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A European multicenter outcome study on the different perioperative airway management policies following midface surgery in syndromic craniosynostosis: a proposal for a Standard Operating Procedure.

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Conflicts of interest

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Abstract

Background: Perioperative airway management following midface advancements in children with Apert and Crouzon/Pfeiffer syndrome can be challenging, and protocols often differ. This study examined airway management following midface advancements and postoperative respiratory complications.

Methods: A multicenter, retrospective cohort study was performed to obtain information about the timing of extubation, perioperative airway management, and respiratory complications after monobloc / le Fort III procedures.

Results: Ultimately, 275 patients (129 monobloc and 146 Le Fort III) were included; 62 received immediate extubation and 162 delayed extubation; 42 had long-term tracheostomies and nine perioperative short-term tracheostomies. Short-term tracheostomies were in most centers reserved for selected cases. Patients with delayed extubation remained intubated for three days (IQR 2 – 5). The rate of no or only oxygen support after extubation was comparable between patients with immediate and delayed extubation, 58/62 (94%) and 137/162 (85%) patients, respectively. However, patients with immediate extubation developed less postoperative pneumonia than those with delayed, 0/62 (0%) versus 24/161 (15%) (P = 0.001), respectively. Immediate extubation also appeared safe in moderate/severe OSA since 19/20 (95%) required either no or only oxygen support after extubation. The odds of developing intubation-related complications increased by 21% with every extra day of intubation.

Conclusions: Immediate extubation following midface advancements was found to be a safe option, as it was not associated with respiratory insufficiency but did lead to fewer complications. Immediate extubation should be considered routine management in patients with no/mild OSA and should be the aim in moderate/severe OSA after careful assessment.

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Introduction

Apert and Crouzon/Pfeiffer syndrome are two forms of syndromic craniosynostosis characterized by multiple suture synostosis, midface hypoplasia, and exorbitism. As a result of their midface hypoplasia, two-thirds of these children are affected by obstructive sleep apnea (OSA).[1] Other potential airway-obstructing abnormalities in these children are choanal atresia, nasal septum deviation, hypertrophic adenoid or tonsils, mandibular hypoplasia, palatal deformities, and tracheal cartilage anomalies.[2-5] Upper airway endoscopy showed that the airway obstruction in these children is often multi-level, and children without OSA can also have partial obstructions.[6,7]

Midface hypoplasia and exorbitism can be surgically treated with a monobloc procedure, Le Fort III, a variant of these procedures (such as Le Fort II with simultaneous zygomatic repositioning) or facial bipartition, and is usually combined with distraction.[8] Blood loss during these advancements can be excessive, and transfusion is generally needed.[9] The difficult airway, high prevalence of OSA, profuse intraoperative bleeding with high transfusion rate, and anticipated postoperative swelling of the upper airway cause anesthesiologic concerns following midface advancements in these children.[9-13]

Little is known about the safety of immediate extubation and (respiratory) complications after midface advancements. Standard Operating Procedures (SOP) differ among hospitals and often lack scientific foundations. This multicenter study aimed: 1) to examine airway management following midface advancement regarding respiratory outcome and complications in children with Apert and Crouzon/Pfeiffer syndrome within several European centers of expertise; 2) to formulate principles for a collective SOP for perioperative airway management following midface surgery in these children.

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Methods

Participating craniofacial centers of expertise

Given the study's retrospective nature, it was exempted from review by the Dutch institutional research ethics committee. University Hospital 12 de Octubre (Madrid, Spain), Sahlgrenska University Hospital (Gothenburg, Sweden), Oxford Craniofacial Unit (Oxford, United Kingdom), Charité University Hospital (Berlin, Germany), Provincial Specialist Children's Hospital (Olsztyn, Poland), Hôpital Necker-Enfants Malades (Paris, France), and Erasmus Medical Centre (Rotterdam, the Netherlands), all members of the European Reference Network CRANIO, participated in this multicenter study.

Outcome variables and data collection

All Apert and Crouzon/Pfeiffer children who had undergone a midface advancement between December 1983 and August 2022 (i.e., monobloc, facial bipartition, Le Fort III, or variant) were eligible for inclusion. The center's inclusion periods could vary based on the availability of older patient files. Patients were split into four groups based on perioperative airway treatment: patients were scored as immediate extubation if they were extubated directly after surgery in the operating room; patients were categorized as delayed extubation if they received prolonged intubation and were extubated later on at the intensive care unit (ICU); patients were scored as short-term/ elective tracheostomy if they were tracheostomized to bridge surgery; patients were scored as long-term tracheostomy if they were tracheostomized in case of severe OSA and not only to bridge surgery.

Primary outcomes were respiratory support after extubation or ceasing mechanical ventilation in tracheostomy patients and postoperative pneumonia. Secondary outcomes were types of postoperative respiratory support and complications. Demographic data (gender, diagnosis, age, OSA), surgical data (type of surgery, indication of surgery, intraoperative estimated blood loss (EBL), intraoperative transfused blood volume), anesthesiologic data

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(timing of extubation, numbers of days intubated, indication for tracheostomy or delayed extubation, respiratory support before and after extubation), and postoperative (respiratory) complications were collected from patients files. Files were scanned until one month postoperatively for complications. The collected intubation-related complications were pneumonia and pressure ulcers.[14-17] The obstructive apnea-hypopnea index (oAHI) obtained from polysomnography was used to classify OSA: no/mild OSA = oAHI < 5; moderate OSA = oAHI ≥ 5 and < 10, severe OSA = oAHI ≥ 10.

Surgical treatment

The type of midface advancement was determined by individual facial abnormalities, the presence of increased intracranial pressure or need for additional forehead advancement, the surgeon's preference and expertise, and the patient's or parent's wishes. Given the severity of midface hypoplasia in both syndromes, there is often an indication of distraction.

Statistical analysis

Data were imported into R statistical software (version 4.1.2, R Foundation for Statistical Computing) for analysis. Histograms and QQ-plots were evaluated to assess the distribution of continuous variables. Normally distributed continuous data are presented as means with standard deviation and skewed data as medians with interquartile ranges (IQR). Categorical data are presented as counts and proportions.

A Chi-square test of independence was performed to assess the relationship between respiratory support after extubation or postoperative pneumonia between patients with immediate and delayed extubation. A Bonferonni correction was used to correct for multiple testing, and a p-value of 0.05/2 = 0.025 was considered statistically significant. Due to the small sample size of patients with tracheostomies, no statistical analysis was performed between patients with short-term and long-term tracheostomies, and only descriptive statistics were provided. Logistic regression was used to investigate the effect size of

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intubation/mechanical ventilation duration on intubation-related complications, corrected for OSA and transfused blood volume (ml/kg). Multiple-imputation-by-chained equation (MICE package) was used to handle missing values. An odds ratio (OR) with a corresponding 95% confidence interval was calculated. Detailed information on the multiple imputation method used can be found in the appendix (see Appendix, Supplemental Digital Content 1). The Hosmer-Lemeshow test (ResourceSelection package) was used to test the goodness-of-fit of the model.

Results

Study population

Eventually, 275 patients, 129 monobloc and 146 Le Fort III procedures, were included; 62 patients received immediate extubation, 162 delayed extubation, 9 short-term tracheostomies, and 42 long-term tracheostomies (Table. 1). Twenty patients from Spain, 89 from the Netherlands, 15 from Sweden, 39 from the United Kingdom, 19 from Germany, 17 from Poland, and 76 from France were included (Fig. 1). The inclusion periods were 2011 – 2022 for Spain, 1983 – 2022 for the Netherlands, 2000 – 2022 for Sweden, 1984 – 2021 for the United Kingdom, 2013 – 2012 for Germany, 2012 – 2022 for Poland, and 2011 – 2022 for France.

Considerations in perioperative airway management strategy

In most centers, the majority of patients had received delayed extubation (Fig. 2). Immediate extubation was routinely used in Spain and the Netherlands. Both have changed their protocol to immediate extubation in the last ten years with gained experience from the anesthesiological team. Short-term tracheostomies were used in 4/7 centers (Sweden, the United Kingdom, Germany, and France), and currently, the center in the United Kingdom has moved to short-term tracheostomies regularly. They changed their protocol to short-term tracheostomies routinely to ensure a straight airway in case of the need for imaging under general anesthesia

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or re-adjustment of the frame during the distraction period. Detailed center-specific considerations can be found in the appendix (see Table, Supplemental Digital Content 2). The primary reported indications for delayed extubation or prolonged mechanical ventilation in tracheostomy patients were routine management in all midface surgeries in 144/200 (72%) patients and severe OSA in 28/200 (14%) (Table 2). In 3/200 (2%) patients, the indication for delayed extubation was failed attempts at the end of surgery. All three were successfully extubated after one day.

Regarding immediate extubation, 50/60 (81%) were done in Spain or the Netherlands. In the other centers, it seemed reserved for selected cases: patients were slightly older (minimum age of 5.8 years), had small amounts of EBL (median 30 ml/kg) or transfused blood volume (median 8.1 ml/kg), and, apart from the center in the United Kingdom, did not have moderate/severe OSA.

Respiratory support before extubation

Patients with delayed extubation remained intubated for 3 days (IQR 2 – 5). Most (86%) received mechanical ventilation during intubation (Table 3). The most frequently reported reasons to keep patients intubated for five days or longer (n = 48) were severe swelling in 15/48 (31%) patients, pneumonia in 5/48 (10%), and macroglossia in 3/48 (6%).

Albeit the numbers were too small to make any definitive statements, total intubation time appeared to be similar among most centers; only in the centers in France and Germany were patients possibly intubated longer (Fig. 3a). Not all differences were due to patient characteristics (Table 4).

After a monobloc procedure, patients remained intubated for a median of 5 days (IQR 3 – 8) compared to 3 days (IQR 3 – 5) after a Le Fort III (Table 5).

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Respiratory support after extubation

Fifty-eight out of 62 (94%) patients with immediate extubation required either no or only oxygen support after extubation, compared to 137/162 (85%) with delayed extubation (Table 3). In both groups, most patients only needed respiratory support for a few hours; median days of respiratory support after extubation were 0 days (IQR 0 – 1) in both groups. A Chi-square of independence did not find a significant association between respiratory support after extubation and perioperative airway management ($\chi 2 = 4.72$, df = 1, p = 0.030). Immediate extubation was effective in patients with moderate/severe OSA: 19/20 (95%) patients with immediate extubation required either no or only oxygen support (3/4 with moderate and 16/16 (100%) with severe OSA), compared to 49/62 (79%) with delayed (21/25 (84%) with moderate and 28/37 (76%) with severe OSA). The same appeared to be true for younger children (< 5 years old): 12/13 (92%) patients with immediate extubation and 38/48 (79%) with delayed required either no or only oxygen support. Likewise, immediate extubation after a monobloc could be contemplated: 35/38 (92%) with immediate versus 50/61 (82%) with delayed extubation received no or only oxygen support (Table 5). The rates were similar for patients treated with a Le Fort III: 23/24 (96%) and 87/101 (86%), respectively.

Ultimately, 1/62 (2%) patients with immediate extubation and 16/161 (10%) with delayed needed to be reintubated or receive a (new) tracheostomy postoperatively. The patient with immediate extubation needed reintubation because of obstructive breathing caused by severe postoperative swelling of the upper airway. Indications for reintubation in patients with delayed extubation were obstructive breathing caused by severe postoperative swelling in 5/10 patients, respiratory distress due to pneumonia in 2/10, accidental self-extubation in 2/10, and unknown cause in 1/10. Four patients with delayed extubation received a (new) tracheostomy postoperatively; 3/4 because of severe swelling and 1/4 due to respiratory deterioration. The tracheostomies were mostly inserted short-term, but one patient required a long-term

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tracheostomy. Two patients with delayed extubation had received both endotracheal reintubation and (new) tracheostomies; one had an accidental self-extubation with reintubation and ultimately received a tracheostomy because of macroglossia, the other received a tracheostomy after multiple extubation failures because of severe swelling. Their tracheostomies were removed after 2 and 8 months, respectively. The patients that needed reintubation were a little younger (median age 6.3 years (IQR 3 – 9)), more often had moderate/severe OSA (64%), and were intubated longer (median of 6 days (IQR 3 – 8)) than the overall group.

Respiratory support in patients with a tracheostomy

Patients with short-term tracheostomies remained ventilated for 3 days (IQR 1 – 6) and long-term tracheostomies for 1 day (IQR 0 – 4). The most frequently reported indications to keep patients ventilated directly after surgery in short- and long-term tracheostomized patients were routine management in all midface surgery (3/9 and 13/29 (45%), respectively) and severe OSA (2/9 and 8/29 (28%) respectively). Similar to intubation time in patients with delayed extubation, ventilation time in patients with long-term tracheostomies appeared to be comparable between most centers, only in the centers in Poland, France, and Germany, ventilation was possibly longer (Fig. 3b).

All patients with short-term tracheostomies received respiratory support after ceasing mechanical ventilation (Table 3). Twenty-six (62%) patients with long-term tracheostomies received respiratory support after ceasing ventilation. Respiratory support was only needed for a short period in both groups; 1 day (IQR 0 – 4) in patients with short-term tracheostomies and 0 days (IQR 0 – 1) in long-term tracheostomies. Two patients with short-term tracheostomies had to be recannulated/ventilation was restarted; in one patient because of accidental decannulation and in the other for reasons unrelated to respiratory status. Four patients with short-term tracheostomies were decannulated within two months after surgery, four were

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decannulated at the end of the distraction period, and one needed a long-term tracheostomy. Ventilation had to be restarted in 3/42 (7%) patients with long-term tracheostomies because of respiratory failure after ceasing mechanical ventilation.

Postoperative complications

There were no deaths related to perioperative airway management in this cohort. A significant association between timing of extubation and postoperative pneumonia was found; patients with immediate extubation were less likely to develop postoperative pneumonia compared to patients with delayed, 0/62 (0%) versus 24/161 (15%), respectively ($\chi 2 = 8.86$, df = 1, p = 0.001). Pressure ulcers developed in 1/62 (2%) patients with immediate and 9/161 (6%) with delayed extubation. Two out of nine with short-term tracheostomies, and none with long-term developed postoperative pneumonia. Pressure ulcers developed in 1/9 patients with short-term tracheostomies and 2/42 (5%) with long-term. The number of patients who had developed postoperative pneumonia was comparable between both surgeries (Table 5): 10/61 (16%) patients after a monobloc procedure and with delayed extubation compared to 14 /101 (14%) after a Le Fort III. More patients after a monobloc procedure and with delayed extubation developed pressure ulcers compared to after a Le Fort III (8/61 (13%) and 1/101 (1%), respectively).

Ultimately 36/275 (13%) patients developed postoperative pneumonia, pressure ulcers, or both. The analysis found an OR of 1.21 (95% CI 1.12 – 1.31) of intubation/mechanical ventilation on intubation-related complications. This means the odds of developing intubation-related complications increased by 21% with every extra day of intubation/mechanical ventilation. The Hosmer-Lemeshow test showed a good model fit ($\chi 2 = 8.35$, df = 8, p = 0.4). Overall postoperative complications are reported in Table 6.

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Discussion

This study aimed to lay the scientific foundation for perioperative airway management following midface advancements in syndromic craniosynostosis and to investigate the possibility of immediate extubation. Perioperative airway management differed among the craniofacial centers of expertise. Delayed extubation was the most frequently used method in most centers, and only in two centers was immediate extubation currently standard care. The use of short-term tracheostomies was limited and was reserved for selected cases in most centers, given their invasive nature.

In most centers, the current choice for the initial type of perioperative airway management, apart from long-term tracheostomies, is mostly independent of clinical factors, like OSA, and primarily based on tradition. Virtually all children remained intubated after surgery, except for the centers in Spain and the Netherlands. Whether the routine use of short-term tracheostomies will be of value remains to be seen with the change in protocol within the United Kingdom.

Our primary analysis showed no association between the number of patients requiring respiratory support after extubation and the timing of extubation, indicating that immediate extubation following midface surgery is a safe option. However, a clear benefit of immediate extubation was found regarding postoperative pneumonia, where patients who had received immediate extubation were less likely to develop postoperative pneumonia than those who had received delayed. Immediate extubation is likely an option in young children or patients with moderate/severe OSA since 92% and 95% of them needed no or only non-invasive respiratory support after extubation. Prolonged endotracheal intubation, with/without mechanical ventilation, has distinct disadvantages; it can lead to immobility-associated prolonged periods of swelling and pressure ulcers,[15,17] it is a risk factor for postoperative stridor and pneumonia,[14,16] and in some cases, the tube can impede the normal blood circulation of the

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tongue, which can initiate or maintain an airway obstruction.[18] Our secondary analysis is in line with the literature and showed that every extra day of intubation/mechanical ventilation increased the odds of developing pneumonia or pressure ulcers by 21%.

Tracheostomies, like prolonged intubation, also have disadvantages: placing or removal of the tracheostomy requires extra surgery with accompanying postoperative complications,[19,20] misplacement of the tracheostomy tube, secretions or blood clots can potentially block the tracheostomy,[19] the complexity of care for patients with tracheostomies and the need for trained nurses and parents,[21] the psychological effect of a noticeable scar on patients, and the rare but severe complication of long-term tracheal stenosis. An additional potential advantage of immediate over delayed extubation and short-term tracheostomies is the possible reduction of the length of stay in the (P)ICU. The number of (P)ICU beds is usually restricted due to high costs and the need for experienced staff. Length of stay in the (P)ICU is the most significant contributor to total (P)ICU cost.[22,23] The indication for ICU-level care is, amongst other factors as hospital nursing protocols, influenced by the type of airway management; changing the type of airway could, therefore, potentially reduce the length of stay.

For many years, extubation has been delayed for several days on the assumption that the anatomically abnormal upper airway in combination with midface surgery would lead to functional obstruction immediately postoperatively. The clinical results of this study show that this belief is unwarranted and that delayed extubation should not be indicated as standard practice. Taking these findings together, the authors recommend the following guidelines for making an SOP in airway management following midface advancements:

1. Immediate extubation should be considered routine management in patients with no/mild OSA.

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2. Immediate extubation should also be the aim in patients with moderate/severe OSA. An attempt for extubation should be contemplated at the end of the surgery, given the found OR of 1.21 for one extra day of intubation on intubation-related complications and because extubation in the operating room by the treating anesthesiologist creates the safest conditions for such a procedure. The following additional factors should be considered: always perform upper airway endoscopy before the midface surgery and perform additional adenoid, tonsil, or adenotonsillectomy when feasible. In carefully selected cases, this could be considered during the midface advancement procedure but preferably is not as this could add to airway challenges. In case of concomitant airway obstruction at the tongue base level, some degree of OSA will persist postoperatively and could influence the timing of extubation. Finally, consider decreasing the degree of OSA postoperatively by directly starting distraction on the operating table to increase the advancement during surgery. In line with this previous concern is the need for postoperative continuance of CPAP therapy and any difficulties fitting the CPAP mask in combination with an external frame. The earlier-mentioned methods to reduce the persistence of postoperative OSA are thus also essential to limit the need to continue postoperative CPAP. In other words, anticipate the degree of OSA that might persist and the need to continue preceding respiratory support postoperatively.
3. Immediate extubation can also be contemplated in young children after considering the abovementioned factors and after the craniofacial team's comprehensive assessment of the individual patient.
4. Case-specific factors, including prematurity, the patient's weight, congenital heart disease, intraoperative blood loss, the severity of OSA, and the presence of multi-

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level airway obstructions (particularly of the tongue base), can be indications for delayed extubation and should thus be taken into account when deciding on extubation timing. Corticosteroids can be contemplated in the perioperative setting to reduce (laryngeal) edema.[24-26]

5. If the decision is made for delayed extubation, consider extubation within the first 24 hours. This decision should be made following a multidisciplinary consultation.

The authors acknowledge several limitations. First, information on operating times was not collected as a covariate. Surgical injury and stress bring on a sequence of systemic responses, ultimately affecting the redistribution of fluid between the intravascular and interstitial space in the inflammatory phase of wound healing, which is clinically noticed as swelling or edema. Prolonged operative duration can therefore be associated with more postoperative swelling and a higher risk of respiratory complications. Furthermore, only information on intraoperative transfused red blood cells was collected, not on postoperative transfusions or other perioperative fluids (e.g., crystalloid or colloid). The total amount of fluid administered and the ratio between transfused blood volume and other fluids highly depend on the anesthesiologist's preference. Therefore, it would likely be different among hospitals and patients. Excessive fluid administration can lead to fluid accumulation in the lungs and may predispose patients to respiratory failure or pneumonia. In future prospective studies, particular emphasis should be placed on establishing standardized definitions for all pertinent perioperative parameters, including fluid resuscitation, airway grade, time in the operating room, or corticosteroids use. These studies should aim to investigate how these variables effect airway management in midface surgeries.

This study lays the foundation for SOPs for perioperative airway management following midface surgery in syndromic craniosynostosis. Immediate extubation following midface surgery is demonstrated to be a safe option associated with a minimal need for

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additional airway support and few complications. Further investigation on its implementation should be directed at individual patient selection, especially regarding levels of airway obstruction in moderate/severe OSA.

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Figure legends

Figure 1. Bar chart showing absolute numbers of patients per perioperative airway management strategy and medical center location.

IEX: immediate extubation, DEX: delayed extubation, STT: short term tracheostomy, LTT: long term tracheostomy. SP: Spain, NETH: Netherlands, SWE: Sweden, UK: United Kingdom, GER: Germany, POL: Poland, FRA: France

Figure 2. Percent stacked bar chart showing distribution of perioperative airway management strategy per medical center location.

IEX: immediate extubation, DEX: delayed extubation, STT: short term tracheostomy, LTT: long term tracheostomy. SP: Spain, NETH: Netherlands, SWE: Sweden, UK: United Kingdom, GER: Germany, POL: Poland, FRA: France

Figure 3. Boxplots showing the median and interquartile ranges of number of days of intubation in patients with delayed extubation (a) and number of days of mechanical ventilation in patient with a long-term tracheostomy (b) per medical center location. Colored dots show distribution of patients and outliers per medical centre.

SP: Spain, UK: United Kingdom, NETH: Netherlands, SWE: Sweden, POL: Poland, FRA: France, GER: Germany

Supplemental Digital Content legend

Supplemental Digital Content 1. Detailed information on the multiple imputation used to handle missing data.

Supplemental Digital Content 2. Summary of center specific considerations/protocols in airway management following midface advancement

IEX: immediate extubation, DEX: delayed extubation, STT: short term tracheostomy, LTT: long term tracheostomy. SP: Spain, NETH: Netherlands, SWE: Sweden, UK: United Kingdom, GER: Germany, POL: Poland, FRA: France

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Table 1. Patient characteristics.

	Timing of extubation / tracheostomy			
	IEX	**DEX**	**STT**	**LTT**
No. of patients	62	162	9	42
Males : females	32 : 30 (52 – 48)	72: 90 (44 – 56)	3 : 6 (33 – 67)	22 : 20 (52 – 48)
Median age (IQR), yrs	8.6 (5.6 – 14.1)	8.6 (4.0 – 14.1)	8.5 (4.0 – 10.2)	4.5 (2.0 – 7.0)
Diagnosis				
Apert	17 (27)	51 (31)	2 (22)	7 (17)
Crouzon/Pfeiffer	45 (73)	111 (69)	7 (78)	35 (83)
OSA classification				
Normal/mild	41 (66)	85 (53)	1 (11)	-
Moderate	4 (6)	25 (15)	2 (22)	4 (10)
Severe	16 (26)	37 (23)	4 (45)	37 (84)
Unknown	1 (2)	15 (9)	2 (22)	1 (6)
Type of surgery				
Monobloc	38 (61)	61 (38)	5 (56)	25 (59)
Le Fort III	24 (39)	101 (62)	4 (44)	17 (41)
Median EBL† (IQR), ml/kg	40 (24 – 60)	43 (28 – 70)	120 (79 – 123)	88 (49 – 231)
Median TBV¶ (IQR), ml/kg	17 (8 – 25)	23 (11 – 43)	24 (7 – 31)	35 (24 – 69)

Values represent number of patients (percentages)

For 1 patient in the IEX, 15 in the DEX, 2 in the STT, and 1 in the LTT the OSA classification was unknown

† For 10 patient in the IEX, 110 in the DEX, 6 in the STT, and 28 in the LTT the EBL was unknown

¶ For 7 patient in the IEX, 28 in the DEX, 3 in the STT, and 5 in the LTT the TBV was unknown

IEX: immediate extubation, DEX: delayed extubation, STT: short term tracheostomy, LTT: long term tracheostomy, OSA: obstructive sleep apnea, EBL: estimated blood loss, TBV: transfused blood volume

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Table 2. Reported indications delayed extubation or prolonged mechanical ventilation in patients with tracheostomies per medical center.

	Craniofacial center							
	SP	**NETH**	**SWE**	**UK**	**GER**	**POL**	**FRA**	**Total**
Routine management in all midface surgeries	1 (33)	42 (88)	2 (22)	13 (41)	13 (76)	16 (94)	57 (77)	144 (72)
Severe OSA	0 (0)	0 (0)	3 (33)	13 (41)	1 (6)	1 (6)	10 (14)	28 (14)
Severe perioperative EBL	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1)
Failed attempt to extubate	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	3 (2)
Severe postoperative swelling	0 (0)	0 (0)	3 (33)	0 (0)	0 (0)	0 (0)	5 (7)	8 (4)
Other/not reported	2 (67)	2 (4)	1 (12)	6 (18)	3 (18)	0 (0)	1 (1)	15 (7)

Values represent number of patients (percentages).

SP: Spain, NETH: Netherlands, SWE: Sweden, UK: United Kingdom, GER: Germany, POL: Poland, FRA: France, OSA: obstructive sleep apnea, EBL: estimated blood loss

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Table 3. Respiratory support and postoperative complications.

	Timing of extubation / tracheostomy			
	IEX	**DEX**	**STT**	**LTT**
No. of patients	62	162	9	42
Days intubated*				
0	62 (100)	-	0 (0)	13 (31)
1	-	32 (20)	3 (33)	10 (24)
2	-	42 (26)	1 (11)	7 (17)
3	-	23 (14)	1 (11)	2 (5)
> 3	-	65 (40)	3 (33)	10 (23)
Respiratory support before extubation†				
Open tube	-	9 (6)	-	-
Oxygen	-	12 (7)	-	-
Mechanical ventilation	-	140 (86)	-	-
Respiratory support after extubation¶				
None	38 (61)	73 (45)	0 (0)	16 (38)
Oxygen	21 (34)	80 (50)	9 (100)	26 (62)
Oropharyngeal airway	3 (5)	4 (2)	0 (0)	0 (0)
CPAP	0 (0)	5 (3)	1 (11)	1 (2)
Endotracheal reintubation	1 (2)	12 (7)	-	-
New tracheostomy	0 (0)	6 (4)	-	-
Restarting mechanical ventilation	-	-	2 (22)	3 (7)
Complications§				
Pneumonia	0 (0)	24 (15)	2 (22)	0 (0)
Pressure ulcer	1 (2)	9 (6)	1 (11)	2 (5)

Values represent number of patients (percentages). Patients could have multiple types of respiratory support or complications.

* In STT/LTT column represents days of mechanical ventilation. In 1 patient in the STT group the number of days of mechanical ventilation was unknown

† In 1 patient type of respiratory support before extubation was unknown

¶ In STT/LTT column represents respiratory support after stopping mechanical ventilation

§In 1 patient in the DEX group complications were unknown

IEX: immediate extubation, DEX: delayed extubation, STT: short term tracheostomy, LTT: long term tracheostomy

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Table 4. Patients characteristics of patients with delayed extubation per medical center.

	Craniofacial center						
	SP	**UK**	**NETH**	**SWE**	**POL**	**FRA**	**GER**
No. of patients	3	18	43	6	14	66	12
Median age (IQR), yrs	10 (8 – 14)	11 (7 – 15)	13 (7 – 18)	7 (7 – 10)	11 (8 – 18)	6 (3 – 12)	5 (4 – 7)
OSA classification							
No/mild	0 (0)	0 (0)	34 (80)	2 (33)	0 (0)	47 (71)	2 (17)
Moderate	1 (33)	3 (17)	3 (6)	0 (0)	6 (43)	12 (18)	0 (0)
Severe	2 (67)	15 (83)	6 (14)	4 (67)	8 (57)	2 (3)	0 (0)
Unknown	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (8)	10 (83)
Median EBL (IQR), ml/kg	47 (27 – 54)	-	43 (28 – 72)	43 (39 – 43)	-	-	-
Median TBV (IQR), ml/kg	33 (20 – 36)	22 (11 - 40)	20 (6 - 43)	-	-	25 (16 – 43)	22 (19 - 84)

Values represent number of patients (percentages)

SP: Spain, UK: United Kingdom, NETH: Netherlands, SWE: Sweden, POL: Poland, FRA: France, GER: Germany, OSA: obstructive sleep apnea,

EBL: estimated blood loss, TBV: transfused blood volume

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Table 5. Patients characteristics, respiratory support, and postoperative complications per type of surgery.

	Monobloc		Le Fort III	
	IEX	**DEX**	**IEX**	**DEX**
No. of patients	38 (38)	61 (62)	24 (19)	101 (81)
Median age (IQR), years	6.3 (4.1 – 9.4)	3.0 (2.0 -5.5)	15.3 (8.6 – 18.4)	12.1 (8.0 – 16.3)
OSA classification				
No/mild	25 (66)	33 (54)	16 (67)	52 (51)
Moderate	2 (5)	9 (15)	2 (8)	16 (16)
Severe	11 (29)	10 (16)	5 (21)	27 (27)
Unknown	0 (0)	9 (15)	1 (4)	6 (6)
Median EBL (IQR), ml/kg	53 (29 – 70)	84 (61 – 124)	27 (21 – 39)	36 (26 – 46)
Median TBV (IQR), ml/kg	22 (17 – 36)	38 (24 – 66)	7 (0 – 15)	16 (6 – 25)
Median days intubated (IQR)	-	5 (3 – 8)	-	3 (3 – 5)
Respiratory support before extubation				
Open tube	-	3 (5)	-	6 (5)
Oxygen	-	5 (8)	-	8 (8)
Mechanical ventilation	-	53 (87)	-	87 (86)
Respiratory support after extubation				
None	24 (63)	28 (46)	14 (58)	45 (45)
Oxygen	12 (32)	25 (41)	9 (38)	55 (54)
Oropharyngeal airway	2 (5)	3 (5)	1 (4)	1 (1)
CPAP	0 (0)	2 (3)	0 (0)	3 (3)
Endotracheal reintubation	1 (3)	5 (8)	0 (0)	7 (7)
New tracheostomy	0 (0)	2 (3)	0 (0)	4 (4)
Complications				
Pneumonia	0 (0)	10 (16)	0 (0)	14 (14)
Pressure ulcer	1 (3)	8 (13)	0 (0)	1 (1)

Values represent number of patients (percentages). One patient could have multiple types of respiratory support or complications.

IEX: immediate extubation, DEX: delayed extubation, OSA: obstructive sleep apnea, EBL: estimated blood loss, TBV: transfused blood volume

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Table 6. Postoperative complications overall.

	Total n = 275	**Monobloc n = 129**	**Le Fort III n = 146**
Pneumonia	26 (9)	11 (9)	15 (10)
Pressure ulcer	13 (5)	11 (9)	2 (1)
Wound infection	26 (9)	18 (14)	8 (5)
Meningitis	3 (1)	1 (1)	2 (1)
Eye cellulitis/keratitis	12 (4)	6 (5)	6 (4)
Corneal ulcer	7 (3)	3 (2)	4 (3)
Cerebrospinal fluid leak	61 (22)	46 (36)	15 (10)
Distraction material migration	14 (5)	6 (5)	8 (5)

Values represent number of patients (percentages). Postoperative complications were unknown in 1 patient.

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Figure 1

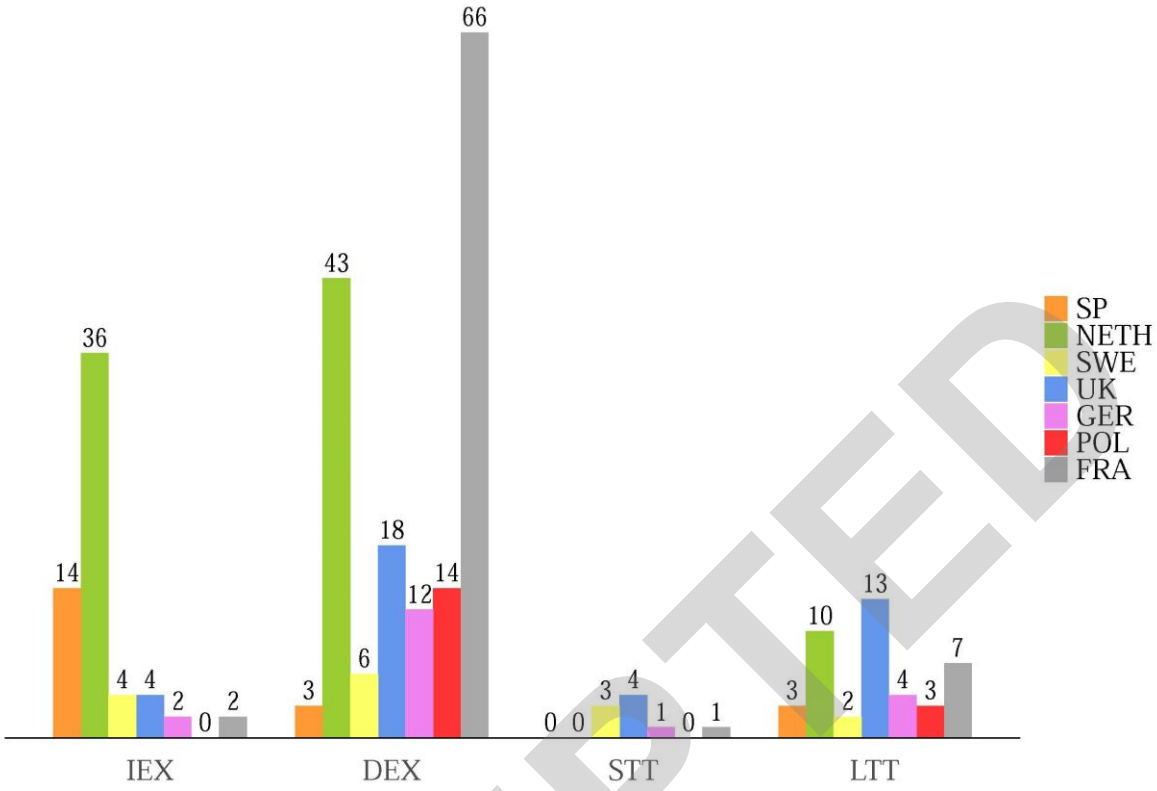

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Figure 2

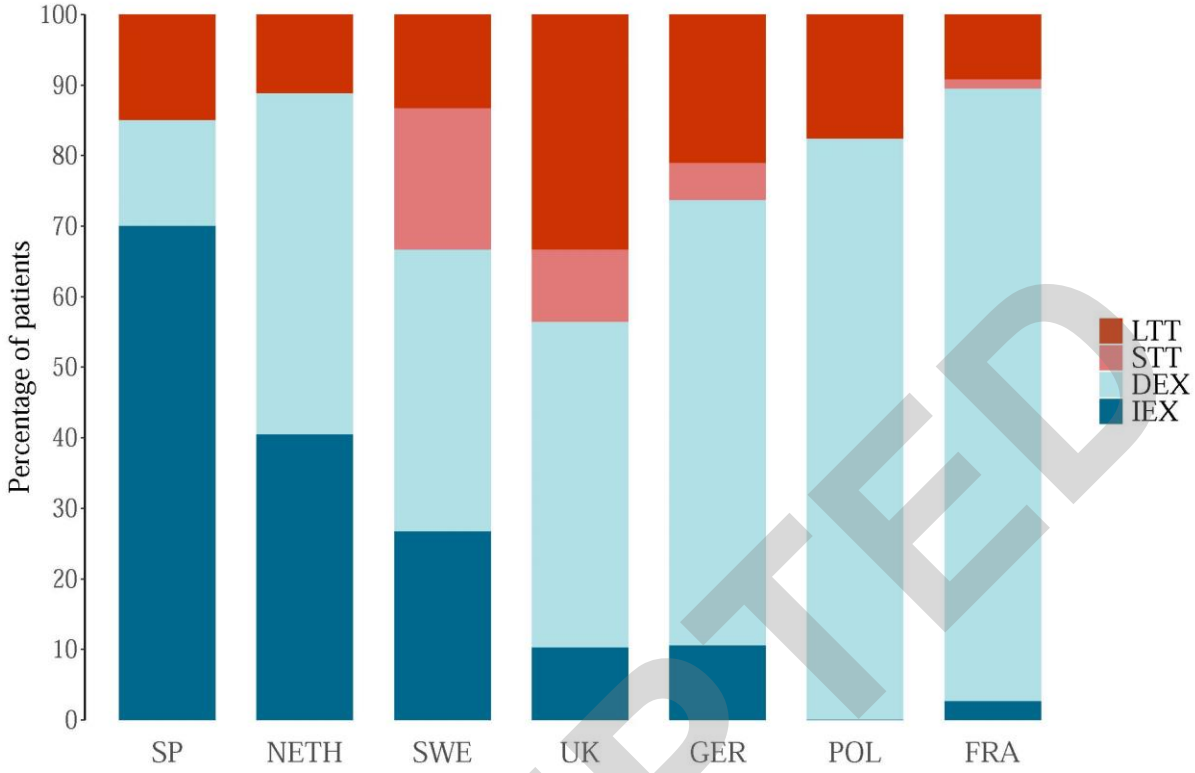

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Figure 3a

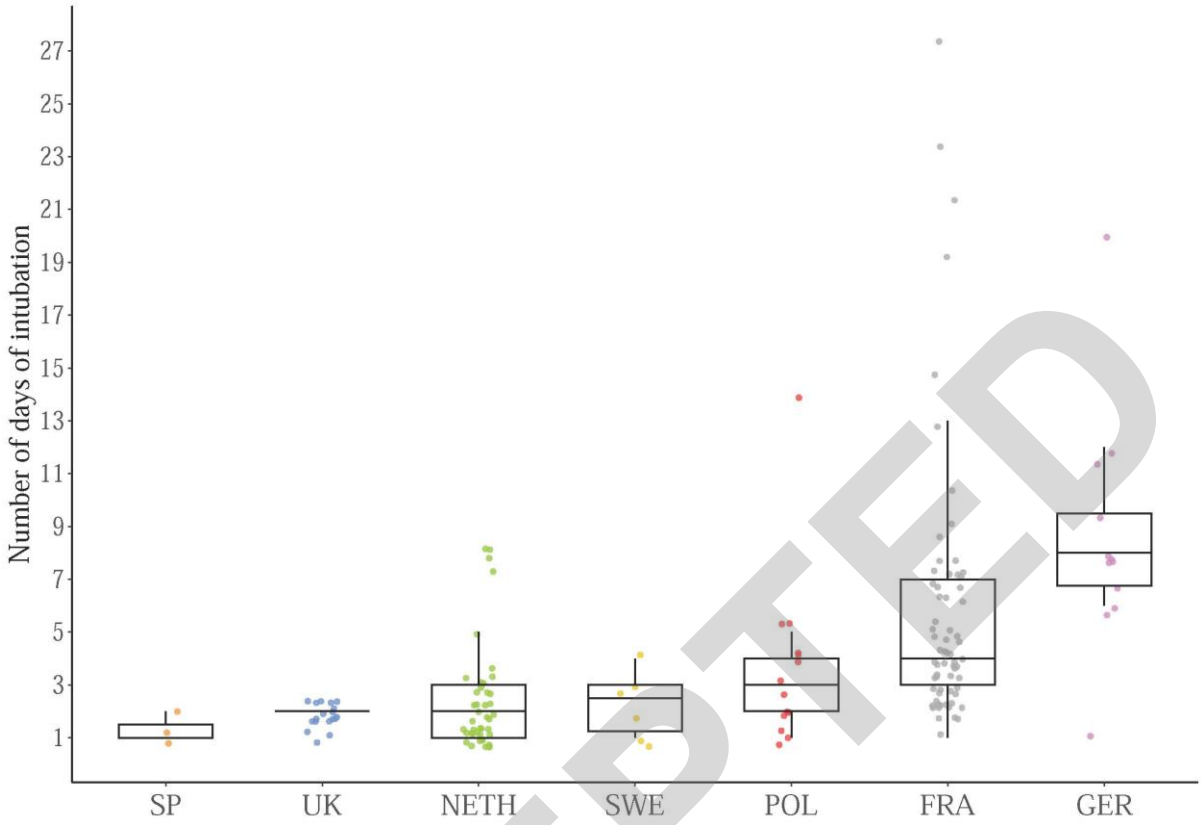

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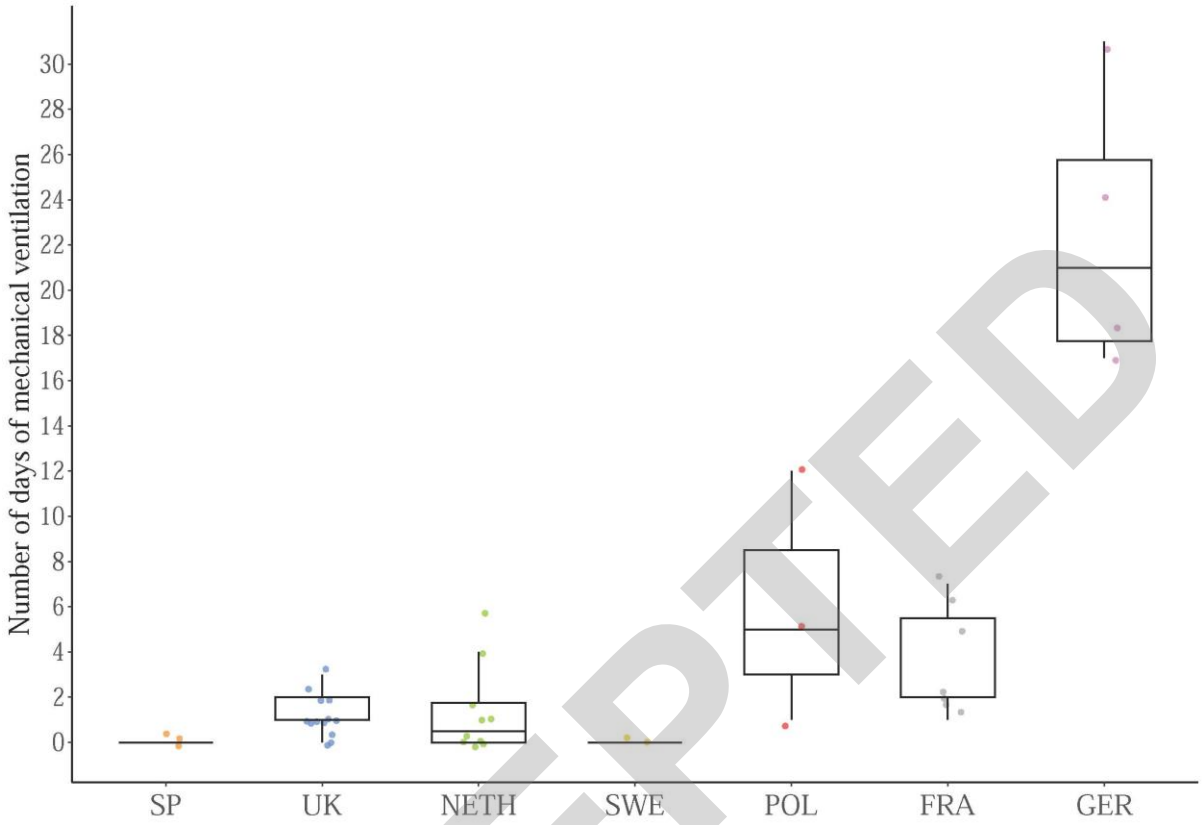
Figure 3b



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Appendix, Supplemental Digital Content 1

Multiple imputation for missing data

Multiple-imputation-by-chained equation (MICE package) in R was used to handle missing values and was based on the method described by van Buuren et al.. The accompanying table gives a summary of the proportion of missing cases and number of missing values per variable. The percentage of missing values ranged between 0% and 56% across the variables. One hundred five out of the 275 (38%) records were incomplete. Missing data pattern was assumed to be missing at random (MAR). Most missing data were in the predictor variables, only in one patient the outcome variable was missing. Most missing values were in estimated blood loss (EBL) and obstructive sleep apnea (OSA) classification. EBL was missing in the centers in the United Kingdom, Germany, and France because only blood transfusion is documented after surgery. In the centre in Poland neither EBL nor blood transfusion could be recovered from the patient files. In Sweden EBL was documented. Most missing values for OSA classification were in Germany since polysomnography was routinely performed at an external facility, limiting the availability of exact OSA classification.

Table. Missing values per variable

Variable	# of patients	% of patients
Study center	0	0
Age	0	0
Gender	0	0
Diagnosis	0	0
Indication surgery	0	0
Type of surgery	0	0
Type of perioperative airway management	0	0

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Type of respiratory support	0	0
Days of intubation	1	0
Intubation related complications	1	0
Days of respiratory support	2	1
OSA present	13	5
Weight	17	6
Classification OSA	19	7
Transfusion	43	16
Transfusion per kg	43	16
Blood loss	154	56
Blood loss per kg	154	56

For the numeric variables the 'predictive mean matching method' was used, for factor columns with two categories the 'logistic regression method', and for columns with more than two categories the 'polytomous logistic regression method'. Passive imputation was used to impute Blood loss per kg by the function 'Blood loss/Weight', and Transfusion per kg by 'Transfusion/Weight'. Care was taken to avoid multicollinearity; Blood loss, Transfusion, and Weight were only used as predictor variables for Blood loss, Transfusion, and Weight. For the other variables, Blood loss per kg and Transfusion per kg were used as predictor variables. Age was not used to impute Weight due to collinearity. Ultimately, 50 imputed datasets were created and analyzed. Convergence was checked and reached. Imputed values were checked to be realistic. Density plots were plotted to check the distribution of the imputed values against the observed values. After multiple imputation, the logistic regression model used for the secondary analysis was applied to each imputed dataset with the '*with*' function. The pooled odds ratio and corresponding 95% confidence interval from the secondary analysis were then gathered by the '*pool*' function.

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Supplemental Digital Content 2

Table 1. Summary of center specific considerations/protocols in airway management following midface advancement

Craniofacial center	IEX - DEX	STT - LTT	Start distraction during surgery
SP	- Since 10 years has IEX been protocol - Indications DEX: severe swelling, hemodynamic instability, or another medical problem - In case of DEX: extubation always within 6 hours	- STTs are not used - LTTs are used in case of severe OSA	+
NETH	- Before 2010, all patients received DEX for 1–3 days - Between 2010-2015 indications for DEX were mainly severe airway swelling or excessive EBL - Since 2015, have all patients received IEX	- STTs are not used - LTTs are used in case of severe respiratory problems in young children (< 2 years old)	+
SWE	- Decisions about airway management are always made after multidisciplinary consultation	- STTs are also used after taking into consideration aforesaid factors	+

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	- Assumed postoperative swelling, EBL, the patients history and the fact that the postoperative care takes place on an adult ICU are taken into consideration		
UK	- Before 2005, most children received DEX for 1-3 days	- Currently, the unit has moved to STTs regularly and STTs are inserted 2 weeks before midface surgery - Patients are ventilated overnight if prolonged surgery or massive EBL	+
GER	- Nearly all children receive DEX - Extubation depends on postoperative swelling and is usually attempted on days 2-5 postoperatively	- STTs are not routinely used but would be considered for very young children with pre-existing severe airway obstruction	-
POL	- Started performing LF3 and MB procedures in 2012 - All children remain intubated for a minimum of 2-3 days	- Midface advancements are not performed before age 7 - LTTs are placed in case of severe OSA in children < 7 years old	-
FRA	- Discussion on extubation from day 2 postoperatively and always after a postoperative CT	- The use of STTs is limited - LTTs are used in young children with severe OSA or children with tracheal anomalies	+

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	- Extubation is based on local edema, fever, CSF leaks, intracranial complications, and response to a decrease in sedation

IEX: immediate extubation, DEX: delayed extubation, STT: short term tracheostomy, LTT: long term tracheostomy. SP: Spain, NETH: Netherlands, SWE: Sweden, UK: United Kingdom, GER: Germany, POL: Poland, FRA: France

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