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ORIGINAL ARTICLE

Epidemiology and incidence of severe respiratory critical events in ear, nose and throat surgery in children in Europe

A prospective multicentre observational study

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BACKGROUND Ear, nose and throat (ENT) surgery, the most frequently performed surgical procedure in children, is a strong predictor for peri-operative respiratory complications. However, there is no clear information about peri-operative respiratory severe critical events (SCEs) associated with anaesthesia management of ENT children in Europe.

OBJECTIVE To characterise the epidemiology and incidence of respiratory SCEs during and following ENT surgery in Europe and to identify the risk factors for their occurrence.

DESIGN A secondary analysis of the Anaesthesia PRactice In Children Observational Trial, a prospective observational multicentre cohort trial.

SETTING The study included 261 centres across 33 European countries and took place over a consecutive 2-week recruitment period between April 2014 and January 2015.

PATIENTS We extracted data from 5592 ENT surgical procedures that were performed on 5572 children aged 6.0 (3.6) years (mean (SD)) from the surgical database and compared these with data from 15 952 non-ENT surgical children aged 6.7 (4.8) years.

MAIN OUTCOME MEASURES The primary outcome was the incidence of respiratory SCEs (laryngospasm, bronchospasm and new onset of postoperative stridor). Secondary outcomes were the differences in epidemiology between ENT children and non-ENT surgical children and the risk factors for the occurrence of respiratory SCEs.

RESULTS The incidence (95% confidence interval) of any respiratory SCE (laryngospasm, bronchospasm and postoperative stridor) was 3.93% (3.46 to 4.48) and was significantly higher than that observed in non-ENT surgical children [2.61% (2.37 to 2.87)], with a relative risk of 1.51 (1.28 to 1.77), P less than 0.0001. Younger age (14% decrease in critical events by increasing year, $P < 0.0001$), history of snoring, recent upper respiratory tract infection and recent wheezing increased the risk of suffering a SCE by over two-fold ($P < 0.0001$). There was also some evidence for a positive association with age below 4.6 years and lower surgical volume thresholds (<20 cases/2 weeks).

CONCLUSION The results of this study provide additional evidence for strong associations between risk factors and respiratory SCEs in children having ENT surgery. These observations may facilitate the implementation of good clinical practice recommendations for ENT patients in Europe.

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Introduction

Ear, nose and throat (ENT) operations are amongst the most frequently performed surgical procedures in the paediatric population. Recently, a large prospective multicentre cohort study confirmed that ENT surgery accounts for more than 20% of all surgical procedures in Europe.[1] Furthermore, there is good evidence from the

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literature that an ENT procedure is a strong predictor for peri-operative respiratory complications,[1–3] particularly when patients are managed by nonspecialist paediatric anaesthesiologists.[4]

Pre-operative assessment of children scheduled for an ENT surgical procedure is generally focused on identifying the risk factors that are known to be associated with a higher incidence of peri-operative respiratory adverse events. These risk factors include age, weight,[5] the presence of a recent upper respiratory tract infection,[1,3] a medical history of airway hypersensitivity[1,3] or symptoms of upper airway obstruction with snoring,[1,6] that is signs of obstructive sleep apnoea.[7,8] Although the results of several studies converge towards identifying comparable risk factors, there is still a dilemma of whether children scheduled for ENT surgical procedures should be managed in specialised paediatric centres. Moreover, determining these risk factors may allow the institution of preventive measures and modification of peri-operative management in an attempt to reduce the incidence of respiratory critical events.

The secondary analysis of the prospective observational multicentre cohort study, Anaesthesia PRactice In Children Observational Trial (APRICOT), was performed to characterise the epidemiology and the incidence of respiratory severe critical events (SCEs) during and following ENT surgery in Europe and to identify the risk factors for the occurrence of three respiratory SCEs: laryngospasm, bronchospasm and new onset postoperative stridor. We hypothesised that the population profile (demographic parameters, medical history) and the incidence of respiratory SCEs in children undergoing ENT surgery were different from those reported during the peri-operative course of children undergoing other surgical procedures.

Methods

The APRICOT study followed a prospective observational multicentre cohort design collecting peri-operative data regarding the anaesthetic management of children undergoing elective, urgent surgical or diagnostic procedures.

The study took place over a consecutive 2-week recruitment period between April 2014 and January 2015 and included 261 centres across 33 European countries. Participating centres registered on a voluntary basis and were free to choose their inclusion period after obtaining local or national formal ethical approval.

All children up to 15 years of age undergoing an inpatient or outpatient surgical procedure, elective or emergency, in-hours or out-of-hours, under sedation or general anaesthesia were eligible for inclusion in the current analysis. We excluded all children having anaesthesia for diagnostic procedures, and those having anaesthesia performed in a neonatal or paediatric intensive care unit. Observations for up to 1 h after anaesthesia and the child's status at 30 days were reported.

Full details of the patient's history, including predefined risk factors as determined from the literature, anaesthetic and airway management, the experience of the anaesthetist in charge and the institution type were recorded. Data obtained from each child were collected on a case report form that was then transcribed anonymously on a secure internet-based electronic case record form (OpenClinica, Boston, Massachusetts, USA).

The primary endpoint was defined as the occurrence of laryngospasm (defined as complete airway obstruction, unrelieved by simple jaw thrust and positive airway pressure manoeuvres and requiring the administration of a medication), bronchospasm (defined as any episode of airway constriction requiring the administration of a bronchodilator) and new-onset postoperative stridor (defined as severe inspiratory flow limitation necessitating the administration of oxygen, intravenous steroids and/or adrenaline) which required immediate intervention and that led or could have led to major disabilities and/or death. The secondary endpoints were the risk factors for the occurrence of respiratory SCEs and the risk profile of ENT patients when compared with other surgical procedures.

Statistical analysis

Study size determination for APRICOT was based on the estimation of approximately 25 000 patients to provide a 95% confidence interval (95% CI) for the overall rate of SCEs with an acceptable confidence width assuming that the lowest incidence of respiratory SCE is 0.1% (i.e. 95% exact CI is 0.065 to 0.147). Statistical analysis was performed using SPSS v. 24 (IBM, Chicago, Illinois, USA) statistical software. Descriptive data are expressed as mean (SD) or percentages for continuous and categorical variables, respectively. Univariate and multivariate relative risk (RR) regression models for correlated observations were applied to identify the potential risk factors for the occurrence of any respiratory SCE. RRs and 95% CI were estimated from the model. Pearson's χ^2 tests and two-sample *t*-tests were applied to compare the two groups of children using the Benjamini–Hochberg procedure with a false discovery rate of 0.05. The level of significance was identified for *P* values less than 0.05. Using age and weight as a continuous variable, receiver operating characteristic analysis was performed to identify a cut-off age and weight where the overlap of the distribution of ages and weights with or without a complication were minimal.

Results

The secondary analysis was performed on 21 524 children aged less than 16 years old who underwent one or multiple surgical procedures under general anaesthesia in 261 centres throughout 33 European countries. The

Table 1 Demographic characteristics and medical history of children undergoing ear, nose and throat operations compared with other surgical procedures

	ENT, *n* (%)	Non-ENT, *n* (%)
n	5572 (25.9)	15 952 (74.1)
Age (years)[b]	6.0 (3.6)	6.7 (4.8)
Sex[a]		
Male	3206 (57.5)	10 398 (65.2)
Female	2366 (42.5)	5554 (34.8)
Weight (kg)[b], *n*	23.9 ± 14.2, 5502	26.2 ± 18.2, 15771
Prematurity[a]		
No	4695 (93.4)	12 913 (91.2)
Yes	333 (6.6)	1240 (8.8)
ASA-PS[a]		
1	3992 (71.4)	10 880 (68.0)
2	1387 (24.8)	3753 (23.4)
3	182 (3.3)	1141 (7.1)
4	28 (0.5)	226 (1.4)
5	1 (0.0)	10 (0.1)
Medical history		
Upper respiratory tract infection in the past 2 weeks[a]		
No	4383 (80.9)	13 745 (88.2)
Yes	1037 (19.1)	1834 (11.8)
Wheezing in the past 12 months[a]		
No	4808 (89.8)	14 359 (95.1)
Yes	546 (10.2)	734 (4.9)
Asthma diagnosis[a]		
No	5051 (91.6)	14 831 (94.4)
Yes	464 (8.4)	886 (5.6)
Atopy[a]		
No	4760 (88.8)	14 164 (92.7)
Yes	599 (11.2)	1114 (7.3)
Allergy[a]		
No	4779 (85.8)	14 035 (88.4)
Yes	792 (14.2)	1846 (11.6)
Snoring[a]		
No	2761 (54.5)	12 081 (90.9)
Yes	2306 (45.5)	1212 (9.1)
Fever[a]		
No	5416 (98.3)	15 143 (96.8)
Yes	91 (1.7)	495 (3.2)
Passive smoking[a]		
No	3382 (82.8)	9303 (84.8)
Yes	704 (17.2)	1668 (15.2)
Medication[a]		
No	4636 (83.4)	12 990 (81.7)
Yes	920 (16.6)	2904 (18.3)
Handicap[a]		
No	5109 (92.3)	14 064 (88.8)
Yes	425 (7.7)	1765 (11.2)

Values are n(%) except for age (mean (SD)) and weight (mean ± SD (*n*)). ASA-PS American Society of Anesthesiologists' Physical Status; ENT, ear, nose, and throat. [a,b] For significance between the two groups of procedures (Pearson's χ^2 test of independence and two sample t-test, respectively, using the Benjamini-Hochberg procedure with a false discovery rate of 0.05).

data represented 5592 exclusively ENT surgical procedures that were performed on 5572 children, and 15 952 children having 16 013 non-ENT operations. Children who had surgery under sedation or regional anaesthesia alone were excluded from the final analysis.

Table 1 describes the characteristics and medical history of the two groups of children representing the studied cohort. Children with ENT surgery were on average younger and had a significantly greater incidence of pre-operative respiratory conditions than those having non-ENT procedures, with recent upper respiratory tract infection in 19% and snoring in 45.5% of the ENT patients. Although there was a difference in the mean weight between the two groups of children ($P < 0.0001$), based on the WHO references,[9] there was no evidence for a difference in the BMI of the two groups (13.6 vs. 12.5% overweight and 7.1 vs. 7.8% obese children in the non-ENT and ENT groups, respectively).

Table 2 shows the distribution of children based on the anaesthesiologist provider and the institutions where the surgery took place. It is of note that in 31% of ENT procedures, anaesthesia was performed by certified anaesthesiologists with occasional paediatric anaesthesia practice, that is less than 50% of their weekly case load, and a high percentage was performed in community institutions. Moreover, the contribution of centres to the cohort varied widely with 38% of the centres reporting more than 20 cases, while 55% of the centres performed less than 20 ENT cases (13% between 16 and 20 cases, 15% between 11 and 15, 13% between six and 10 and finally 14% between one and five cases) within the 2-week recruitment period. Children who had their ENT surgery in a community hospital were older (6.7 years, 95% CI 6.4 to 6.9) than those admitted to an academic specialist paediatric institution (5.7 years, 95% CI 5.5 to 5.8) or a mixed adult-paediatric teaching hospital (6.1 years, 95% CI 6.0 to 6.3) ($P < 0.05$).

Premedication was administered more frequently in children undergoing ENT surgery (63%) vs. 52% for non-ENT surgery ($P < 0.0001$), with oral midazolam being the most frequently administered agent (approximately 48% in both groups). Anaesthesia management varied widely with no clinical evidence for a difference between the two groups of children. Exclusive use of inhalational anaesthesia was employed in a third of the cohort with another third having a combination of intravenous induction and inhalational maintenance. Only 10% of children in both groups had total intravenous anaesthesia (Appendix A, http://links.lww.com/EJA/A188). This variability can also be noticed in the various anaesthetic agents used for induction with no evidence for a difference between the two groups of children (Appendix B, http://links.lww.com/EJA/A188). Finally, a higher percentage of ENT children had tracheal intubation without the administration of a neuromuscular blocking agent (NMBA) than non-ENT children (53 vs. 26.9%, $P < 0.001$). Significantly, 70% of the ENT children who were intubated without a NMBA had inhalational induction of anaesthesia with or without propofol, while 70% of those who had intravenous induction received a NMBA to facilitate intubation ($P < 0.0001$). Independent of the use of a NMBA for tracheal intubation, the duration of the procedure was shorter in ENT than in non-ENT intubated children (41.3 (42) vs. 92.9 (84) min with NMBA and 35.2 (39) vs. 70.9 (70) min without NMBA, respectively, $P < 0.0001$).

Table 2 Distribution of the surgical cases based on the frequency of paediatric anaesthesia practice and on the type of institutions layered by ASA physical status (ASA) and by the presence or not of snoring

	ENT procedures, *n* (%)				Non-ENT procedures, *n* (%)			
	ASA I-II	ASA III-V	No snoring	Snoring	ASA I-II	ASA III-V	No snoring	Snoring
Anaesthesia team								
Certified anaesthesiologist with mainly paediatric practice (>80%)	2420 (45.0)[a]	148 (70.1)	1332 (48.2)[a]	1024 (44.4)[a]	8702 (59.5)	988 (71.8)	7494 (62.0)	622 (51.3)
Certified anaesthesiologist with frequent paediatric anaesthesia cases (50 to 80%)	786 (14.6)[a]	20 (9.5)	377 (13.7)[a]	372 (16.1)[a]	2022 (13.8)	161 (11.7)	1756 (14.5)	187 (15.4)
Certified anaesthesiologist with occasional paediatric anaesthesia cases (<50%)	1692 (31.5)[a]	33 (15.6)	813 (29.4)[a]	711 (30.8)[a]	2711 (18.5)	172 (12.5)	1960 (16.2)	311 (25.7)
Anaesthesiologist in training, anaesthetic nurse or technician	481 (8.9)[a]	10 (4.7)	293 (8.7)[a]	199 (8.6)[a]	1198 (8.2)	56 (4.1)	871 (7.2)	92 (7.6)
Classification of institutions								
Paediatric hospital (academic)	1851 (34.4)[a]	116 (55.0)	1032 (37.4)[a]	768 (33.3)[a]	6057 (41.4)	683 (49.6)	5109 (42.3)	416 (34.3)
Mixed adult-paediatric teaching (academic)	2511 (46.7)[a]	87 (41.2)	1280 (46.4)[a]	1080 (46.8)[a]	6916 (47.3)	635 (46.1)	5702 (47.2)	648 (53.5)
Community hospital	824 (15.3)[a]	7 (3.3)	344 (12.5)[a]	390 (16.9)[a]	1281 (8.8)	53 (3.8)	982 (8.1)	131 (10.8)
Private institution	193 (3.6)[a]	1 (0.5)	105 (3.8)[a]	68 (2.9)[a]	379 (2.6)	6 (0.4)	288 (2.4)	17 (1.4)
Years of experience of most senior team member mean ± SD, *n*	14.59 ± 9.89	14.81 ± 9.83	15.10 ± 9.82	13.96 ± 9.89[b]	14.82 ± 9.28	15.36 ± 9.10	15.06 ± 9.25	14.95 ± 9.12

ENT, ear, nose and throat. [a,b]For significance between the two groups of procedures (Pearson's chi-square test of independence and two-sample t-test, respectively, using the Benjamini-Hochberg procedure with a false discovery rate of 0.05).

The details of airway management and devices used in children with ENT surgery are summarised in Table 3. Although 69% of the children had their airway secured with a tracheal tube, 18% had a laryngeal mask airway (LMA). There were 15 patients who required more than three attempts to secure the airway with a tracheal tube and in two patients, tracheal intubation was unsuccessful. Finally, most children were extubated awake (68.5%) or had their LMA removed while they were fully awake (68.5%). It is interesting to note that 130 centres used only cuffed tubes for ENT patients, while eight used only uncuffed tubes, and both cuffed and uncuffed tracheal tubes were employed in 96 centres.

Table 3 Airway management and airway devices used in children with ear–nose–throat surgeries

	ETT, *n* (%)	SGA, *n* (%)
Tube type		
Classic	2268 (59.1)	456 (45.6)
Preformed Tubes (RAE)	1169 (30.4)	–
Reinforced tube	369 (9.6)	500 (50.0)
Nasal preformed	17 (0.4)	–
Other	17 (0.4)	44 (4.4)
ETT type		
Cuffed	2747 (71.5)	–
Uncuffed	1093 (28.5)	–
Insertion location		
First attempt	3590 (93.6)	935 (93.7)
Second attempt	229 (6.0)	56 (5.6)
More than 3 attempts	15 (0.4)	7 (0.7)
Unsuccessful	2 (0.1)	0 (0.0)
Cormack–Lehane score		
1	3331 (86.8)	–
2	464 (12.1)	–
3	37 (1.0)	–
4	4 (0.1)	–
Removal		
Awake	2630 (68.5)	677 (68.5)
Deep anaesthesia	1169 (30.4)	312 (31.5)
Left Intubated	41 (1.1)	–
Total	3840 (68.7)	1000 (17.9)

Data are presented as absolute numbers (*n*) and percentages (%). ETT, endotracheal tube; SGA, supraglottic airway.

There was an increased risk of the occurrence of perioperative laryngospasm, bronchospasm and postoperative stridor in ENT children when compared with non-ENT children. Table 4 summarises the RRs and 95% CIs of the respiratory SCEs. Laryngospasm occurred primarily during induction (n=33, 38%) and at awakening (n=48, 56%) while bronchospasm was reported at induction (n=34, 40%), maintenance (n=21, 25%) and awakening (n=40, 47%). Further analysis failed to demonstrate an effect of BMI on the incidence of respiratory SCEs (data not shown). Moreover, comparing the most frequent anaesthesia management strategies revealed a higher incidence of laryngospasm, bronchospasm and stridor in children who had combined inhalational-intravenous induction followed by those with purely inhalational maintenance (Table 5). However, no association could be detected between the incidence of respiratory complications and the induction technique *per se* (data not shown). Of those who received no NMBA for intubation, the incidence of respiratory SCEs (laryngospasm, bronchospasm and/or stridor) was 5.1 vs. 4.4% in those who were paralysed for intubation in the ENT group (RR = 0.87, 95% CI 0.64 to 1.56) and 4.2 vs. 3.3% in the non-ENT children (RR = 0.78, 95% CI 0.61 to 1.02).

The identified risk factors for the occurrence of respiratory SCEs in children undergoing ENT operations are shown in Table 6. Medical history of prematurity and the presence of airway susceptibility (recent upper respiratory tract infection, wheezing in the last 12 months and atopy) significantly increased the risk of respiratory SCEs. Moreover, children who experienced respiratory SCEs were younger and the presence of snoring was a significant risk factor, as well as the American Society of Anesthesiologists' physical status. There was no evidence for an effect of the type of institution where ENT surgery was performed but, independent of age, centres performing more than 20 ENT cases in the 2-week period had a significantly lower incidence of respiratory SCEs.

Table 4 Relative risks and 95% confidence intervals of severe respiratory critical events for ear, nose and throat operations compared with other surgical procedures (total ear, nose and throat = 5592, other = 16 013)

	ENT		Non-ENT			
	n	% (95% CI)	*n*	%	*P*	RR (95% CI)
Laryngospasm	86	1.54 (1.25 to 1.90)	191	1.19 (1.04 to 1.37)	0.049	1.29 (1.00 to 1.66)
Bronchospasm[a]	85	1.52 (1.23 to 1.88)	184	1.15 (1.00 to 1.33)	0.032	1.32 (1.02 to 1.71)
Postoperative stridor[a]	78	1.39 (1.12 to 1.74)	83	0.52 (0.42 to 0.64)	<0.0001	2.69 (1.98 to 3.66)
Any of these[a]	220	3.93 (3.46 to 4.48)	418	2.61 (2.37 to 2.87)	<0.0001	1.51 (1.28 to 1.77)

RR, relative risk. [a] For significance between the two groups of procedures (relative risk regression using the Benjamini–Hochberg procedure with a false discovery rate of 0.05).

Regarding airway management, the use of a LMA and its removal while the child was fully awake was associated with a lower risk of a respiratory SCE. However, no difference could be detected in the incidence of respiratory SCEs with the removal technique of the tracheal tube, even when considering complications at awakening and recovery (2.6% for deep vs. 1.8% for awake removal, respectively, RR = 1.44, 95% CI 0.91 to 2.26).

Figure 1 shows the distribution of the number of ENT procedures across the participating centres in the 33 European countries and the incidence of respiratory SCEs by country. A cut-off age for the occurrence of respiratory SCEs was found around 4.6 years but the area under the curve is only 0.645.

There was some evidence of a higher incidence of snoring in Hispanic children (59%) than in other ethnic origins (44% for white, 48% for Asian or Arabic and 46% for African children). However, and in line with a recent publication,[10] African children had a higher incidence of respiratory SCEs (8 vs. 3.7% for white or Hispanic, 4.5% for Asian or Arabic) giving them a RR of 2.19 (95% CI 1.29 to 3.69, $P = 0.003$). There was no difference in the incidence of stridor between uncuffed and cuffed tracheal tubes (RR = 1.031, 95% CI 0.61 to 1.74, $P = 0.908$). Finally, the presence of snoring did not seem to determine the use of NMBA for tracheal intubation overall.

Discussion

The results of this secondary analysis of the prospective observational European multicentre cohort study, APRICOT, provide additional evidence of the higher incidence of severe respiratory critical events in children having ENT surgery than in those having other surgical procedures. The younger age and the higher incidence of respiratory symptoms in their medical history contribute largely to the increased risk. Although these children were managed more frequently by specialist anaesthesiologists with occasional paediatric practice and in community or private hospitals, there was no evidence for the effect of experience of the physician or the institution on the occurrence of respiratory SCEs. However, there was some evidence for age and surgical case volume thresholds with less than 4.6 years and less than 20 cases in 2 weeks, respectively, possibly being associated with a higher occurrence of respiratory SCE.

In agreement with previous large cohort studies,[1,3] the presence of recent upper respiratory tract infection, recent wheezing, and atopy were identified in the current study as independent risk factors for respiratory SCE. Because these factors were observed more frequently in ENT patients, these children are expected to have chronic airway inflammation, which leads to airway hypersensitivity and increased risk of respiratory complications. It is therefore very important to identify those children at risk and apply individualised anaesthesia management.[11] As expected, the results of the current study confirm that a history of snoring was significantly more frequent in children admitted for ENT surgery. Although there were no specific questions assessing sleep-related breathing disorders, respiratory SCEs were more than twice as likely to occur in children with a history of snoring. This increased risk of perioperative respiratory adverse events is of the same order

Table 5 Absolute numbers (percentages) and relative risks (95% confidence interval) of severe respiratory critical events when considering anaesthesia management strategy (compared with purely inhalational induction and maintenance) in children undergoing ear, nose and throat surgery

	Purely inhalational induction + purely inhalational maintenance, *n*=1946	Combined inhalational-intravenous induction + purely inhalational maintenance, *n*=909		Purely intravenous induction + purely inhalational maintenance, *n*=1610		Purely intravenous induction + propofol intravenous maintenance, *n*=587	
Critical event	*n* (%)	*n* (%)	RR (95% CI)	*n* (%)	RR (95% CI)	*n* (%)	RR (95% CI)
Laryngospasm	29 (1.5)	24 (2.6)	1.77 (1.04 to 3.03)*	23 (1.4)	0.96 (0.56 to 1.65)	3 (0.5)	0.34 (0.11 to 1.12)
Bronchospasm	24 (1.2)	25 (2.8)	2.23 (1.28 to 3.88)*	21 (1.3)	1.06 (0.59 to 1.89)	4 (0.7)	0.55 (0.19 to 1.59)
Postoperative stridor	23 (1.2)	21 (2.3)	1.97 (1.10 to 3.54)*	13 (0.8)	0.69 (0.35 to 1.35)	6 (1.0)	0.86 (0.35 to 2.11)

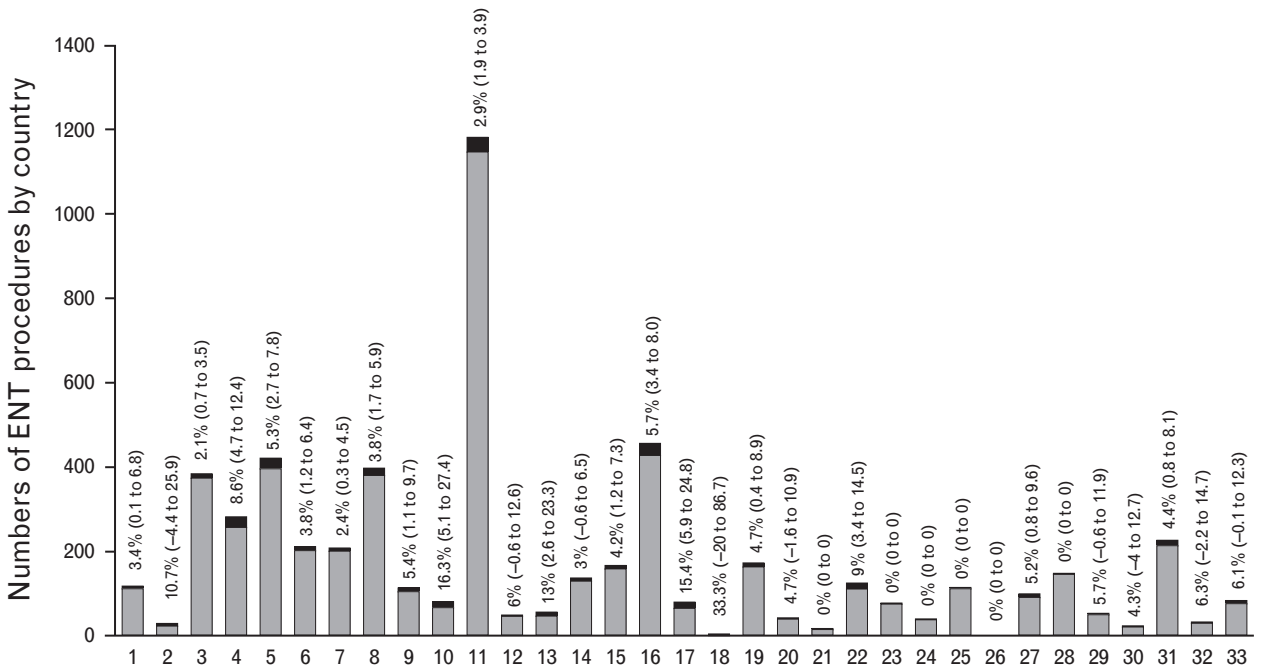
RR, relative risk. * $P < 0.05$.

Table 6 Relative risks and 95% confidence intervals of the risk factors associated with the occurrence of severe respiratory critical events (peri-operative laryngospasm, bronchospasm or postoperative stridor) in children undergoing ear, nose and throat procedures

	Univariate model									Multivariate model[a]		
	Yes			No			*P*	RR	95% CI	*P*	RR	95% CI
Risk factor	**Total**	***n***	**%**	**Total**	***n***	**%**						
Age, mean (SD)	4.5 (3.1)			6.1 (3.6)			<0.0001	0.86	0.82 to 0.91	<0.0001	0.85	0.80 to 0.90
Sex: male vs female	3218	123	3.82	2374	97	4.09	0.615	0.94	0.72 to 1.21	0.103	0.80	0.62 to 1.05
Weight, mean (SD) [RR adjusted for age]	18.21 (9.31)			24.12 (14.36)			0.131	0.97	0.93 to 1.01			
Airway sensitivity[b]										<0.0001	1.91	1.44 to 2.52
Upper respiratory tract infection in the past 2 weeks	1037	81	7.81	4383	137	3.13	<0.0001	2.50	1.92 to 3.26			
Wheezing in the past 12 months	546	52	9.52	4808	155	3.22	<0.0001	2.95	2.18 to 3.99			
Asthma diagnosis	464	25	5.39	5051	193	3.82	0.097	1.41	0.94 to 2.11			
Passive smoking	704	38	5.40	3382	133	3.93	0.079	1.37	0.96 to 1.95			
Environmental sensitivity[c]										0.167	1.24	0.92 to 1.67
Atopy	599	35	5.84	4760	172	3.61	0.008	1.62	1.13 to 2.30			
Allergy	792	33	4.17	4779	184	3.85	0.677	1.08	0.75 to 1.55			
Physical condition[d]										0.029	1.40	1.03 to 1.89
Prematurity	333	27	8.11	4710	173	3.67	<0.0001	2.21	1.49 to 3.26			
Fever	91	7	7.69	5416	211	3.90	0.066	1.97	0.96 to 4.07			
Handicap	425	20	4.71	5109	198	3.88	0.397	1.21	0.77 to 1.90			
Snoring	2306	126	5.46	2761	70	2.54	<0.0001	2.16	1.62 to 2.87			
Medication	920	51	5.54	4636	169	3.65	0.007	1.52	1.12 to 2.06			
ASA grade												
ASA 2 vs. ASA 1	1387	69	4.97	3992	138	3.46	0.011	1.44	1.09 to 1.91			
ASA 3 to 5 vs. ASA 1	211	13	6.16	3992	138	3.46	0.040	1.78	1.03 to 3.09			
Anaesthesia provider												
Type of centre												
Mixed adult-paediatric hospital vs. paediatric hospital	2599	105	4.04	1968	70	3.56	0.404	1.13	0.84 to 1.53			
Community or private hospital vs. paediatric hospital	1025	45	4.39	1968	70	3.56	0.261	1.23	0.85 to 1.78			
Anaesthesia team												
Specialist anaesthesiologist with frequent paediatric anaesthesia cases (50 to 80%) vs. specialist anaesthesiologist with mainly paediatric practice (>80%)	807	44	5.45	2569	82	3.19	0.003	1.71	1.19 to 2.44			
Specialist anaesthesiologist with occasional paediatric anaesthesia cases (<50%) vs. specialist anaesthesiologist with mainly paediatric practice (>80%)	1725	68	3.94	2569	82	3.19	0.190	1.23	0.90 to 1.69			
Anaesthesiologist in training, anaesthetic nurse or technician vs. specialist anaesthesiologist with mainly paediatric practice (>80%)	491	26	5.30	2569	82	3.19	0.021	1.66	1.08 to 2.55			
Type of centre combined with anaesthesia team[e]												
Occasional vs. paediatric										0.075	1.31	0.97 to 1.76
Trainee vs. paediatric										0.011	1.77	1.14 to 2.74
Number of ENT cases per centre >20 vs. ≤20	4094	133	3.25	1498	87	5.81	<0.0001	0.56	0.43 to 0.73	<0.0001	0.56	0.43 to 0.74
Years of experience of most senior team member, mean (SD)	13.52 (9.23)			14.64 (9.91)			0.092	0.99	0.98 to 1.00	0.452	0.99	0.98 to 1.01
Intravenous induction vs. inhalational (RR adjusted for age)	2425	74	3.05	3157	146	4.62	0.266	0.85	0.65 to 1.13	0.017	0.71	0.54 to 0.94
Interface for airway management												
SGA vs. TT	1000	24	2.40	3840	184	4.79	0.001	0.50	0.33 to 0.76	0.001	0.50	0.33 to 0.76
Face mask vs. TT	651	5	0.77	3840	184	4.79	<0.0001	0.16	0.07 to 0.39	<0.0001	0.13	0.05 to 0.31
Uncuffed vs. cuffed TT	1093	52	4.76	2747	132	4.81	0.971	0.99	0.73 to 1.36			
Deep vs. awake TT removal	1169	61	5.22	2630	121	4.60	0.420	1.13	0.84 to 1.53			
Deep vs. awake SGA removal	312	12	3.85	677	11	1.62	0.036	2.37	1.06 to 5.31			
Muscle relaxant	1857	82	4.42	3732	138	3.70	0.193	1.19	0.91 to 1.56			

For data presented as mean (SD) the first column relates to those with respiratory SCE, and the second column to those with no SCE. For data presented as option 1 vs option 2 the first set of data in the "Yes" columns refer to option 1, the second set of data in the "No" columns refer to option 2. ASA, American Society of Anesthesiologists' physical status; ENT, ear, nose and throat; RR, relative risk; SCE, respiratory severe critical events; SGA, supraglottic airway; TT, tracheal tube; URI, upper respiratory infection. [a] Variables in the multivariate model: age, sex, airway sensitivity, environmental sensitivity, physical condition, type of centre combined with anaesthesia team, number of ENT cases, years of experience of most senior team member, induction type, interface for airway management. [b] Airway sensitivity (positive respiratory history): URI less than 2 weeks or wheezing or asthma or passive smoking. [c] Environmental sensitivity: allergy or atopy. [d] Physical condition: prematurity or fever or handicap or snoring or medication or ASA status more than 2. [e] Type of centre combined with anaesthesia team: paediatric: all specialist and frequent in paediatric or mixed hospital, occasional: all occasional and frequent in community or private institution.

Fig. 1



Distribution of the number of ear, nose and throat procedures among the 33 European countries and the incidence of at least one severe respiratory critical event (95% confidence intervals) within each country.

of magnitude as that reported with the use of the STBUR (Snoring, Trouble Breathing, Un-Refreshed) questionnaire, which translates snoring into five scoring-related symptoms and correlates with the sleep-related disorders identified by polysomnography.[12,13] Considering that snoring was also found as an independent risk factor for respiratory SCEs in the whole dataset of the current cohort study,[1] it is therefore advisable to implement the STBUR questionnaire, or a similar one, in paediatric preoperative assessment, particularly in children admitted for ENT surgery.

There is still a debate in the literature about the appropriate age to refer children to dedicated paediatric centres and/or to be managed by paediatric anaesthesiologists.[14–16] Although the current secondary analysis failed to demonstrate the role of the anaesthesiologist as well as the institution, age was a strong predictor of respiratory SCEs. This finding is consistently highlighted as a risk factor in several previous publications.[2–4,17,18] We were able to identify an age threshold of 3.77 years for severe peri-operative critical events on the whole APRICOT dataset.[1] Applying similar receiver operating analysis on the ENT dataset revealed a higher age threshold for respiratory SCEs. These findings suggest that age should be part of any national or regional guidelines for the harmonisation of paediatric anaesthesia management in Europe. In addition, we observed a strong association between the volume of cases and the incidence of respiratory complications. This finding may also need to be considered in health planning where regrouping ENT services may contribute to increase patient safety.

A large variability in practice was observed among the participating centres of the different European countries, reflected also by a wide variability in case volume among centres (data not shown) and countries (Fig. 1). In contrast to the results obtained with APRICOT and those recently reported in a randomised controlled study,[19] we failed to demonstrate an effect of type of induction on the occurrence of respiratory SCEs. This discrepancy may be explained by the fact that children admitted for ENT procedures exhibit chronic airway inflammation and thus bronchial hypersensitivity that results more frequently in the occurrence of bronchospasm (Table 5), particularly if they have tracheal intubation. In addition, the current study focused on severe respiratory events and excluded minor and transient ones. Along the same lines, we observed a significantly higher incidence of respiratory SCEs with the use of tracheal intubation than with the use of a supraglottic airway device. Although this expected finding agrees with previous reports,[3,20] the lack of information about the indication for tracheal intubation and the details of the ENT procedures renders interpretation of the role of the airway device particularly hazardous. In addition, children undergoing adeno-tonsillectomies have more respiratory risk factors and these

procedures are more likely to expose the patients to a greater risk of blood aspiration. Therefore, it might be inappropriate to conclude that airway management *per se* is a risk factor for severe respiratory critical events. It is rather airway stimulation in the presence of acute or chronic inflammation of the airways and potentially a too light level of anaesthesia that may explain the higher rate of complications. Another potential factor may be related to tracheal intubation without the use of a NMBA.[1] However, the use of NMBAs varied largely between countries (a range over nine-fold) which may explain the lack of association between their use to facilitate tracheal intubation[21] and the occurrence of respiratory SCEs.

The type and incidence of reported difficult airway management in this subtype analysis of children scheduled for ENT surgery did not differ from those reported from the whole database.[22] However, it is worth mentioning that failure to intubate occurred in two ENT patients and cardiac arrest occurred in one of those, who suffered a tension pneumothorax.[22] In neither case was a NMBA given to facilitate tracheal intubation. Also of note, tracheal extubation or removal of a supraglottic airway (SGA) occurred in almost one-third of the children while they were still deeply anaesthetised. Although there was no evidence for an association between the technique of removal of the tracheal tube or SGA and the incidence of respiratory SCEs, children who had their SGA device removed when they were awake had significantly less respiratory adverse events. These results are in contrast with previous studies reporting the preventive effect of removing the tracheal tube in awake children.[3] However, to the best of our knowledge, there are still no robust studies to date focusing on the timing of the removal of the tracheal tube in the context of ENT surgery. The single identified randomised controlled trial (RCT) was not sufficiently powered to detect the occurrence of SCEs.[23] In contrast, a recent study revealed no difference in the timing of SGA device removal on the incidence of respiratory adverse events.[24] However, the authors reported more respiratory SCEs with the awake removal in the postanaesthesia care unit (PACU), which may be explained by the possible decrease in the level of monitoring in the PACU during the awakening stage of the child. In any case, the contrasting results obtained in the literature advocate for well designed large RCTs to investigate the effect of time and technique of removal of a tracheal tube or SGA device in the context of ENT surgery.

The APRICOT study was not designed primarily to investigate the specific ENT population, but this large observational cohort study reveals that ENT is the most frequently performed surgery in Europe, and thus detailed information on the management strategies of these children and on the incidence of respiratory SCEs is of great interest for future guidelines and harmonisation of best care in Europe. Despite the lack of details of the surgical procedures, the current study highlights the large variability in the incidence of respiratory SCEs and provides evidence for strong associations between known risk factors and respiratory adverse events. These observations should be taken into account while implementing good clinical practice recommendations for ENT procedures in Europe. Moreover, the current study identifies areas for targeting education and research to improve safety and quality of care in paediatric anaesthesia.

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