors have enrolled patients with controlled airways,⁵⁵ breathing through a tight fitting face-mask,³⁹ or during stays in intensive care⁵⁶ or postanesthesia recovery units.^{38,54} These settings allow for more control over sensor and cannula placement than during PRS and allow intervention by clinicians when patients mouth breathe or remove the capnometry sampling cannula. Mouth breathing during PRS may contribute to false-positive EtCO₂ alarms. Use of a dual oral/nasal oxygen supply and capnometry cannula may provide a different result than what we found. We were not able to demonstrate a relationship between low PSI and respiratory depression, similar to a report of PSI monitoring of children during PRS.⁵⁷

The study has some limitations. We did not randomize patients to the standard or advanced group during a single time window, but instead used an observational before-after comparison model. Random assignment could have allowed procedural sedation teams to alter practice during sedation of standard patients by using experience gained while viewing RRA and PSI parameters during sedation of advanced patients. The time interval between study parts allowed sedation teams to gain familiarity with acoustic respiratory monitoring. It is possible that experience gained during this interval could have contributed to the difference in alarm events we found. However, the sedation nurses involved in these procedures had a minimum of 10 years prior experience participating in procedural sedation teams. In light of that experience, the additional case experience gained in the interval is unlikely by itself to have altered their sedation practices. We did not obtain respiratory rate from a source that could be considered an independent standard to compare RRA and

Table 3. Analysis of Respiratory Rate ≤ 4 BPM Events Reported by Nasal Cannula Capnometry (EtCO₂) or RRA in the 44 Standard Patients

Monitor	Detected respiratory pauses		Retrospective analysis		Positive predictive value, %
	Respiratory rate ≤ 4 BPM reported, n	Verified as true positive, n (%)	Verified as false positive, n (%)		
EtCO ₂	166	49 (30)	117 (70)		29.5
RRA	100	78 (78)	22 (22)		78.0

The proportion of true-positive respiratory rate ≤ 4 BPM alarm events reported by acoustic respiratory monitoring was greater than for nasal cannula capnometry (Wald difference, 48.5%; 95% confidence interval, 37.0%–58.3%; $P < 0.0001$).

BPM = breaths per minute; EtCO₂ = end-tidal carbon dioxide; RRA = acoustic respiratory monitor.

EtCO₂ against, instead using the sound files from RRA for the comparative standard. Thus, we did not attempt to calculate a false-negative rate. In this observational study of GI and IR procedures, having a research assistant continuously auscultate breath sounds was not practical. In addition, this auscultation could have interfered with procedure performance or altered assessment of the patient's sedation level by the procedural sedation teams based on patient response to stethoscope placement and movement. Furthermore, we compared RRA to EtCO₂ from nasal cannula capnometry. Problems with nasal cannula capnometry include poor accuracy if patients mouth breathe³³ and obstruction of the sample path by secretions. Future research could compare combined nasal/oral cannula capnometry to RRA. Finally, as this was an observational study, we did not specify sedation medications or indications for additional sedative medication administration. A prospective study designed to target specific PSI or RRA targets could be designed to more thoroughly investigate the possible impact of these monitors on sedation practice.

In conclusion, the use of advanced monitoring during planned moderate PRS was associated with fewer alarm events, patients experiencing desaturation, and patients experiencing respiratory depression alarm events. It is possible that increased use and familiarity with RRA could alert practitioners before the need for clinical intervention and thus perhaps result in fewer episodes of hypoventilation and desaturation. The findings of this pilot study suggest that further study into the safety and outcome impacts of advanced monitoring during PRS is warranted. ■■

DISCLOSURES

Name: Richard L. Applegate II, MD.

Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript. Richard L. Applegate, II, MD, was the Principal Investigator for this study; the LLU Department of Anesthesiology received funding for his role in the conduct of this study.

Attestation: Richard L. Applegate II has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

Conflicts of Interest: Richard L. Applegate II received research funding from Masimo.

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