

ORIGINAL ARTICLE

Association between capnography and recovery time after procedural sedation and analgesia in the emergency department

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Abstract

Aim: Capnography is recommended for use in procedural sedation and analgesia (PSA); however, limited studies assess its impact on recovery time. We investigated the association between capnography and the recovery time of PSA in the emergency department (ED).

Methods: This study was a secondary analysis of a multicenter PSA patient registry including eight hospitals in Japan. We included all patients who received PSA in the ED between May 2017 and May 2021 and divided the patients into capnography and no-capnography groups. The primary outcome was recovery time, defined as the time from the end of the procedure to the cessation of monitoring. The log-rank test and multivariable analysis using clustering for institutions were performed.

Results: Of the 1265 screened patients, 943 patients who received PSA were enrolled and categorized into the capnography ($n = 150$, 16%) and no-capnography ($n = 793$, 84%) groups. The median recovery time was 40 (interquartile range [IQR]: 25–63) min in the capnography group and 30 (IQR: 14–55) min in the no-capnography group. In the log-rank test, the recovery time was significantly longer in the capnography group ($p = 0.03$) than in the no-capnography group. In the multivariable analysis, recovery time did not differ between the two groups (adjusted hazard ratio, 0.95; 95% confidence interval, 0.77–1.17; $p = 0.61$).

Conclusion: In this secondary analysis of the multicenter registry of PSA in Japan, capnography use did not associate with shorter recovery time in the ED.

KEY WORDS

capnography, conscious sedation, deep sedation, emergency departments, patient monitoring

INTRODUCTION

Procedural sedation and analgesia (PSA) is performed during painful procedures or examinations to attenuate anxiety, pain, or motion.¹ In the emergency department (ED), PSAs are often unscheduled; therefore, PSA in the ED may have some potential risks for adverse events,^{2–4} and may require close monitoring to prevent adverse events.^{2–6} Capnography, which continuously expresses the carbon dioxide concentration in exhaled breath,^{7–9} is recommended during PSA,

especially in moderate-to-deep sedation, to monitor the ventilation status of the patient.^{5,6}

Although guidelines recommend the use of capnography, a recent systematic review and meta-analysis showed that the use of capnography was not significantly associated with adverse events.¹⁰ Capnography, along with standard monitoring for patients undergoing PSA in the ED, does not decrease cardiorespiratory events compared with standard monitoring alone.¹¹ In contrast, a subgroup analysis of the same study revealed a significant increase in the

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rate of airway interventions in adults in the capnography group.¹¹

Recovery time was defined as the time from the end of the procedure to the cessation of monitoring.¹² Patients who receive PSA should be monitored until they are no longer at risk for respiratory depression and hemodynamic instability and they return to their baseline level of consciousness.⁶ A systematic review and meta-analysis that examined the usefulness of capnography showed little evidence on the relationship between the use of capnography and recovery time.¹¹

We hypothesized that by using capnography, physicians may quickly assess and intervene in hypoventilation; therefore, appropriate sedation can contribute to shortening the recovery time. A longer recovery time could lead to longer length of stay in the ED and ED crowding, which is associated with mortality and a higher rate of individuals who leave without being seen in the ED.¹³

Therefore, the effectiveness of capnography on the recovery time of patients receiving PSA in EDs must be evaluated. The present study analyzed PSA registry data with the aim of investigating the association of capnography with shortening of recovery time after PSA.

METHODS

Study design and setting

This is a secondary analysis of a multicenter PSA patient registry database in Japan (Japanese Procedural Sedation and Analgesia Registry [JPSTAR]).¹⁴ Eight urban hospitals that have an emergency medicine residency program were included in the JPSTAR. The JPSTAR prospectively collected data on all patients undergoing PSA in ED since May 2017. PSA was defined as parenteral administration of sedative medication (with or without analgesics) to facilitate procedures or examinations (including computed tomography, magnetic resonance imaging, fluoroscopy, and endoscopy).^{14,15} The registry did not include patients who received sedation for airway management or agitation control. Data collected in JPSTAR included patient age, height, weight, body mass index, sex, time from last meal and drink, provider status, risk factors for tracheal intubation and bag valve mask ventilation, consultation for anesthesia, monitoring, target depth of sedation set before the procedure, American Society of Anesthesiologists physical status (ASA-PS), use of supplemental oxygen, indication for PSA, pre-PSA medication such as antiemetics, medication choices (both sedative and analgesic), route of medication administration, dose of medications, time course of PSA, ancillary methods such as regional block, procedure success, adverse events, and satisfaction with the provider and patients. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of New Mexico as previously described.^{14,15} This study was approved by the relevant institutional review boards of all the hospitals, which waived

the requirement for informed patient consent to ensure participant anonymity as stipulated in the Japanese government guidelines. This study followed the Strengthening the Reporting of Observational studies in Epidemiology statement checklist for observational studies.

Participants

In this study, we included all patients who received PSA in the ED and registered their data between May 2017 and May 2021. The following patients were excluded: (i) those who were administered antihistamines or antipsychotics as sedatives, (ii) those who were administered analgesics only, (iii) those whose route of sedatives administration was unknown, (iv) those with missing data, and (v) those with outliers of recovery time. Outliers of recovery time were defined as those with recovery times <1 min or >24 h (1440 min).

Exposure and outcome measures

The exposure was capnography use. The indication for capnography was not defined and was left to the discretion of the physicians. The primary outcome was recovery time, which was defined as the time from the end of the procedure to the cessation of monitoring.¹² The timing of the cessation of monitoring was also left to the physician's discretion. Although the individual protocols about the policy and procedures for ED sedation were maintained by each institution, all the participating EDs were staffed by emergency attending physicians, and all patients were treated at the discretion of the treating physicians and supervised by attending physicians. The secondary outcomes were: (i) hypoxemia ($\text{SpO}_2 < 90\%$) and (ii) the composite of apnea, glossoptosis (posterior displacement of the tongue), and hypoxemia.

Sample size estimation

Estimated mean recovery time with the capnography and without capnography were 30 min and 40 min, with standard deviations of 10 min. A minimum of 128 samples were required to achieve 80% power and a significance level of $\alpha = 0.05$.

Data analysis

The patients were categorized into the capnography and no-capnography groups. Between both groups, the baseline characteristics of the patients were summarized using medians and interquartile ranges (IQR) for continuous variables and counts and percentages for categorical variables. The Mann-Whitney U test was used to compare the medians of the continuous variables between the groups. The χ^2 test or Fisher's exact test was used to compare the

proportions of categorical variables between the groups. The primary analysis used the log-rank test to compare recovery times between the groups. A Kaplan–Meier curve was used to summarize the results. In this analysis, there are no censoring events because the cessation of monitoring occurs in all cases. Further, a multivariate Cox proportional hazard model was used to compare the groups with adjustment for confounding variables including patient age, sex, target depth of sedation (light, moderate, or deep), ASA-PS (1–2 or 3–5), use of supplemental oxygen, indication for PSA (cardioversion, gastrointestinal procedure such as endoscopy, fracture or dislocation reduction, abscesses or wound treatment, diagnostic test such as magnetic resonance imaging, and others), choice of sedative medication (ketamine, propofol, midazolam, thiopental, dexmedetomidine, diazepam, and combination use), and choice of analgesics (opioids, non-opioids, or not). The proportional hazards were evaluated using the Schoenfeld residual test. A multivariate logistic regression test was used to analyze the relationship between capnography use and adverse events (hypoxemia and composite outcome). To consider the differences in practice and training systems between institutions, a generalized estimating equation (GEE) with clustering for institutions was used. A sensitivity analysis including outliers of the recovery time was performed to examine the robustness of our inference. Missing values were assumed to occur randomly and the complete case analysis was applied. The 95% confidence intervals (CI) are reported for each result. *p*-Values were based on a significance level of 0.05, and all the tests were two-sided. Statistical analyses were performed using the STATA (Version 16.1, Stata Corp, USA) software package.

RESULTS

Patient selection

During the study period, 1265 patients were registered with JPSTAR. Of these, 322 (25%) were excluded: 12 used antihistamines or antipsychotics, 10 used analgesics only, three had

unknown routes of sedative administration, 92 had missing data, and 205 were outliers of recovery time, resulting in 943 (75%) patients in the analysis (Figure 1).

Baseline characteristics

The median age of the included patients was 69 years (IQR: 48–79), and 528 patients (56%) were men. Most patients (76%) were categorized into ASA class 1 or 2. Capnography was performed in 150 (16%) patients. Table 1 shows the characteristics of the patients in each group. The patients in the capnography group were significantly younger than those in the no-capnography group (43 [IQR: 14–70] versus 70 [IQR: 57–80], $p < 0.001$). Regarding indication, the capnography group had the highest number of fractures and dislocation reductions (45%), whereas the no-capnography group had the highest number of cardioversions (47%). Regarding sedatives, in the capnography group, 40% used propofol, and 34% used ketamine, whereas in the no capnography group, 37% used thiopental and 32% used midazolam. Table 2 provides information on the rate of capnography use across institutions.

Recovery time

The median recovery time was 40 (IQR: 25–63) min in the capnography group and 30 (IQR: 14–55) min in the no-capnography group. Kaplan–Meier cumulative incidence curves (Figure 2) showed that the recovery time was longer in the capnography group, which was confirmed using the log-rank test ($p = 0.03$). In the multivariable analysis using the Cox proportional hazards model with clustering for institutions, there was no difference in recovery time between the two groups (adjusted hazard ratio, 0.95; 95% CI, 0.77–1.17; $p = 0.61$) (Table 3). However, the Schoenfeld residual test demonstrated non-proportional hazards in the Cox proportional hazards model analysis ($p < 0.001$). In the analysis including the outliers of recovery time, the result was consistent (adjusted hazard ratio, 0.86; 95% CI, 0.67–1.12; $p = 0.26$).

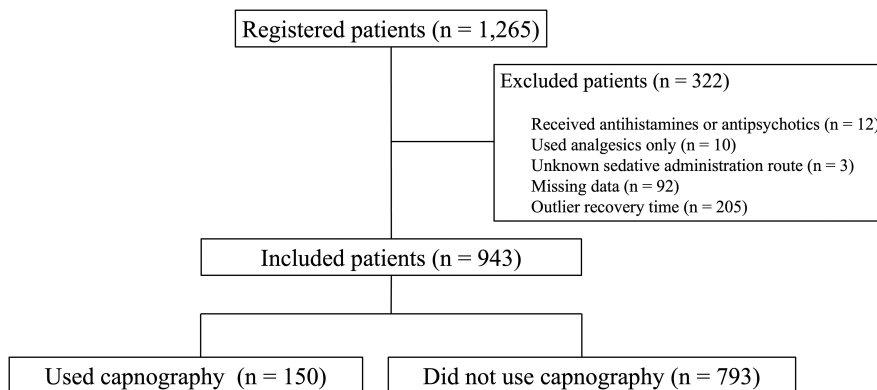


FIGURE 1 Study participant selection.

TABLE 1 Patients and clinical management characteristics of patients who underwent procedural sedation and analgesia according to capnography use.

Variables	Capnography group	No-capnography group	p Value
	n = 150 (16%)	n = 793 (84%)	
Age, year, median (IQR)	43 (14–70)	70 (57–80)	<0.001
Female sex	60 (40)	355 (45)	0.28
Target depth of sedation ^a			
Light	61 (41)	230 (29)	<0.001
Moderate	79 (53)	236 (30)	
Deep	10 (7)	327 (41)	
ASA-PS			
1–2	129 (86)	589 (74)	0.002
3–5	21 (14)	204 (26)	
Supplemental oxygen	65 (43)	481 (61)	<0.001
Indication			
Cardioversion	17 (11)	369 (47)	<0.001
Gastrointestinal procedure	4 (3)	200 (25)	
Fracture or dislocation reduction	67 (45)	104 (13)	
Abscesses or wounds treatment	38 (25)	27 (3)	
Examinations	8 (5)	23 (3)	
Others ^b	16 (11)	70 (9)	
Sedatives ^a			
Ketamine	51 (34)	32 (4)	<0.001
Midazolam	24 (16)	256 (32)	
Propofol	60 (40)	156 (20)	
Thiopental	0 (0)	292 (37)	
Dexmedetomidine	0 (0)	28 (4)	
Diazepam	0 (0)	6 (1)	
Combination use ^c	15 (10)	23 (3)	
Analgesics			
Opioids	51 (34)	34 (4)	<0.001
Non-opioids ^d	10 (7)	101 (13)	
No use	89 (59)	658 (83)	

Note: Data are shown as n (%), unless otherwise specified.

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; IQR, interquartile range.

^aThe sum of the percentages may not equal 100 because of rounding.

^bIncludes coronary angiography, chest drain insertion, use of continuous positive airway pressure mask, lumbar puncture, interventional radiology, bronchoscopy, transesophageal echocardiography, observation of larynx or pharynx with a laryngoscope, burn treatment, changing of the tube for gastric fistula, or physical examination after sexual abuse.

^cDefined as the use of two or more sedatives.

^dIncludes acetaminophen, pentazocine, non-steroidal anti-inflammatory drug, and lidocaine via oral route, intravenous, and local injections.

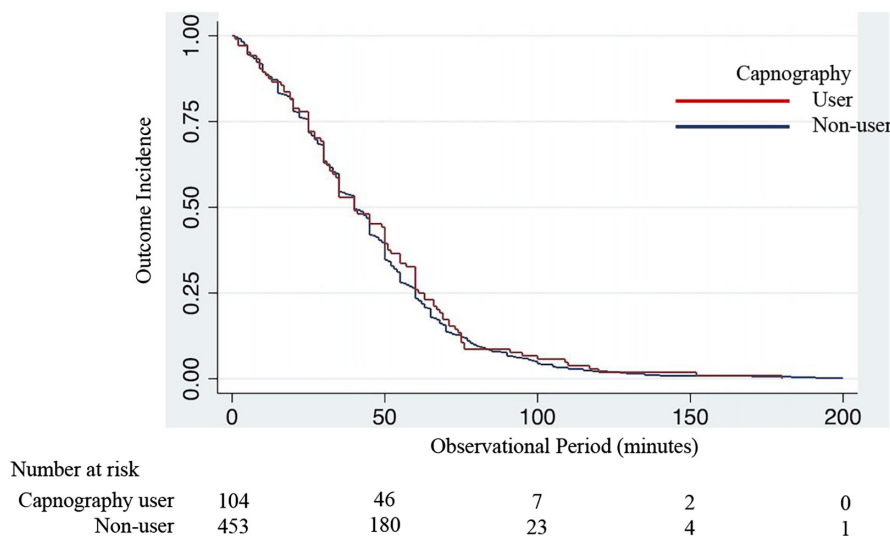
Adverse events

With regard to secondary outcomes, 98 of 943 (10%) patients had hypoxemia ($\text{SpO}_2 < 90\%$), and 144 of 943 (15%) had the composite outcome of apnea, glossoptosis, and hypoxemia. Hypoxemia occurred in 16 of 150 (11%) and 82 of 793 (10%) patients in the capnography and no-capnography groups, respectively. The odds ratios between the two groups did not differ significantly (unadjusted odds ratio, 0.81; 95% CI, 0.29–2.31; $p = 0.69$). The composite outcome occurred in

18/150 (12%) and 126 of 793 (16%) patients in the capnography and no-capnography groups, respectively, showing no significant difference between the two groups (unadjusted odds ratio, 0.83; 95% CI, 0.34–2.03; $p = 0.68$). Multivariate logistic regression with GEE showed no significant difference between the two groups in the secondary outcomes (hypoxemia: adjusted odds ratio, 1.05; 95% CI, 0.80–1.37, $p = 0.73$) (Table 4) (composite of apnea, glossoptosis, and hypoxemia: adjusted odds ratio, 1.02; 95% CI, 0.67–1.56, $p = 0.93$) (Table 5).

TABLE 2 Rate of capnography use across institutions.

Institutions	Capnography group (n = 150)	No-capnography group (n = 793)	Total (n = 943)	Rate of capnography use (%)
A	141	50	191	73.8
B	1	324	325	0.3
C	3	314	317	0.9
D	1	9	10	0.1
E	0	16	16	0
F	0	40	40	0
G	4	17	21	23.5
H	0	23	23	0

**FIGURE 2** Kaplan–Meier estimates of the probability of recovery from procedural sedation and analgesia with and without capnography.

DISCUSSION

In this multicenter prospective observational study that investigated recovery time in the ED among patients who underwent PSA with or without capnography, the use of capnography was not significantly associated with shorter recovery time of PSA after adjusting for possible confounders. Despite increasing interest, there is insufficient literature on the association between capnography and recovery time.¹¹ A practice guideline for moderate PSA recommends the continuous monitoring of ventilation at regular intervals (e.g., every 5–15 min) until patients are suitable for discharge.⁵

Capnography is useful for identifying airway obstruction because of glossoptosis or hypercapnia induced by inappropriate deep sedation.^{16,17} However, capnography can only detect sedation to the level leading to serious respiratory adverse events and cannot identify sedation deeper than the planned level without respiratory depression. Therefore, capnography may not be useful for maintaining optimal sedation depth. Our secondary analysis showed no difference in the occurrence of respiratory adverse events between the capnography and no-capnography groups, corroborating

the results of a previous study.¹¹ Although capnography is useful for the early detection of adverse events, other factors such as the amount of medication used to induce and maintain optimal sedation are more important in relation to adverse events. Therefore, the usefulness of capnography is limited considering the proportion of occurrence of adverse events.

The occurrence of respiratory adverse events was not significantly different between the capnography and no-capnography groups for PSA in the ED. This was concordant with the results of a recent systematic review and meta-analysis, which showed no differences in the rate of oxygen desaturation (risk ratio, 0.89; 95% CI, 0.48–1.63; $n = 1272$, three trials; moderate-quality evidence) and airway interventions (risk ratio, 1.26; 95% CI, 0.94–1.69; $n = 1272$, three trials; moderate-quality evidence).¹¹ In our study, hypoxemia and apnea occurred more frequently (i.e. hypoxemia, 10%; apnea, 6%) than in previous studies (hypoxemia, 4%; apnea, 1%).⁴ In addition, glossoptosis occurred in 2% of patients, and the proportion of total respiratory adverse events (hypoxemia, apnea, and glossoptosis) was high at 15%.

Regarding the usefulness of capnography with respect to adverse events, capnography could detect respiratory events

TABLE 3 Adjusted association of capnography use with recovery time.

Variables	Adjusted hazard ratio (95% CI)	p Value
Capnography	0.95 (0.77–1.17)	0.61
Covariates		
Male (versus female) sex	1.18 (0.95–1.47)	0.14
Sedation depth		
Light sedation	[reference]	
Moderate sedation	0.53 (0.34–0.82)	<0.01
Deep sedation	0.38 (0.22–0.67)	<0.01
ASA-PS (3–5)	0.84 (0.62–1.12)	0.24
Age	0.99 (0.99–1.00)	0.54
Indication		
Cardioversion	[reference]	
Gastrointestinal procedure	2.08 (1.02–4.26)	0.045
Fracture or dislocation reduction	1.08 (0.87–1.33)	0.49
Abscess or wound treatment	0.57 (0.36–0.92)	0.02
Diagnostic tests	0.68 (0.38–1.22)	0.19
Others ^a	0.91 (0.65–1.26)	0.56
Supplemental oxygen	1.38 (1.22–1.57)	<0.01
Sedative medication		
Ketamine	[reference]	
Propofol	0.86 (0.69–1.07)	0.18
Midazolam	1.53 (1.27–1.85)	<0.01
Thiopental	1.59 (1.27–1.98)	<0.01
Dexmedetomidine	1.62 (0.95–2.76)	0.08
Diazepam	1.95 (1.48–2.57)	<0.01
Combination use	0.70 (0.53–0.91)	0.01
Analgesics medication		
Opioids	[reference]	
Non-opioids	0.91 (0.76–1.10)	0.34
No-use	1.08 (0.75–1.55)	0.69

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; CI, confidence interval.

^aDefined as coronary angiography, chest drain insertion, use of continuous positive airway pressure mask, lumbar puncture, interventional radiology, bronchoscopy, transesophageal echocardiography, observation of larynx or pharynx with a laryngoscope, burn treatment, changing of the tube for gastric fistula, or physical examination after sexual abuse.

early^{18,19}; however, as discussed above, it may not prevent adverse events. The high complication rate in this study could be because the study included older patients who were more likely to have complications than those in previous studies. The median age in most studies included in the systematic review and meta-analysis ranged from 30 to 50,⁴ and the median age of the included patients in our study was 69 years (IQR: 48–79). PSA in the elderly needs further investigation because the proportion of PSA would increase especially in

TABLE 4 Adjusted association of capnography use with hypoxemia.

Variables	Adjusted odds ratio (95% CI)	p Value
Capnography	1.05 (0.80–1.37)	0.73
Covariates		
Male (versus female) sex	0.75 (0.80–1.37)	0.73
Sedation depth		
Light sedation	[reference]	
Moderate sedation	1.81 (1.07–3.06)	0.03
Deep sedation	2.81(0.67–11.76)	0.16
ASA-PS (3–5)	1.50 (1.00–2.26)	0.05
Age	1.02 (1.00–1.03)	0.01
Indication		
Cardioversion	[reference]	
Gastrointestinal procedure	0.39 (0.42–3.51)	0.40
Fracture or dislocation reduction	0.48 (0.21–1.13)	0.09
Abscess or wound treatment	1.39 (0.3–5.77)	0.65
Diagnostic tests	0.65 (0.24–1.76)	0.40
Others ^a	1.40 (0.37–5.23)	0.62
Supplemental oxygen	0.31 (0.21–0.46)	<0.01
Sedative medication		
Ketamine	[reference]	
Propofol	0.74 (0.29–1.88)	0.53
Midazolam	1.77 (1.21–2.61)	<0.01
Thiopental	0.50 (0.32–0.76)	<0.01
Dexmedetomidine	0.57 (0.31–1.02)	0.06
Diazepam	0.55 (0.24–1.27)	0.16
Combination use	1.62 (0.44–6.02)	0.50
Analgesics medication		
Opioids	[reference]	
Non-opioids	0.85 (0.33–2.18)	0.74
No-use	0.72 (0.36–1.42)	0.34

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; CI, confidence interval.

^aDefined as coronary angiography, chest drain insertion, use of continuous positive airway pressure mask, lumbar puncture, interventional radiology, bronchoscopy, transesophageal echocardiography, observation of larynx or pharynx with a laryngoscope, burn treatment, changing of the tube for gastric fistula, or physical examination after sexual abuse.

developed countries because of the aging society. Moreover, because apnea was not well defined and was subjectively assessed by the physicians in this study, it cannot be accurately compared with that in previous studies.

Although our null hypothesis was not rejected, our study could provide a foundation for further research on the recovery time of PSA. Studies on high-risk patient groups, such as older patients, patients who needed moderate-to-deep sedation, or unstable vital signs, could find differences by using capnography.

TABLE 5 Adjusted association of capnography use with composite outcome^a.

Variables	Adjusted odds ratio (95% CI)	p Value
Capnography	1.02 (0.67–1.56)	0.93
Covariates		
Male (versus female) sex	0.92 (0.53–1.59)	0.76
Sedation depth		
Light sedation	[reference]	
Moderate sedation	1.71 (0.98–3.01)	0.06
Deep sedation	3.23 (0.59–17.60)	0.17
ASA group (3–5)	1.06 (0.85–1.33)	0.58
Age	1.02 (1.01–1.03)	<0.01
Indication		
Cardioversion	[reference]	
Gastrointestinal procedure	0.29 (0.05–1.62)	0.16
Fracture or dislocation reduction	0.58 (0.16–2.12)	0.41
Abscess or wound treatment	1.37 (0.33–5.72)	0.66
Diagnostic tests	0.65 (0.24–1.74)	0.40
Others ^b	0.99 (0.29–3.34)	0.98
Supplemental oxygen	0.33 (0.28–0.39)	<0.01
Sedative medication		
Ketamine	[reference]	
Propofol	1.13 (0.61–2.07)	0.70
Midazolam	1.92 (1.61–1.85)	2.28
Thiopental	0.94 (0.59–1.50)	0.79
Dexmedetomidine	0.85 (0.68–1.07)	0.17
Diazepam	0.66 (0.46–0.95)	0.03
Combination use	1.31 (0.35–4.96)	0.69
Analgesics medication		
Opioids	[reference]	
Non-opioids	1.43 (0.72–2.89)	0.31
No-use	0.94 (0.52–1.70)	0.83

Abbreviations: ASA-PS, American Society of Anesthesiologists Physical Status; CI, confidence interval.

^aThe composite outcome included apnea, glossoptosis (posterior displacement of the tongue), and hypoxemia.

^bDefined as coronary angiography, chest drain insertion, use of continuous positive airway pressure mask, lumbar puncture, interventional radiology, bronchoscopy, transesophageal echocardiography, observation of larynx or pharynx with a laryngoscope, burn treatment, changing of the tube for gastric fistula, or physical examination after sexual abuse.

Limitations

This study had several limitations. First, there were no common criteria for patient recovery in the eight participating facilities, rather, it depended on the discretion of the physicians. Although recovery from PSA is defined as the time of the return of the patient's consciousness to baseline in JPSTAR, there are no objective indicators for consciousness. Second, the definition of outliers of

recovery time could lead to selection bias. Of the 1265 (16.2%) patients, 205 were excluded from the data analysis because their recovery times were presumed to be outliers because of registration errors (recovery time >1440 min [24 h] or <1 min). Because 1440 min (24 h) or more recovery time in the ED is considered equivalent to hospitalization, we set the upper limit of the cutoff to 1440 min (24 h). In addition, we excluded a recovery time of 0 min because it is not common for patients to return home immediately after finishing a procedure involving PSA. However, the findings were consistent across the different statistical assumptions, including those with outliers. In addition, the rate of outliers was as high as 16%, which may impair the reliability of the analysis. The system needs to be revised to return an error when entering unrealistic values into the database. Third, as with any observational study, there was a lack of unmeasured confounders (e.g., dose of medication or achieved sedation depth) in the practice and patient factors that contribute to the recovery time. In addition, although we adjusted for severity, physicians could have used capnography in patients with severe conditions, which could lead to confounding by indication. Fourth, because capnography is used in limited institutions, the analysis might only compare differences between institutions. To adjust this dispersion, we conducted a GEE with clustering for institutions. Finally, the study sample predominantly consisted of academic EDs in Japan. Although formal validation in other practice settings is warranted, the observed relationships were clinically plausible and likely present in different settings.

CONCLUSION

In this multicenter prospective observational study, capnography was not associated with shorter recovery time or adverse respiratory events in patients who received PSA in the ED in Japan. Our data should facilitate further investigations into the development of optimal monitoring during PSA, which will, in turn, lead to better outcomes of patients in the ED.

ACKNOWLEDGMENTS

We acknowledge the following study and research personnel for their contributions to this project: Sendai City Hospital (Hiroshi Takase, MD, Yuji Murata, MD, PhD), Tokyobay Urayasu Ichikawa Medical Center (Hikaru Funakoshi, MD, MPH, PhD), Osaka Police Hospital (Yasuaki Mizushima, MD, PhD, Takashi Noma, MD), Kenwakai Otemachi Hospital (Akihikari Shimosato, MD), Kyoto Prefectural University of Medicine (Nobunaga Okada, MD), National Center for Global Health and Medicine (Kentaro Fukano, MD), Tane General hospital (Atsushi Kitamura, MD), Fukui Prefectural Hospital (Minoru Hayashi, MD), and all personnel at participating hospitals who contributed the data.

FUNDING INFORMATION

No funding information provided.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ETHICS STATEMENT

Approval of the Research Protocol: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. The Ethics Committee of Tokyobay Urayasu Ichikawa Medical Center approved this study (reference number is 251 and 510).

Informed Consent: This study was approved by the relevant institutional review boards of all the hospitals, which waived the requirement for informed patient consent to ensure participant anonymity as stipulated in the Japanese government guidelines.

Registry and Registration No. of the Study/Trial: The registry is the Japanese Procedural Sedation and Analgesia Registry; JPSTAR. The registration number is not applicable.

Animal Studies: Not applicable.

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How to cite this article: Shirane S, Funakoshi H, Takahashi J, Homma Y, Norii T. Association between capnography and recovery time after procedural sedation and analgesia in the emergency department. *Acute Med Surg.* 2023;10:e901. <https://doi.org/10.1002/ams2.901>