

## ORIGINAL ARTICLE

## Endoscopy and Procedures

# Assessment of risk factors for adverse events in analgo-sedation for pediatric endoscopy: A 10-year retrospective analysis

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**Abstract**

**Objectives:** Data regarding the occurrence of complications specifically during pediatric anesthesia for endoscopic procedures is limited. By evaluating such data, factors could be identified to assure proper staffing and preparation to minimize adverse events and improve patient safety during flexible endoscopy.

**Methods:** This retrospective cohort study included children undergoing anesthesia for gastroscopy, colonoscopy, bronchoscopy, or combined endoscopic procedures over 10-year period. The primary study aim was to evaluate the incidence of complications and identify risk factors for adverse events.

**Results:** Overall, 2064 endoscopic procedures including 1356 gastroscopies (65.7%), 93 colonoscopies (4.5%), 235 bronchoscopies (11.4%), and 380 combined procedures (18.4%) were performed. Of the 1613 patients, 151 (7.3%) patients exhibited an adverse event, with respiratory complications being the most common (65 [3.1%]). Combination of gastrointestinal endoscopies did not lead to an increased adverse event rate (gastroscopy: 5.5%, colonoscopy: 3.2%). Diagnostic endoscopy as compared to interventional had a lower rate. If bronchoscopy was performed, the rate was similar to that of bronchoscopy alone (19.5% vs. 20.4%). Age < 5.8 years or body weight less than 20 kg, bronchoscopy, American Society of Anesthesiologists status  $\geq 2$  or pre-existing anesthesia-relevant diseases, and urgency of the procedure were independent risk factors for adverse events. For each risk factor, the risk for events increased 2.1-fold [1.8–2.4].

**Conclusions:** This study identifies multiple factors that increase the rate of adverse events associated anesthesia-based endoscopy. Combined gastrointestinal procedures did not increase the risk for adverse events while combination of bronchoscopy to gastrointestinal endoscopy showed a similar risk as bronchoscopy alone.

Jan de Laffolie and Michael Sander contributed equally to this study.

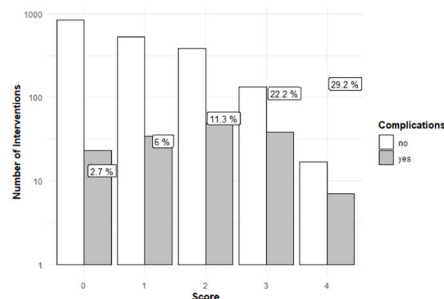
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## Risk factors during anaesthesia for paediatric endoscopy

### Score including independent risk factors for adverse events during anaesthesia for paediatric endoscopy

Score item	Point
Age < 5.8 years or body weight < 20 kg	1
ASA status > 2 or Pre-existing cardiac, respiratory, myopathic, or syndromal diseases	1
High urgency	1
Bronchoscopy	1
Sum	(Max. points: 4)



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### KEYWORDS

bronchoscopy, colonoscopy, gastroscopy, pediatric anesthesia, risk stratification

## 1 | INTRODUCTION

Anesthesia for endoscopic procedures in children represents a common, yet challenging, area of consideration in health care. A recent analysis of the American National Anesthesia Clinical Outcomes Registry showed that of 2,236,788 pediatric anesthetic encounters involving nonoperating room anesthesia, only 147,130 (6.6%) patients underwent endoscopic procedures.<sup>1</sup>

Typical complications experienced by sedated children are oversedation with hypoventilation and desaturation, aspiration, broncho-, and laryngospasm.<sup>2,3</sup> Despite the impact on a significant number of pediatric patients, recent data on the complication rate of endoscopic procedures in this population is limited, especially because a homogenous definition of adverse events during pediatric anesthesia is lacking. The Pediatric Endoscopy Database System Clinical Outcomes Research Initiative revealed an anesthesia-associated complication rate of 2.3% during pediatric gastrointestinal endoscopy.<sup>2</sup> Also, a newer study on gastrointestinal endoscopy by Kramer and Narkewicz showed an adverse event rate of 2.6%.<sup>4</sup> However, the analyses included data for American healthcare institutions and for gastrointestinal endoscopies only. A recent study of 2022 from Belgium also included next to gastrointestinal endoscopies also bronchoscopies and showed an overall adverse event rate of 2%.<sup>5</sup>

For evaluation and improvement of quality of care, collection of complication rates and exploratory identification of influencing factors from various centers is important. We report data from a single center with a severely diseased pediatric population over 10 years and aim to describe the incidence of complications to identify risk factors for adverse outcomes.

### What is Known

- Nonoperating room anesthesia is associated with an increased risk for adverse events. Pediatric endoscopy might be a relevant factor in this context.

### What is New

- The overall complication rate during pediatric endoscopy was 7.3%, which is higher than that in the general pediatric anesthesia population.
- An age < 5.8 years or body weight < 20 kg, patients with American Society of Anesthesiologists status > 2 or relevant diseases, bronchoscopies, and urgent endoscopies were independent risk factors presenting an increased risk of complications.
- Combined gastrointestinal procedures did not increase the risk for adverse events while combination of bronchoscopy and gastrointestinal endoscopy show a similar risk as bronchoscopy alone.

## 2 | METHODS

### 2.1 | Ethics

Ethical approval for this single-center study, retrospective cohort study (Ethical Committee N° AZ197/20) was provided by the Ethical Committee of the Justus-Liebig-

University of Giessen, Giessen, Germany (Chairperson Prof. Dr. H. Tillmanns) on October 13, 2020. The methods and results are reported according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines. Data were collected anonymously for all patients aged 0–17 years who underwent endoscopy at the University Hospital of Giessen between April 1, 2011, and March 31, 2021.

## 2.2 | Data acquisition and definition of study parameters

All patients were treated at the University Hospital of Giessen, a tertiary care center in Germany. Patients were included if their age was under 18 years and if they underwent any type of endoscopy with anesthesia care. Exclusion criteria were endoscopies which were performed without anesthetic support. Patients were identified automatically in the local electronic patient data management system by using a data query via the internet protocol address of the pediatric endoscopy electronic administration unit. Additionally, the anesthetic electronic patient data management system (Narkodata<sup>®</sup>) was automatically searched for the German operating code (Operationen- und Prozedurenschlüssel) encoding for either gastroscopy (synonymously esophago-gastroduodenoscopy), colonoscopy (synonymously ileocolonoscopy), or bronchoscopy to include locations for endoscopies other than the primary pediatric endoscopy laboratory.

The primary study outcome was the incidence of complications, which were defined as a composite endpoint of the following documented complication: need for intensive care unit (ICU) treatment or resuscitation, death, any emergency, or unplanned intubation after the beginning of the procedure, exceptionally difficult venous access (defined as prolonged search for venous access > 30 min), as well as the need for catecholamine therapy. Secondary study parameters were the chosen type of anesthesia, airway management, and medications. Patient characteristics included age, type of endoscopy, the medical indication of endoscopy, and underlying additional diseases, in particular, anesthesia-relevant diseases. The latter were defined as cardiac (e.g., congenital heart diseases, arrhythmias, heart transplantation, and Fontan circulation) and respiratory diseases (e.g., asthma, cystic fibrosis, congenital lung diseases), as well as severe liver and kidney insufficiency, metabolic (e.g., M Pompe, mucopolysaccharidoses, as well as others [except diabetes mellitus]) and neuropediatric diseases (e.g., epilepsy), complex congenital syndromes, and myopathies.

## 2.3 | Statistical analysis

A descriptive statistical analysis was performed. Categorical data are reported as absolute or relative frequencies whereas numeric measurements are expressed as median (interquartile range). Standard deviation scores of the body mass index (SDS BMI), weight (SDS weight), and size (SDS height) were calculated according to Kromeyer-Hauschild et al.<sup>6</sup> and by using R-package *childsds* (version 0.8.0). Analysis of differences in anesthesia times between endoscopy types was performed by using analysis of variance procedure followed by Tukey honestly significant difference test. Since several patients have been treated twice or even more, strictly speaking the data set contains repeated measurements. In terms of relation to complication rate, we did not find a significant influence of multiple treatment by logistic regression analysis [ $p = 0.65$ , odds ratio, OR: 1.08 (0.77–1.53)]. In addition, a certain period of time might have elapsed between the successive treatments, so that the numerical parameters such as height, weight, and age have also changed. Additionally, multiple treatments occurred relatively rarely. Therefore, we did not correct repeated measures in our data by means of mixed models.

To design a risk score for the prediction of adverse events, the following steps were performed. First, univariable logistic regression analysis was used to identify possibly influencing risk factors (defined as statistically significant  $p \leq 0.05$ ). Second, receiver operating characteristic (ROC) was calculated for each relevant risk factor to infer applicable cut-off values by exploiting the highest Youden index giving an indication of the optimal combination of sensitivity and specificity, respectively. The raw values for body weight were additionally converted into percentile values. Since significances were comparable to those from raw body weight, the latter ones were used for better interpretability. The model for the multivariable logistic regression analysis was optimized based on the results from univariable logistic regression analysis and the Youden index resulting from ROC analysis. Since body weight and age as well as American Society of Anesthesiologists (ASA) status and pre-existing relevant diseases are strongly correlated according to Pearson's correlation coefficient, a combination of both, respectively, was used for the design of the multivariable model. Based on the resulting model, a score incorporating six relevant variables into one single value running from 0 to 4 was generated by adding score points each of the following aspects: (1) bronchoscopy (yes/no), (2) urgency (yes/no), (3) representing high ASA or belonging to a special patient group, and (4) weight or age below respective thresholds. Recursive partitioning and

graphical display were performed with R package rpart (version 4.1.19).<sup>7</sup> Finally, logistic regression for the resulting score was calculated. All statistical analyses were performed using statistical software R version 4.2.3 (2023-03-15 ucrt) ([www.r-project.org](http://www.r-project.org)).

### 3 | RESULTS

In total, over a period of 10 years, 2064 endoscopic interventions in 1613 patients were included in the study. 1348 (83.6%) patients were examined once, while 265 (16.4%) patients received more than one endoscopic procedure at different time points (of these 166 [10.3%] twice). No patient was excluded. Baseline characteristics are shown in Table 1 while details on the pre-existing diseases which were

**TABLE 1** Basic characteristics of the study population and characteristics of the endoscopy.

Parameter	Values
Age (years)	9.1 [4.1–14.2]
Sex	
Female	1034 [50.1%]
Age groups (%)	
Infant (1–12 months)	124 (6.0)
Toddler (12 months to <6 years)	567 (27.5)
Schoolchild (≥6–<12 years)	662 (32.1)
Adolescents (≥12–<18 years)	711 (34.4)
Total body weight (kg)	
Infant (1–12 months)	6.6 [5.6–8.1]
Toddler (12 months to <6 years)	13 [10.5–16]
Schoolchild (≥6–<12 years)	30 [24–39]
Adolescents (≥12–<18 years)	54 [45–65]
SDS body weight	
Infant (1–12 months)	−1.01 (−1.93 to −0.02)
Toddler (12 months to <6 years)	−0.66 (−1.65 to 0.21)
Schoolchild (≥6–<12 years)	−0.57 (−1.55 to 0.33)
Adolescents (≥12–<18 years)	−0.37 (−1.56 to 0.53)
ASA (%)	
I	524 (25.4)
II	1130 (54.7)

**TABLE 1** (Continued)

Parameter	Values
III	389 (18.8)
IV	21 (1.0)
Disease leading to endoscopy (%)	
Cardiac	15 (0.7)
Central nervous system	36 (1.7)
Gastrointestinal	1713 (83)
Consequence of preterm birth	3 (0.1)
Metabolic	11 (0.5)
Respiratory	246 (11.9)
Oncologic	33 (1.6)
Other syndromes	7 (0.3)
Patients with pre-existing disease relevant for anesthesia according to following groups (%) <sup>a</sup>	644 (31.2)
Complex congenital heart disease	163 (7.9)
Moderate to severe respiratory diseases	268 (13.0)
Severe liver disease	12 (0.6)
Severe kidney disease	21 (1.0)
Severe metabolic and myopathic diseases	180 (8.7)
Severe neuropediatric disease	294 (14.2)

*Note:* Data are presented either as median and interquartile range (square brackets) or as percentage (round brackets) of absolute numbers.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; SDS, standard deviation score.

<sup>a</sup>Multiple pre-existing diseases/disease groups in one patient were possible.

assumed relevant for the anesthesia can be found in Supporting Information S1: Table 1.

### 3.1 | Endoscopic management

Gastroscopy was the most often performed procedure ( $n = 1356$  [65.7%]) followed by combined procedures ( $n = 380$  [18.4%]), bronchoscopies (235 [11.3%]), colonoscopies (93 [4.5%]). Most frequently, endoscopy was performed for biopsies (or other removal of pathologic tissues,  $n = 909$  [44%]) or for diagnostic purposes/follow-ups (693 [33.6%]). In 86.7% of cases, the procedure was planned electively. Details on the

endoscopic procedures are shown in Supporting Information S1: Table 2; Figures 1 and 2.

### 3.2 | Anesthetic management

All patients were treated by a board-certified anesthesiologist and an anesthetic nurse. Summarized over all included patients, sedation under spontaneous ventilation and oxygen supplementation was the most favored type of anesthesia for endoscopy ( $n = 1649$  [79.9%]). If airway management was conducted before the procedure, patients were intubated with an endotracheal tube in 185 cases (9.0%) and a laryngeal mask in 52 cases (2.5%), while mask ventilation was performed in 165 cases (8.0%), respectively. In 0.6% of cases, no data was available regarding the type of ventilation. Supporting Information S1: Tables 3 and 4 provide an overview of the used airway techniques in dependence of the age and type of endoscopy. In 1513 (73.4%) cases, the patients received opioids for analgesia.

Pharmacologic anesthetic management included a variety of drugs. In summary, 1513 (73.4%) of patients received opioids for analgesia. For opioids, pethidine ( $n = 1534$  [74.3%]) was used most frequently, while fentanyl ( $n = 187$  [9.1%]), piritramide ( $n = 60$  [2.9%]), remifentanyl ( $n = 24$  [1.2%]), and nalbuphine ( $n = 7$  [0.3%]) were less often used. The most used hypnotics and sedatives were propofol ( $n = 1437$  [69.6%]) and midazolam ( $n = 1360$  [65.9%]). Inhalative anesthetics were used in 283 (13.7%) of cases, in which sevoflurane was most often used ( $n = 266$ , 12.8%).

### 3.3 | Adverse events

In total, 151 (7.3%) cases with adverse events were registered, of which 73 suffered from two or more complications. No patient died during the observation period; one child (0.0004%) was successfully resuscitated after a hypoxia-related cardiac arrest, and 41 (2.0%) patients were transferred unplanned to the ICU after endoscopy. The child in need of resuscitation suffered from a cardiac arrest during the induction of sedation before the endoscopy. Beyond, it was considered as ASA III because of pre-existing congenital heart disease and trisomy 21. Respiratory complications were most common (65 [3.2%]), followed by cardiovascular events (23 [1.1%]), allergic reactions (11 [0.5%]), exceptionally difficult venous access (four [0.2%]), and cerebral convulsions (three [0.1%]). In 12 cases (0.6%), endoscopic problems led to a change of the anesthetic regime. Thirty-three adverse events were characterized by more than one problem making it impossible to define retrospectively the primary cause of complication

(e.g., combined respiratory and circulatory failure leading to cerebral convulsions, intubation, and ICU admission). Yearly complication rates were stable over the observation period ( $7.2\% \pm 2.5\%$ , Supporting Information S1: Figure 3). In this setting, no child suffered from long-term sequelae of adverse events in this setting.

The duration of the induction of narcosis, anesthesia, and the endoscopic procedure was significantly associated with the onset of complications (induction: OR: 1.09 [1.07–1.12], endoscopy: OR: 1.01 [1.01–1.02], duration of anesthesia: OR: 1.03 [1.02–1.03], all  $p < 0.001$ ). Respiratory adverse events included 28 (1.4%) cases of severe bronchospasms, 19 (0.9%) cases of hypoventilation-induced hypoxemia, six (0.3%) patients with life-threatening laryngospasm, respectively, six (0.3%) patients with stridor. In three cases each (0.14%), either tracheal intubation was described as difficult or pulmonary aspiration occurred. In summary, 41 (2.0%) patients were intubated unplanned. Patients who were intubated endotracheally showed a similar rate of adverse events (32.4% [60/185]) compared to those with a laryngeal mask (34.6% [18/52]), while patients with spontaneous breathing experienced the lowest risk (3.2% [52/1649]). The type of medication did not influence the rate of adverse events.

In relation most complications were present during bronchoscopies but in absolute numbers most complications occurred during gastroscopies because of the higher number of procedures. The combination of different types of gastrointestinal endoscopies did not result in an increase of complications but if bronchoscopies were additionally performed, the complication rate was comparable to bronchoscopies alone (19.5 vs. 20.4%, Table 2). Diagnostic gastroscopies showed an adverse event rate of 5.5% (75/1356), while it was higher in cases of percutaneous endoscopic gastrostomy insertion (13.5%, 30/221) and removal of foreign bodies (10.5%, 11/105). Although colonoscopy was associated with a low risk (3.2%, 3/93), the risk increased in patients with lower intestinal bleeding (14.3%, 1/7). Regarding their complication rates, diagnostic bronchoscopies were safer than interventional bronchoscopic procedures (16.7% [8/48] vs. 21.4% [40/187]). The highest rate of adverse events, at 32.5% (13/40), was observed during the removal of foreign bodies, while the second lowest rate occurred during bronchoscopic biopsies, at 19.1% (27/141).

Univariable analysis revealed that age, weight, ASA status, pre-existing relevant diseases, urgent endoscopies, and especially bronchoscopy put the patients at odds for adverse events, while nil per os (NPO) status did not influence these odds (Table 3). A subanalysis revealed that congenital heart disease and moderate to severe respiratory conditions increased particularly the risk for complications, while neuropediatric and metabolic diseases did not influence the rate of

**TABLE 2** Demonstration of the complications in dependence of the type of endoscopy.

	•	•	•	•	•	•	•
Bronchoscopy							
Gastroscopy							
Colonoscopy							
Total	(n = 235)	(n = 1)	(n = 26)	(n = 2)	(n = 1356)	(n = 93)	(n = 351)
Overall complications							
Yes	48 (20.4)	0 (0)	5 (19.2)	0 (0)	75 (5.5)	3 (3.2)	20 (5.7)
No	187 (79.6)	1 (100)	21 (80.8)	2 (100)	1281 (94.5)	90 (96.8)	331 (94.3)
Unexpected ICU admission	3 (1.3)	0 (0)	1 (3.8)	0 (0)	13 (1)	1 (1.1)	1 (0.3)
Need for catecholamines	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	1 (0.3)
Emergency intubation	12 (5.1)	0 (0)	2 (7.7)	0 (0)	5 (0.4)	1 (1.1)	1 (0.3)
Unexpected ICU admission	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
General reactions	0 (0)	0 (0)	1 (3.8)	0 (0)	8 (0.6)	0 (0)	1 (0.3)
Need for catecholamines	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	0 (0)
Respiratory events	17 (7.2)	0 (0)	0 (0)	0 (0)	19 (1.4)	1 (1.1)	4 (1.1)
Alterations of the central nervous system	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.3)
Unexpected ICU admission	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.2)	0 (0)	1 (0.3)
Need for catecholamines	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.1)	0 (0)	0 (0)
Emergency intubation	3 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Emergency intubation with unexpected ICU admission	7 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.6)
Hemodynamic reactions	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	0 (0)
Need for catecholamines	3 (1.3)	0 (0)	0 (0)	0 (0)	8 (0.6)	0 (0)	3 (0.9)
Emergency intubation, and need for catecholamines	0 (0)	0 (0)	1 (3.8)	0 (0)	1 (0.1)	0 (0)	0 (0)
Unexpected ICU admission and need for CPR	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	0 (0)
Respiratory event and emergency intubation	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Respiratory event, emergency intubation, and need for catecholamines	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	0 (0)
General lesions	1 (0.4)	0 (0)	0 (0)	0 (0)	2 (0.1)	0 (0)	0 (0)
Unexpected ICU admissions	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	0 (0)
Central nervous system	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.2)	0 (0)	1 (0.3)
Others							
Unexpected ICU admissions	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.1)	0 (0)	1 (0.3)
Emergency intubation	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	1 (0.3)
Emergency intubation and unexpected	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	1 (0.3)
ICU admissions	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	1 (0.3)

Abbreviations: CPR, cardiopulmonary resuscitation; ICU, intensive care unit.

complications (Table 3). Subsequently, ROC analysis was performed for numerical variables age and weight, which resulted in an area under the receiver operating curve (AUCROC) = 0.67 for weight and AUC = 0.66 for age. To identify appropriate thresholds, we referred to the Youden index and found the most appropriate threshold for age to be 5.8 years (Youden's index = 1.28, specificity = 0.70, sensitivity = 0.58, AUCROC =

0.64) and for weight to be 19.9 kg (Youden's index = 1.31, specificity = 0.67, sensitivity = 0.64, AUCROC = 0.67). The Youden's index for 20 kg was identical and, therefore, used for practicability.

According to logistic regression analysis, the odds for adverse events decreased by 3% per increase of 1 kg body weight (Table 3). Further, the deviation of the children size expressed as SDS BMI, SDS weight, or

**TABLE 3** Results of the univariable analysis.

Factor	n	Odds ratio	Confidence Interval	p Value
Age (per age class)				
Infant (1–12 months)	124	5.36	2.98–9.62	<0.001
Toddler (12 months to <6 years)	567	3.15	2.01–4.95	<0.001
Schoolchild (≥6–<12 years)	662	1.19	0.71–2.00	0.50
Adolescents (≥12–<18 years, control)	711			
Age (per year gain)	2064	0.90	0.87–0.93	<0.001
Sex	2064	1.36	0.97–1.90	0.085
Body weight (kg) (per weight class)				
>60 (control)	251			
50–60	237	0.86	0.35–2.12	0.74
40–50	258	0.97	0.41–2.28	0.95
30–40	247	0.73	0.29–1.85	0.51
20–30	315	1.17	0.53–2.56	0.70
15–20	214	1.88	0.86–4.11	0.11
10–15	285	3.26	1.63–6.53	<0.001
5–10	229	4.46	2.23–8.93	<0.001
0–5	28	2.73	0.71–10.46	0.14
Increase per kg body weight gain	2064	0.97	0.96–0.98	<0.001
SDS BMI	2064	0.97	0.88–1.07	0.61
SDS body weight	2064	0.94	0.87–1.02	0.16
SDS body height	2064	0.94	0.86–1.02	0.15
Type of endoscopy				
Gastroscopy	1735	0.33	0.23–0.48	<0.001
Bronchoscopy	264	1.16	1.12–1.20	<0.001
Colonoscopy	440	0.58	0.36–10.93	<0.05
NPO status				
NPO	2004			
Not NPO	53	1.37	0.54–3.49	0.51
ASA unit	2064	1.61	1.27–2.04	<0.001
ASA				
I	524			
II	1130	1.26	0.81–1.97	0.31
III	389	2.14	1.30–3.53	<0.01
IV	21	7.09	2.55–19.66	<0.001

**TABLE 3** (Continued)

Factor	n	Odds ratio	Confidence Interval	p Value
Urgency of the endoscopy				
Elective patients 1790				
12–24 h	113	1.31	0.65–2.66	0.46
6–12 h	19	4.03	1.32–12.36	<0.05
<6 h	70	3.45	1.83–6.49	<0.001
Next free endoscopic capacity				
Immediately	18	4.32	1.40–13.35	<0.05
Relevant diseases				
Patients without 1420				
Patients with 644				
Type of diseases				
Complex congenital heart disease	163	3.67	2.36–5.70	<0.001
Moderate to severe respiratory diseases	268	3.21	2.17–4.77	<0.001
Severe liver disease	12	1.15	0.15–8.99	0.89
Severe kidney disease	21	2.13	0.62–7.33	0.23
Severe metabolic and myopathic diseases	147	1.29	0.75–2.22	0.36
Severe neuropaediatric disease	294	1.31	0.83–2.07	0.25

Note: Age categories were compared to the group of adolescents, while colonoscopy was the control group in the category “endoscopy,” and weight compared to weight >60 kg body weight. Fasting was compared to patients with appropriate fasting, ASA to ASA score I, and sex to female sex. Last, urgency of endoscopy refers to elective patients.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; NPO, nil per os; SDS, standard deviation score.

SDS height did not influence the incidence of complications.

### 3.4 | Risk prediction

To develop a risk score, we included all statistically significant variables, considering their respective thresholds into a multivariable model (Table 4). Because the variables age and weight (Pearson's correlation coefficient 0.86;  $p < 0.001$ ) as well as ASA

**TABLE 4** Results of the multivariable analysis.

Factor	Odds ratio	Confidence Interval	p Value
Bronchoscopy	2.77	1.87–4.09	<0.001
Age < 5.8 years or weight < 20 kg	2.43	1.68–3.52	<0.001
Age < 5.8 years	1.12	0.59–2.11	0.73
Weight < 20 kg	2.26	1.18–4.32	<0.05
ASA status > 2 or relevant diseases	1.58	1.10–2.27	<0.05
ASA status > 2	1.03	0.67–1.58	0.88
Patients with relevant diseases	1.80	1.21–2.71	<0.01
Urgency of the endoscopic procedure (not elective)	1.69	1.11–2.56	<0.05

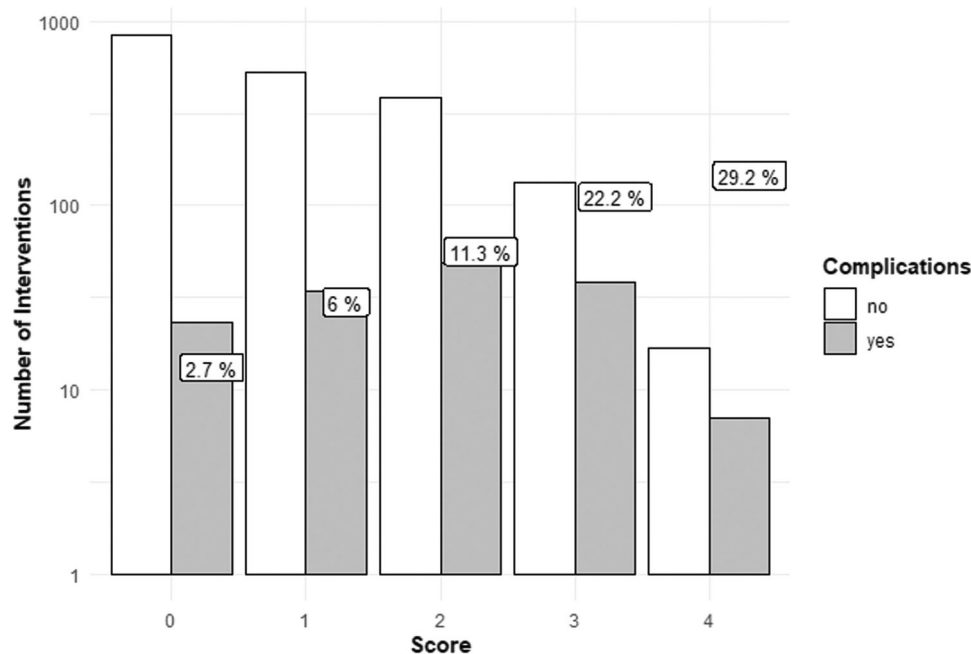
Abbreviation: ASA, American Society of Anesthesiologists.

status and pre-existing diseases (Pearson's correlation coefficient 0.48;  $p < 0.001$ ) were correlated, we combined both into one variable, respectively (Table 4).

Finally, the score consisted of four items of the multivariable analysis, resulting in four points at maximum (Table 4, Supporting Information S1: Table 5). On average each increase of the score value of one point resulted in a 2.1-fold ([1.8–2.4],  $p < 0.001$ ) increase of odds for complications (Figure 1). The rate of adverse events when four points are fulfilled is 29.2%. The score showed a sensitivity for complication of 0.62 and specificity of 0.72 (AUCROC 0.72; Supporting Information S1: Figure 4). It reflected an age and weight-dependent increase of risks for

adverse events, with the highest risk predicted when combined with the other risk factors “bronchoscopy” and “pre-existing diseases.”

To facilitate the risk score for daily practice, we performed recursive partitioning and included next to bronchoscopy (in terms of the strongest risk factor) also SDS weight and SDS height because of its pivotal role in pediatric daily practice. The resulting decision tree is depicted in Supporting Information S1: Figure 4 and shows an increase of risks for adverse events already for application of bronchoscopy procedure. In cases, where other procedures than bronchoscopy are applied, the risk increases for extremely undersized and underweight children. This applies to 7% of the patients [ $n = 138$ ].



**FIGURE 1** Logarithmic demonstration of number of cases with complications along score categories. Percentages nominate the proportion of cases with complications in each score category (128 out of 151 cases, with complications having a score higher than zero).

## 4 | DISCUSSION

Pediatric endoscopy remains a challenge to the anesthetist but also to the interventional pediatrician and requires, therefore, a multiprofessional and carefully planned approach.<sup>8</sup> The study (i) showed an overall complication rate of 7.3%, (ii) identified an age < 5.8 years, a body weight < 20 kg, bronchoscopy, pre-existing relevant diseases, ASA status  $\geq 2$ , and urgent endoscopies as the main contributors for an increased risk for adverse events, and (iii) provides a score with the aim for risk stratification.

At first, the overall complication rate appears higher than in comparable studies, but it is important to highlight that this study included gastrointestinal endoscopies and bronchoscopies. This is of importance because bronchoscopies are one of the main drivers for an increased risk for adverse events. Nevertheless, we chose not to exclude bronchoscopies from the analysis because it would not reflect daily life. Particularly, in the United States (but also in Europe), aerodigestive specialist centers are enhancing and address diseases of the upper digestive tract as well as of the respiratory organs in a holistic approach. This gains increasing recognition and many university hospitals have already implemented them.<sup>8–10</sup> Consequently, in our department (and many others in Europe) the anesthetist faces all types of endoscopies and, particularly, an increasing number of combined procedures such as gastroscopy and bronchoscopy during one anesthetic session including also interventional procedures which show even higher complication rates than diagnostic procedures. This reduces stress for the child and the family and adds to a decrease of the disease burden but on the other hand must be recognized in the risk prediction especially if bronchoscopic interventions are planned.

Even though the complication rate appears high, it is comparable to other studies. The pediatric sedation research consortium database performed a subanalysis on 12,030 gastrointestinal endoscopic procedures and revealed an overall adverse event rate of 4.8% which is comparable to our results (gastroscopy 5.5% and colonoscopy 3.8%).<sup>11</sup> Similar to our results, there were no descriptions of lethal complications or need for resuscitation, and respiratory problems were the most common sources of adverse events. Still, the rate of adverse events was higher in our cohort; this can most likely be explained by the inclusion of bronchoscopic procedures, as they displayed an independent risk factor for adverse events in our study but also in comparable studies.<sup>12</sup> For example, a retrospective analysis of 670 children undergoing anesthesia for bronchoscopy in a tertiary center demonstrated a complication rate of 7.2%.<sup>13</sup> Last, our study included more patients with an ASA score  $\geq 3$  (19.8% vs. 6.8%) which is most likely caused by the monocentric design

of our study. The study by Kramer and Narkewicz revealed a lower complication rate but cannot be compared with our study because we concentrated on anesthetic complications and not on procedural adverse events like Kramer and Narkewicz.<sup>4</sup> From the patients' view it is of high importance to describe all types of complications because they will not differentiate between endoscopic and anesthetic complications.

The most prominent study about adverse events in general pediatric anesthesia remains the anesthesia practice in children observational trial (APRICOT) study; it revealed a complication rate of 5.2% (95% confidence interval: 5.0–5.5), indicating that pediatric anesthesia for endoscopy is associated with an elevated risk for adverse events.<sup>14</sup> It showed that compared to surgery, nonsurgical procedures were associated with less risks for adverse events (relative risk 1.19 [1.02–1.39],  $p = 0.025$ ). However, this did not reach statistical significance in the multivariable analysis. This indicates that nonsurgical anesthesia is not less dangerous than surgery. It remains unclear if anesthesia for endoscopy might increase the risk for complication in such manner that it is comparable with surgery. On the other hand, it must be mentioned that only a small number of endoscopies and particularly bronchoscopies were included. Further, compared to our study, the APRICOT study included significantly fewer patients with an ASA status  $\geq 3$  (19.8% vs. 11.3%) which might also explain the lower complication rate. Notably, as in our study, most adverse events were of respiratory origin. In all mentioned studies, anaphylaxis was a rare (<0.1%) complication.<sup>11,13–15</sup>

Multivariable analysis showed that an age < 5.8 years, a body weight < 20 kg, bronchoscopy, pre-existing relevant diseases, ASA status  $\geq 2$ , and urgent endoscopies displayed independent risk factors for complications, whereas NPO status did not influence the children's risk. While other studies examining general pediatric anesthesia populations specifically identified toddlers and infants as patients with an increased risk for adverse events, this study demonstrates that the complication rate during anesthesia for endoscopy already rises in preschool children under the age of 5.8 years.<sup>11,16</sup> This was substantiated by a secondary analysis of the APRICOT study, which showed that especially neonates and small children were associated with an increased risk for intubation failure.<sup>17,18</sup> Due to its retrospective design, the study cannot conclusively determine whether the method of airway management (endotracheal intubation or laryngeal mask) itself poses a risk factor for adverse events. It was not feasible to ascertain whether a protected airway was primarily chosen for critically patients, although this assumption seems reasonable. The potential correlation between complex patient conditions and the choice of a protected airway could cause a selection bias. Consequently, isolating the risk solely

attributable to either intubation or laryngeal mask use is unfeasible, and the study is confined to delineating the heightened incidence of adverse events linked to airway management. Further, it was surprising that neither SDS BMI, SDS weight, nor SDS height influenced the risk for complications indicating that the absolute size of the child matters for the anesthetic management rather than age-related deviation regarding weight or size. While it is well-described that obesity is a risk factor for anesthesiologic complications, only little is known on the complication rate of moderate underweight patients.<sup>19,20</sup> The fact that our study included moderately underweighted children on average might explain why the neither the SDS BMI, SDS weight, nor the SDS height were associated with the rate of adverse events.

Our findings indicate that congenital heart and moderate to severe respiratory diseases are the main contributors to the risk factor “pre-existing diseases” which is supported by the literature.<sup>21–23</sup> Patients with congenital heart disease may experience varying degrees of risk depending on the type and severity of their cardiac defect and its correction. In this study, approximately a third of patients suffered from severe cardiac conditions explaining the strong influence on the onset of adverse events.<sup>21</sup> Nevertheless, to the opinion of the authors also neuropsychiatric and metabolic diseases should be addressed with care because they commonly suffer from muscle weakness affecting respiratory function.<sup>24</sup>

Another important finding from the multivariable analysis is that bronchoscopies increase the risk for adverse events by an OR of 2.7. This underlines the fact that from a clinical point of view, pediatric gastrointestinal endoscopy cannot be compared with bronchoscopy. Still, both types of endoscopies are declared as nonoperating room anesthesia procedures and are, therefore, planned and performed in a similar way. The anesthetist should be aware of a higher risk for respiratory events in these patients and plan the procedure thoroughly in a team with the pediatrician. It is well-known that a multiprofessional and experienced team is able to reduce the risk for adverse events.<sup>14,25,26</sup> As mentioned earlier, this finding is particularly significant for specialized aerodigestive centers, where combined procedures and interdisciplinary decision-making are integral to their holistic approach. Although a longer duration of narcosis induction, anesthesia, and endoscopic procedures was associated with an increased risk of adverse events, it cannot be definitively concluded that these procedures caused this outcome. Given the retrospective design of the study, no definitive conclusions can be drawn regarding underlying causal relationships; however, it seems reasonable to consider that managing complications may have contributed to prolonged procedure durations. The risk of combined

gastrointestinal endoscopies was not higher than of sole gastro- or colonoscopies and comparable to the abovementioned studies. But if combined with bronchoscopies the incidence of adverse events was significantly higher underlining their influence on the risk development.

We summarized the independent risk factors deriving from the multivariable analysis in a score with six score items. Some of the score items confirm the results of Biber et al., who identified an age under 5 years, an ASA status >2, combined procedures, and diseases accompanied with obesity or lower airway diseases as anesthesia-related risk factors in children undergoing gastroscopy and colonoscopy, but not bronchoscopy.<sup>11</sup>

To the knowledge of the authors, this study presents the first score for the risk prediction for anesthesia in pediatric endoscopy. Per positive risk factor, the odds for the occurrence of complications doubled. However, it must be mentioned that with an AUCROC of 0.72, the predictive value is only moderate. This is mainly explainable by the low sensitivity of the score, which might be caused by the relatively wide range of body weight and age. Since the predictive value of the score is limited, we chose to characterize the score items in combination with the SDS weight and size by using recursive partitioning which showed that the risk of adverse events increased with extreme deviation of size (SDS < -3) and weight (< -2.1) especially if the risk is not already increased by the use of bronchoscopy.

There are some limitations to this study. First, due to its retrospective design, no causative conclusions about the risk factors can be drawn and the results need to be validated by a prospective cohort. This is particularly relevant for the chosen anesthetics and airway strategies. Complicated cases likely received adaptations to the anesthetic regimen, which may have introduced selection bias. Due to the retrospective design, it is not possible to investigate how these adapted strategies influenced patient outcomes. An internal validation cohort was not feasible due to the limited number of these patients in our study cohort. Second, it cannot be ruled out that especially minor complications have not been documented properly, which also might have influenced the rate of complications. Nevertheless, due to their consequences (e.g., ICU admission, unplanned intubation, rescue medication), it can be assumed that all severe complications were documented and, therefore, are also part of the study. Third, it was not possible to test the type of anesthetic on its influence on adverse events because they were commonly combined (e.g., midazolam and propofol or propofol for the induction of narcosis and inhalative agents). Finally, the experience of the anesthetist or the interventionalist was not analyzed due to the absence of quantifiable data on their actual

experience in the field of pediatric anesthesia or endoscopy, despite all patients being treated by consultant specialists.

## 5 | CONCLUSION

In summary, the overall complication rate among these patients is 7.3%, which is higher than that in the general pediatric anesthesia population. An age < 5.8 years or body weight < 20 kg, patients with ASA status > 2 or relevant diseases, bronchoscopies, and urgent endoscopies were independent risk factors presenting an increased risk of complications. Combined gastrointestinal procedures did not increase the risk for adverse events while the combination of bronchoscopy and gastrointestinal endoscopy show a similar risk as bronchoscopy alone. This finding might help to identify high-risk procedures in advance that need to be staffed by a specialized dedicated pediatric anesthesia team.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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