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ORIGINAL ARTICLE

Procedural sedation and analgesia in the emergency department in Japan: interim analysis of multicenter prospective observational study

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Abstract

Purpose Procedural sedation and analgesia (PSA) is widely performed outside of the operating theater, often in emergency departments (EDs). The practice and safety of PSA in the ED in an aging society such as in Japan have not been well described. We aimed to characterize the practice pattern of PSA including indications, pharmacology and incidence of adverse events (AEs) in Japan.

Methods We formed the Japanese Procedural Sedation and Analgesia Registry, a multicenter prospective observation registry of ED patients undergoing PSA. We included all patients who received PSA in the ED. PSA was defined as any systemic pharmacological intervention intended to facilitate a painful or uncomfortable procedure. The main variables in this study were patients' demographics, American Society of Anesthesiologists (ASA) physical status, indication of PSA, medication choices, and AEs. The primary outcome measure was overall AEs from PSA.

Results We enrolled 332 patients in four EDs during the 12-month period. The median age was 67 years (IQR, 46–78). In terms of ASA physical status, 79 (23.8%), 172 (51.8%), and 81 (24.4%) patients were class 1, 2, 3 or higher, respectively. The most common indication was cardioversion (44.0%). The most common sedative used was thiopental (38.9%), followed by midazolam (34.0%) and propofol (19.6%). Among all patients, 72 (21.7%, 95% confidence interval, 17–26) patients experienced one or more AEs. The most common AE was hypoxia (9.9%), followed by apnea (7.2%) and hypotension (3.5%). All of the AEs were transient and no patient had a serious AE.

Conclusion In a multicenter prospective registry in Japan, PSA in the ED appears safe particularly since the patients who underwent PSA were older and had a higher risk profile compared to patients in previous studies in different countries.

Keywords Procedural sedation · Safety · Emergency department

Introduction

Procedural sedation and analgesia (PSA) is widely performed outside of the operating theater, often in emergency departments (EDs) [1]. An increasing number of

The members of the Japanese Procedural Sedation andAnalgesia Registry investigators were listed in the Acknowledgements section.

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studies have shown that PSA can be safely performed in the ED [2–4]. The practice and safety of PSA in the ED in an aging society, such as in Japan, have not been well described.

Japan is an extremely aging society. Individuals 65 years or older comprised 27.7% of the population in 2017 [5]. Similar to many countries, the number of visits to EDs in Japan has been significantly trending up [6–8]. The Japanese Fire and Disaster Management Agency reported that 5.62 million patients were transported to the EDs in 2016 [6]. This represents a 2.6% increase from 2015 and an almost 10% increase since 2005. Patients in the ED often require PSA for their medical conditions, such as cardioversion for unstable dysrhythmias or reduction of displaced fractures.

Japan has been facing a significant shortage of anesthesiologists nationwide, including university hospitals [9]. Potentially due to the increasing demand and lack of anesthesiologist coverage, non-anesthesiologists including emergency physicians and residents often perform PSA in EDs in Japan. This leads to a unique situation where high-risk patients receive PSA by non-anesthesiologist in the ED. We aimed to characterize the practice pattern of PSA, indications, pharmacology and incidence of adverse events (AEs) in Japanese EDs.

Methods

Study design

This is the interim analysis of the Japanese Procedural Sedation and Analgesia Registry (JPSTAR), a multicenter prospective observation registry of patients undergoing PSA in the ED, formed in 2017. Currently, four teaching hospitals in Japan participate in the registry (Fig. 1). The Institutional Review Boards of each participating hospital as well as the University of New Mexico have approved the study design. PSA was defined as any systemic pharmacological intervention intended to facilitate a painful or uncomfortable procedure. The main variables in this study were patient demographics including age, gender, American Society of Anesthesiologists (ASA) physical status classification [10], indication of PSA, medication choices and doses, procedure success rate, patient and physician satisfaction, AEs and disposition.

Table 1 shows the complete list of AEs in the registry. AEs included both serious and other less serious AEs and were defined as any undesirable events associated with the use of medications including both sedatives and analgesics. AEs did not include events that were not associated with the use of medications, for example, if the patient

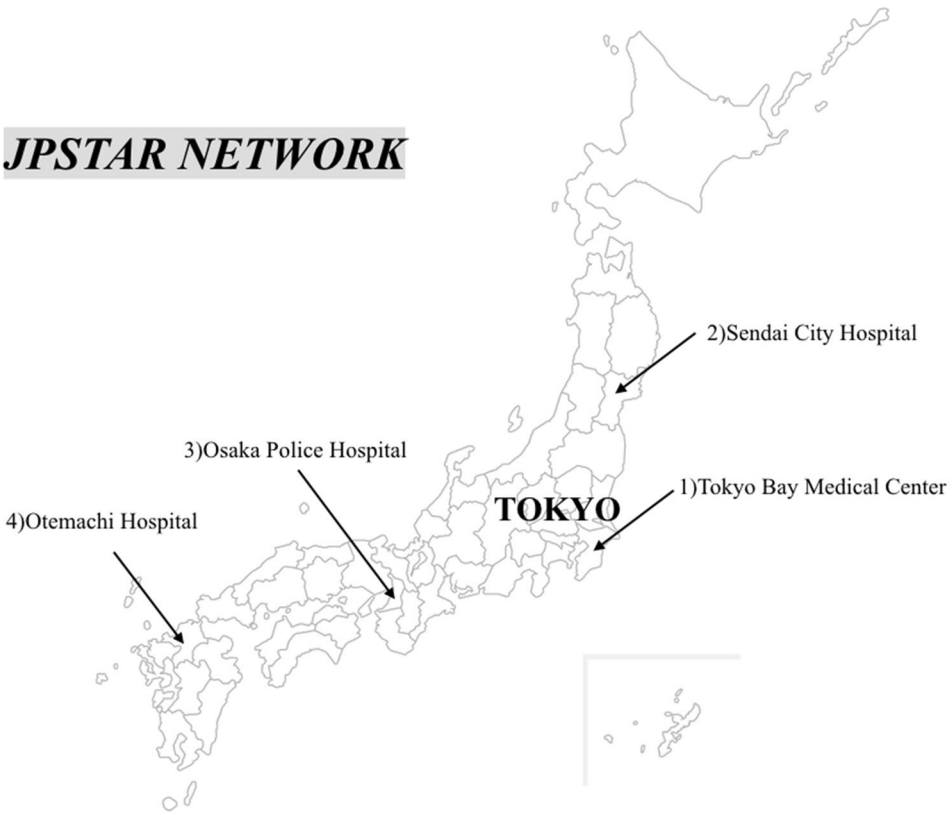

Fig. 1 The locations of participating hospitals in the Japanese Procedural Sedation and Analgesia Registry (JPSTAR)

Table 1 List of adverse events from procedural sedation and analgesia

Serious adverse events
Cardiac arrest
Anoxic brain injury
Non-serious adverse events
Apnea
Glossoptosis (posterior displacement of the tongue)
Hypoxia (SpO_2 < 90%)
Laryngospasm
Hypersalivation requiring intervention
Hypertension (systolic blood pressure > 180 mmHg)
Hypotension (systolic blood pressure < 90 mmHg)
Tachycardia (heart rate > 120 bpm)
Bradycardia (heart rate < 60 bpm)
Other dysrhythmias
Vomiting with aspiration
Vomiting without aspiration
Agitation
Prolonged sedation
Nightmare
Local anesthetic toxicity
Other minor adverse events
Intervention
Simple manual airway maneuvers (e.g., jaw-thrust, head-tilt/chin-lift)
Endotracheal intubation
Use of extraglottic airway devices
Bag-valve-mask ventilation
Fluid bolus
Vasopressor administration
Reversal agent administration
Other minor interventions[a]

[a]Others including stimulate, oxygen administration and nasal airway insertion

was already hypotensive or hypoxic before the use of medication due to his/her medical condition, they were not recorded as an adverse event. Serious AEs included cardiac arrest and anoxic brain injury. Other AEs included transient apnea, hypoxia (defined as SpO_2 < 90%), vomiting and other. Because continuous capnography is not routinely used in EDs in Japan, we defined apnea as the temporary cessation of breathing that required any intervention such as jaw-thrust or bag-valve mask (BVM) ventilation. If apnea was adequately treated before causing hypoxia, only apnea (but not hypoxia) was recorded as an AE. We used a visual analog scale (VAS) that ranged from 0 (extreme dissatisfaction) to 100 (extreme satisfaction) to assess the patient and physician satisfaction.

Study setting

JPSTAR was initiated in May 2017. This registry is used in four hospitals across Japan. These hospitals include both academic and community hospitals. All of the hospitals are located in urban areas and all have an emergency medicine residency program. Three of these hospitals are equivalent to a level 1 trauma center in the US system and one hospital is equivalent to a level 2 trauma center. The average census of the EDs is 20,112 (range 13,000–30,000). All of the hospitals have anesthesiology departments. PSA in the ED is typically performed by emergency physicians (EPs), emergency residents, or non-emergency residents who rotate in the ED.

Selection of participants

We included all patients who received PSA in the ED. If the patient's care is still under the EP's service, we included patients who received PSA in adjacent clinical areas (e.g., MRI rooms, gastrointestinal endoscopy suites). We excluded patients who received sedation for airway management or excited delirium.

Data collection

Study data were collected and managed using the REDCap electronic data capture tools hosted at the University of New Mexico [11]. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources. Physicians who performed PSA primarily entered the data. In order to capture all PSA cases, an investigator for each hospital obtained a monthly list of patients who received sedatives or analgesics in the ED from the pharmacy department. If the data were not entered by the provider performing PSA, the site investigators interviewed providers who performed PSA and obtained clinical information from medical charts to complete the data entry form. The investigator of each hospital also reviewed a nursing record of each case for data quality assurance.

Measurement

The primary outcome measure was an overall AEs from PSA.

Table 2 Demographics of patients in the Japanese Procedural Sedation and Analgesia Registry ($n=332$)

	Patient demographics ($n=332$) *N* (%)
Age (years)	
Mean (SD)	59.4 (16.7)
Median	67.0
IQR	46–78
Male	191 (57.5)
Female	141 (42.5)
ASA class	
1	79 (23.8)
2	172 (51.8)
3	71 (21.4)
4	10 (3.0)
Medical comorbidities	
Heart failure	71 (21.4)
Dysrhythmia	139 (41.9)
Hypertension	140 (42.2)
COPD	3 (0.9)
DM	67 (20.2)
CVA	31 (9.3)
Schizophrenia	0 (0.0)
Others[a]	94 (28.3)
Any	248 (74.7)

COPD chronic obstructive pulmonary disease, *DM* diabetes mellitus, *CVA* cerebrovascular accident

[a]Dyslipidemia, hypothyroidism, epilepsy, coronary artery disease, chronic kidney disease, aortic aneurysm

Statistical analysis

We analyzed the data with simple descriptive statistics with 95% confidence intervals (95% CIs). We described continuous variables as means (SD) and medians (IQR). Categorical variables were presented as percentages. We used both SAS statistical software (SAS version 9.3, The SAS Institute, Cary, NC) and the R statistical language [12] for analysis and for graphing.

Results

Characteristics of study subjects

During the 12-month period from May 2017 to April 2018, we enrolled 332 patients. Table 2 summarizes patient demographics. Figure 2 shows the age distribution of patients in the registry. There were slightly more male patients ($n=191$, 57.5%) and the median age was 67 years (IQR, 46–78). Thirty-nine (11.7%) patients were pediatric (18 years or younger). There were 188 (56.6%) patients who were 65 years or older. In terms of ASA physical status, 79 (23.8%), 172(51.8%), 71 (21.4%), and 10 (3.0%) patients were class 1, 2, 3 and 4, respectively. No patients were classified as class 5. As reflected in ASA class, the majority of the patients had at least one medical comorbidity ($n=248$, 74.7%). Of these cases, the most common medical comorbidity was hypertension ($n=140$, 42.2%). The list of other medical comorbidities and their frequencies among patients in the registry are shown in Table 2.

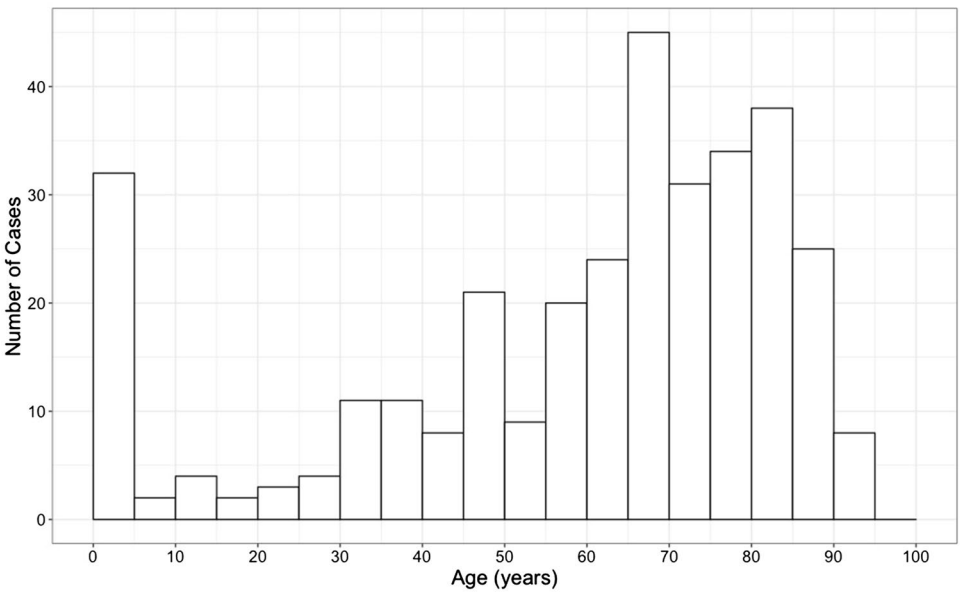

Fig. 2 Age distribution in 5-year increments for the study participants ($n=332$)

Indication and location

Table 3 shows primary indications for PSA and procedure success rates. The most common indication for PSA was cardioversion ($n=146$, 44.0%), which was followed by gastrointestinal endoscopy ($n=71$, 21.4%) and reduction of joint dislocations or fracture ($n=59$, 17.8%). In 325 (97.9%) cases, procedures were successfully completed. In seven cases, procedures (generally, reduction of large joint dislocations) were unsuccessful. Unsuccessful procedures were due to the technical difficulty of procedures, not to PSA-related issues. These procedures were later completed under general anesthesia in the operating theater or at another facility.

Monitoring

Pulse oximetry was used for all cases ($n=332$, 100%). ECG and non-invasive blood pressure monitors were used for the majority of cases ($n=310$, 93.4%, $n=309$, 93.1%, respectively). Continuous capnography was less frequently used than other monitors ($n=55$, 16.6%). The minority of patients received continuous arterial line monitoring ($n=6$, 1.8%). No patient received bispectral index (BIS) monitoring for PSA.

Pharmacology

Table 4 summarizes medications used for PSA and incidence of AEs who received medication. The most common sedative used was thiopental ($n=129$, 38.9%), followed by midazolam ($n=113$, 34.0%) and propofol ($n=65$, 19.6%). There were 33 (9.9%) patients who received ketamine. The initial and total doses of each sedative including ketamine are shown in Table 5.

There were 104 (31.3%) patients who received at least one analgesic including ketamine for PSA. The two most common analgesics used were pentazocine ($n=39$, 11.7%) and fentanyl ($n=34$, 10.2%). Intravenous formulation of acetaminophen was also used in a minority of cases ($n=11$, 3.3%). Sedatives used for each selected procedure including cardioversion, reduction of fractures or joint dislocations, and laceration repair are shown in Tables 6, 7 and 8, respectively. Midazolam was used for all patients ($n=71$, 100%) who underwent gastrointestinal endoscopy. Among those who had PSA for gastrointestinal endoscopy, 10 (14.1%) patients had one or more adverse events.

Among patients who were 18 years or younger ($n=39$), the most common sedative was midazolam ($n=19$, 48.7%), followed by ketamine ($n=17$, 43.6%). Propofol was used in 3 cases (7.7%). The most common indication in this group was laceration repair ($n=20$, 51.3%).

Among the 188 patients who were 65 years or older, the most common sedative was thiopental ($n=80$, 42.6%), followed by midazolam ($n=68$, 36.1%) and propofol ($n=36$, 19.1%). The two most common analgesics used in geriatric patients were pentazocine ($n=22$, 11.7%) and fentanyl ($n=13$, 6.9%). The most common indication in this group was cardioversion ($n=92$, 48.9%).

Adverse events

There were 72 (21.7%, 95% CI17–26) patients who experienced one or more AEs. Table 9 shows the complete list of AEs and interventions performed. The two most common AEs were hypoxia ($n=33$, 9.9%) and apnea ($n=24$, 7.2%). Among 310 patients who had non-invasive blood pressure monitors or continuous arterial monitoring, 11 (3.5%) patients experienced hypotension. There were seven (2.1%) patients who had vomiting. No patient experienced

Table 3 Indications for PSA and procedure success rates ($n=332$)

	Procedures		Adverse events		Procedure success	
	N	%	*N*	% (95% CI)	*N*	% (95% CI)
Total	332	–	72	21.7 (17–26)	325	97.9 (96–99)
Cardioversion	146	44.0	45	30.8 (24–39)	145	99.3 (96–100)
Fracture or dislocation reduction	59	17.8	9	15.3 (8–27)	54	91.5 (82–96)
Laceration repair	23	6.9	2	8.7 (2–27)	23	100.0 (86–100)
Abscess I&D	1	0.3	0	0.0 (0–79)	1	100.0 (21–100)
Tube thoracostomy	3	0.9	0	0.0 (0–56)	3	100.0 (44–100)
Gastrointestinal endoscopy	71	21.4	10	14.1 (8–24)	70	98.6 (92–100)
Lumbar puncture	7	2.1	2	28.6 (8–64)	7	100.0 (65–100)
CT	5	1.5	0	0.0 (0–43)	5	100.0 (36–92)
MRI	8	2.4	0	0.0 (0–32)	8	100.0 (68–100)
Miscellaneous[a]	8	2.4	4	50.0 (22–78)	8	100.0 (68–100)

I&D incision and drainage, *CT* computed tomography, *MRI* magnetic resonance imaging

[a]Includes burn care, contrast enema, ileus tube, non-invasive positive ventilation

Table 4 Medication use and incidence rate of adverse events for each medication ($n = 332$)

	Cases receiving sedatives		Cases with any adverse events		Cases with respiratory adverse events[c]		Cases with hypotension		Cases with vomiting	
	N	%[a]	*N*	% (95% CI)[b]	*N*	% (95% CI)	*N*	% (95% CI)[b]	*N*	% (95% CI)[b]
Sedative										
Ketamine	33	9.9	5	15.2 (7–31)	1	3.0 (1–15)	0	0.0 (0–10)	2	6.1 (2–20)
Midazolam	113	34.0	17	15.0 (10–23)	9	8.0 (4–14)	6	5.3 (2–11)	3	2.7 (1–8)
Propofol	65	19.6	27	41.5 (30–54)	23	35.4 (25–48)	3	4.6 (2–13)	3	4.6 (2–13)
Thiopental	129	38.9	28	21.7 (15–30)	22	17.1 (12–24)	3	2.3 (1–7)	1	0.8 (1–7)
Dexmedetomidine	2	0.6	1	50.0 (9–91)	0	0.0 (0–66)	0	0.0 (0–66)	1	50.0 (9–91)
Other sedatives[d]	6	1.8	0	0.0 (0–39)	0	0.0 (0–39)	0	0.0 (0–39)	0	0.0 (0–39)
Analgesics										
Fentanyl	34	10.2	7	20.6 (10–37)	7	20.6 (10–37)	1	2.9 (1–15)	1	2.9 (1–15)
Morphine	1	0.3	0	0.0 (0–79)	0	0.0 (0–79)	0	0.0 (0–79)	0	0.0 (0–79)
Pentazocine	39	11.7	6	15.4 (7–30)	4	10.3 (4–24)	1	2.6 (0–13)	0	0.0 (0–9)
Acetaminophen (intravenous)	11	3.3	2	18.2 (5–48)	1	9.1 (2–38)	0	0.0 (0–26)	0	0.0 (0–26)
Any analgesic including ketamine	104	31.3	17	16.3 (10–25)	11	10.6 (6–18)	2	1.9 (1–7)	3	2.9 (1–8)

[a]Percentage of patients who received medication. Some cases received more than one medication, so the sum of percentages is greater than 100%

[b]Percentage of patients receiving medication who experienced an adverse event

[c]Respiratory adverse events including apnea, hypoxia, glossoptosis and laryngospasm

[d]Others including diazepam, hydroxyzine, and haloperidol

Table 5 Initial and total doses of each sedative agent

Sedatives[b]	Initial dose (mg/kg)[a]		Total dose (mg/kg)[a]	
	Median	IQR	Median	IQR
Ketamine ($n = 33$)	0.77	0.63–0.97	1.04	0.77–1.33
Midazolam ($n = 110$)	0.04	0.03–0.05	0.06	0.04–0.10
Propofol ($n = 62$)	0.50	0.37–0.73	0.77	0.49–1.05
Thiopental ($n = 126$)	1.89	1.50–2.39	2.11	1.73–2.96

Doses of sedatives used for procedural sedation and analgesia ($n = 332$)

[a]Body weight data are missing in ten patients, thus excluded from this analysis

[b]Some cases received more than one medication

Table 6 Sedatives used for cardioversion and incidence of adverse events for each agent ($n = 146$)

Sedatives	Cases receiving sedatives		Cases with adverse events	
	N	%[a]	*N*	% (95% CI)[b]
Ketamine	1	0.7	0	0.0 (0–79)
Midazolam	4	2.7	2	50.0 (15–85)
Propofol	23	15.8	16	69.6 (49–84)
Thiopental	120	82.2	27	22.5 (16–31)
Dexmedetomidine	0	0.0	–	–
Other sedatives	0	0.0	–	–

[a]Percentage of patients who received medication. Some cases received more than one medication, so the sum of percentages is greater than 100%

[b]Percentage of patients receiving medication who experienced an adverse event

aspiration. Respiratory AEs are more common than any other AE for all sedatives except ketamine (Table 4). All of the AEs were transient and no patient had a serious AE. Figure 3 describes the incidence of AEs for each age group. Increasing age was associated with higher rate of AEs. Figures 4, 5 and 6 show the types of AE in each age group. Throughout all age groups, respiratory AE was the most common type of AE.

Adverse events due to medication co-administration

Among patients who received propofol ($N = 65$), 21 (32.3%) also received fentanyl. We observed similar rates of AEs in the propofol only (22/44, 50.0%) and propofol + fentanyl groups (5/21, 23.8%) ($p = 0.0823$). Among patients who received midazolam ($N = 113$), 11 (9.7%) also received fentanyl. Rates of AEs were similar in the midazolam only (14/102, 13.7%) and the midazolam + fentanyl groups (3/11, 27.3%) ($p = 0.4531$).

Table 7 Sedatives used for fracture or dislocation reduction and incidence of adverse events for each agent ($n=59$)

Sedatives	Cases receiving sedatives		Cases with adverse events	
	N	%[a]	*N*	% (95% CI)[b]
Ketamine	14	23.7%	1	7.1 (1–31)
Midazolam	7	11.9%	1	14.3 (3–51)
Propofol	35	59.3%	7	20.0 (10–36)
Thiopental	6	10.2%	1	16.7 (3–56)
Dexmedetomidine	0	0.0%	–	–
Other sedatives[c]	1	1.7%	0	0.0 (0–79)

Fracture or dislocation reduction ($N=59$)

[a]Percentage of patients who received medication. Some cases received more than one medication, so the sum of percentages is greater than 100%

[b]Percentage of patients receiving medication who experienced an adverse event

[c]Others including diazepam, hydroxyzine, and haloperidol

Table 8 Sedatives used for laceration repair and incidence of adverse events for each agent ($n=23$)

Sedatives	Cases receiving sedatives		Cases with adverse events	
	N	%[a]	*N*	% (95% CI)[b]
Ketamine	13	56.5	2	15.4 (4–42)
Midazolam	7	11.9	1	14.3 (3–51)
Propofol	2	3.4	0	0.0 (0–66)
Thiopental	1	1.7	0	0.0 (0–79)
Dexmedetomidine	0	0.0	–	–
Other sedatives[c]	3	5.1	0	0.0 (0–56)

Laceration repair ($N=23$)

[a]Percentage of patients who received medication. Some cases received more than one medication, so the sum of percentages is greater than 100%

[b]Percentage of patients receiving medication who experienced an adverse event

[c]Others including diazepam, hydroxyzine, and haloperidol

Disposition

After completion of PSA, 201 (60.5%) patients were discharged home and 131 (39.5%) patients were admitted to the hospital for acute medical conditions. No patients had an unplanned admission due to complications from PSA.

Patient and physician satisfaction

Patient and physician satisfaction surveys were completed after PSA in 91 (27.4%) cases and 104 (31.3%) cases, respectively. Among those cases, both patient and physician satisfaction scores were high. The mean and median patient satisfaction scores were 84.4 and 90.0 (IQR 80–100), respectively. The mean and median physician satisfaction scores were 86.4 and 90.0 (80–100).

Discussion

In a multicenter prospective registry in Japan, we found that PSA is safely performed in EDs for a variety of indications in patients with wide age range of 1–94 years. A variety of sedatives and analgesics were used for PSA. We also observed relatively uniform use of standard monitoring devices and limited use of the continuous capnography monitor. To the best of our knowledge, our study is the first multicenter registry study of PSA in EDs in Asia.

Previous registry-based studies in the US and other countries demonstrated that PSA can be safely performed in the ED [2, 4, 13]. In those studies, the incidence rate of AEs ranged from 4.1 to 11.3% which is lower than the AE rate in our study. In our study, patients were significantly older (median age: 67) and more patients had an ASA class of 3 or 4 (21.4%, and 3.0%, respectively) compared to studies conducted in different countries. For example, the registry-based study conducted by Sacchetti et al. [2] in the community EDs in US had patients with a median age of 31 and only 4.1% of patients were classified as ASA class 3 or higher. Previous studies have shown that elderly patients tend to have more AE compared to young adults [4, 14]. Consistent with these studies, we also found that increasing age was associated with higher rate of AEs. Among all AEs, respiratory AEs were the most common AE in elderly patients. Although a previous study has shown that PSA is safely performed in geriatric patients in the ED [15], Japanese healthcare providers should realize that PSA is often performed on high-risk patients in the ED and the necessity of training on PSA, particularly focusing on skills and knowledge of preventing and resuscitating respiratory AEs, such as pre-PSA evaluation and bag-valve-mask ventilation, should be emphasized.

The higher incidence of AEs might also be related to PSA indications in our registry. The studies of PSA in EDs in the US, UK, and the Netherlands showed that only 0.8%, 9%, and 1.1% of patients received PSA for cardioversion, respectively, compared to 44.0% in our study [2, 4, 13]. We found that patients who received PSA for cardioversion had a particularly high AE incidence rate. Consistent with our finding, Krauss et al. [3] reported that 40% of patients who had PSA for cardioversion received some clinical intervention for apnea. The optimal PSA strategy to prevent AE during cardioversion is still controversial, particularly in geriatric patients, and it should be investigated in future studies.

We found that medications used for PSA significantly varied in Japanese EDs and physicians occasionally choose

Table 9 Adverse events and interventions in patients who received PSA ($n=332$)

	Adverse events and interventions in patients who received PSA ($n=332$)[a] *N* (%)
Serious adverse events	
Cardiac arrest	0 (0.0)
Anoxic brain injury	0 (0.0)
Non-serious adverse events	
Apnea	24 (7.2)
Glossoptosis (posterior displacement of the tongue)	9 (2.7)
Hypoxia ($SpO_2 < 90\%$)	33 (9.9)
Laryngospasm	0 (0.0)
Hypersalivation requiring intervention	1 (0.3)
Hypertension (systolic blood pressure > 180 mmHg)[c]	4 (1.3)
Hypotension (systolic blood Pressure < 90 mmHg)[c]	11 (3.5)
Tachycardia (heart rate > 120 bpm)	1 (0.3)
Bradycardia (heart rate < 60 bpm)	2 (0.6)
Other dysrhythmias	1 (0.3)
Vomiting with aspiration	7 (2.1)
Vomiting without aspiration	0 (0.0)
Agitation	1 (0.3)
Prolonged sedation	0 (0.0)
Nightmare	1 (0.3)
Local anesthetic toxicity	0 (0.0)
Other minor adverse events	2 (0.6)
Cases with any adverse events	72 (21.7)
Intervention	
Simple manual airway maneuvers (e.g., jaw-thrust, head-tilt/chin-lift)	16 (4.8)
Endotracheal intubation	0 (0.0)
Use of extraglottic airway devices	0 (0.0)
Bag-valve-mask ventilation	37 (11.1)
Fluid bolus	6 (1.8)
Vasopressor administration	1 (0.3)
Reversal agent administration	0 (0.0)
Other minor interventions[b]	25 (7.5)
Cases with any interventions	72 (21.7)

[a]Some cases had more than one adverse event or required more than one intervention

[b]Others including stimulation, oxygen administration and nasal airway insertion

[c]310 Patients had non-invasive blood pressure monitors and/or continuous arterial line monitoring, thus 310 is the total number of cases included in the analysis of these variables (denominator)

to administer medications that are not commonly used for PSA in North America. For example, thiopental was commonly used in our study. Although thiopental has been used in many countries for PSA and is considered as an appropriate sedative choice for PSA [16, 17], it often causes apnea and hypotension similar to other barbiturates and propofol [18]. Some of the medications used for PSA in other countries including etomidate are not approved in Japan. This might be a reason why thiopental is commonly used for PSA in Japanese EDs.

In contrast to other studies in the US and Australia, only a small portion of patients received opioid analgesics in our study [2, 14]. Opioids, including fentanyl and morphine, are strictly regulated in Japan and many Japanese EDs do not stock these in the department, apart from pentazocine. This is likely the cause of infrequent use of fentanyl as an analgesic for PSA. The differences in indications for PSA between our study and other studies might also explain why opioid analgesics were not commonly used. Controversy exists regarding the potential benefits and risks of adding

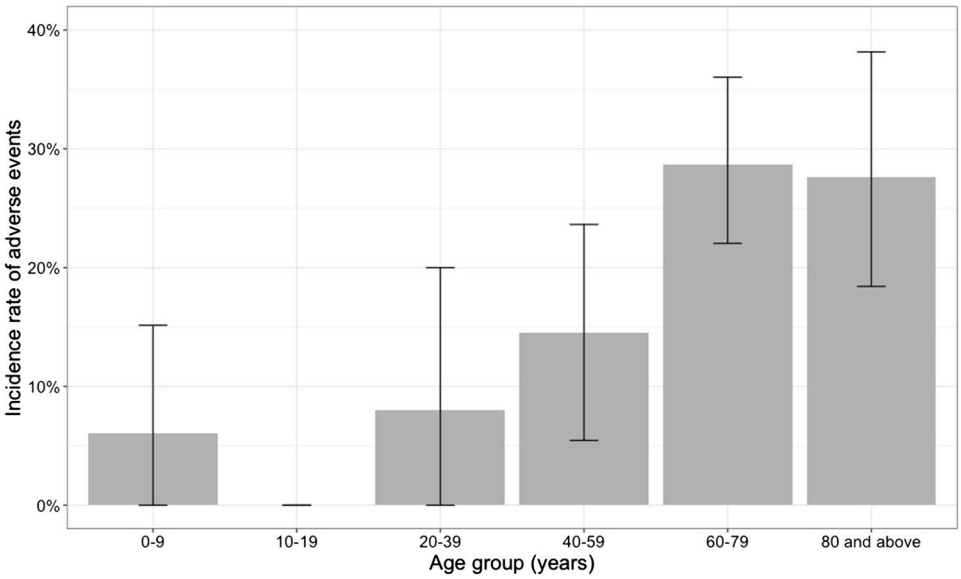

Fig. 3 Incidence of any adverse events in each age group ($n = 332$). Error bars represent 95% CI

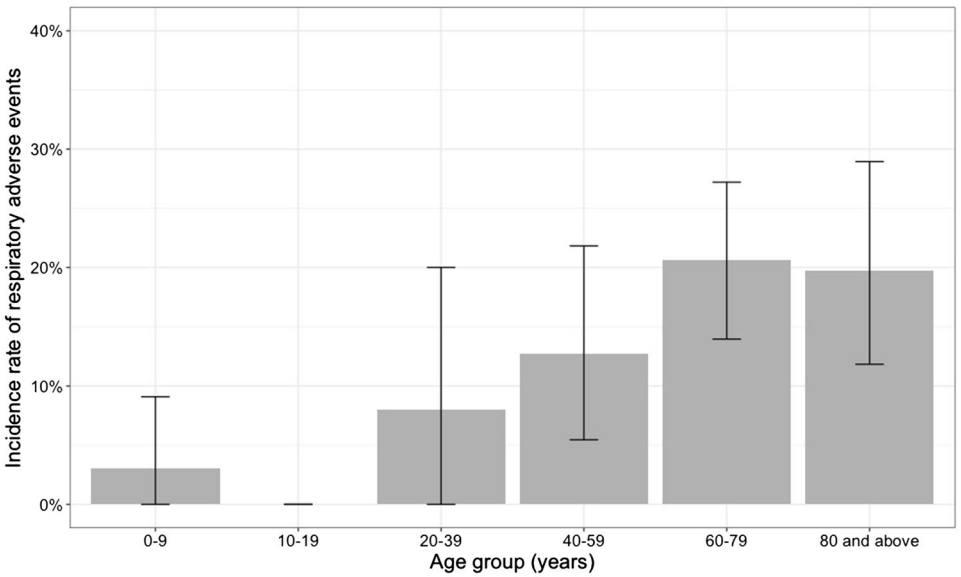

Fig. 4 Incidence of respiratory adverse events in each age group ($n = 332$). Respiratory adverse events include apnea, hypoxia, glossoptosis and laryngospasm. Error bars represent 95% CI

opioid analgesics to sedatives [19]. Previous studies have shown that supplemental opioid use increases the risk of respiratory depression [20, 21]. Although our small size precludes a meaningful statistical analysis of effects of adding opioid analgesics, future studies including a larger sample should be conducted to investigate the effect, particularly in geriatric population.

It was not our intent to compare the incidence of AE of specific sedative or analgesic agents with other agents in this preliminary analysis because a variety of medications were used in a heterogeneous population for different indications. However, we observed a particularly higher incidence of AE with propofol compared to other agents in our study. Sacchetti et al. [2] reported that the incidence of AE was only 0.8% in the propofol group compared to 9.5% in the fentanyl group and 6.4% with the midazolam group. As discussed above, the study was conducted in the community EDs in US and the patients in the study were significantly younger than ours. A more recent study conducted in 2011 in Australia which included more geriatric patients showed that the incidence rate of an airway event was significantly higher with propofol when compared to other agents [14]. Midazolam, fentanyl and propofol are all known to cause AEs, particularly airway or respiratory issues [21], however, little is known regarding the relative safety of agents for PSA in geriatric patients. The small sample size precludes the use of multivariable methods to adjust for potential

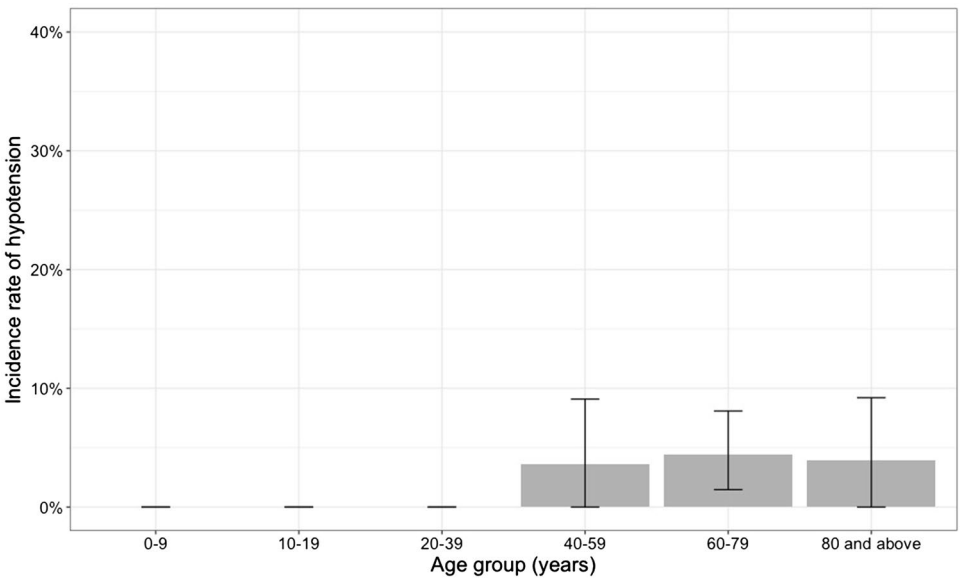

Fig. 5 Incidence of hypotension in each age group ($n=310$). Among the total 332 patients, 22 patients had neither non-invasive blood pressure monitors nor continuous arterial monitoring, thus only 310 cases were included in this analysis. Error bars represent 95% CI

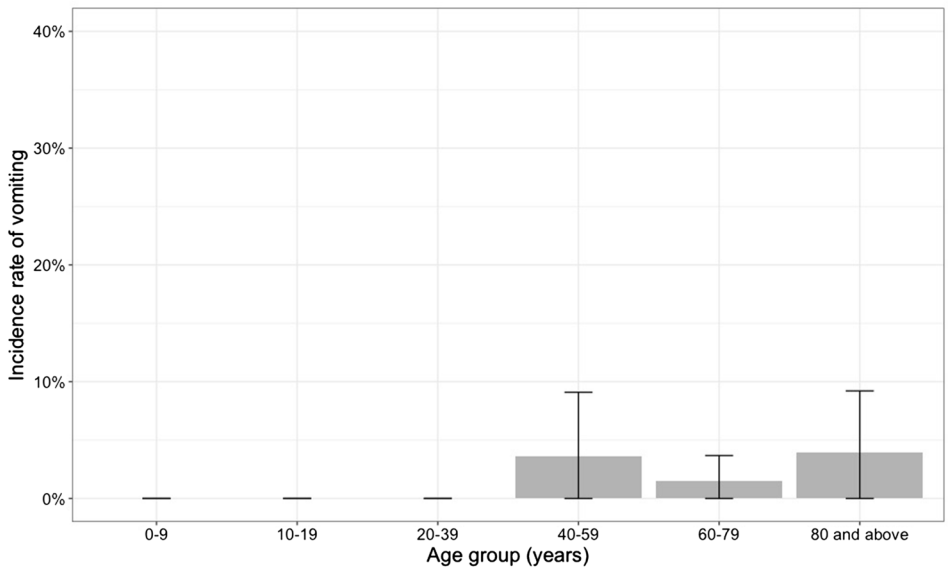

Fig. 6 Incidence of vomiting in each age group ($n=332$). Error bars represent 95% CI

confounders in our study. Future studies with a larger sample size should focus on identifying sedative agents with fewer AE in geriatric patients.

Our previous survey study showed that continuous capnography monitoring is not routinely performed for PSA in Japan and it is consistent with the results of this study [22]. The benefit of routine capnography use for PSA in low-risk patients is still being debated. However, given the fact that patients with higher ASA class receive PSA in Japanese EDs and respiratory adverse events are common, more frequent use of capnography might need to be considered.

Limitations

We should acknowledge several limitations of our study. Similar to other registry studies, we rely on physicians' reports and the results might suffer from reporting bias. However, the site investigator for each hospital compared entries to a list of patients who received sedatives for data compliance purposes and also reviewed a nursing record of each patient in order to minimize the risk of under-reporting.

There is also a risk of under-reporting AEs, particularly transient apnea. Because continuous capnography was not often used, transient apnea might not be noticed in some

cases; however, any case of apnea requiring clinical intervention was recorded in the registry. Further, a transient apneic episode which does not require intervention is usually not clinically relevant.

Since all of the participating hospitals are located in Japan, the results might differ in other countries. PSA in the ED has not been standardized in Japan. Guidelines regarding PSA practice in the ED do exist in some countries including the US, Canada, Australia and New Zealand [1, 23, 24]. In Japan, some medical societies including the Japan Gastrointestinal Endoscopy Society and Japanese Society of Anesthesiologists have developed guidelines on PSA, but not for the ED [25]. However, many countries including the majority of those in Asia are still at the same stage and our results might be applicable in those places.

Conclusion

In a multicenter prospective registry in Japan, we observed that PSA is safely performed in EDs for a variety of indications despite the fact that physicians face challenges, including performing PSA on high-risk patients.

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Compliance with ethical standards

Conflict of interest All authors deny any conflict of interest.

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