ANESTHESIOLOGY

Adverse Events Associated with Airway Management in Pediatric Anesthesia: A Prospective, Multicenter, Observational Japan Pediatric Difficult Airway in Anesthesia (J-PEDIA) Study

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ABSTRACT

Background: The incidence of adverse events and desaturation during airway-securing procedures (a sequence from preoxygenation to completion of tracheal intubation or supraglottic airway placement) under general anesthesia in children remains underexplored. Thus, this study investigated the incidence of adverse and desaturation events and associated risk factors.

Methods: This was a prospective, multicenter, observational study conducted between June 2022 and January 2024 in 10 tertiary care (6 pediatric and 4 university [mixed adult–pediatric]) hospitals in Japan. A standardized data collection system was applied through the recruited institutions to collect 95% or more of cases. The primary and secondary outcomes were adverse events and a 10% or greater drop in oxygen saturation (desaturation) associated with airway-securing procedures.

Results: There were 17,007 airway management procedures in 16,695 children (mean ± SD age, 6.3 ± 4.8 yr). Any adverse events occurred in 346 of 17,007 (2.0%; 95% CI, 1.8 to 2.3) children, including 189 of 17,007 (1.1%; 0.96 to 1.3) respiratory adverse events. Desaturation occurred during 395 of 17,007 (2.3%; 2.1 to 2.6) procedures, with 66 of 308 (21.4%; 17.0 to 26.4) in neonates and 210 of 2,298 (9.1%; 8.0 to 10.4) in infants. Multilevel regression analysis showed younger age (adjusted odds ratio, 0.92; 95% CI, 0.90 to 0.95; $P < 0.001$), airway management in radiation diagnostic/therapy rooms (5.7, 1.64 to 19.9; $P = 0.006$), airway sensitivity (1.46, 1.09 to 1.94; $P = 0.010$), craniocervical surgery (1.41, 1.09 to 1.83; $P = 0.009$), and presence of one anatomical difficult airway feature (1.74, 1.02 to 2.95; $P = 0.042$) *versus* two or more anatomic difficult airway features (2.82, 1.21 to 6.6; $P = 0.017$) as risk factors of any adverse events. Supraglottic airway device usage at the first attempt (0.42, 0.288 to 0.62; $P < 0.001$) and muscle relaxant administration (0.62, 0.43 to 0.89; $P = 0.009$) showed beneficial effects.

Conclusions: The Japan Pediatric Difficult Airway in Anesthesia (J-PEDIA) study demonstrated adverse event and desaturation incidences and the impact of clinically relevant risk factors during airway-securing procedures in Asian children. This study can help anesthesiologists to identify high-risk children and create a safe airway-securing strategy.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Failure to secure the airway is a common cause of critical adverse events in children
- Recognizing risk factors for adverse events when securing the airway may promote safe anesthesia in children

What This Article Tells Us That Is New

- In a Japanese prospective, multicenter, observational study involving 17,007 airway management procedures in children, the adverse airway event rate was 1.1%
- Adverse events were more likely in younger children, procedures in radiation diagnostic/therapeutic rooms, children with airway sensitivity, craniocervical surgery, and children with anatomic features of a difficult airway
- Adverse events were less likely when a supraglottic device or muscle relaxation was used

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Abbreviations: **aOR**, adjusted odds ratio; **APRICOT**, Anesthesia Practice In Children Observational Trial; **CT**, computed tomography; **J-PEDIA**, Japan Pediatric Difficult Airway in Anesthesia; **MRI**, magnetic resonance imaging; **PeDI**, Pediatric Difficult Intubation; **SGD**, supraglottic airway device; **Spo_2**, oxygen saturation measured by pulse oximetry; **STROBE**, Strengthening the Reporting of Observational Studies in Epidemiology

Perioperative life-threatening adverse events occur more frequently in children than in adults based on their unique anatomic and physiologic characteristics.[1] Failure to secure the airway is still a common cause of critical adverse events in children due to intolerance to apnea.[1–4] Therefore, recognition of the risk factors of adverse events while securing the airway is essential to promote safe anesthesia in children.

Previous pediatric studies based on real-world data have reported the incidence and risk factors of adverse events during the perianesthesia period. The Anesthesia Practice In Children Observational Trial (APRICOT) study in Europe showed the epidemiologic data of adverse events throughout the perianesthesia period in children.[5] However, the APRICOT study was not designed for collecting data specifically related to airway management (*e.g.*, discipline of providers, devices for securing the airway, medications during airway management). The Pediatric Difficult Intubation (PeDI) registry study in the United States reported the incidence of adverse events during airway management under general anesthesia in children.[2] However, the PeDI study cohort was composed of children with difficult airways that do not represent the entire pediatric population.[6] In addition, this limited study population may restrict the estimation of risks for adverse events attributed to airway management.

Previous studies reported the different craniofacial and oropharyngeal anatomical features and anesthetic sensitivity between Asian and Caucasian persons.[7–10] The occurrence of adverse events and the risks during airway management in Asian persons can be different from those in previous studies in Europe and the United States. However, there is a lack of pediatric multicenter, real-world studies based on prospectively collected data in the Asian regions regarding the adverse events and risk factors associated with airway management during general anesthesia.

This study aimed to describe the current airway management practice in children and the incidence of adverse events associated with airway management during general anesthesia. This study also explored potential risk factors of clinical relevance for adverse events and desaturation during a sequence of airway-securing procedures in children under general anesthesia.

Materials and Methods

Study Design and Participants

This is a prospective, multicenter, observational study conducted between June 2022 and January 2024 in 10 tertiary care hospitals (6 pediatric and 4 university [mixed adult–pediatric] hospitals) in Japan. The local institutional review board, Aichi Children's Health and Medical Center's review board, approved the study protocol (approval No. 2021051, September 29, 2021). All participating institutions obtained ethical approval from their local institutional ethical committees. An opt-out procedure was applied to obtain consent for using anonymized data in this study. This study was registered in the University Hospital Medical Information Network (registration No. UMIN00047351; April 1, 2022; principal investigator: Taiki Kojima). We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[11] The study protocol, including the research term definitions and the data analysis plan, had been published as a study protocol article before initiating the data collection.[12]

This study recruited children aged less than 18 yr who received advanced airway management at least once under general anesthesia or sedation, with or without regional anesthesia, for scheduled or emergency surgeries and tests in operating suites, catheterization laboratory rooms, radiological imaging and procedure rooms, or general wards conducted by anesthesiologists or supervised anesthesia providers. An airway-securing procedure was defined as a sequence from preoxygenation to completion of tracheal intubation or supraglottic airway device (SGD) placement.

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Advanced airway management was defined as placing a tracheal tube or SGD or securing a surgical airway by applying techniques that include direct or video laryngoscopy, fiberoptic intubation, ridged bronchoscopy, cricothyroidotomy, tracheostomy, or a combination of these. Children were excluded if airway management was performed outside operating suites where anesthesiologists were consulted, in emergency rooms or intensive care units, if they were previously enrolled in this study, or if they or their families opted out of participation.

Data Collection

We prospectively collected data on patient comorbidities, surgery types, anesthesia provider training levels, devices (*e.g.*, video laryngoscope, flexible bronchoscope), equipment (*e.g.*, tracheal tube, SGD), medications used during airway management, number of attempts to place airway securing equipment, occurrence and types of adverse events, treatments for adverse events, and oxygen saturation measured by pulse oximetry (Spo_2) at the start and lowest Spo_2 during airway management.[12] Data regarding airway management practices included reasons for initiating airway management, administered medications, airway securing routes, types and sizes of tracheal tube/SGD, presence of cricoid pressure/external laryngeal manipulation, and glottic opening scores.[12]

Definitions

For data collection, we defined "encounter" and "attempt" regarding airway management. "Encounter" referred to one sequence of airway management procedures, including preoxygenation, jaw thrust, face mask attachment, and positive pressure ventilation, until the assigned anesthesia providers ensured the child's respiratory and hemodynamic stability upon airway-securing device placement. "Attempt" was defined as one trial to place a tracheal tube or SGD, starting with the insertion of airway-securing devices (*e.g.*, laryngoscope, bronchoscope) until its removal from the child's airway (*i.e.*, mouth, nose, and tracheal stoma). Therefore, one encounter can include multiple airway-securing attempts. Other definitions of research terms are provided in Supplemental Digital Content 1 (https://links.lww.com/ALN/E119).[13,14] The encounters and attempts were recorded when anesthesia providers initiated airway-securing procedures at any point during the peri-anesthesia period, including data regarding anesthesia induction, intraoperative period, anesthesia emergence, and recovery period at postanesthesia care units.

Outcomes

The primary outcome was the occurrence of adverse events associated with airway management during general anesthesia. Adverse events were reported if they occurred during the encounters (from preoxygenation/mask ventilation to the completion of airway-securing device placement with stable respiratory and hemodynamic conditions of the patient). "Any adverse events" included at least one hemodynamic and airway-related complication, such as cardiac arrest, upper airway obstruction, laryngospasm, severe cough lasting 10 s or longer, bronchial intubation, esophageal intubation, vomiting with aspiration, hypotension, hypertension, tooth injury, pneumothorax, mediastinal emphysema, bronchospasm (asthma exacerbation), atelectasis, pulmonary edema, stridor, airway trauma, arrhythmia, and airway securing device dislodgement.[12] Respiratory adverse events included upper airway obstruction, laryngospasm, severe cough lasting 10 s or longer, esophageal intubation with desaturation, vomiting with aspiration, pneumothorax, mediastinal emphysema, bronchospasm (asthma exacerbation), atelectasis, pulmonary edema, stridor, and airway trauma. These adverse events and their severity were defined based on NEAR4KIDS, a national registry for quality improvement during emergency tracheal intubation in pediatric intensive care units primarily located in North America.[13]

The secondary outcome was desaturation, defined as a Spo_2 drop of 10% or more between the initiation of airway management and the lowest value during the procedure. There is no consensus regarding the validated Spo_2 cutoff for clinical research. We defined the secondary outcome through discussions among board-certified pediatric anesthesiologists in specialized centers, using the PeDI study criteria.[15] We focused on Spo_2 drop rather than the single lowest values, as our data included patients with congenital cardiac diseases with reduced baseline SpO_2.

Quality Control of Data Collection

We recruited site-specific research leaders to ensure data collection quality. They conducted standardized data verification processes to minimize reporting bias and missing data. Before initiating local data collection, these readers educated anesthesia providers on research term definitions based on a research-operational manual. They reviewed paper-based forms daily for missing cases and information. For missing data, they collected the necessary information from case-assigned anesthesia providers and reviewed medical records. Our goal was to achieve a capture rate of 95% or higher across all institutions before initiating data collection. This data-verification process was standardized among all sites.

Site-specific research leaders used Slack (Slack Technologies, USA) to communicate uncertainties regarding data collection (*e.g.*, research-term definitions). The collected paper form–based data was anonymized and registered in the Research Electronic Data Capture (REDCap, Japan) system hosted at the National Center for Child Health and Development. REDCap is a secure, web-based platform designed to support data capture for research studies.[16]

Sample Size Estimation

A previous pediatric study reported an adverse event rate of 5.2% during the perianesthesia period, including 1.9% involving cardiovascular instability.[5] Based on this, we applied 2.0% as the assumed adverse event incidence rate for sample size estimation, resulting in approximately 16,000 participants, assuming a 99% probability of obtaining a 95% Wilson CI with a ±0.3% half-width for critical adverse events.

Statistical Analyses

Continuous variables are presented as means and SDs or medians and interquartile ranges, depending on data distribution normality. Categorical variables are described as numbers and percentages. Univariate analysis used chi-square or Fisher's exact tests for categorical variables and Student's *t* test and Mann–Whitney U test for numerical variables. A composite dichotomous variable identified groups with and without at least one difficult airway feature, including preoperative recognition of a possible difficult airway, difficult airway history, limited cervical range of motion, short hyomental distance, upper airway obstruction, midface hypoplasia, macroglossia, micrognathia, and macrocephaly.

Univariate and multilevel logistic regression with mixed effects analyses analyzed the association between outcomes (*i.e.*, adverse events and desaturation) and patient, surgery, provider, and clinical practice characteristics. Random effects were adjusted for clustering by individuals with repetitive measurement as level 2. In addition, to adjust for variances in local airway management practices at each institution that could not be captured in detail, the institution was incorporated into the regression models as a level 3 random effect.[17] We excluded subsequent anesthesia cases from the same patients to ensure the independence of samples but adjusted for cases in which multiple airway encounters occurred during the same surgery by incorporating the patient's research identification number as a random effect. The odds ratios obtained from the multilevel logistic analysis are conditional estimates for the random effects.

The variables (assumed potential risk factors) incorporated into the multivariable regression models were selected through discussion among board-certified pediatric anesthesiologists based on their clinical experience and previous research findings.[5] To develop multivariable regression models, composite dichotomous variables were created by classifying the potential risks based on clinical relevance. These composite variables were: (1) respiratory comorbidity (*e.g.*, respiratory support, hypoxemia, apneic events, upper airway obstruction, laryngeal abnormalities); (2) airway sensitivity including active or within 14 days upper respiratory infection symptoms, asthma, living with an active smoker; (3) environmental sensitivity (*e.g.*, food or medication allergies, allergic rhinitis, atopic dermatitis); (4) cardiovascular conditions (*e.g.*, shock, cardiac arrest, congenital cardiac diseases, pulmonary hypertension); (5) physical conditions (*e.g.*, American Society of Anesthesiologists [Schaumburg, Illinois] Physical Status of III or better, decreased muscle strength, preterm birth, low birth weight); and (6) gastrointestinal conditions, (*e.g.*, noncompliance to *nil per os*, full-stomach pathophysiology, nausea, or vomiting). Anatomical features of difficult airway were categorized as none, presence of one feature, and presence of two or more features, including limited cervical range of motion, limited mouth opening, short hyomental distance, upper airway obstruction, midface hypoplasia, macroglossia, micrognathia, and macrocephaly. The regression analysis revealed independent associations between the outcomes and the odds of each patient, anesthesia, and airway-management factor after adjusting for potential confounders.

We used the REDCap registration system, which prevents the data registration process from proceeding when missing data are present for most variables. Further, site-specific research leaders reviewed collected data daily to identify any missing data. According to these structural prevention strategies, we performed a complete case analysis, assuming minimal missing data. The data were analyzed using Stata V.18.0 (StataCorp, USA), with a two-sided P value of < 0.05 as the criterion for rejecting the null hypothesis.

Data Sharing Statement

The anonymized data that support the findings of this study can be provided by the principal investigator upon reasonable request.

Results

The final Japan Pediatric Difficult Airway in Anesthesia (J-PEDIA) study data set included 16,695 children, 17,007 encounters, and 19,733 airway-securing attempts across 10 tertiary-care hospitals between June 2022 and January 2024.

Patient Characteristics

Table 1 presents the characteristics of enrolled children. The mean ± SD age was 6.3 ± 4.8 yr: 308 of 17,007 (1.8%) were neonates, 1,990 of 17,007 (11.7%) were infants, 6,860 of 17,007 (40.3%) were preschool children, 5,791 of 17,007 (34.1%) were school children, and 2,058 of 17,007 (12.1%) were adolescents. Regarding preoperative comorbidity, 771 of 17,007 (4.5%) children needed preoperative respiratory support, and 507 of 17,007 (3.0%) experienced hypoxemia. Regarding premature birth week, preterm birth (28 to less than 37 weeks) was reported in 1,118 of 17,007 (6.6%) and very preterm birth in 197 of 17,007 (1.2%). In total, premature birth weight was reported in 2,212 of 17,007 (13.0%) children: low birth weight (1,500 to 2,500 g) in 1,655 of 17,007 (9.8%), very low birth weight (1,000 to 1,500 g) in

Table 1. Characteristics of Patients and Surgery (n = 17,007)

Characteristics	Data
Age, yr, mean ± SD	6.3 ± 4.8
Neonates (< 1 month), No. (%)	308 (1.8)
Infants (1 to 11 months), No. (%)	1,990 (11.7)
Preschool children (1 to 5 yr), No. (%)	6,860 (40.3)
School children (6 to 12 yr), No. (%)	5,791 (34.1)
Adolescents (13 to 17 yr), No. (%)	2,058 (12.1)
Female, No. (%)	7,045 (41.4)
Body weight, kg, median (IQR)*	17.5 (10.6, 29.3)
Body mass index, kg · m^{-2}, median (IQR)†	16.2 (15.0, 17.9)
Preoperative comorbidity, No. (%)	
Preoperative respiratory support	771 (4.5)
Oral intubation	33 (0.19)
Nasal intubation	7 (0.041)
Tracheostomy	224 (1.3)
Oral or nasal airway	13 (0.076)
Oxygen administration	291 (1.7)
High-flow nasal cannula	167 (0.98)
Mechanical ventilation	107 (0.63)
ECMO or VAD‡	5 (0.029)
Hypoxemia§	507 (3.0)
Apneic events	101 (0.59)
Upper airway stenosis or obstruction	381 (2.2)
Active URI symptoms	422 (2.5)
URI symptoms within 14 days	486 (2.9)
Asthma exacerbation‖	195 (1.2)
Laryngomalacia	117 (0.69)
Tracheomalacia	135 (0.79)
Vocal cord paralysis	41 (0.24)
Subglottic or tracheal stenosis	131 (0.77)
Nausea and vomiting	132 (0.78)
Unstable hemodynamics	51 (0.30)
History of congenital cardiac diseases	2,355 (13.9)
Pulmonary hypertension	193 (1.1)
Decreased muscle strength	200 (1.2)
Decreased airway reflexes	18 (0.11)
Low birth weight (1,500 to 2,500 g)	1,655 (9.8)
Very low birth weight (1,000 to 1,500 g)	267 (1.6)
Extremely low birth weight (< 1,000 g)	290 (1.7)
Preterm birth (28 to < 37 weeks)	1,118 (6.6)
Very preterm birth (< 28 weeks)	197 (1.2)
Post-term birth (≥ 42 weeks)	10 (0.059)
Allergy for food or medications	807 (4.8)
Symptomatic allergic rhinitis	463 (2.7)
Atopic dermatitis	407 (2.4)
Living with active smokers	2,048 (12.0)
Chromosomal abnormality#	
Trisomy 21	327 (1.9)
Trisomy 13	16 (0.094)
Trisomy 18	20 (0.12)
Others	314 (1.9)
Syndrome assuming difficult airway	270 (1.6)

The data are described as numbers (%), means (SDs), or medians (IQRs).

*Body weight included one missing value. †Body mass index included 19 missing values. ‡All children on ECMO or VAD underwent scheduled tracheal intubation during anesthesia induction in the operating rooms. One child was on high-flow nasal cannula preoperatively. §Hypoxemia was defined as a peripheral arterial oxygen saturation of less than or equal to 94% on room air. ‖Presence of asthma attack was defined either as an asthma attack occurring at least once within 1 month or three times or more within 1 yr. #Chromosomal abnormalities included 10 missing values.

ECMO, extracorporeal membrane oxygenation; IQR, interquartile range; MRI, magnetic resonance imaging; URI, upper respiratory infection; VAD, ventricular assist device.

267 of 17,007 (1.6%), and extremely low birth weight (less than 1,000 g) in 290 of 17,007 (1.7%; table 1).

Surgery and Anesthesia Characteristics

Craniocervical and pharyngeal surgeries were performed in 5,815 of 17,007 (34.2%) encounters, cardiac surgeries were performed in 705 of 17,007 (4.1%), and emergency surgeries were performed in 1,076 of 17,007 (6.3%). A total of 14,423 of 17,007 (84.8%) encounters were conducted in pediatric hospitals, with 16,624 of 17,007 (97.8%) occurring in operating rooms. Further, 2,445 of 17,007 (14.7%) were classified as American Society of Anesthesiologists Physical Status III or higher (table 2). Encounters with one difficult airway feature and two or more difficult airway features were reported in 530 of 17,007 (3.1%) and 141 of 17,007 (0.83%), respectively. Children with two or more anatomical features of difficult airway were more likely to have difficult airway syndromes than those with none or one (67 of 141 [47.5%] *vs.* 292 of 16,858 [1.73%]; $P < 0.001$ [with eight missing cases]). Difficult mask ventilation occurred in 152 of 17,007 (0.89%) encounters. Anesthesia induction methods included 11,067 of 17,007 (65.1%) inhalational, 5,675 of 17,007 (33.4%) intravenous, and 246 of 17,007 (1.4%) rapid sequence induction (table 2). Tracheal intubation in cardiac catheter laboratory and computed tomography (CT)/magnetic resonance imaging (MRI)/radiation therapy rooms was performed in 170 of 261 (65.1%) and 7 of 49 (14.3%) children, respectively, while SDG placement was performed in 89 of 261 (34.1%) and 34 of 49 (69.4%) children, respectively. A respective 1,991 of 2,354 (84.6%) and 344 of 2,354 (14.6%) children with congenital cardiac diseases received tracheal intubation and SGD placement.

Incidence and Treatment of Adverse Events

The incidence of any adverse events associated with airway management was 346 of 17,007 (2.0%; 95% CI, 1.8 to 2.3), including 168 of 17,007 (0.99%; 95% CI, 0.84 to 1.14) respiratory adverse events. Overall, desaturation events occurred in 395 of 17,007 (2.3%; 95% CI, 2.1 to 2.6) encounters. Among respiratory adverse events, laryngospasm was the most frequent (69 of 17,007 [0.41%]), followed by severe cough, upper airway obstruction, bronchospasm, esophageal intubation with desaturation, atelectasis, vomiting with aspiration, and stridor (table 3).

Within different age groups, the incidence of any adverse events was 18 of 308 (5.8%; 95% CI, 3.5 to 9.1) in neonates and 65 of 1,995 (3.3%; 95% CI, 2.5 to 4.1) in infants. Respiratory adverse events were 8 of 308 (2.6%; 95% CI, 1.1 to 5.1) in neonates and 36 of 1,990 (1.8%; 95% CI, 1.3 to 2.5) in infants, which were higher than other older age groups (figs. 1 and 2). Desaturation predominantly affected neonates (66 of 308, 21.4%; 95% CI, 17.0 to 26.4) and infants (144 of 1,990, 7.2%; 95% CI, 6.1 to 8.5; fig. 3).

Table 2. Characteristics of Surgery and Anesthesia (n = 17,007)

Characteristics	No. (%)
Surgery type*	
Cerebral	636 (3.7)
Thoracic, mediastinal	157 (0.92)
Cardiovascular	705 (4.1)
Thoracic and abdominal	41 (0.24)
Upper abdominal	575 (3.4)
Lower abdominal	1,092 (6.4)
Craniocervical, pharyngeal	5,815 (34.2)
Thoracic wall, abdominal wall, perineal	3,056 (18.0)
Spinal	319 (1.9)
Hip, extremity	2,346 (13.8)
Catheterization for examination or treatments	1,292 (7.6)
Examinations except for catheterization	1,097 (6.5)
Implantation	39 (0.23)
Others	224 (1.3)
Emergency surgery	1,076 (6.3)
Intraoperative position, No. (%)	
Supine	15,374 (90.4)
Prone	989 (5.8)
Decubitus	828 (4.9)
Lithotomy	536 (3.2)
Reverse Trendelenberg	24 (0.14)
Trendelenberg	36 (0.21)
Others	19 (0.11)
Type of institution, No. (%)	
Pediatric	14,423 (84.8)
Mixed adult–pediatric	2,584 (15.2)
Location, No. (%)†	
Operating rooms	16,624 (97.8)
Catheter laboratory rooms	262 (1.54)
CT, MRI, radiation therapy rooms	49 (0.29)
General wards	4 (0.024)
Others	65 (0.38)
Noncompliance to *nil per os*	291 (1.7)
Full stomach status‡	379 (2.2)
Drainage of gastric contents before airway management§	564 (3.3)
Premedication‖	5,610 (33.0)
ASA-PS#	
I	8,885 (52.2)
II	5,676 (33.4)
III	2,197 (12.9)
IV	243 (1.43)
V	4 (0.024)
VI	1 (0.0059)
Difficult airway features	
History of difficult airway	145 (0.85)
Limited cervical range of motion	70 (0.41)
Limited mouth opening	78 (0.46)
Short hyomental distance	27 (0.16)
Upper airway obstruction	122 (0.72)
Midface hypoplasia	74 (0.44)
Macroglossia	87 (0.51)
Micrognacia	348 (2.1)
Macrocephaly	47 (0.28)
Others	143 (0.84)
Difficult mask ventilation**	152 (0.89)
Types of anesthesia induction	
Inhalational	11,067 (65.1)
Intravenous	5,675 (33.4)
Rapid sequence††	246 (1.4)
Others	19 (0.11)

*Surgery type included one missing value. †Location included three missing values. ‡Full stomach status included two missing values. §Drainage of gastric contents before airway management included eight missing values. ‖Premedication included two missing values. #ASA-PS included one missing value. **Difficult mask ventilation included three missing values. ††Rapid sequence anesthesia induction was defined as the procedure that sedatives and muscle relaxants were administered simultaneously to minimize the time until tracheal intubation with or without mask ventilation.

ASA-PS, American Society of Anesthesiologists Physical Status; CT, computed tomography; MRI, magnetic resonance imaging.

Table 3. Incidence and Treatments of Adverse Events (n = 17,007)

Adverse Events and Treatments	No. (%)
Adverse events	
Any adverse events*	346 (2.0)
Respiratory adverse events†	168 (0.99)
Desaturation‡	395 (2.3)
Cardiac arrest (survive)	0 (0)
Cardiac arrest (death within 48 h)	0 (0)
Laryngospasm	69 (0.41)
Upper airway obstruction	27 (0.16)
Severe cough	34 (0.20)
Bronchial intubation	40 (0.24)
Esophageal intubation (absence of desaturation)	86 (0.51)
Esophageal intubation (presence of desaturation)	16 (0.094)
Vomiting (absence of aspiration)	8 (0.047)
Vomiting (presence of aspiration)	2 (0.012)
Hypotension	3 (0.018)
Hypertension	1 (0.0059)
Tooth injury	24 (0.14)
Pneumothorax, mediastinal emphysema	0 (0)
Bronchospasm	20 (0.12)
Atelectasis	9 (0.053)
Pulmonary edema	2 (0.012)
Stridor	4 (0.024)
Airway trauma	2 (0.012)
Arrhythmia (including bradycardia)	25 (0.15)
Dislodgement of airway securing devices	13 (0.076)
Others	27 (0.16)
Treatments for adverse events	
Sedatives	68 (0.40)
Muscle relaxants	49 (0.29)
Ventilatory support with tracheal tube	7 (0.041)
Bronchodilator	16 (0.094)
Intratracheal suctioning	36 (0.21)
Positive pressure ventilation	74 (0.44)
Inhalational epinephrine	11 (0.065)
Intravenous epinephrine	3 (0.018)
Atropine	12 (0.071)
Inotropes, vasopressors	6 (0.035)
Intravenous steroid	16 (0.094)
Surgical airway secure	3 (0.018)
Defibrillation, cardioversion	0 (0)
Bolus infusion	3 (0.018)
Anti-arrhythmic medications	1 (0.0059)
Cardiopulmonary resuscitation	4 (0.024)
Extracorporeal membrane oxygenation	0 (0)
Reversal medications§	2 (0.012)
Diuretics	0 (0)
Unscheduled admission to the ICU‖	12 (0.071)
Others	45 (0.26)

*Any adverse events included hemodynamic and airway-related complications, such as cardiac arrest, upper airway obstruction, laryngospasm, severe cough lasting 10 s or longer, bronchial intubation, esophageal intubation, vomiting with aspiration, hypotension, hypertension, tooth injury, pneumothorax, mediastinal emphysema, bronchospasm (asthma exacerbation), atelectasis, pulmonary edema, stridor, airway trauma, arrhythmia, and airway securing device dislodgement. †Respiratory adverse events included upper airway obstruction, laryngospasm, severe cough lasting 10 s or longer, esophageal intubation with desaturation, vomiting with aspiration, pneumothorax, mediastinal emphysema, bronchospasm (asthma exacerbation), atelectasis, pulmonary edema, stridor, and airway trauma. ‡Desaturation was defined as a drop in Spo2 greater than or equal to 10% between the initiation of airway management and the lowest value during the procedure. §Reversal medications were used for upper airway obstruction in two cases. ‖Unscheduled ICU admissions were attributed to adverse events related to airway management.

ICU, intensive care unit; Spo_2, oxygen saturation measured by pulse oximetry.

Esophageal intubation occurred more frequently among children with two or more difficult airway features (6 of 359 [1.7%] and 96 of 16,648 [0.58%], $P = 0.008$) and younger age (mean ± SD age, 4.2 ± 4.8 and 5.8 ± 4.8; $P < 0.001$). However, no significant differences were found in hospital types (81 of 14,423 [0.56%] and 21 of 2,584 [0.81%]; $P = 0.13$), specialists and other providers (26 of 3,695 [0.70%] and 76 of 13,312 [0.57%]; $P = 0.36$), or video laryngoscopy and direct laryngoscopy (24 of 2,015 [1.2%] and 77 of 9,978 [0.77%]; $P = 0.060$).

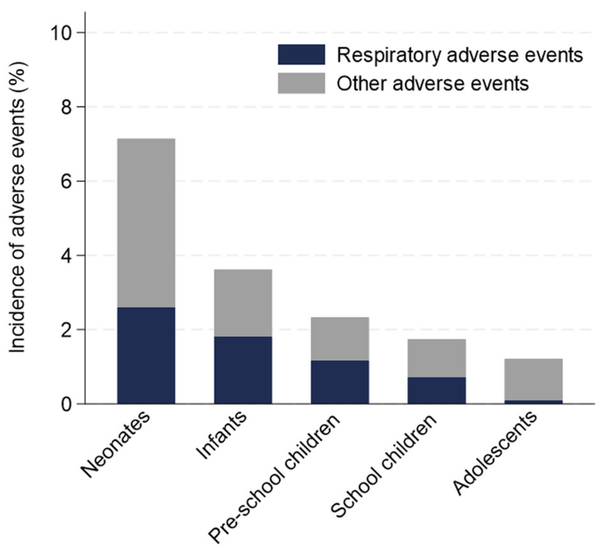

Fig. 1. Incidence of all adverse events by age group. The age groups were defined as neonates (less than 1 month old), infants (1 to 11 months old), preschool children (1 to 5 yr old), school children (6 to 12 yr old), and adolescents (13 to 17 yr old).

Risks for Adverse Events

A multilevel logistic regression analysis of 16,990 encounters showed that increasing age was associated with decreased odds of any adverse events (adjusted odds ratio [aOR], 0.92; 95% CI, 0.90 to 0.95; $P < 0.001$) and providing anesthesia in CT, MRI, or radiation therapy rooms rather than in operating rooms (aOR, 5.7; 95% CI, 1.64 to 19.9; $P = 0.006$); airway sensitivity (aOR, 1.46; 95% CI, 1.09 to 1.94; $P = 0.010$); craniocervical surgery (aOR, 1.41; 95% CI, 1.09 to 1.83; $P = 0.009$); and the presence of one (aOR, 1.74; 95% CI, 1.02 to 2.95; $P = 0.042$) or two or more (aOR, 2.82; 95% CI, 1.21 to 6.6; $P = 0.017$) anatomical difficult airway features were associated with increased odds of any adverse events. Conversely, SGD insertion at the first attempt (aOR, 0.42; 95% CI, 0.288 to 0.62; $P < 0.001$) and muscle relaxant use at the first airway-securing attempt (aOR, 0.62; 95% CI, 0.43 to 0.89; $P = 0.013$) were associated with decreased odds of any adverse events (table 4). External laryngeal manipulation, when compared with tracheal intubation, was associated with increased odds of any adverse events (aOR, 1.90; 95% CI, 1.41 to 2.56; $P < 0.001$). Risk factors for respiratory adverse events are shown in Supplemental Digital Content 2 (https://links.lww.com/ALN/E120).

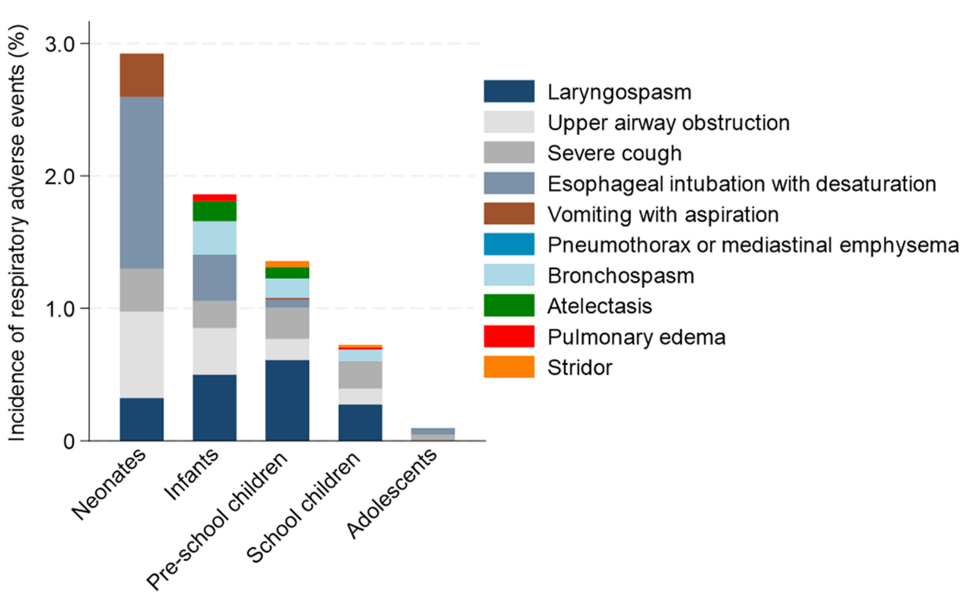

Fig. 2. Incidence of respiratory adverse events by age group. The age groups were defined as neonates (less than 1 month old), infants (1 to 11 months old), preschool children (1 to 5 yr old), school children (6 to 12 yr old), and adolescents (13 to 17 yr old).

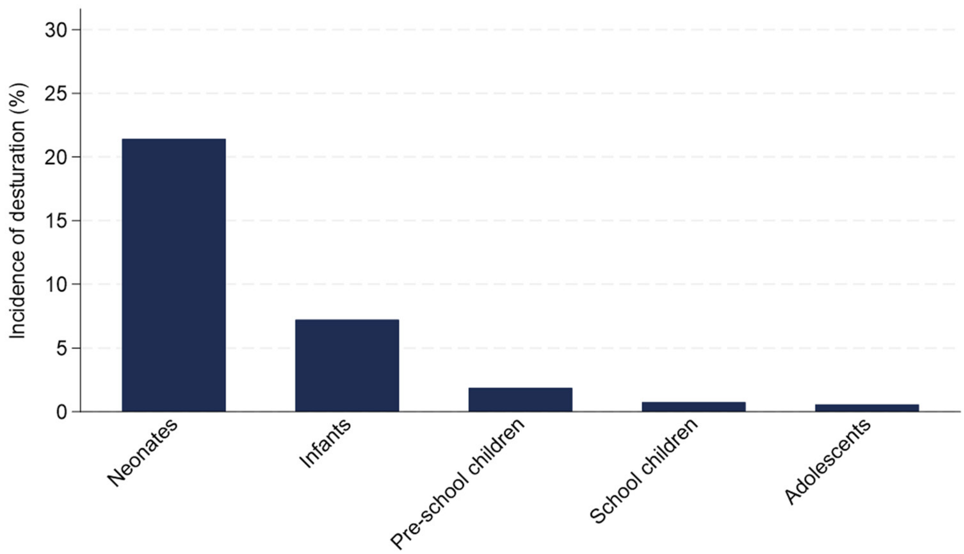

Fig. 3. Incidence of desaturation (oxygen saturation measured by pulse oximetry [Spo_2] greater than or equal to 10% drop) by age group. The age groups were defined as neonates (less than 1 month old), infants (1 to 11 months old), preschool children (1 to 5 yr old), school children (6 to 12 yr old), and adolescents (13 to 17 yr old).

Risks for Desaturation

Multilevel logistic analysis of 16,990 encounters revealed that increasing age was associated with decreased odds of desaturation (aOR, 0.78; 95% CI, 0.75 to 0.82; $P < 0.001$), and providing anesthesia in catheter laboratories (aOR, 2.76; 95% CI, 1.39 to 5.5; $P = 0.004$) and CT, MRI, or radiation therapy rooms (aOR, 4.3; 95% CI, 1.14 to 16.0; $P = 0.031$) compared with that performed in operating rooms, respiratory comorbidities (aOR, 1.51; 95% CI, 1.07 to 2.12; $P = 0.017$), and physical conditions (aOR, 1.94; 95% CI, 1.44 to 2.61; $P < 0.001$) were associated with increased odds of desaturation. In addition, cardiac (aOR, 1.75; 95% CI, 1.11 to 2.76; $P = 0.016$) and emergency (aOR, 1.58; 95% CI, 1.03 to 2.42; $P = 0.036$) surgeries, nonspecialist anesthesiologists (aOR, 1.63; 95% CI, 1.04 to 2.55; $P = 0.032$), and anesthesia trainees (aOR, 1.56; 95% CI, 1.10 to 2.22; $P = 0.014$) compared with pediatric anesthesia specialists, video laryngoscope usage at the first attempt (aOR, 1.93; 95% CI, 1.35 to 2.76; $P < 0.001$) when compared with tracheal intubation, and intravenous induction (aOR, 1.71; 95% CI, 1.28 to 2.30; $P < 0.001$) and rapid sequence induction (aOR, 3.12; 95% CI, 1.50 to 6.5; $P = 0.002$) when compared with inhalational induction were associated with increased odds of desaturation (table 5).

Discussion

This large prospective cross-sectional study explored the incidence and risks of adverse events in pediatric airway management during general anesthesia in Japan. Adverse events and desaturation occurred in approximately 2.0% of airway management courses. Desaturation predominantly occurred in neonates and infants when compared with other age groups. Risk factors included younger age, providing anesthesia outside operating rooms, airway sensitivity, craniocervical surgeries, two or more preoperatively confirmed difficult airway features, and external laryngeal manipulation. This study also highlighted the benefits of using SGDs and muscle relaxants before the first airway-securing attempt.

Our results showed a lower adverse event incidence during airway management than those reported in APRICOT, the largest multicenter prospective study in Europe, which reported a severe adverse event rate of 5.2%.[5] However, this study included adverse events throughout the perianesthesia period, not exclusively those related to airway management. In contrast, this study specifically focused on adverse events during airway-securing procedures, accounting for the lower incidence of adverse events observed.

The PeDI registry, which prospectively collected data on adverse events during tracheal intubation from pediatric-specialized centers in several countries, reported at least one adverse event in 20% of children[2]; however, the entire PeDI study population had difficult airways, which is not representative of the general pediatric anesthesia population. In contrast, our study included all children undergoing general anesthesia, with only 671 of 17,007 (3.9%) airway-securing courses performed for children with at least one anatomical difficult airway feature and 487 of 17,007 (2.9%) courses requiring three or more airway-securing attempts, likely contributing to our lower adverse event incidence (2.0%). Additionally, several previous single-

Table 4. Odds Ratio and 95% CI for the Risk Factors Associated with Any Adverse Events during Airway Management

Patient and Airway Management Characteristics	Univariate Analysis (n = 17,007)					Multivariable Analysis (n = 16,990)
	Yes		No			
	Total	SD, IQR, or No. (%)	Total	SD, IQR, or No. (%)	OR (95% CI); *P* Value	OR (95% CI); *P* Value
Mean age, yr	4.7	4.4	6.3	4.8	0.92 (0.90–0.94); *P* < 0.001	0.92 (0.90–0.95); *P* < 0.001
Sex (male *vs.* female)	9,959	227 (2.3)	7,045	119 (1.7)	1.39 (1.10–1.76); *P* = 0.007	1.42 (1.12–1.80); *P* = 0.004
Median body weight, kg*	13.9	8.5, 21.2	17.5	10.7, 29.5		
Place for airway management						
Mixed adult–pediatric hospital *vs.* pediatric hospital	2,584	58 (2.2)	14,423	288 (2.0)		
Catheter laboratory *vs.* operating room†	262	4 (1.5)	16,624	337 (2.0)	1.00 (0.349–2.89); *P* = 0.99	1.01 (0.337–3.02); *P* = 0.99
CT, MRI, radiation therapy rooms *vs.* operating room‡	49	4 (8.2)	16,624	337 (2.0)	5.3 (1.59–17.3); *P* = 0.006	5.7 (1.64–19.9); *P* = 0.006
Respiratory comorbidity						
Respiratory support	771	25 (3.2)	16,236	321 (2.0)		
Hypoxemia§	507	12 (2.4)	16,500	334 (2.0)		
Apneic events	101	2 (2.0)	16,906	344 (2.0)		
Upper airway obstruction	381	13 (3.4)	16,626	333 (2.0)		
Laryngeal abnormalities	376	6 (1.6)	16,631	340 (2.0)		
Respiratory comorbidity	1,561	41 (2.6)	15,446	305 (2.0)	1.36 (0.96–1.94); *P* = 0.086	0.78 (0.51–1.20); *P* = 0.258
Airway sensitivity						
Active URI symptoms	422	20 (4.7)	16,585	326 (2.0)		
URI within 14 days without active symptoms	486	18 (3.7)	16,521	328 (2.0)		
Asthma	195	7 (3.6)	16,812	339 (2.0)		
Living with an active smoker	2,048	38 (1.9)	14,959	308 (2.1)		
Airway sensitivity	2,983	79 (2.7)	14,024	267 (1.9)	1.47 (1.11–1.96); *P* = 0.008	1.46 (1.09–1.94); *P* = 0.010
Environmental sensitivity						
Allergy for food or medication	807	17 (2.1)	16,200	329 (2.0)		
Allergic rhinitis	463	9 (1.9)	16,544	337 (2.0)		
Atopic dermatitis	407	6 (1.5)	16,600	340 (2.1)		
Environmental sensitivity	1,532	30 (2.0)	15,475	316 (2.0)	0.97 (0.65–1.45); *P* = 0.883	1.09 (0.73–1.65); *P* = 0.667
Cardiovascular comorbidity						
Shock status or cardiac arrest	51	2 (3.9)	16,956	344 (2.0)		
Congenital cardiac diseases	2,355	51 (2.2)	14,652	295 (2.0)		
Pulmonary hypertension	193	4 (2.1)	16,814	342 (2.0)		
Cardiovascular conditions	2,403	53 (2.2)	14,604	293 (2.0)	1.16 (0.84–1.59); *P* = 0.367	1.09 (0.74–1.62); *P* = 0.658
Physical condition						
ASA-PS score of III or higher	2,445	59 (2.4)	14,562	287 (2.0)		
Decreased muscle strength	200	3 (1.5)	16,807	343 (2.0)		
Preterm birth	2,448	68 (2.8)	14,559	278 (1.9)		
Low birth weight	2,222	60 (2.7)	14,785	286 (1.9)		
Physical condition	4,368	107 (2.5)	12,639	239 (1.9)	1.27 (0.99–1.62); *P* = 0.058	1.11 (0.84–1.48); *P* = 0.467
Chromosomal abnormality‖						
Trisomy 21 *vs.* none	327	5 (1.5)	16,320	328 (2.0)		
Trisomy 13 *vs.* none	16	1 (6.3)	16,320	328 (2.0)		
Trisomy 18 *vs.* none	20	2 (10.0)	16,320	328 (2.0)		
Other abnormalities *vs.* none	314	10 (3.2)	16,320	328 (2.0)	1.64 (0.82–3.28); *P* = 0.160	
Gastrointestinal condition						
Noncompliance to *nil per os*	291	11 (3.8)	16,716	335 (2.0)		
Full-stomach pathophysiology#	379	16 (4.2)	16,626	330 (2.0)		
Nausea or vomiting	132	6 (4.6)	16,875	340 (2.0)		
Gastrointestinal condition	604	25 (4.1)	16,403	321 (2.0)	2.28 (1.44–3.63); *P* < 0.001	1.73 (0.97–3.07); *P* = 0.061
Type of surgery						
Cerebral	636	13 (2.0)	16,371	333 (2.0)		
Cardiac surgery	705	13 (1.8)	16,302	333 (2.0)	0.93 (0.51–1.67); *P* = 0.796	0.70 (0.36–1.36); *P* = 0.296
Craniocervical	5,803	138 (2.4)	11,204	208 (1.9)	1.24 (0.98–1.56); *P* = 0.074	1.41 (1.09–1.83); *P* = 0.009
Emergency surgery	1,076	36 (3.4)	15,931	310 (2.0)	1.77 (1.21–2.58); *P* = 0.003	1.47 (0.91–2.38); *P* = 0.116
Difficult airway evaluation						
Syndrome assuming difficult airway	359	25 (7.0)	16,648	321 (1.9)	3.98 (2.41–6.6); *P* < 0.001	

(*Continued*)

Table 4. (Continued)

Patient and Airway Management Characteristics	Univariate Analysis (n = 17,007)					Multivariable Analysis (n = 16,990)
	Yes		No			
	Total	SD, IQR, or No. (%)	Total	SD, IQR, or No. (%)	OR (95% CI); *P* Value	OR (95% CI); *P* Value
Difficult mask ventilation**	152	25 (16.5)	16,555	314 (1.9)	9.7 (5.6–17.1); *P* < 0.001	
Preoperative difficult airway evaluation						
History of difficult airway	145	8 (5.5)	16,862	338 (2.0)	3.17 (1.41–7.1); *P* = 0.005	
Anatomical features of difficult airway						
Limited cervical range of motion	70	1 (1.4)	16,937	345 (2.0)	0.64 (0.081–5.0); *P* = 0.669	
Limited mouth opening	78	6 (7.7)	16,929	340 (2.0)	4.3 (1.66–11.4); *P* = 0.003	
Short hyomental distance	27	2 (7.4)	16,980	344 (2.0)	3.60 (0.70–18.7); *P* = 0.127	
Upper airway obstruction	122	5 (4.1)	16,885	341 (2.0)	2.01 (0.75–5.4); *P* = 0.167	
Midface hypoplasia	74	1 (1.4)	16,933	345 (2.0)	0.58 (0.075–4.5); *P* = 0.604	
Macroglossia	87	3 (3.5)	16,920	343 (2.0)	1.75 (0.50–6.1); *P* = 0.380	
Micrognacia	348	21 (6.0)	16,659	325 (2.0)	3.39 (2.00–5.7); *P* < 0.001	
Macrocephaly	47	1 (2.1)	16,960	345 (2.0)	1.09 (0.14–8.8); *P* = 0.932	
Preoperative difficult airway features						
One feature *vs.* none	530	20 (3.8)	16,336	317 (1.9)	2.00 (1.20–3.32); *P* = 0.007	1.74 (1.02–2.95); *P* = 0.042
Two or more features *vs.* none	141	9 (6.4)	16,336	317 (1.9)	3.49 (1.59–7.7); *P* = 0.002	2.82 (1.21–6.6); *P* = 0.017
Airway management						
Attempt frequency (three times or more)	487	68 (14.0)	16,520	278 (1.7)	13.3 (8.3–21.5); *P* < 0.001	
Reason for initiating a course						
Airway issue *vs.* planned	157	33 (21.0)	16,850	313 (1.9)		
Least experienced provider in each course						
Frequent or occasional *vs.* specialist	2,199	45 (2.1)	3,434	92 (2.7)	0.82 (0.53–1.26); *P* = 0.363	0.88 (0.57–1.37); *P* = 0.575
Trainee *vs.* specialist	10,158	180 (1.8)	3,434	92 (2.7)	0.77 (0.57–1.04); *P* = 0.086	0.80 (0.59–1.09); *P* = 0.159
Airway devices at first attempt						
Uncuffed ETT *vs.* cuffed ETT	965	21 (2.2)	11,502	262 (2.3)		
SGD placement *vs.* direct laryngoscopy††	4,762	63 (1.3)	12,118	280 (2.3)	0.46 (0.340–0.62); *P* < 0.001	0.42 (0.288–0.62); *P* < 0.001
Video laryngoscopy *vs.* direct laryngoscopy	2,015	67 (3.3)	9,978	219 (2.2)	1.82 (1.32–2.50); *P* < 0.001	0.70 (0.45–1.08); *P* = 0.109
Supportive maneuvers at first attempt						
Cricoid pressure	399	17 (4.3)	16,608	329 (2.0)		
External laryngeal manipulation	2,107	76 (3.6)	14,900	270 (1.8)	2.22 (1.66–2.96); *P* < 0.001	1.90 (1.41–2.56); *P* < 0.001
Apneic oxygenation	191	9 (4.7)	16,816	337 (2.0)		
Anesthesia management						
Induction method						
Intravenous *vs.* inhalational	5,921	118 (2.0)	11,067	223 (2.0)	0.92 (0.73–1.18); *P* = 0.526	1.05 (0.78–1.41); *P* = 0.749
Rapid sequence	246	8 (3.3)	16,761	338 (2.0)	1.65 (0.76–3.59); *P* = 0.204	0.88 (0.36–2.15); *P* = 0.781
Muscle relaxant use at first attempt	12,481	240 (1.9)	4,526	106 (2.3)	1.02 (0.78–1.34); *P* = 0.890	0.62 (0.43–0.89); *P* = 0.009
Premedication	5,324	118 (2.2)	11,683	228 (2.0)		

The data are described as numbers (%), means ± SDs, or medians (IQRs). The mean ± SD or median (IQR) values are shown in continuous variables (age and weight) by the presence (yes) and absence (no) of adverse events. The number (%) shows the occurrence of adverse events in nominal variables (sex [male *vs.* female], place for airway management (mixed adult–pediatric hospital *vs.* pediatric hospital; catheter laboratory *vs.* operating room; CT, MRI, or radiation therapy room *vs.* operating room), perioperative difficult airway features, reasons for initiating a course, least experienced provider in each course, airway devices at first attempt, and induction method). The multivariable regression analysis included the variables reported in the multivariable analysis columns. The maximal value of variance inflation factor of incorporated variables in the multilevel logistic regression model was 1.45.

*Median body weight included one missing value. †Catheter laboratory vs. operating room included three missing values. ‡CT, MRI, radiation therapy rooms vs. operating room included three missing values. §Hypoxemia was defined as a peripheral arterial oxygen saturation of 94% or lower on room air. ‖Chromosomal abnormality included 10 missing values. #Full-stomach pathophysiology included two missing values. **Difficult mask ventilation included three missing values. ††SGD placement *vs.* direct laryngoscopy included seven missing values.

ASA-PS, American Society of Anesthesiologists Physical Status; CT, computed tomography; ETT, endotracheal tube; IQR, interquartile range; MRI, magnetic resonance imaging; OR, odds ratio; SGD, supra glottic device; URI, upper respiratory infection.

center, self-reported surveys showed higher respiratory adverse event rates, possibly due to differences in study design, definitions of outcomes, and study populations.[18–20] In our study, the adverse event incidence rates in children with one difficult airway feature or two or more difficult airway features were 20 of 530 (3.8%) and 9 of 141 (6.4%), respectively (table 4), lower than that in the PeDI registry (204 of 1,018 [20%]).[2] This discrepancy might be due to

Table 5. Odds Ratio and 95% CI for the Risk Factors Associated with the Occurrence of Desaturation during Airway Management

Patient and Airway Management Characteristics	Univariate Analysis (n = 17,707)					Multivariable Analysis (n = 16,990)
	Yes		No			
	Total	SD, IQR, or No. (%)	Total	SD, IQR, or No. (%)	OR (95% CI); *P* Value	OR (95% CI); *P* Value
Mean age, yr	2.4	3.6	6.3	4.8	0.75 (0.73–0.78); $P < 0.001$	0.78 (0.75–0.82); $P < 0.001$
Sex (male *vs.* female)	9,959	217 (2.2)	7,045	178 (2.5)	0.86 (0.69–1.07); $P = 0.181$	0.86 (0.68–1.09); $P = 0.21$
Median body weight,* kg	7.7	3.8, 13.0	17.7	10.9, 29.7		
Location for airway management						
Mixed adult–pediatric hospital *vs.* pediatric hospital	2,584	113 (4.4)	14,423	282 (2.0)		
Catheter laboratory *vs.* operating room†	262	20 (7.6)	16,624	370 (2.2)	5.7 (2.94–10.9); $P < 0.001$	2.76 (1.39–5.5); $P = 0.004$
CT, MRI, radiation therapy rooms *vs.* operating room‡	49	4 (8.2)	16,624	370 (2.2)	6.3 (1.71–23.0); $P = 0.006$	4.3 (1.14–16.0); $P = 0.031$
Respiratory comorbidity						
Respiratory support	771	64 (8.3)	16,236	331 (2.0)		
Hypoxemia§	507	47 (9.3)	16,500	348 (2.1)		
Apneic events	101	5 (5.0)	16,906	390 (2.3)		
Upper airway obstruction	381	9 (2.4)	16,626	386 (2.3)		
Laryngeal abnormalities	376	16 (4.3)	16,631	379 (2.3)		
Respiratory comorbidity	1,561	103 (6.6)	15,446	292 (1.9)	5.3 (3.60–7.8); $P < 0.001$	1.51 (1.07–2.12); $P = 0.017$
Airway sensitivity						
Active URI symptoms	422	19 (4.5)	16,585	376 (2.3)		
URI within 14 days without active symptoms	486	15 (3.1)	16,521	380 (2.3)		
Asthma	195	3 (1.5)	16,812	392 (2.3)		
Living with an active smoker	2,048	35 (1.7)	14,959	360 (2.4)		
Airway sensitivity	2,983	67 (2.3)	14,024	328 (2.3)	1.01 (0.74–1.38); $P = 0.940$	1.19 (0.87–1.63); $P = 0.283$
Environmental sensitivity						
Allergy for food or medication	807	10 (1.2)	16,200	385 (2.4)		
Allergic rhinitis	463	5 (1.1)	16,544	390 (2.4)		
Atopic dermatitis	407	6 (1.5)	16,600	389 (2.3)		
Environmental sensitivity	1,532	20 (1.3)	15,475	375 (2.4)	0.56 (0.34–0.92); $P = 0.023$	1.05 (0.63–1.75); $P = 0.841$
Cardiovascular comorbidity						
Shock status or cardiac arrest	51	6 (11.8)	16,956	389 (2.3)		
Congenital cardiac diseases	2,355	120 (5.1)	14,652	275 (1.9)		
Pulmonary hypertension	193	23 (11.9)	16,814	372 (2.2)		
Cardiovascular comorbidity	2,403	124 (5.2)	14,604	271 (1.9)	3.79 (2.74–5.2); $P < 0.001$	0.82 (0.57–1.19); $P = 0.307$
Physical condition						
ASA-PS score or III or higher	2,445	171 (7.0)	14,562	224 (1.5)		
Decreased muscle strength	200	3 (1.5)	16,807	392 (2.3)		
Preterm birth	2,448	89 (3.6)	14,559	306 (2.1)		
Low birth weight	2,222	83 (3.7)	14,785	312 (2.1)		
Physical condition	4,368	214 (4.9)	12,639	181 (1.4)	4.7 (3.43–6.4); $P < 0.001$	1.94 (1.44–2.61); $P < 0.001$
Chromosomal abnormality‖						
Trisomy 21 *vs.* none	327	8 (2.5)	16,320	374 (2.3)		
Trisomy 13 *vs.* none	16	2 (12.5)	16,320	374 (2.3)		
Trisomy 18 *vs.* none	20	2 (10.0)	16,320	374 (2.3)		
Other abnormalities *vs.* none	314	9 (2.9)	16,320	374 (2.3)		
Gastrointestinal condition						
Noncompliance to *nil per os*	291	10 (3.4)	16,716	385 (2.3)		
Full-stomach pathophysiology#	379	25 (6.6)	16,626	370 (2.2)		
Nausea or vomiting	132	8 (6.1)	16,875	387 (2.3)		
Gastrointestinal condition	604	32 (5.3)	16,403	363 (2.2)	2.81 (1.76–4.5); $P < 0.001$	0.85 (0.49–1.49); $P = 0.569$
Type of surgery						
Cerebral	636	23 (3.6)	16,371	372 (2.3)		
Cardiac surgery	705	67 (9.5)	16,302	328 (2.0)	7.1 (4.5–11.1); $P < 0.001$	1.75 (1.11–2.76); $P = 0.016$
Craniocervical	5,803	76 (1.3)	11,204	319 (2.9)	0.41 (0.305–0.55); $P < 0.001$	0.78 (0.57–1.06); $P = 0.112$
Emergency surgery	1,076	58 (5.4)	15,931	337 (2.1)	2.80 (1.95–4.0); $P < 0.001$	1.58 (1.03–2.42); $P = 0.036$
Difficult airway evaluation						

(*Continued*)

Table 5. (Continued)

Patient and Airway Management Characteristics	Univariate Analysis (n = 17,707)					Multivariable Analysis (n = 16,990)
	Yes		No			
	Total	SD, IQR, or No. (%)	Total	SD, IQR, or No. (%)	OR (95% CI); *P* Value	OR (95% CI); *P* Value
Syndrome assuming difficult airway	359	19 (5.3)	16,648	376 (2.3)	2.65 (1.49–4.7); *P* = 0.001	
Difficult mask ventilation**	152	22 (14.5)	16,555	360 (2.2)	9.6 (4.8–19.4); *P* < 0.001	
Preoperative difficult airway evaluation						
History of difficult airway	145	9 (6.2)	16,862	386 (2.3)	3.50 (1.52–8.1); *P* = 0.003	
Anatomical features of difficult airway						
Limited cervical range of motion	70	5 (7.1)	16,937	390 (2.3)	3.90 (1.26–12.1); *P* = 0.018	
Limited mouth opening	78	3 (3.9)	16,929	392 (2.3)	1.83 (0.48–7.0); *P* = 0.376	
Short hyomental distance	27	0 (0)	16,980	395 (2.3)	NA	
Upper airway obstruction	122	6 (4.9)	16,885	389 (2.3)	2.38 (0.89–6.4); *P* = 0.085	
Midface hypoplasia	74	5 (6.8)	16,933	390 (2.3)	3.22 (1.05–9.9); *P* = 0.041	
Macroglossia	87	2 (2.3)	16,920	393 (2.3)	0.95 (0.20–4.6); *P* = 0.950	
Micrognathia	348	16 (4.6)	16,659	379 (2.3)	2.17 (1.18–3.99); *P* = 0.013	
Macrocephaly	47	5 (10.6)	16,960	390 (2.3)	7.43 (2.21–24.9); *P* = 0.001	
Anatomical difficult airway features						
One risk *vs.* none	530	19 (3.6)	16,336	366 (2.2)	1.63 (0.94–2.80); *P* = 0.080	0.98 (0.55–1.75); *P* = 0.948
Two or more risks *vs.* none	141	10 (7.1)	16,336	366 (2.2)	4.1 (1.81–9.3); *P* = 0.001	2.03 (0.86–4.8); *P* = 0.108
Airway management						
Attempt frequency (three times or more)	487	65 (13.4)	16,520	330 (2.0)	10.3 (6.3–16.9); *P* < 0.001	
Reason for initiating a course						
Airway issue *vs.* planned	157	39 (24.8)	16,850	356 (2.1)		
Least experienced provider in each course						
Frequent or occasional *vs.* specialist	2,199	83 (3.8)	3,434	67 (2.0)	1.55 (1.01–2.38); *P* = 0.043	1.63 (1.04–2.55); *P* = 0.032
Trainee *vs.* specialist	10,158	233 (2.3)	3,434	67 (2.0)	1.20 (0.86–1.68); *P* = 0.279	1.56 (1.10–2.22); *P* = 0.014
Airway devices at the first attempt						
Uncuffed ETT *vs.* cuffed ETT	965	49 (5.1)	11,502	301 (2.6)		
SGD placement *vs.* direct laryngoscopy††	4,762	48 (1.0)	12,118	343 (2.8)	0.338 (0.237–0.48); *P* < 0.001	0.76 (0.49–1.20); *P* = 0.242
Video laryngoscopy *vs.* direct laryngoscopy	2,015	119 (5.9)	9,978	225 (2.3)	3.04 (2.17–4.3); *P* < 0.001	1.93 (1.35–2.76); *P* < 0.001
Supportive maneuvers at first attempt						
Cricoid pressure	399	11 (2.8)	16,608	384 (2.3)		
External laryngeal manipulation	2,107	68 (3.2)	14,900	327 (2.2)	1.65 (1.21–2.25); *P* = 0.001	1.28 (0.93–1.76); *P* = 0.134
Apneic oxygenation	191	9 (4.7)	16,816	386 (2.3)		
Anesthesia management						
Induction method						
Intravenous *vs.* inhalational	5,921	214 (3.6)	11,067	175 (1.6)	2.40 (1.85–3.12); *P* < 0.001	1.71 (1.28–2.30); *P* < 0.001
Rapid sequence	246	19 (7.7)	16,761	376 (2.2)	4.77 (2.51–9.0); *P* < 0.001	3.12 (1.50–6.5); *P* = 0.002
Muscle relaxant use at first attempt	12,481	323 (2.6)	4,526	72 (1.6)	1.65 (1.21–2.26); *P* = 0.002	0.79 (0.52–1.18); *P* = 0.251
Premedication	5,324	73 (1.4)	11,683	322 (2.8)		

The data are described as numbers (%), means ± SDs, or medians (IQRs). The mean ± SD or median (IQR) values are shown in continuous variables (age and weight) by the presence (yes) and absence (no) of adverse events. The number (%) shows the occurrence of adverse events in nominal variables (sex [male *vs.* female], place for airway management (mixed adult–pediatric hospital *vs.* pediatric hospital; catheter laboratory *vs.* operating room; CT, MRI, or radiation therapy room *vs.* operating room), perioperative difficult airway features, reasons for initiating a course, least experienced provider in each course, airway devices at first attempt, and induction method). The multivariable regression analysis included the variables reported in the multivariable analysis columns. The maximal value of the variance inflation factor of incorporated variables in the multilevel logistic regression model was 1.86.

*Median body weight included one missing value. †Catheter laboratory vs. operating room included three missing values. ‡CT, MRI, radiation therapy rooms vs. operating room included three missing values. §Hypoxemia was defined as the status where the preoperative Spo2 was 94% or lower on room air. ‖Chromosomal abnormality included 10 missing values. #Full-stomach pathophysiology included two missing values. **Difficult mask ventilation included three missing values. ††SGD placement *vs.* direct laryngoscopy included seven missing values.

ASA-PS, American Society of Anesthesiologists Physical Status; CT, computed tomography; ETT, endotracheal tube; IQR, interquartile range; MRI, magnetic resonance imaging; NA, Not applicable; OR, odds ratio; SGD, supra glottic device; Spo_2, oxygen saturation measured by pulse oximetry; URI, upper respiratory infection.

reporting and measurement biases, misclassification, and inclusion of different pediatric populations.

Our multivariable analysis emphasized the impact of younger age on the risk of adverse events and desaturation during a sequence of airway-securing procedures, consistent with previous pediatric literature across the perianesthesia period (*i.e.*, APRICOT) that recorded desaturation events except for during airway management.[5,18] Our study, focusing specifically on airway management, showed that approximately 21% of neonates and 7% of infants experienced desaturation, which was higher than that in other age groups. Neonates' unique physiologic and anatomical characteristics can explain this hypoxic progression tendency.[1] Additionally, cardiac surgery was linked to an increased desaturation risk, possibly due to neonates with congenital cardiac diseases with right-to-left intracardiac shunts, which reduces tolerance to apnea. In some cases, preoxygenation with high-concentration oxygen is restricted for neonates with the hemodynamics and pulmonary artery flow reliance on patent ductus arteriosus.[21] The higher desaturation incidence in neonates in our study highlights the necessity for shorter tracheal intubation time and higher first-attempt success rates in neonates. Our data showed that approximately 40% of respiratory adverse events in neonates involved esophageal intubation with hypoxia. In addition, overall esophageal intubation occurred more frequently among younger children. Recent European guidelines recommend video laryngoscopes for neonatal tracheal intubation, as they allow multiple anesthesia providers to confirm glottic exposure.[22] Our data revealed that approximately 40% of the reasons for tracheal intubation failure in airway-securing attempts with video laryngoscopy comprised the inability to lead the tracheal tube to the vocal cords even with optimal glottic exposure, suggesting the necessity of training to guide a tracheal tube under video laryngoscopy visualization.

This study evaluated the risk of preoperative patient history and anatomical features of difficult airway for adverse events and desaturation during airway-securing attempts. Univariate analysis showed that syndromic difficult airway, preoperative recognition of a possibility of difficult airway, history of difficult airway, limited mouth opening, and micrognathia were associated with adverse events. Limited cervical motion, midface hypoplasia, and macrocephaly were associated with desaturation. Limited mouth opening hinders the insertion of airway-securing devices (*e.g.*, laryngoscope, tracheal tube). During intrauterine development, micrognathia results from the posterior displacement of the tongue base with a decreased oropharynx space.[23] In children with micrognathia, glottic exposure and insertion and manipulation of airway devices are challenging. Our univariate analysis revealed that overall esophageal intubation was more common among children with two or more difficult airway features. The higher esophageal–tracheal intubation rate in children with difficult airway features may result from limited mouth opening and oropharyngeal space for manipulating laryngoscopes. This could lead to difficulty in identifying the vocal cords and smoothly guiding the tracheal tube to them, which may result from insufficient training and experience among anesthesia providers. Efficient training for manipulating laryngoscopes to achieve a sufficient glottic view and smooth guidance of the tracheal tube to the vocal cords is essential to secure the airway of children with difficult airway features.

Regression analysis showed that the presence of at least one difficult airway feature was a risk factor for adverse events during airway-securing procedures. The risk of adverse events was deemed higher in children with two or more difficult airway features than in those with one feature. Combined features across different sites could interactively increase management difficulty. In our data set, approximately half of the children with two or more difficult airway features had difficult airway syndrome, suggesting an extensive degree of anatomical challenges.

Our data revealed that desaturation (a potential adverse event precursor) occurred more often during procedures performed by nonspecialist anesthesiologists than by specialist anesthesiologists, even without increased risk for adverse events. Hypoxia is a common cause of critical adverse events during airway management in children. Our results might reflect the occurrence of "near-miss" hypoxic events that did not progress to critical adverse events, which more likely occurred during airway management by nonspecialists and trainees.

Regarding other risk factors, providing anesthesia in CT, MRI, and radiation therapy rooms was an independent risk factor associated with adverse events after adjusting for potential patient and anesthesia risks. This implies that environmental factors outside the operating rooms, including resources (*e.g.*, height-unadjusted table for airway management and inexperienced anesthesia assistants), may be associated with adverse events. Most children who underwent CT/MRI/radiation therapy received monitored anesthesia care without tracheal intubation or SDG placement, while most children who underwent cardiac catheterization received tracheal intubation or SDG placement. Our study only included children who underwent tracheal intubation or SGD placement. These children could be considered high-risk, leading clinicians to apply airway-securing procedures. In addition, craniocervical surgeries, emergency surgeries, and composite variables such as airway sensitivity, including current and recent (2 weeks) upper respiratory infection symptoms, and physical conditions, including preterm birth and low birth weight, were associated with adverse events.[5] Conversely, SGD (instead of tracheal intubation) and muscle relaxant usage at the first airway-securing attempt were associated with a decrease in adverse events. Further research, including the type of SGDs, may help identify the features of SGDs that are associated with the failure of airway securing attempts. Consistent with previous pediatric studies in intensive care units,[24] we found that external laryngeal manipulation increased the risk of adverse events in general anesthesia settings. Unlike a previous randomized controlled study,[25] our data showed that intravenous anesthesia induction was associated with an increased risk of hypoxemia after adjusting for potential confounders. This finding may be explained by several assumptions. First, intravenous anesthetics might hinder subsequent bag-mask ventilation due to events such as opioid-induced (*i.e.*, fentanyl, remifentanil, and morphine) wooden chest syndrome and cough. Second, the initiation of mask ventilation might have been delayed after spontaneous breathing disappeared due to a delay in its recognition by the anesthesia providers. In children who resist preoxygenation, desaturation is more likely to occur when mask ventilation is delayed. Our real-world data might reflect the gap between the real-world practice and the results of studies conducted under experimental conditions, including patients' comorbidities, use of various types of airway-securing devices, and lack of sufficient preoxygenation. However, the remaining unmeasured confounders (*e.g.*, absence of sufficient preoxygenation) might have influenced the results. Finally, unadjusted confounders, including difficult airway history, severe comorbidities causing difficult mask ventilation, or rapid hypoxemia progression (*e.g.*, abdominal distention in GI surgery cases, pulmonary hypertension), may be involved. Further studies evaluating opioid-induced adverse events during anesthesia induction adjusting for potential confounders are needed.

This study has some limitations. First, reporting bias may arise since data collection relied on self-reports from assigned anesthesiologists, which may cause inaccurate memory and misunderstandings of research terminology. In addition, clinical judgment and interpretation of adverse event definitions (*e.g.*, laryngospasm) might have differed at the reporter level. Second, selection bias may occur due to missing cases for inclusion. To minimize these biases, we applied a standardized data collection and verification system, in which local research leaders checked for missing data and educated anesthesia providers regarding research terminology using a manual. Additionally, research collaborators clarified any uncertainties regarding definitions or event classification through communication software (Slack). Local research leaders encouraged anesthesiologists to complete data collection within a few days to accurately recall airway management details, aiming for a data capture rate of 95% or higher. Site-specific leaders were tasked with confirming the submission of data collection forms for all applicable cases. Third, unmeasured confounders (*e.g.*, experiences of pediatric anesthesia fellowship training) may bias the results. We addressed this by carefully reviewing previous literature to select potential confounders, which were verified by experienced board-certified anesthesiologists during protocol development.[12] Fourth, missing data could distort the results. We utilized the REDCap data registration system, configured to reject registrations with missing data, which was enforced for most variables. Fifth, as our data set recorded outcomes per encounter that could include multiple attempts utilizing different airway-securing devices (*e.g.*, tracheal tube, SGD), the exact incidence of adverse events according to tracheal intubation or SGD placement was unknown. Therefore, regarding multivariable analysis, the odds ratios of variables in the subcategory "airway devices at the first attempt" required cautious interpretation due to unadjusted confounding in cases with multiple attempts with different airway-securing devices during each course. Sixth, we selected the clinically relevant variables for multivariable regression models to evaluate their impact on the outcomes. However, the complexity of the models can cause model fitting issues, and further investigation of the prediction models is needed. Finally, the Hawthorne effect may have influenced anesthesia providers' performance during the study period, necessitating careful interpretation of the results considering this behavioral bias.

In conclusion, this large prospective, multicenter, real-world, observational study conducted in Japan reported the incidence of adverse events and evaluated their risks during airway-securing procedures. The findings from the J-PEDIA study can help recognize airway management risks and increase safety during airway management under general anesthesia in children.

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Competing Interests

The authors declare no competing interests.

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Supplemental Digital Content

Supplemental Digital Content 1. Definitions for research terminologies, https://links.lww.com/ALN/E119

Supplemental Digital Content 2. Risks for respiratory adverse events and desaturation, https://links.lww.com/ALN/E120

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