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Choanal atresia, a rare occurrence and its treatment

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To my mother

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Choanal Atresia – a rare occurrence and its treatment

1. Introduction

1.1 Definition and Epidemiology

Choanal Atresia is a congenital condition where the passage from the nasal cavity to the nasopharynx is blocked. Between 1 and 3 in 10,000 live births present with choanal atresia, either isolated or as part of a syndrome (Case & Mitchell, 2011; Harris, Robert, & Kallen, 1997). According to the data from the German statistical Institute (Statistisches Bundesamt), out of the 787523 infants born in 2018, there were 216 new reported cases of patients diagnosed with choanal atresia. This translates in an incidence that year of 2.74 in 10.000 live births.

It presents bilaterally in 30% to 50% of cases and unilaterally in 50% to 70% (Harris et al., 1997; Kancherla et al., 2014), with the right side as most commonly affected (Ramsden, Campisi, & Forte, 2009).

It was reported to affect females more often than males (Samadi, Shah, & Handler, 2003).

When cases of atresia were compared to controls, the patients had lower birth weight (<2500 g), higher chances of being born preterm (<37 weeks of gestation) and a family history of choanal atresia (Kancherla et al., 2014).

Additionally, motherly age was high, the mothers had higher rates of type 1 or 2 diabetes and had active periconceptional cigarette smoking (Kancherla et al., 2014; Samadi et al., 2003).

Bilateral choanal atresia is the most common indication for surgical intervention involving the nose in infants (Friedman, Mitchell, Bailey, Albert, & Leighton, 2000).

1.2. Embryology of choanal atresia

In humans, as in all vertebrates, the development of the skeleton of the head and pharynx is based on the chondrocranium supporting the brain, the sensory capsules, the olfactory organs, the membrane bones roofing the skull and the viscerocranium supporting the pharyngeal arches and their derivatives. These structures form in the first weeks of embryonic development.

There is a mesenchymal condensation within each arch, deriving from neural crest ectomesenchyme. This gives rise to pharyngeal arch cartilages, which in turn develop the structures that form the viscerocranium. The human embryo is composed of 6 arches, which form in cranio-caudal succession.

The development of the face, the nasal cavity and pharyngeal structures happens between the fifth and seventh weeks (Tamarin, 1982; Tamarin & Boyde, 1977).

The nose forms from the medial unpaired frontonasal process (Tamarin & Boyde, 1977).

The nasal placodes, which are a pair of ectodermal thickenings, appear on the frontonasal process. The ectoderm at the center invaginates and forms an oval nasal pit.

The nasal passages form then by the deepening of the nasal pits. They are separated from the oral cavity by the nasal fin, an epithelial structure at the posterior part of the lambdoidal region. It then thins out and becomes the oronasal membrane. The complete breakdown of this membrane during the seventh week forms the primitive choana. This is due to processes such as cell death and or epithelial mesenchymal transformation (Kurosaka, Wang, Sandell, Yamashiro, & Trainor, 2017; Sun, Baur, & Hay, 2000; Tamarin, 1982).

The complete obstruction between the nasal cavity and nasopharynx that presents in choanal atresia can be membranous, bony or mixed. It may be uni- or bilateral.

There are a few accepted theories for the development of choanal atresia, many derived from other vertebrate models.

These involve:

1. the persistence of bucopharyngeal membrane (Flake & Ferguson, 1964);
2. the formation of adhesions in the nasochoanal region due to abnormal persistence or formation of mesoderm (Hengerer & Strome, 1982);
3. abnormal persistence of the nasobuccal membrane of Hochstetter (Flake & Ferguson, 1964);
4. abnormal development of the cranial neural crest, due to misdirection of migration and mesodermal flow (Hengerer, Brickman, & Jeyakumar, 2008; Kurosaka et al., 2017).

An important step for the embryology analysis was the discovery of the induced craniofacial anomalies by high doses of Vitamin A in studies from the 1970's and 1980's (Newell-Morris, Sirianni, Shepard, Fantel, & Moffett, 1980)
However, the study of the anomalies leading to choanal atresia is impeded by the lack of proper models. While the development of the frontonasal region seems to be quite similar among species, the development of the primitive choana seems to differ (Abramyan, Thivichon-Prince, & Richman, 2015; Kurosaka et al., 2017).

Interestingly, choanal atresia often appears linked to syndromic abnormalities. Gene mutations are related to signaling pathways, possibly also leading to abnormal neural crest development (Andrade et al., 2005; Burrow et al., 2009; Stieve, Kempf, & Lenarz, 2009).

Several examples of disorders associated with both neurocristopathy and choanal atresia are described below.

CHARGE Syndrome

CHARGE syndrome is characterized by **C**oloboma, **H**eart defects, choanal **A**tresia, **R**etarded growth and development, **G**enital abnormalities, and **E**ar anomalies. In 65% of patients with the diagnosis of CHARGE, choanal atresia is present. There is a reported mutation in the gene CHD7 in 90%-95% of patients

(Hsu et al., 2014; Johnson et al., 2006; Vissers et al., 2004). This gene seems involved in cranial neural crest and olfactory neuroectoderm development and in the retinoid signaling pathway, which is important for organs such as the inner ear, brain and palate (Asad et al., 2016; Bajpai et al., 2010; Bosman et al., 2005; Dupe et al., 2003; Hurd et al., 2007; Kurosaka et al., 2017; Micucci et al., 2014; Schulz et al., 2014; Sperry et al., 2014).

Treacher Collins-Franceschetti

Patients with this association are characterized by down-slanting palpebral fissures, lower eyelid colobomas, microtia, and malar and mandibular hypoplasia. It presents with a defect in genes TCOF1, POLR1C and POLR1D (Terrazas, Dixon, Trainor, & Dixon, 2017; Valdez, Henning, So, Dixon, & Dixon, 2004), genes that are important for ribosomal RNA production and ribosome biogenesis. The interruption of such production impedes the nasal airway connection to the nasopharynx. These patients in some cases present with choanal atresia. (Andrade et al., 2005)

Di George Syndrome

Di George Syndrome is another type of neurocristopathy associated with choanal atresia among other craniofacial anomalies. There is a hemizygous deletion of chromosome 22q11.2. Major gene mutations are in TBX1, which plays a very important role in neural crest cell development (Epstein, 2001; Funato, Nakamura, Richardson, Srivastava, & Yanagisawa, 2015; Jerome & Papaioannou, 2001; Lindsay et al., 2001; Merscher et al., 2001).

Other syndromes such as Crouzon or Apert are caused by mutations in fibroblast growth factor receptors (FGFRs). These patients present with craniosynostosis, and may also present choanal atresia (Burrow et al., 2009; Stieve et al., 2009; Upmeyer, Bothwell, & Tobias, 2005; Xie, De, & Selby, 2016).

Patients presenting with choanal atresia present chromosomal defects in 50% of the cases, and are not always associated to syndromes (Case & Mitchell, 2011; Harris et al., 1997).

CHD7 mutation in CHARGE cases is present in 38% of patients with choanal atresia, according to a review gathering 247 cases from 26 studies (Zentner, Layman, Martin, & Scacheri, 2010). This percentage could reach 55%, as it is possible that clinical data may be incomplete (Bergman et al., 2011).
In the case of non-syndromic choanal atresia, anti-thyroid medication may play a role (Corrales & Koltai, 2009; Johnsson, Larsson, & Ljunggren, 1997).

1.3 History

Congenital atresia was first described in 1830 in Friedrich-Wilhelm University of Breslau by the anatomy professor Adolf Wilhelm Otto, in his Book “Lehrbuch der pathologischen Anatomie des Menschen und der Tiere”. Then in 1854, Professor Carl Emmert from the University of Bern reported about the operation he performed on a seven-year-old boy with bilateral atresia. He operated through the nose with a curved trocar. He then placed metal tubes and fixed them in front of the nasal septum. Later, he replaced them and inserted larger ones. After six months he removed the stents and the boy was then asymptomatic. Later in 1859, Hubert von Luschka who was the professor of Anatomy between 1849-1875 at the Eberhard Karls University of Tübingen, described in detail the anatomical features of a bilateral choanal atresia as well as other craniofacial and cardiovascular deformities in the body of a female infant who had died shortly after birth. Not much later, in Stockholm, a man in his twenties was operated on by Dr. Santesson in 1867. One year later, Voltolini, again in Breslau, operated on a medical student with a unilateral case. Meanwhile, Dr. Jacob da Silva Solis Cohen, a laryngologist from New York (USA), successfully operated the first

infant with bilateral choanal atresia with an endonasal approach. It was reported that afterwards, the child's nutrition improved markedly.

In the early twentieth century, the endonasal technique with submucous septal resection was spread worldwide, following the example of Gustav Killian from Freiburg and Otto Freer in Chicago. Later in 1908 and 1909, the transseptal and transmaxillary techniques were developed. Uffernorde in Göttingen and Brunk in Rostock performed some of the first successful transseptal and transpalatinal surgeries. Then the transmaxillary approach was used by Lannois and Jacod on a man who had four transnasal unsuccessful operations before (Pirsig, 1986).

Stankiewicz first approached this pathology endoscopically in 1990 (Stankiewicz, 1990).

1.4 Clinical importance

The presentation of bilateral choanal atresia is usually at birth, because newborns are obligate nasal breathers due to the high position of the epiglottis (Schraff, Vijayasekaran, Meinzen-Derr, & Myer, 2006). For this reason, newborns need an oro-tracheal intubation or a bridging device such as a Guedel tube, maximizing breath intake through the mouth. Therefore, management of bilateral atresia has to be performed early after birth after a short assessment for other risk factors.

Unilateral choanal atresia can be diagnosed either early, through an examination by the attending neonatologist after birth, or later in childhood or even adulthood due to increasing symptoms of nasal congestion and rhinorrhea (Schraff et al., 2006). In a recently published consensus for the diagnosis and treatment of choanal atresia (Moreddu, Rizzi, et al., 2019), it was determined that the optimal timing for surgery for unilateral choanal atresia is after 6 or 12 months of age.

The diagnosis should be made upon a nasal endoscopy (Figure 1) and using computerized tomography of the nasal cavity and face in order to confirm the presence of choanal atresia and to be able to further plan surgery.

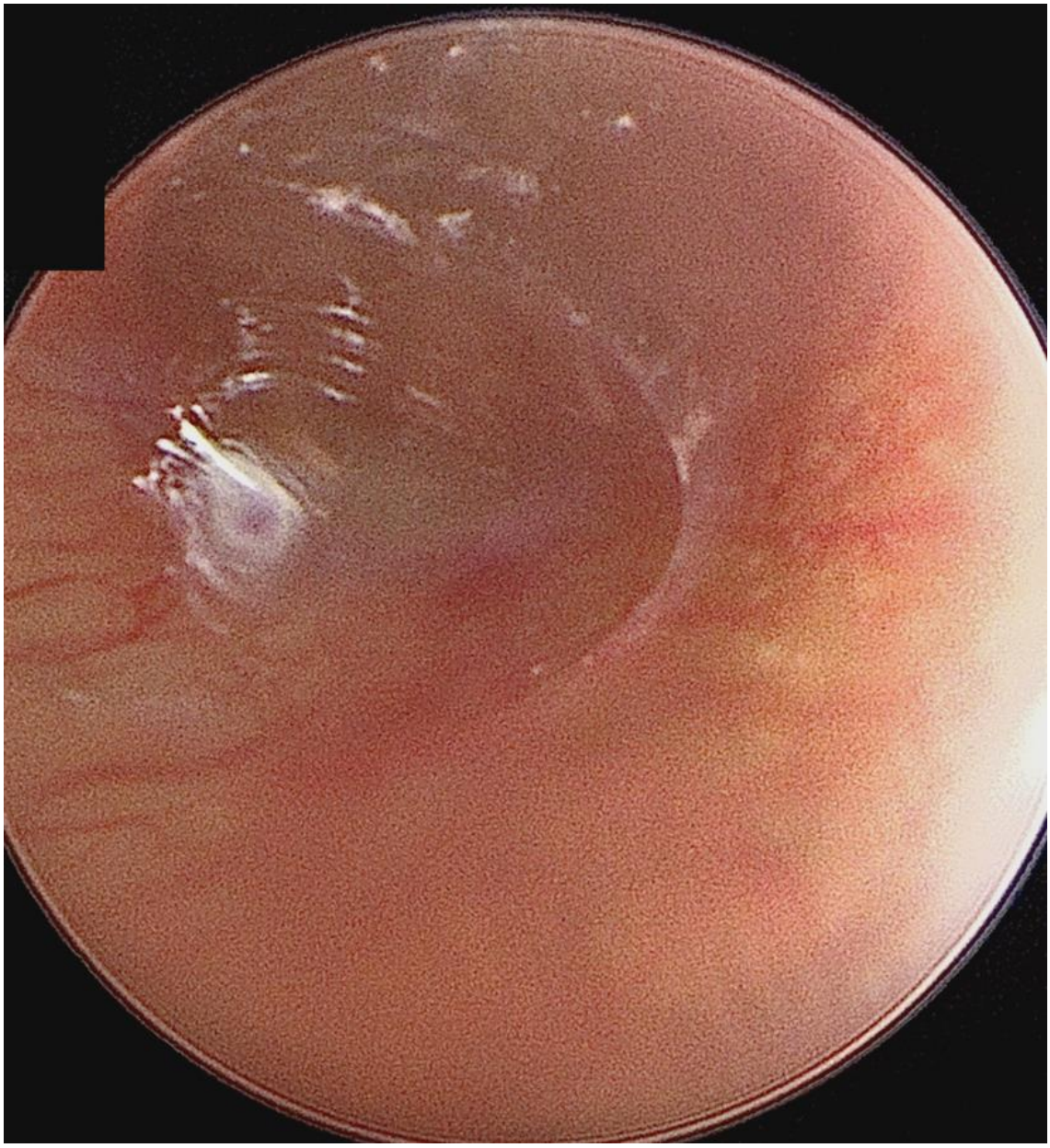

Figure 1 Choanal Atresia: Endoscopic view with a 0 degree, 2.3mm diameter, rigid Hopkins telescope, showing the left nasal cavity in a patient presenting a bilateral choanal atresia.

1.5 Current treatment

As mentioned above, there are several approaches for treatment of choanal atresia. Of the four, endonasal, transseptal, transpalatinal and transmaxillary, endonasal is the preferred approach. This is possible nowadays due to the immense advance in knowledge and technical possibilities that have occurred since the 1990's. The development of endoscopic endonasal surgery was based on the creation of specific and further refined instruments as well as improvement of the image provided by the endoscopes and cameras.

The endonasal endoscopic technique used in the treatment of the choanal atresia is surgeon dependent, respecting the principles of the endonasal functional surgery and involving the use of a rigid scope and endonasal cutting instruments. It is performed in general anesthesia, with the patient lying down. First, pledgets with anti-congestive medication are placed in the nasal cavity.

Then, if bilateral, an incision is made in the mucosa on both sides of the nose at the transition from the nasal septum to the nasal floor. The passage from the nose to the epipharynx is enlarged with cutting instruments and often with the help of a burr. The posterior vomer is removed, and the opening is enlarged laterally to the medial pterygoid plates, superiorly to the roof of the nasopharynx and inferiorly to the palatine bone. This is performed with a nasal endoscope, with a view of 0 or 30 degrees.

Some centers propose the removal of the atresia plate transeptally, with the preparation of the septal mucosa (Wormald, Zhao, et al., 2016). Many authors proposed the use of mucosa flaps (Brihaye et al., 2017; Karligkiotis et al., 2017; Wormald, Zhao, et al., 2016) in order to reduce stenosis by covering the denuded bone created by the removal of the atretic plate.

The postoperative care includes the irrigation of the nasal cavities with nasal saline. Some centers advocate the use of proton pump inhibitors, others the administration of nasal steroids. Some authors use tubes postoperatively that need to be removed after one to several weeks, while some advocate that they may not be needed at all (Strychowsky, Kawai, Moritz, Rahbar, & Adil, 2016; Wormald, Zhao, et al., 2016).

Ideally, follow up should extend for two years according to the guidelines (Moreddu, Rizzi, et al., 2019).

The transpalatinal approach used to be performed more often in the past and in fact was still the favored method. It has advantages in terms of visualization, especially when the nasal cavity is very small. However it sometimes led to more complications, such as fistula and crossbite (Jung, 1994). The operation is performed under general anesthesia with head down. The palate is visualized under the microscope. A mucosal U Flap is prepared, showing the hard palate and its dorsal end, with care not to damage the vessels. Then the atretic plate is removed with the burr, until the nasopharyngeal mucosa comes to view. The posterior end of the vomer is removed. The mucosal flaps are then repositioned and often a tube will be placed for a few days or a few weeks (Jung, 1994).

Classification of surgical and functional success or failure varies widely among studies. Some authors adopt Teissier definition, which combines endoscopical and clinical features, while others define success or failure only by the need for revision. (Teissier, Kaguelidou, Couloigner, Francois, & Van Den Abbeele, 2008). Further follow-up procedures may be considered by some authors as part of the treatment (Wormald, Zhao, et al., 2016).

Recently, a multicentric retrospective study proposed a new classification. The authors grouped the results in four grades, as illustrated in table 1 (Karligkiotis et al., 2017). In the same year, Brihaye adopted a similar classification, also with four categories (Brihaye et al., 2017).

Recently, Moreddu and colleagues also classified their results in a similar fashion, but spread their results into three groups. They classified their results in normal patency, partial restenosis, and complete stenosis (Moreddu, Rossi, Nicollas, & Triglia, 2019).

These above-mentioned proposed classifications are summarized in table 1.

Whatever the classification adopted, the international consensus recommends early revision surgery in case of appearance of re-stenosis and symptoms (Moreddu, Rizzi, et al., 2019).

Table 1 Surgical results: Classification by author

Authors	**Grading of surgical results**			
Teissier et al 2008		Restenosis when lumen < endoscope diameter and symptoms		
Karligkiotis et al 2017	Grade A Surgical success Patent choana Asymptomatic	Grade B Anatomical Failure Partial stenosis Asymptomatic	Grade C Functional failure Partial stenosis Symptomatic	Grade D Surgical failure Complete stenosis Symptomatic
Brihaye et al 2017	Type I Patent choana Asymptomatic	Type II Limited scar Asymptomatic	Type III Limited restenosis Moderate symptoms	Type IV Severe restenosis Severe symptoms
Moreddu, Rizzi et al 2019	Normal patency <50% restenosis Asymptomatic		Partial restenosis >50% Symptomatic	Complete stenosis

1.6 Aim of the Study

The primary goal of the current retrospective study is to describe the characteristics of the cohort of patients presenting with choanal atresia to the department of otolaryngology of the University Hospital of Tübingen as well as the details of their treatment. The second goal is to analyze factors related to the success or failure of the surgery and the number of surgeries needed to achieve

success based on the characteristics of this cohort and surgical technique performed.

- Are age, weight and the size of the neochoana determinant for the success of the surgery?
- Is there an implication of the use of stents of different types in these results?
- Are there complications related to the use of stents in these group of patients?

2. Material and Methods

2.1 Population

We performed a retrospective observational study based on the analysis of the files of 33 patients diagnosed with congenital choanal atresia, operated on in the Department of Otorhinolaryngology, Head and Neck Surgery at the University Hospital of Tübingen, Germany between 2004 and 2019.

Data was retrieved from the digital database contained within the Hospital working software system (SAP ®), which was introduced in 2004.

Patients presenting with bilateral atresia were referred either from the neonatology or pediatric unit from our institution, or from these departments from another hospital located in the same region. Patients presenting with unilateral atresia were referred from other Otolaryngologists practicing in the area about 200km around Tübingen.

2.2 Diagnosis

In patients presenting with bilateral choanal atresia at birth, the diagnosis was made after impossibility to pass a suction catheter through the nose into the pharynx by the neonatologist. These newborns presented with respiratory

distress. The diagnosis was confirmed after performing an endoscopy by a trained senior Otolaryngologist, either with a flexible rhinolaryngoscope with 2mm or 4mm diameter (ENF P4, Olympus, Japan) or a rigid Hopkins Telescope with a thickness of 2.3 or 4mm, with an angled end of 30 degree (7220 BA, Karl Storz SE and Co. KG, Germany) connected to a light source. A triplane computerized tomography with bone window following a protocol for sinus cavities and with a slice thickness of 1.5mm was performed in the majority (72.4%) of cases.

Most of the cases presenting with unilateral atresia were diagnosed by a nasal endoscopy in the otolaryngology clinic. For this purpose, either a flexible rhinolaryngoscope or a rigid Hopkins Telescope as mentioned above were used, similarly to the bilateral cases. These patients presented symptoms such as nasal obstruction or increased nasal secretions. Some additional patients were presented by the neonatologist in cases with concomitant malformations associated with respiratory distress.

2.3 Surgical treatment

After a routine check-up for other pathologies, surgery was planned between the pediatric and Otorhinolaryngology departments. Patients with bilateral atresia or concomitant pathologies were admitted to the pediatric ward, most of the time staying at the intensive care unit for neonatology. For these infants, airway was secured by the use of an orotracheal tube or by a Guedel tube inserted in the oral cavity.

When patients were transferred to the operating room of the Department of Otorhinolaryngology, Head and Neck Surgery the senior anesthetist would perform general anesthesia. The temperature of the room would be elevated to between 23 and 25 degrees Celsius.

The patients were lying down, with the head placed in a circular head rest. The surgeon introduced cotton pledgets soaked in xylometazoline 0.025% in both nasal cavities before beginning surgery in order to decongest the nasal mucosa.

Patient documentation and imaging were analyzed. After counselling with the team according to the World Health Organization guidelines, the face of the infant would be cleaned and a sterile draping would be applied. Then, the nasal cavities were approached. This was performed with a 2.3 or 4mm rigid 0 degree Hopkins telescope (Karl Storz SE and Co.KG, Germany or Fentex Medical GmbH, Germany) presented in Figure 2, coupled to a high definition or 4K definition camera (Storz SE and Co.KG) and observed in a screen, presented in Figure 3.

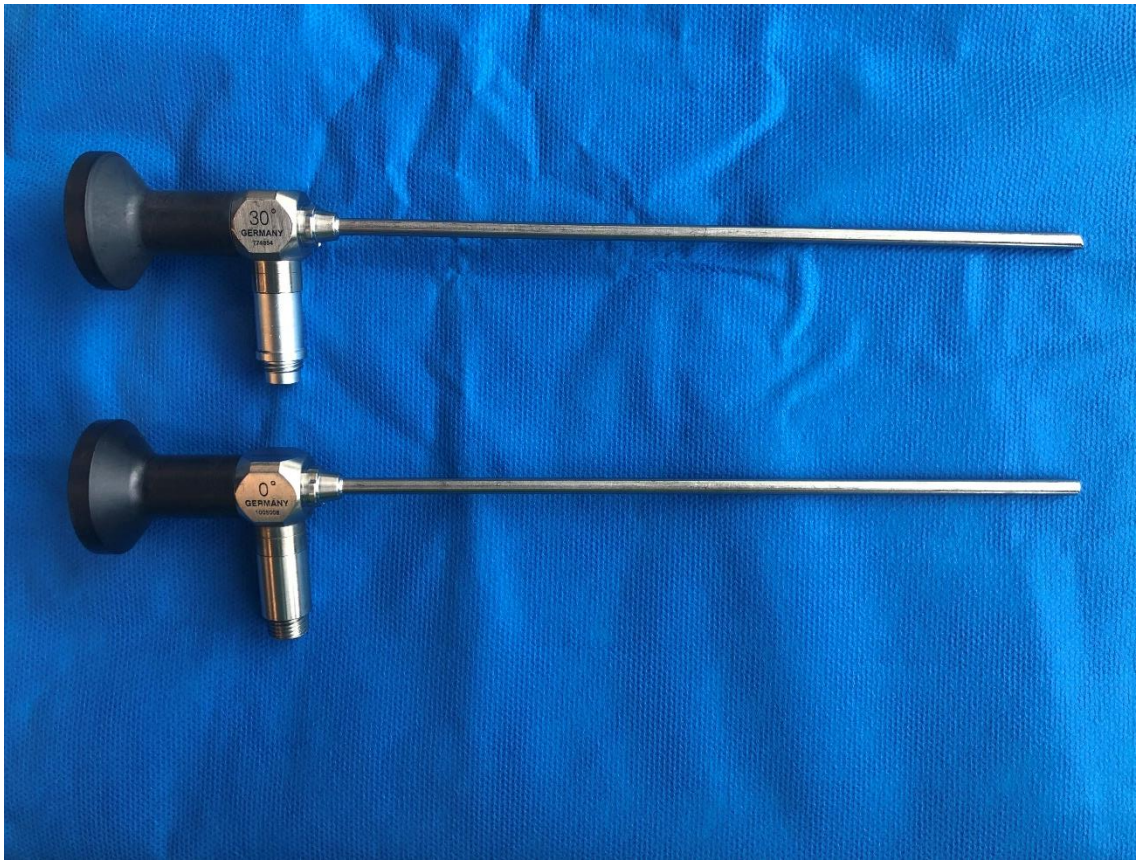

Figure 2 Rigid Telescope: Hopkins Telescope 0 and 30 degrees view, 4mm diameter (Fentex, Germany)

Figure 3 4k Camera and Screen: Telescope connected to the camera, the image transmitted to a 4K Quality screen (Storz, Germany)

In general, CT- guided navigation was not used. After confirming the occurrence of choanal atresia, noting the side and type of atresia, the nasal mucosa was incised in the region of the membranous or osseous part of the atretic plate and removed or carefully taken to the side. In other cases, a medial and caudal perforation to the nasopharynx would be done with the straight suction. If this was not possible due to a predominant osseous component, the choanal atresia plate and posterior part of the vomer were then approached with a 4mm, 15 degree burr with simultaneous irrigation of NaCl and suction at 12000 or 30000 rotations per minute (Medtronic, USA). Otherwise cutting instruments for pediatric functional endoscopic sinus surgery (Storz SE and Co.KG) were used to create a neochoana until the nasopharynx was seen. The wound would be then enlarged until an appropriate opening for the age was achieved, by carefully removing bone and mucosa as needed. The level of the middle turbinate was determined as superior limit, in order to protect the skull base. Finally, mucosa was readjusted.

In some patients a CO2 laser was used instead to perform the initial incision of the mucosa over the atretic plate.

Then, in the majority of cases, tracheal tubes (Vygon) of adequate size were inserted uni- or bilaterally depending on the pathology of the patient. These are presented in Figure 4.

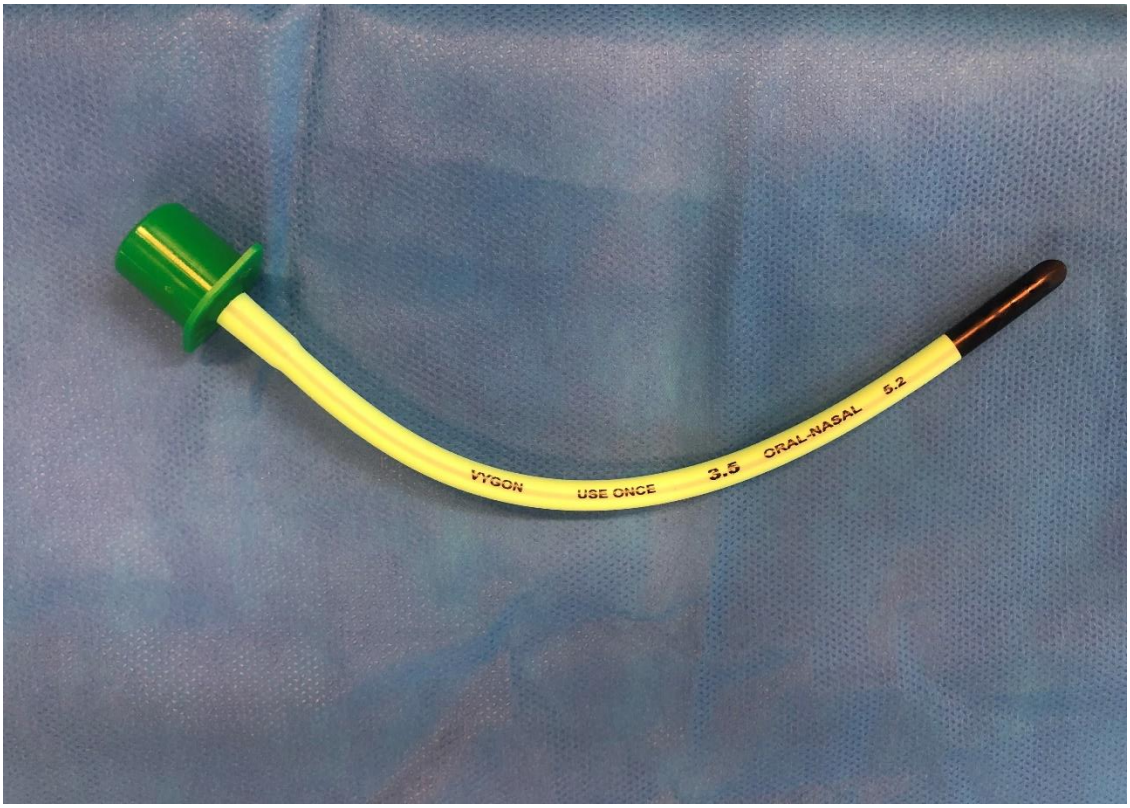

Figure 4 Stent: Tracheal Tube Vygon (Vygon, France), 3.5, External diameter 5.3mm. These tubes are then fashioned to fit in the nasal cavity with the black extremity placed in the nasopharynx

These tubes were fashioned to fit in the nasal cavity and neochoana and then stitched to the nasal septum anteriorly with nonresorbable material. In general, these tubes were left in place for several weeks. In some patients, septal silicon foils were used and stitched to the nasal septum. Only a few patients had a nasal packing placed in the nasal cavity for a few days.

In other cases, a resorbable steroid eluting stent delivering fluticasone for 4 weeks (propel mini ^{R}) was placed in the neochoana at the end of the procedure. This is demonstrated in Figure 5.

The intraoperative measurement of the size of the neochoana was performed based on the tubes placed or calculated according to the diameter of the surgical instruments used.

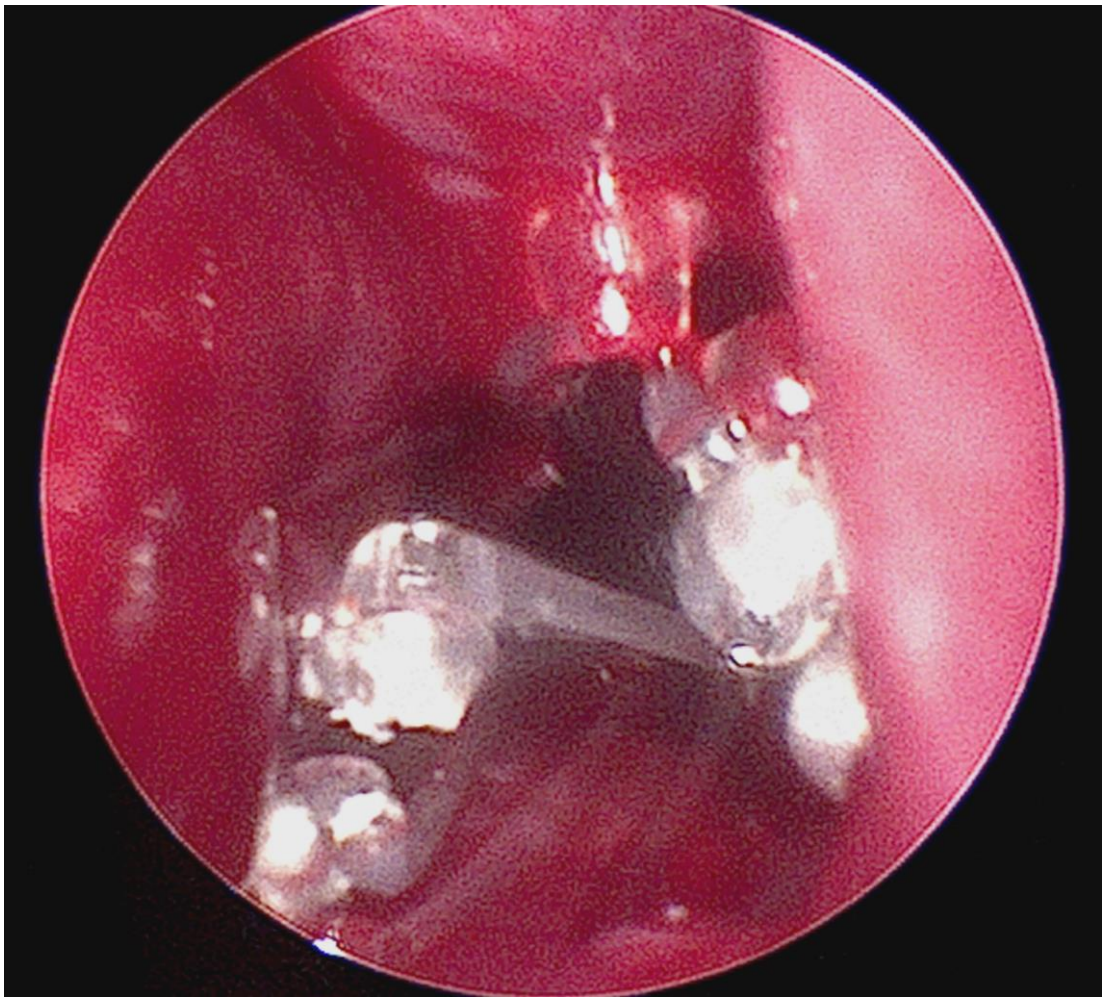

Figure 5 Drug eluting stent: Intraoperative image of a drug eluting stent placed in the neochoana after the surgical treatment of a bilateral choanal atresia.

2.4 Postoperative management

All caregivers, either the medical staff of the neonatal or pediatric unit or the parents, were carefully instructed about the postoperative treatment. The administration of saline drops several times per day in the nasal cavity or in the

tubes was recommended, as well as the cleaning and/or suction of the tubes or of the nostrils postoperatively. If discharged home, the parents received a portable suction device and received instructions on its use. Then, follow-up appointments were scheduled. These included endoscopy and removal of the tubes, as well as removal of crusting or granulation tissue.

2.5 Data management and statistical analysis

In a group of thirty-three patients who underwent operations between 2004 and 2019 for choanal atresia, four were lost during the follow up phase. The rest of the population came to the scheduled post-op appointments in the Department of Otorhinolaryngology, Head and Neck Surgery with the surgeon and/or with the attending otolaryngologist if so planned.

For these twenty-nine patients we retrieved the following data:

- Demographic characteristics: age, gender, weight at surgery, presence of other malformations, presence of a congenital syndrome. Also, the type of atresia, if bilateral, unilateral and on which side it was located was noted.
- Diagnostic procedures: findings of endoscopy, pre-operative computerized tomography (Figures 6 to 8) of the nose, face and sinus.

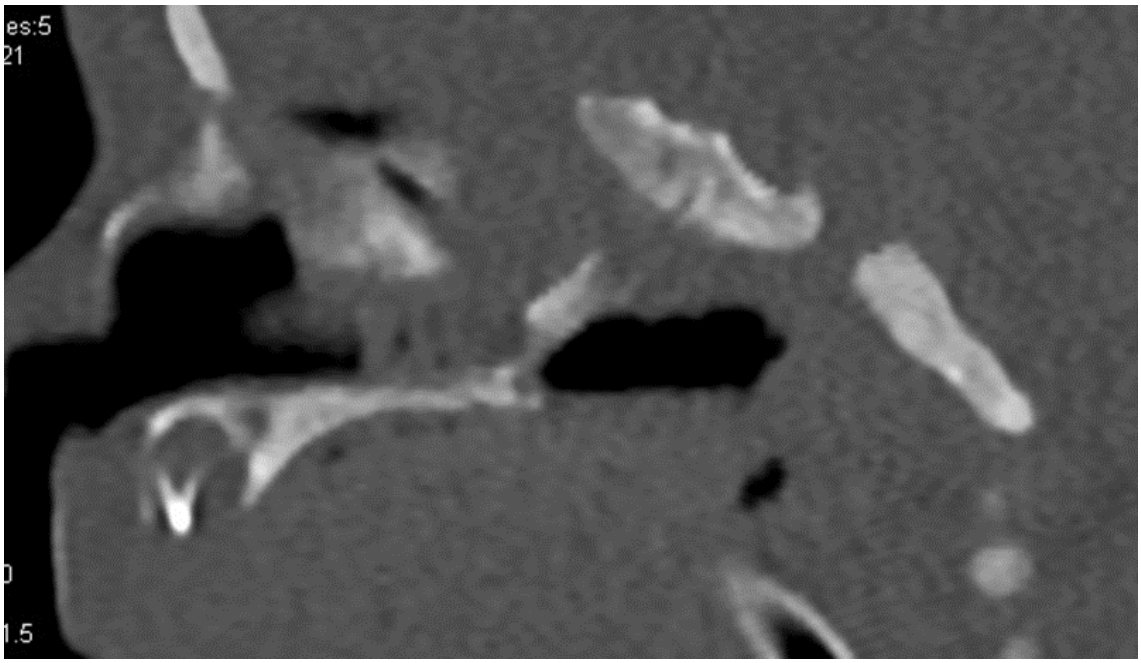

Figure 6 CT scan: Computerized tomography image in sagital plane with bone window of a patient presenting with bilateral choanal atresia, revealing a mixed bony and membranous component

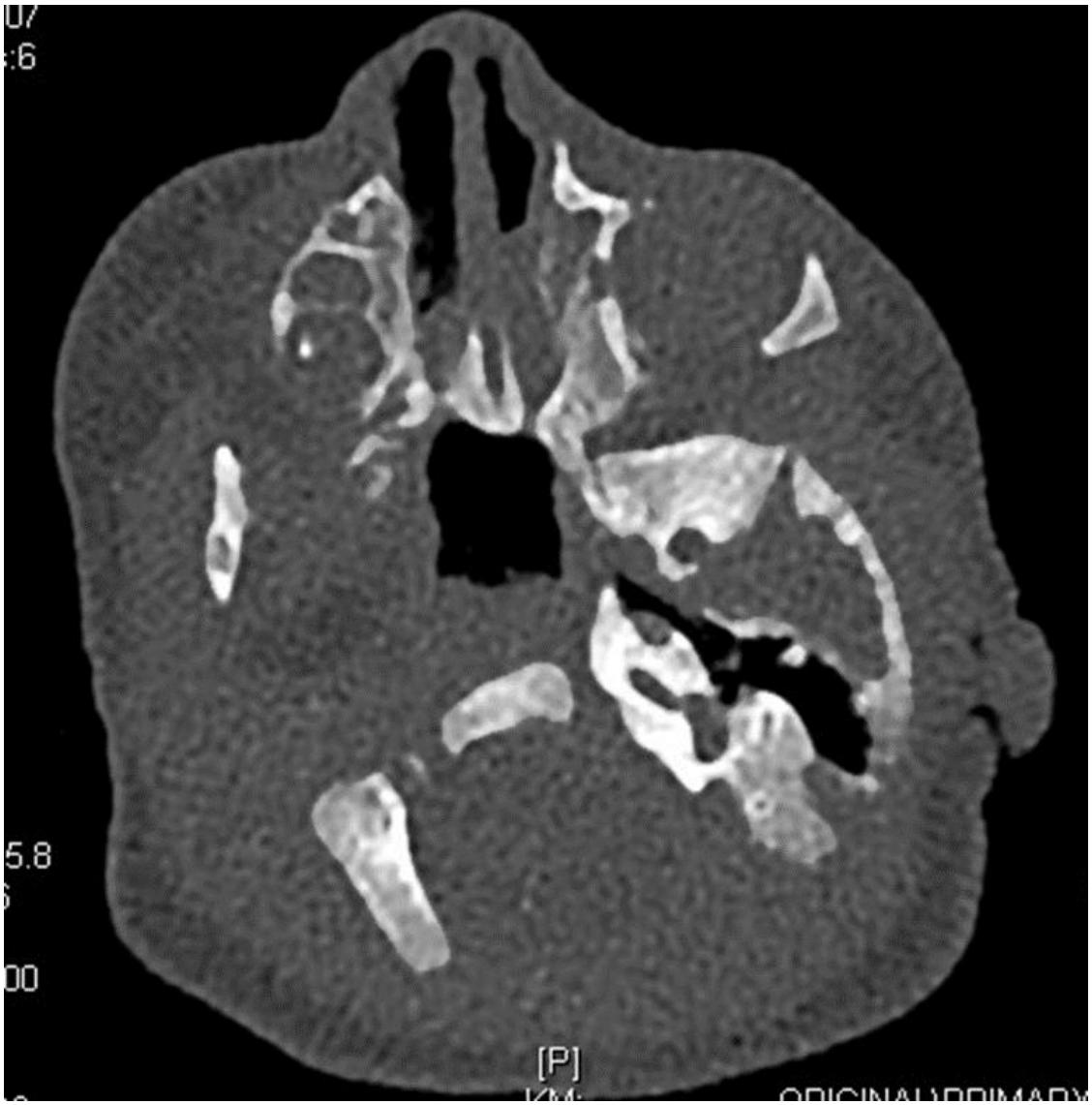

Figure 7 CT-scan: Computerized tomography image in axial plane with bone window of a patient presenting with a bilateral mixed choanal atresia.

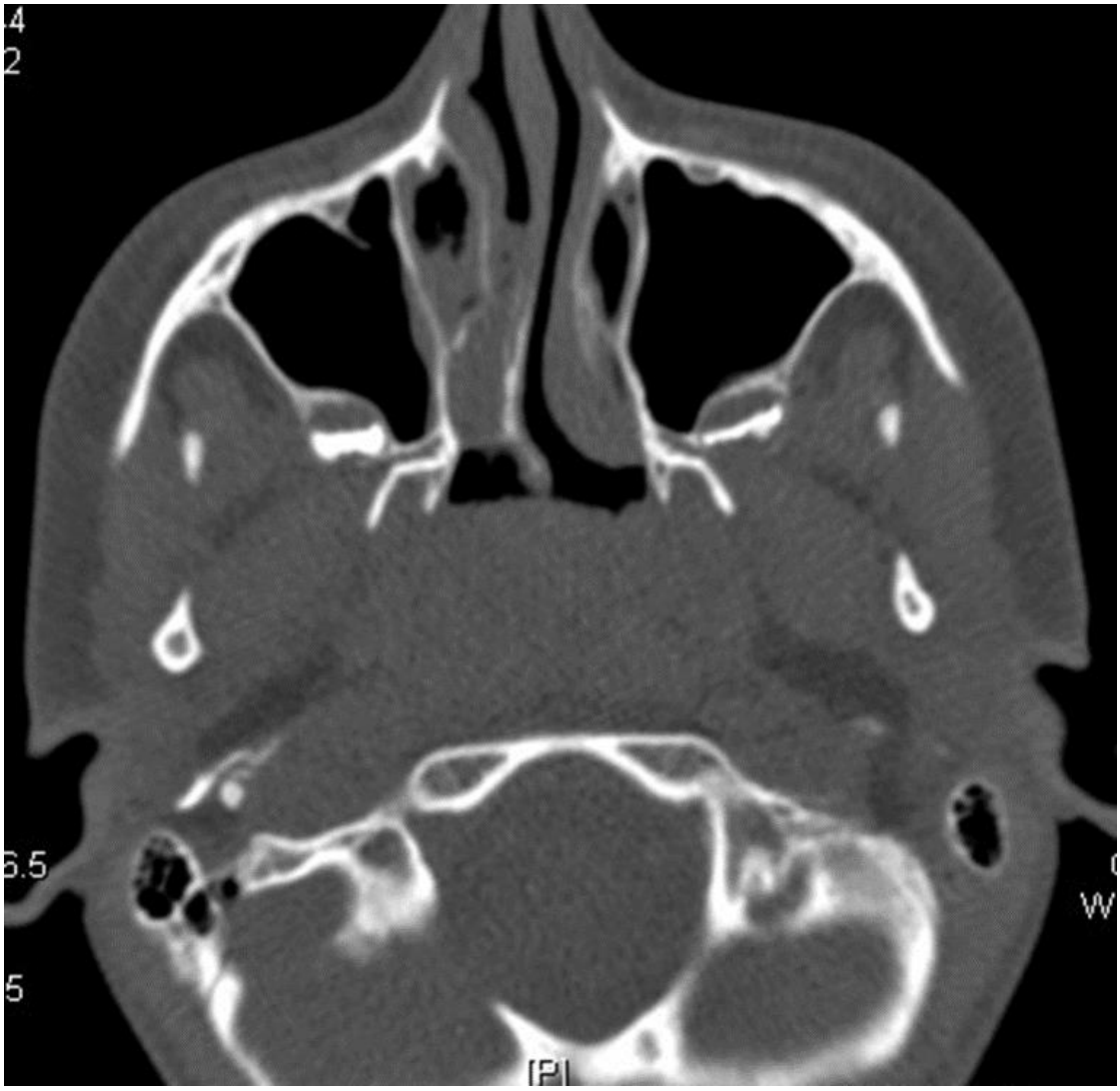

Figure 8 CT scan: Computerized tomography, in axial plane with bone window, of a patient presenting with unilateral atresia on the right side, being in this case the osseous component less predominant

- Surgical details: number of procedures in general anesthesia, use and type of stent, duration of stent applied. Operation time as well as surgical technique used were noted. Measurement of the perioperative surgical size of the neochoana using the applied tube or tubes as well as the sinus surgery instruments (Figure 9).

- Complications: The incidence of early or late onset complications was recorded, as well as its treatment.
- Follow up: The duration of follow up was noted, as well as the findings of endoscopy and the presence of symptoms.

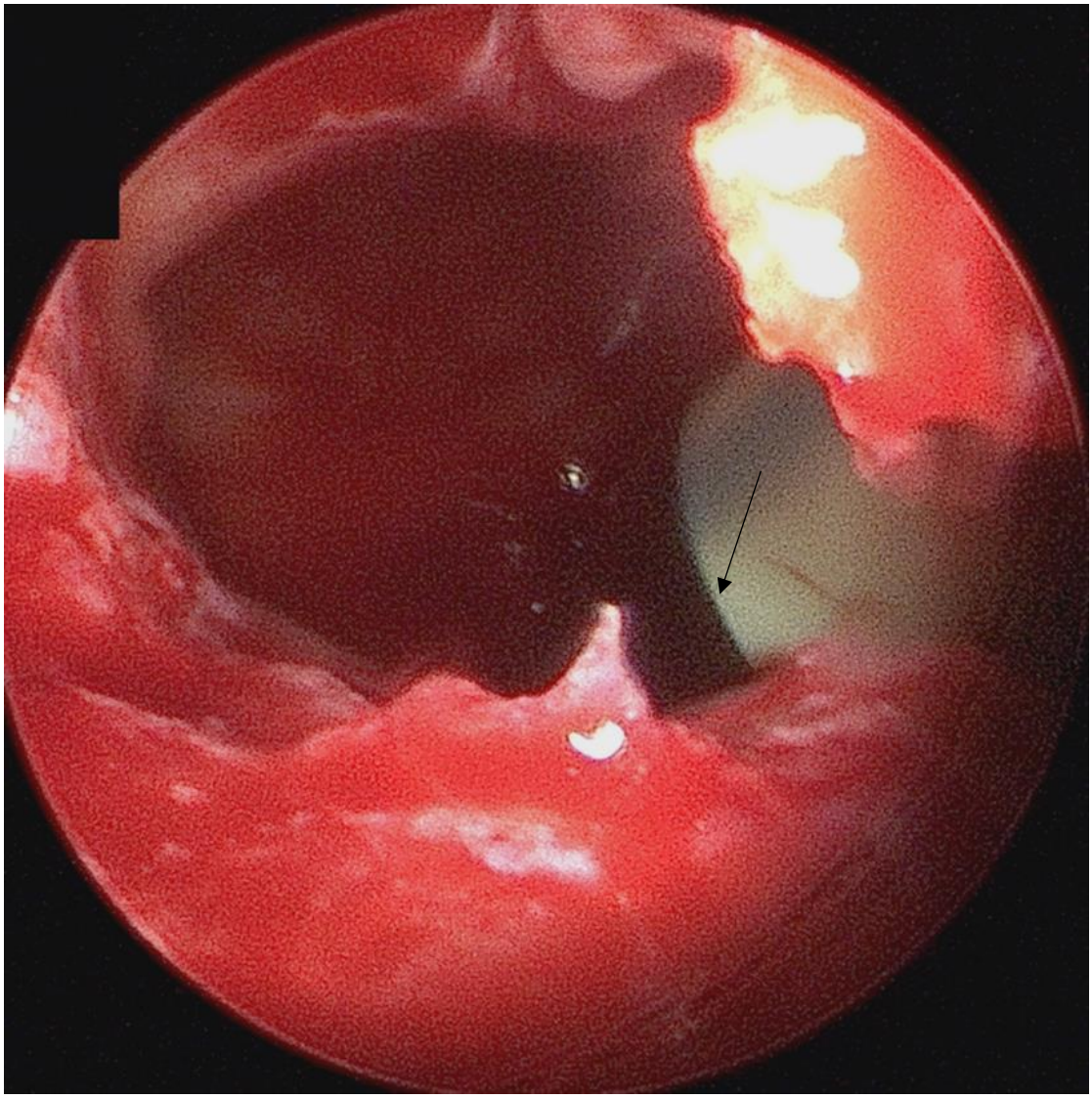

Figure 9 Intraoperative view of a patient presenting with bilateral atresia after opening a neochoana. Arrow showing a tube inserted perioperatively on the contralateral side

The anatomical and functional results that determined success or failure of the surgery were grouped according to the classification published in 2017 by Karligkiotis (Karligkiotis et al., 2017) as shown in Table 1. This classification is applied based on the clinical and endoscopical findings. It was important to note the absence or presence of dyspnea or nasal obstruction as well as the intake of food in order to judge the patient as asymptomatic or symptomatic. Additionally, in order to classify the anatomical result, it was important to note the passage of the flexible endoscope in the postoperative examination, the aspect of the surgical wound, and the presence, if any, of granulation tissue or scarring. These examinations were performed for at least one year postoperatively, either at the department or by another fellow otolaryngologist, in order to classify the results. Patients lost to follow up were not considered in the final analysis.

For the statistical analysis we used SPSS version 25 (IBM). A multinomial logistic regression was applied for categorical values. Comparisons were performed using the Fisher/Chi Square test where applicable.
We considered a significance level of 0.05.

3. Results

3.1 Demographics

Our population was comprised of twenty-nine patients, of which 37.9% (11/29) were male and 62.1% (18/29) were female.
The youngest patient was two days and the oldest twenty-six years old, with a mean of 5.8 years and SD 7.93. The patient who was twenty-six was a young man presenting for revision for bilateral choanal atresia. He was operated on when he was a child in another country.
The weight of the patients varied between 1.8 kg and 85.0 kg, with a mean of 21.6 and SD 25.1.

Patients presented a unilateral choanal atresia in 58.6% of the cases, occurring on the right side in 8 patients and on the left in 9. It was bilateral in 41.4% of this population.

Four subjects underwent one previous surgery at another institution and later sought treatment in our department through referrals.

These features further distributed as shown in Figure 10 and in Table 2.

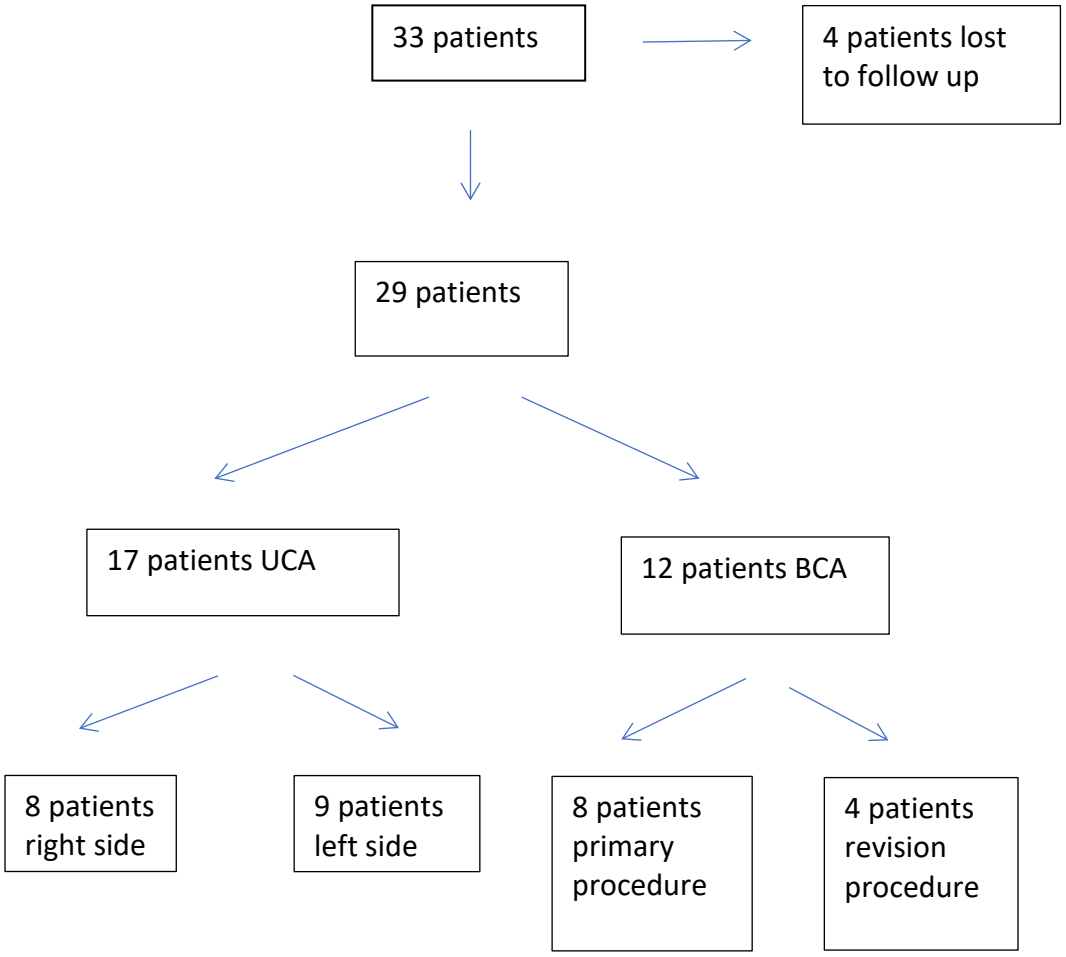

Figure 10 Choanal atresia Patients: Distribution of patients operated for choanal atresia in the Department of Otolaryngology and Head and Neck surgery in Tübingen. UCA - unilateral choanal atresia, BCA - bilateral choanal atresia

Table 2 Patients demographic details:. UCA – unilateral choanal atresia. BCA – bilateral choanal atresia, SD standard deviation, M- male, F- female

Patient details	**N**	**Age in months (mean, SD min, max,)**	**Weight in kg (mean, SD, min, max,)**	**Gender**	**Associated Syndrome**	**Previous surgery**
UCA	17	99.6 88.4 3.50 249	30.2 24.1 3.6 85.0	6 M 11 F	6 present 11 absent	17 none
BCA	12	27 91.4 0.07 318	9.4 21.9 1.8 79	5 M 7 F	7 present 5 absent	4 yes 8 none
Total	29	69.8 95.2 0.07 318	21.6 25.1 1.8 85	11 M 18 F	13 present 16 absent	4 yes 25 none

3.2 Type of atresia

According to the perioperative reports, the atresia was classified by computerized tomography or intraoperatively as bony, mixed or membranous. There was only

one patient presenting with a purely membranous atresia. The remaining patients had a combination of bone and soft tissue.

3.3 Associated malformations

Patients presented with an associated syndrome in 44.8% of the cases.
Often associated syndromes such as CHARGE and Treacher-Collins-Franceschetti, were present in 4 and 3 patients respectively. The distribution of other associated anomalies is depicted in Table 3.

In 55.2% of the patients no other malformation was reported. Three of the children were born pre-term.

Table 3 Presence of concomitant pathologies: UCA – unilateral choanal atresia, BCA bilateral choanal atresia, CHARGE - Coloboma, Heart defects, Atresia choanae, growth Retardation, Genital abnormalities, Ear abnormalities

Medical comorbidities	**UCA**	**BCA**	**Total**
CHARGE	2	2	4
Treacher-Collins-Franceschetti	1	2	3
Prader Willi	1	0	1
Trisomie 21	0	1	1
Chromossome 1 Anomaly	0	2	2
Dandy Walker	1	0	1
Caudal Regression	1	0	1
Total	6	7	13

3.4 Diagnostic computerized tomography

A pre-operative computerized tomography of the head, according to the pediatric European guidelines (Moreddu, Rizzi, et al., 2019) was performed in 72.4% of the patients.
Figure 6 to 8 show images of computerized tomographies of patients presenting bilateral and unilateral atresia. Of notice the different preponderance of bony and membranous tissue obstructing the choana.

3.5 Surgical Technique

Our population of patients was in all cases operated on endoscopically through the nose, with a 2.3 or 4 mm rigid 0-degree Hopkins Endoscope (Storz-Germany). A CO^2 Laser was used in four patients.
Due to the anatomical characteristics of the atresia, a diamant high speed drill with 12 to 30 000 R/min, with a diameter of 4mm and angled to 15 ° (Medtronic, USA) was needed in 44.8% of the subjects. Therefore in 55.2% of the cases the surgery was performed with standard or pediatric cutting cold steel instruments for sinus surgery.

3.6 Number of Procedures in General Anesthesia

In total, the number of procedures per patient performed in general anesthesia varied from one to nine, with a mean of 2.38 and a standard deviation of 2.1.
Patients presenting with bilateral atresia needed more surgical procedures in order to achieve success than patients with unilateral atresia (4.1 ± 2.5 SD vs. 1.2 ± 0.6 SD, $p = 0.001$). The procedures in general anesthesia were performed in order to change the tube placed in the nasal cavity when it was dislodged or to

proceed to its removal. When there were postoperative signs for presence of granulation tissue or scarring, revision surgery was indicated.

All except three patients had one to three procedures performed while under general anesthesia in the Department of Otorhinolaryngology, Head and Neck Surgery of the University Hospital in Tübingen.

The number of procedures distributed in respect to the presence of unilateral or bilateral atresia is stated in table 4.
Mean operating time was highly variable depending on the type of procedure performed such as primary surgery, revision surgery, or tube exchange/removal, and whether there was a secondary procedure associated. The primary procedure in our institution lasted for an average of 66.3 minutes, with a standard deviation of 31.4.

Table 4 Surgical details: under consideration were the application of a stent and its duration as well as the number of procedures performed in general anesthesia; BCA – bilateral choanal atresia, UCA – unilateral choanal atresia, SD – standard deviation, Min – Minimum, Max - Maximum

Surgical details	**Stent/Tube applied intraoperatively**	**Duration of Stent – weeks (mean, SD, Min-Max)**	**Number of procedures in general anesthesia (mean, SD, Min-Max)**
BCA	11 yes 1 no	5.0 3.1 0-12	4.0 2.5 2 - 9
UCA	10 yes 7 no	2.9 3.4 0-12	1.2 0.6 1 – 3
Total	21 yes 8 no	3.8 3.4 0-12	2.4 2.1 1-9

3.7 Stenting

A stent was placed in the majority of the patients in this cohort, yet predominantly and for longer duration in cases of bilateral atresia.

For twenty-one patients, a tube was inserted in the nasal cavity at the time of the first surgery in our department. This tube was placed for a duration of 0 to 12 weeks. In almost all patients an endotracheal Vygon tube was used (Vygon, code 525, France). Its size was chosen according to the nasal cavity anatomy and its length was tailored so that its end presented in the nasopharynx. In general, tubes sized between 2.0 und 5.2 (inner diameter) were used. In one patient, a McGill

tube (McGill, USA) was applied. In another patient, a Nitinol stent (micro-tech-Europe), an expanding device typically used in vascular procedures, was placed intraoperatively.

Using the logistic model, we could not find a significant relationship between the success of the surgery as classified by Karligkiotis (and used in this cohort) and the use of a stent in this population (p 0.497), as described in detail in Table 4.

3.8 Drug eluting stent

A drug eluting stent (Propel mini (R), Intersect ent, USA) was applied in four patients, enumerated below as patients 20, 21, 23, and 24.

Patient 20 underwent a second revision surgery at ten months of age. The right side of the neochoana was narrow and the child was symptomatic. A corticosteroid eluting stent was applied, subsequently achieving surgical success such as defined by Karligkiotis.

Patient 21, who presented with unilateral atresia, was five years old and weighed 23 kg. No tube had been placed in the first surgery, and this patient had to go through revision surgery. A drug-eluting stent was placed at the time of the endoscopic revision. Postoperative surgical success was achieved.

Patient 23 presented with bilateral choanal atresia and weighed 1.8 kg at the time of the first operation. A Vygon tube (Vygon, France) was placed for four weeks. In the second procedure performed in general anesthesia the tube was removed as well as granulation tissue and a drug-eluting stent was inserted. This child underwent two procedures in general anesthesia with resulting surgical success.

Another drug-eluting stent was used in the primary surgery for patient 24. He presented with unilateral choanal atresia and concomitant CHARGE syndrome,

had a weight of 6.10 kg at the time of surgery and was three months old. Surgical success was achieved in this patient. Further details are noted in Table 5.

Table 5 Patient cohort: Patients who received a drug-eluting stent; BCA - bilateral choanal atresia, UCA - unilateral choanal atresia

Patient N	**BCA/UCA**	**Age at surgery**	**Weight in kg**	**Use of drug eluting stent**	**Classification of results (as in table 1 according to Karligkiotis)**
Patient 20	BCA	5 days	3	By 2. Revision	A
Patient 21	UCA	5 years	23	1. Revision	A
Patient 23	BCA	3days	1.8 at 1. Operation	At stent (Vygon tube) removal	A
Patient 24	UCA CHARGE	3 months	6.10	At stent (Vygon tube) removal	A

3.9 Size of the Neochoana

The maximal size of the neochoana created was dependent on the patient's weight and was distributed according to the presence of unilateral or bilateral atresia as stated in Table 6.

Table 6 Neochoana: Size of the Neochoana in mm

Size of the neochoana	Mean in mm	SD
Unilateral choanal atresia	9.4	2.7
Bilateral choanal atresia	6.8	4.5

There was a linear relationship between the weight of the patient and the possible size of the choana perioperatively R^2= 0.673 (Figure 11).

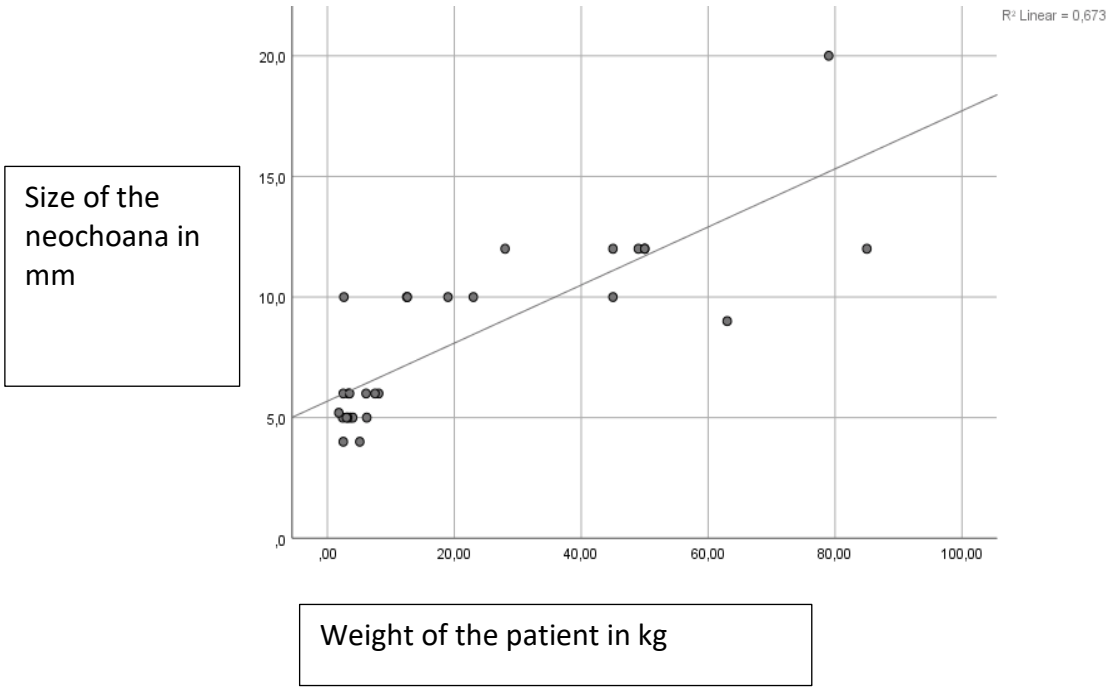

Figure 11 Neochoana size/ weight: Relationship between neochoana size in mm (y) and weight in kg (x) of the patient.

3.10. Complications

Within the study population, one patient suffered from epistaxis occurring one week after surgery. Silicon foils had been placed in the patient presenting with

unilateral choanal atresia, and one of them was displaced. This was removed and a nasal packing was placed for two days. After its removal there was no further event.

Another patient, nine years of age and presenting with unilateral atresia, had a silicon foil stitched to the septum that dislodged two days later. It required an additional surgery in general anesthesia to replace it.

Two other patients, one two days old and another seven days old, both presenting with bilateral choanal atresia, had dislocation of the tube, respectively, four days and one week after the first procedure respectively. They required repositioning of the tubes.

The two-day-old infant with bilateral atresia in whom the Nitinol stent was applied required removal due to migration. It was then replaced by tracheal tubes.

3.11 Factors for failure and need of revision surgery

In this study, the results of surgery were classified according to the publication from Karligkiotis as shown in Table 1. The following results achieved after first surgery distributed as follows: A: 55.2%, B 27.6%, C 6.9%, D 10.3%.

This is shown in detail according to the presence of unilateral or bilateral atresia in Table 7.

Table 7 Results: Distribution of results according to the classification published by Karligkiotis in 2017 (Karligkiotis et al., 2017), as described in Table 1.

Classification	**A – surgical success Example in Figure 12**	**B – functional success**	**C- functional failure**	**D – surgical failure**	**Total**
Unilateral Choanal atresia	8	7	2	0	17
Bilateral Choanal atresia	8	1	0	3	12
Total	16	8	2	3	29

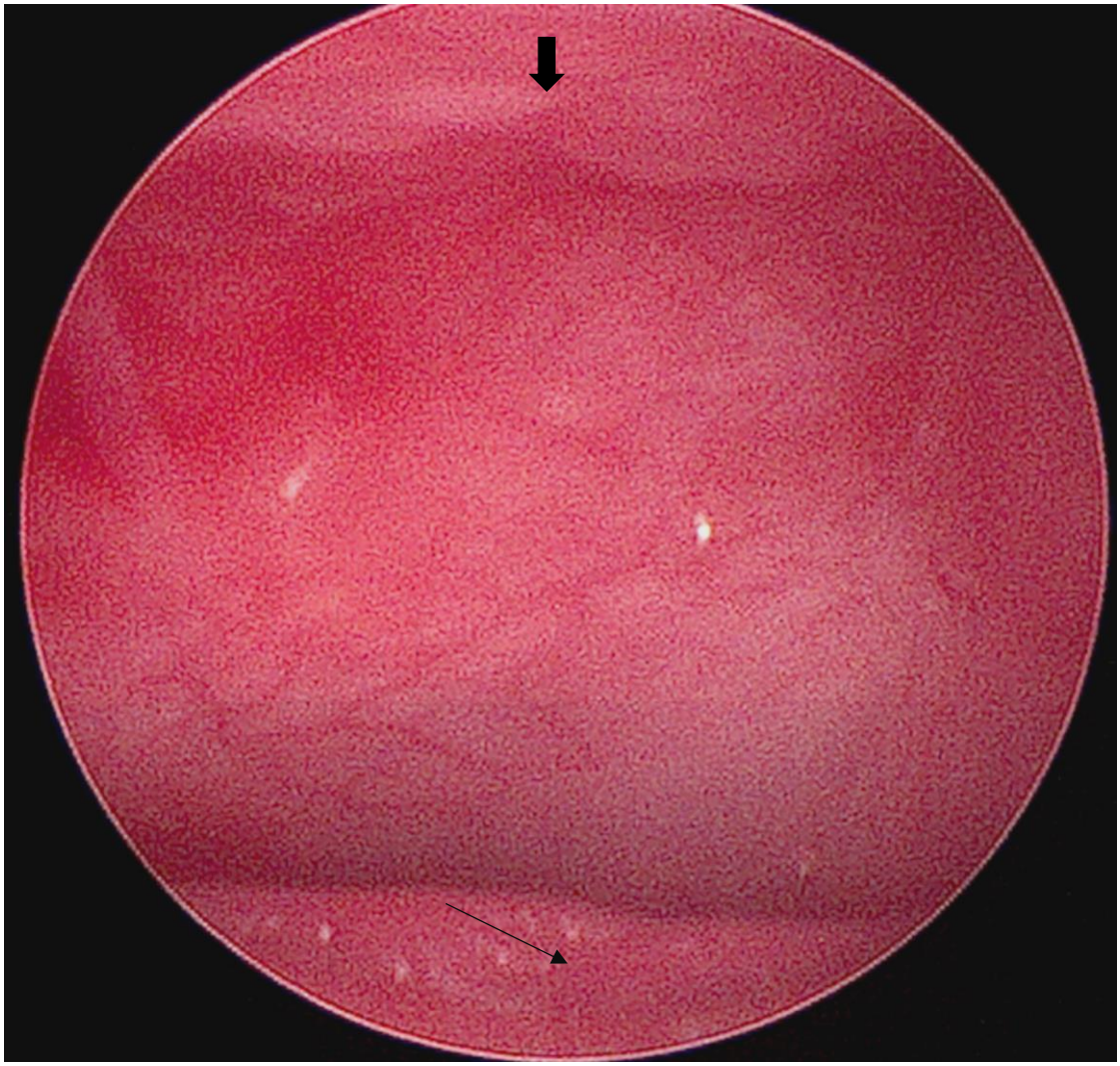

Figure 12 Postoperative result: Example of a postoperative view showing a surgical success, Type A

The wound is well healed, with a smooth contour with a look at the nasopharynx from a neochoana after surgery for bilateral atresia. The roof of the soft palate is seen at a placement of 6 o'clock (fine arrow) above we recognize the roof of the nasopharynx (broad arrow).

There were two patients that underwent surgery for unilateral choanal atresia that presented postoperatively with stenosis. They did not present symptoms, and have decided not to go through revision surgery.

The logistic regression model results showed that there were two important factors determinant for success at first surgery. These factors reached statistical significance, and they were the weight of the child and age at the time of surgery as described in Table 8.
In our population, neither the isolated presence of bilateral or unilateral atresia nor the presence of a concomitant syndrome reached statistical significance.

The use of any particular instrument, such as a drill, did not impact the results (p 0.383) or the placement of a stent (p 0.497) in the logistic regression model (Table 8).

Table 8 Logistic Regression Model: Implication of patients' characteristics in the success of surgery

Patient characteristics at time of surgery **N 29**	**Mean, Standard Deviation or percentage**	**p value**
Weight in kg	21.6, 25.1	0.002*
Age in months	69.8, 95.2	0.001*
Bilateral or unilateral Atresia	41.4%/58.6%	0.390
Associated Syndrome	44.8%	0.237

In detail, we identified 3 patients in this population of 29 patients who needed revision surgery and underwent more than three procedures in general anesthesia: subjects 6, 10, and 21. They presented with bilateral choanal atresia. Two of them had concomitant pathology.
Patient 6 underwent dilatation nine months after the first surgery, and later underwent a revision surgery after nine years.
Patient 10 went through revision surgery three months after first surgery.

Patient 21 was re-operated on four months after the first surgery and underwent another procedure six months later.

These patients all presented with weight inferior to 3 kg at the time of the first surgery.

We analyzed the importance of presenting with a weight inferior to 3 kg performing a Chi Square test, which showed to be highly significant (p=0.003*), described in Table 9.

Table 9 Demographics: patients requiring revision:

Subject	**Demographic**	**Data**
Patient 6	3 days, bilateral atresia	2.6 kg, trisomy 21
Patient 10	7 days, bilateral atresia	2.5 kg, caudal regression
Patient 21	5 days, bilateral atresia	3 kg, no syndrome

3.12 Follow up

Our patients were followed up for a least one year, in person by either the surgeon or a fellow ENT colleague, and through telephone contact.

Follow up in our department alone was on average of 93.2 weeks, with a minimum of nine weeks, maximum of 843 weeks.

The total rate of success in patients with bilateral and unilateral atresia, combining surgical and functional success, was 82.8%.

As for unilateral choanal atresia, a surgical and functional success was attained in 88.2% of the cases. In bilateral cases it reached 75**%.**

4. Discussion

4.1 Methodology

4.1. 1. Strengths and weaknesses

The current study has some weaknesses that are worthy of comment. First, the current study is a retrospective observational study. Therefore, there may be an information bias. In a retrospective study, data is not always introduced in the files in a standardized manner and there is larger group of healthcare workers involved in diagnosis and treatment as well as in the introduction of the data in the files.

Second, it reports over a population of patients presenting with unilateral and bilateral choanal atresia in a combined analysis. There may be some heterogeneity caused by the different demographic characteristics of these populations.

Third, the current study included different surgeons operating on the population described. This fact may include variabilities in the techniques performed. Limitations in the analysis of the technique as a factor contributing to the success or failure of the surgery further reduces the statistical power.

Fourth, the fact that some patients were lost to follow up may again introduce a bias. There were insufficient records of these children, and no reasons for missed appointments were noted.

Fifth, reporting over a small, specific population may limit the statistical power of the study. The focus on small children in the study population limits the possibilities for performing large prospective randomized studies.

In contrast to the limitations just elucidated, the current study exhibits several strengths in comparison to previous publications.

To begin with, it has the advantage of being based on a digital filing system, thus allowing a more detailed description of the characteristics of the patients and of the care performed, and without the risk of losing information related to manual

records. As it follows international standards in the level of care, essential pieces of information were always available.

Furthermore, the diagnosis of choanal atresia in this study follows the current guidelines (Moreddu, Rizzi, et al., 2019). What this means is that a nasal endoscopy was always performed by a trained otolaryngologist, enabling the correct identification of the medical condition, and that the nasal cavity was scanned with a computerized tomography, which in the current study was performed in 72.4% of the cases.

Additionally, in the present study we report in detail the number of procedures performed in general anesthesia as well as the complications encountered. A detailed description of the indication to engage in each procedure performed in general anesthesia has been provided. As there are associated risks of procedures in general anesthesia, especially for young children, we believe this information is relevant.

Finally, in our group of patients the type of tubes or stents used are reported in detail, as well as the complications associated with their use. Descriptions of different techniques or devices utilized for the treatment of choanal atresia provides additional information regarding their safety.

4.1.2. Discussion of the success measures

The size of the neochoana achieved postoperatively was measured by the surgeon either with the help of the tubes applied, or by the instruments used to perform the surgery. This may be an approximate estimation of the neochoana, bringing error in the preciseness of the measurement by some millimeters. However, an alternative method was not always available. For instance, the use of a computerized tomography could introduce exposure to unnecessary radiation.

The success of the surgery was evaluated according to Karligkiotis classification system, a relatively easy application considering the resources and clinical follow

up performed in our institution, even though the endoscopic findings may have been dependent on the observer. Additionally, it has the advantage of increasing detail in the analysis of results, evaluating both the endoscopic findings as well as the clinical description of the symptoms. The fact that varied centers already used this classification or a similar one may increase uniformity in the reporting of results (Karligkiotis et al., 2017).

The diversity in observers performing follow up may cause an information bias, nevertheless it also helped to sustain a very long and multifaceted observation period in most cases.

4.2. Discussion of Results

In the last twenty years, several authors published the results of their surgical treatment of choanal atresia. Over thirty papers reported populations ranging from 7 to 114 patients and include patients operated by an endonasal approach in the majority of cases. This was made possible due to the technical advances in endoscopic sinus surgery since the end of the 1990s. It includes the development of rigid endoscopes with various degrees of view and of several thicknesses, the ability to couple these to high-definition cameras connected to screens of optimal resolution, combined with the know-how for producing delicate as well as powered instruments exclusively designed for the endoscopic surgery. This development was optimized through cooperation among surgeons and the medical industry in order to bring technique into uniformity and perfection.

There is a natural demographic separation in the treatment of unilateral and bilateral atresia. Children presenting with bilateral atresia are diagnosed after birth almost exclusively. As newborns are uniquely nasal breathers, the necessity to address this condition presents in the first days or weeks of life. Patients presenting with unilateral atresia can in the majority of the cases wait until the anatomical conditions are more favorable to undergo surgical treatment.

However, opinions largely differ in the use of tubes or stents intraoperatively as well as raising mucosal flaps.

The majority of the publications consist of retrospective studies. There are only three prospective studies from otolaryngologists practicing in Egypt addressing this pathology.

There is a constant need to improve treatment of this condition and reach optimal results with as small a number of procedures and complications possible.

4.2.1 Demographics

In the present study there was a preponderance of cases in female subjects, which correlates to other observations from colleagues working in different parts of the globe. The group of patients in this study comprised twenty-nine patients, of which 37.9% were male and 62.1% were female, with a rate of 1.66:1. Samadi and colleagues described population presented at a rate of 1.6:1 (Samadi et al., 2003); Eladl and Khafagy published a report on one hundred and twelve children presenting bilateral atresia and comprising a rate of 3.5: 1 female to male. (Eladl & Khafagy, 2016).

Choanal atresia presented as unilateral in 58.6% of the cases. It appeared on the right side in eight patients and on the left side in nine patients. It was diagnosed as bilateral in 41.4% of the cases. The observations of this study reflect the findings of other publications, in reference to both types of atresia. Samadi and colleagues reported 55% bilateral cases in a large population of seventy-eight children (Samadi et al., 2003); Hengerer and co-workers in 2008 analyzed seventy-three cases of choanal atresia and reported 38% bilateral atresia cases (Hengerer et al., 2008). In a population of one hundred and fourteen patients treated in the Children's Hospital La Timone in Marseille, 32.5% had a bilateral atresia (Moreddu, Rossi, et al., 2019). In a Belgian population of children treated for bilateral or unilateral atresia, 38.7% were bilateral (Brihaye et al., 2017).

The definition of atresia as membranous, bony or combined is very much dependent on the method used to detect its characteristics. In the present study, a computerized tomography was not performed in all cases before the surgery. This left the evaluation up to the judgement of the surgeon, who then chose

surgical instruments accordingly. A combined type was reported in over 90% of the cases. There was only one case of purely membranous choanal atresia encountered; not surprising, since according to conclusions from Hengerer, purely membranous atresia is quite rarely encountered (Hengerer et al., 2008).
The age at which first surgery is performed is intrinsically related to the presence of unilateral or bilateral atresia. The combination with syndromic conditions and its symptomatology may also play a role. In this study, the youngest patient was operated on at two days old and the oldest was twenty-six years old, with a mean of around five years (69.8 months) with a standard deviation of 95.2. This was substantially earlier in the case of bilateral atresia. The majority of the cases of bilateral atresia were operated on before two months of age, an age that correlates well with the most current publications. In a Belgian population, for example, the age of first surgery reached a mean of ten days and this value was four days in another population in Germany comprising fifty children presenting choanal atresia (Brihaye et al., 2017; Velegrakis, Mantsopoulos, Iro, & Zenk, 2013).

The percentage of patients presenting concomitant medical problems reaches in the current study 44.8%. As previously mentioned, patients diagnosed with CHARGE association and Treacher-Collins-Franceschetti are often presenting choanal atresia, due to the genetical defects occurring at a cellular level. This value is in agreement with several other series analysing this population, and varies from 25% to about 52% (Brihaye et al., 2017; Hengerer & Strome, 1982; Uzomefuna, Glynn, Al-Omari, Hone, & Russell, 2012).

4.2.2 Reported success rate and number of surgeries

The surgical and functional rate of success documented in previous literature is dependent on the classification adopted. Although some authors, for example Karligkiotis and team as well as Brihaye and colleagues, adopt similar definitions of success, standard postoperative procedures can be quite disparate from surgeon to surgeon, having an impact how success is determined (Brihaye et al.,

2017; Karligkiotis et al., 2017). While some authors consider every endoscopic procedure to remove granulation or crusting a revision (Kim et al., 2012), others include these in the standard of care (Romeh & Albirmawy, 2010; Wormald, Zhao, et al., 2016).

In the current study, the performed surgical procedure reached a functional success of 82.8% at first approach, which is slightly inferior to the one reported by the above authors who adopted the same or similar classification. This may be due to demographic characteristics, but may also be a result of technical details such as raising mucosal flaps, the absence of use of a tube or stent perioperatively, or even the postoperative care. Both authors mention however the necessity of executing a very close follow up in order to keep the wound clear from crusting and granulation tissue and, when necessary, in tandem with sedation or general anesthesia. Karligkiotis and colleagues notice that in infants presenting with bilateral choanal atresia, the combined percentage of functional and surgical success is lower than in cases of unilateral atresia. In this study, which analyzed a large population of 84 patients from Northern Italy, of which twenty-nine presented with bilateral atresia, it reached an overall success rate of 93%, yet achieving 86.2% for bilateral cases. The mean age for bilateral cases was relatively high in this report, with a value of two years (Karligkiotis et al., 2017).

Brihaye and colleagues reached a clinical success of 94%. They applied a purely endoscopic technique, applying no stent perioperatively and instead using mucosal flaps fixed with fibrin glue. This team referred to the necessity of wound cleaning postoperatively (Brihaye et al., 2017).

In an earlier report from 2010, Ibrahim and colleagues did not use a stent. They presented an 85.7% success rate, slightly superior to the present study. This team also described the necessity of a regular debridement of the wound postoperatively (Ibrahim, Magdy, & Hassab, 2010).

Our results correlate well with another large population analyzed by Moreddu and colleagues, presenting an overall success rate of 79.8%. It included thirty-seven patients presenting bilateral atresia. However, only 10 were treated endonasally,

the rest underwent operations using a transpalatinal approach. In the majority of cases there was a stent applied intraoperatively (Moreddu, Rossi, et al., 2019).
De Freitas and Berkowitz in 2012 reported a 70% success at first surgery, which also correlates well with our results in children with bilateral atresia. They analyzed their results of surgery only in patients presenting this condition. A stent was applied perioperatively in all cases. It is worthwhile to mention that this population had low weight, with a mean of 2.7 kg, and a high percentage of further anomalies reaching 87% (De Freitas & Berkowitz, 2012).

Other colleagues from Ireland, when analyzing their results of the surgical treatment of thirty-one children with choanal atresia, concluded that the use of a stent may have contributed to a worse result, suggesting however the possibility of age and the presence of bilateral atresia as the intrinsic factor contributing to this conclusion, as stents are mostly used in this group of patients (Uzomefuna et al., 2012).
Not every publication reported in detail the number of surgeries needed to achieve patency, inhibiting any larger comparisons.
In the present study, almost all patients achieved patency after one to three procedures. However, three patients needed more than three procedures in general anesthesia to achieve a satisfactory result. All of these children presented with a bilateral atresia. Our results correlate well with the study from Samadi and colleagues. They wrote that the number of procedures to achieve patency was on average 2.7 for unilateral cases of choanal atresia while for cases of bilateral atresia this was higher with a value of 4.9 (Samadi et al., 2003).
Hengerer in 1982 also reported 4.2 procedures on average in patients presenting with bilateral atresia in order to achieve success (Hengerer & Strome, 1982).

4.2.3. Reasons for restenosis

In this study we identified two factors with statistical significance for the occurrence of restenosis: these were age and weight of the patient at the time of

the first surgery. In particular, we reported over three patients with a weight under 3 kg when treated for the first time endoscopically. All cases needing revision, indicating surgical failure, weighed less than 3 kg at the time of the first surgery. This factor was statistically significant. These patients had a very high rate of restenosis, needing more procedures in order to achieve patency. We identified this weight at first surgery as the cutoff for worse results.
The current study shows that the surgical result is dependent on age and weight of the child at the time the surgery is performed.

Additionally, the maximal possible size of the resulting neo choana is directly dependent on the weight of the patient.

Our results confirm the observations from a previous report by Moreddu and colleagues identifying the influence of age, weight and the presence of bilateral atresia in the success of the surgery (Moreddu, Rossi, et al., 2019).
In contrast to this publication, the cut off weight we identified as having implications in the success of the surgery was 3 kg. In the publication from the colleagues from Marseille, 5 kg of weight at first surgery was stated as having implications on treatment failure. The reason for this discrepancy could be that the majority of their cases of bilateral choana were addressed through operations using transpalatinal approach. They reported over 37 children presenting with bilateral atresia, of which only 10 were operated endoscopically.
Our results also relate to another publication from South Korea identifying age as a factor contributing to success of the treatment, although not presenting a cutoff value (Kim et al., 2012).
The presence of bilateral atresia did not reach statistical significance in our logistic regression model, as opposed to the reports from Kinis and team and Velegrakis and colleagues (Kinis et al., 2014; Velegrakis et al., 2013). This may be due to the distribution of our population.
As previously mentioned, some colleagues propose that the use of stents is deleterious to the success of the surgery (Tatar et al., 2017; Teissier et al., 2008). In our group of patients, it was not possible to compare the use of stents versus

no stent, possibly because almost all of the bilateral atresia cases were stented or a tube was inserted. A stent was kept in place on average for three weeks in cases of unilateral atresia, and on average for five weeks for children presenting with bilateral atresia.

Again here, we could not draw conclusions about the effect of the duration of stenting in the surgical results, as proposed by Romeh and Albirmawy (Romeh & Albirmawy, 2010). This reluctance to observe a relationship between treatment and success was additionally reported in a metanalysis studying cases with bilateral atresia by Strychowsky and colleagues in 2016 (Strychowsky et al., 2016). It included 3 prospective and 10 retrospective studies. It concluded that there was no difference in the results using or not using a stent perioperatively. Yet the application for a short duration of less than seven days had a tendency to achieve better results with p value of 0.03. Surgical success reached 82% in cases of shorter duration of application of the stent versus 60% in cases of longer application. Still authors pointed to the fact that there were only two studies approaching this question, with differences in the age at the time of the procedure.

In the present population of patients, a tube was not inserted perioperatively in older children. Except in one case, all children that did not have a stent applied were older than two years. With the exception of one case, all the children presented with a unilateral atresia. In these, the use of a tube or stent is, as shown, not necessary. The airway is secured, and only one patient did not achieve a good result postoperatively.

In this cohort of patients there was only one case presenting with bilateral atresia in whom a stent was not placed. This was an infant that was operated on at fifteen days of age, and presented with bilateral atresia. He weighed 3.5 kg. Surgical success was achieved. This child was followed up by our department for over two years.

A small group of patients received a different peri- or postoperative care. Four patients with choanal atresia received at the second procedure or at the time of revision surgery a drug-eluting stent releasing corticosteroids to the wound for

about four weeks. Although it was in a small number of patients, these children seemed to perform better going through less procedures in general anesthesia. Two of them were under 3 kg at the time of the first surgery.

This result agrees with some case reports, which showed use of a corticosteroid eluting stent to be a possible factor in reducing the number of procedures in general anesthesia (Wilcox et al., 2020).

However, there remains speculation that postoperative treatment of the wound with corticosteroids, which is not standard for all authors, may have had some impact.

This was described in detail in the publication from Belgium, which comprised nebulization with Fluticasone Proprionate three times a day for two months and later application of Mometason Furoate Nasal spray twice daily for the duration of six months (Brihaye et al., 2017).

The present study's observations, when considered with the results included in these publications, may show a benefit for use of locally applied corticosteroid in the surgical success after procedures for choanal atresia.

4.3. Other surgical endonasal wounds

Other endonasal surgical wounds compare to the one created after removal of a choanal atresia plate, resulting in a neo-choana. It results in a circular wound, being important to remove part of the vomer posteriorly to reduce this effect (Romeh & Albirmawy, 2010).

In patients undergoing endonasal endoscopical functional surgery for chronic rhinosinusitis, there may be a resulting postoperative stenosis in ostia, in about 15% to 27 % of cases (Ramadan, 1999)**.** The enlargement of the frontal recess in particular also may result in a circular wound, depending on the anatomy, which is highly variable, calling for the meticulous technique removing the cells around the drainage pathway of the frontal sinus (Wormald, Hoseman, et al., 2016). Here, the size of the maximal enlargement seems to play a role, as well as

transforming the shape of the wound and reducing mucosal damage (Hosemann, Kuhnel, Held, Wagner, & Felderhoff, 1997) (DeConde & Smith, 2016).

The effect of the perioperative care in this particular region is well known among the scientific community, particularly the local application of corticosteroids which is standard treatment and recommended in the international guidelines recently revised (Fokkens et al., 2020). Additionally, the application of corticosteroids locally with permanent release for a certain amount of time may be superior to the twice daily application, and may bypass the otherwise inevitable scarring during the healing time, allowing a better and larger size of the drainage (Beule et al., 2008).

In order to reduce scarring immediately postoperatively, these self-resorbing steroid releasing devices, which have been especially designed for use in the ethmoid cavity as well as the frontal sinus, have been tested in several trials in adult patients. This population followed a standard postoperative treatment of antibiotics and nasal spray with corticosteroids. A pooled analysis has shown some positive effects, reducing the need for postoperative interventions at day thirty. There were no adverse events reported with the use of these devices (Singh et al., 2019).

In the present study, we conclude that patients weighing less than 3 kg at the time of the first procedure and therefore with a smaller achievable neo-choana have a risk of needing a larger number of procedures in order to achieve a satisfactory connection between the nose and the nasopharynx.

In this group of patients, two infants presenting with bilateral choanal atresia with weights inferior to 3 kg received a drug-eluting stent perioperatively. One of the infants had it placed at removal of the fashioned tubes applied in the nasal cavity, while the other received it at the time of the second revision surgery. In total they went through less procedures in general anesthesia compared to the infants that had only received fashioned tracheal tubes places in the nasal cavity. Some authors reported the use of a drug-eluting stent in the case of choanal atresia. Wilcox and team reported its use in five patients, of which two had bilateral atresia. They also reported the reduced need to revision surgery, which relates

to our findings. There were no complications reported (Wilcox et al., 2020). Other colleagues from Michigan reported its use in two patients presenting with bilateral atresia, one as a primary procedure and the other in a revision surgery. They noted the reduced need of revision, after a twelve-month follow up (Bangiyev, Govil, Sheyn, Haupert, & Thottam, 2017). Adverse events also were not recorded. Their report corroborates the observations made in this study.
Improvement of the standard postoperative care can be expedited through the use of local steroids for reducing inflammation and scar formation, in addition to other surgical wounds in the nasal cavity such as mentioned above.

In addition to the size of the frontal sinus, much importance is placed on the achievable size of the neo-choana. This is directly dependent on the weight of the patient, and as such weight is a limiting factor for the success of the surgery.

The use of corticosteroids via nebulization or as drug-eluting stents peri and post-operatively may lead to better results. This issue needs to be further studied.

4.4 Complication rate

Not all publications are very detailed when reporting the rate of complications.
In the current study, most complications were related to the dislocation of the tube or silicon foil, occurring in four patients. They were then either replaced by another fashioned tracheal tube or foil, or they were removed.
In one of these patients, a nitinol stent was placed after the treatment for bilateral choanal atresia. These stents migrated and the child needed a further procedure to remove the remnant stent. Also, there was some scarring which made this process more difficult. These stents are successfully used for vascular procedures for many years (Abdoli, Katz, & Ochoa, 2020) and experimentally in the trachea (Choi et al., 2018). However, they did not seem to be adequate for this particular pathology.

Another patient had to be treated for epistaxis postoperatively, one week after the surgery.

Strychowsky and colleagues had published in 2016 a systematic review with metanalysis about the effect of using a stent in the treatment of bilateral choanal atresia and found nine articles which referred their complications (Strychowsky et al., 2016). In publications reporting cases using tubes or stents, dislocation was the most common occurring complication. Such reports relate well to the present study. Epistaxis was also noted, which occurred in one of our patients as mentioned.

However, in the present study further complications that have been previously described such as scarring of the columella, perforation of soft palate, serious bleeding or penetration of the skull base have not been detected (De Freitas & Berkowitz, 2012; Stieve et al., 2009; Velegrakis et al., 2013; Wormald, Zhao, et al., 2016).

4.5 Postsurgical care and follow up

In this group of patients, the post-operative care consisted mainly of rinsing the nose with saline, and in case of young children applying suction to the tubes, which was taught to the parents. This treatment is consistent with most of the other studies where tubes are applied (Hengerer et al., 2008; Tatar et al., 2017). Follow up, on average, surpassed the one year recommended in the recently published consensus (Moreddu, Rizzi, et al., 2019).

4.6 Clinical importance

The current study facilitates the pre-operative identification of possible risk factors associated with a worse surgical result and may help define the framework for further multicentric studies analyzing this group of patients.
Furthermore, the information obtained may improve counselling of the caregivers as well as contribute to boosting peri- and /or postoperative care in order to improve success or detect failure earlier.
In summary, multicentric randomized trials using steroid-eluting stents or postoperative corticosteroids for bilateral atresia could be very helpful in answering the question of its efficacy in improving surgical results.

5. Summary and Conclusion

Choanal atresia is a rare congenital occurrence which may present unilaterally or bilaterally and is often associated with other defects. The most vulnerable cases are found in newborns who, as nasal breathers, are under serious threat.

The medical community in the nineteenth century offered the first description of this pathology along with recommended surgical treatments. However, two centuries later, there still remains a need to optimize care of these patients, most often presenting at a very early and fragile age.
The present study had therefore a primary goal to describe the characteristics of the cohort of patients presenting with choanal atresia to the Department of Otolaryngology at the University of Tübingen as well as the treatments performed.
The second goal was to identify the factors for success or failure in the treatment of choanal atresia and to trace the occurrences of complications and / or effect of the use of stents.

With the analysis of our results, we could demonstrate that age and weight of the patient at the time of surgery are determinant to the results of the surgical endoscopical treatment of choanal atresia. Even with a relatively small population, we could apply a logistical regression model in order to analyze possible factors. Indeed, both these characteristics showed a statistically significant result.

Children of young age needed to go through a higher number of procedures, and this correlated well to the weight of the patients.

We demonstrated a cutoff weight that is especially relevant for the success of the surgery with an exclusively endoscopic endonasal approach. In particular, we could demonstrate that patients under 3 kg have to undergo more procedures in order to achieve patency.

In this study we showed that there is, as expected, a direct relationship of the size of the neochoana achievable related to the weight of the patient. This matter is of particular importance. As compared to other wounds in the nose, size has been found to be one of the limiting factors for success in achieving a patent ostium.

Unfortunately, we could not infer the influence of the use of a stent versus no stent for the results of the surgery.

With our population we could however have a glimpse of a possible advantage of the use of a drug-eluting stent in the reduction of the number of procedures performed in general anesthesia.

When analyzing complications or safety profile associated with the use of stents, we could report that there may be dislocation of both silicon foils and tracheal tubes fashioned to the neochoana and stitched to the septum. With this occurrence, a further procedure in general anesthesia is imperative.

We did not demonstrate any complications resulting from using a drug-eluting stent.

However, further studies in a larger number of patients are needed to ascertain their efficacy and safety in treatment.

Finally, we believe that the role of corticosteroids in general in the management of the surgical wound after treatment for choanal atresia, either perioperatively or postoperatively, needs to be further studied.

Choanalatresie, eine seltene Krankheit und deren Behandlung

Choanalatresie ist eine seltene angeborene Pathologie, welche einseitig oder beidseitig auftreten kann und oft mit anderen Defekten verbunden ist. Die vulnerabelsten Fälle finden sich bei Neugeborenen, die als Nasenatmer ernsthaft bedroht sein können.

Erste Beschreibungen dieser Erkrankung zusammen mit empfohlenen chirurgischen Behandlungen lassen sich auf das 19. Jahrhundert zurückführen. Zwei Jahrhunderte später besteht jedoch immer noch die Notwendigkeit, die Versorgung dieser Patienten, die sich meist in einem sehr frühen und fragilen Alter präsentieren, zu optimieren.
Das primäre Ziel der vorliegenden Studie ist die Charakteristika der Kohorte von Patienten mit Choanalatresie in der Klinik für Hals-Nasen-Ohren-Heilkunde der Universität Tübingen sowie die durchgeführten Behandlungen zu beschreiben. Das zweite Ziel ist es, die Faktoren für Erfolg oder Versagen bei der Behandlung der Choanalatresie zu identifizieren und das Auftreten von Komplikationen und/oder Auswirkungen des Einsatzes von Stents zu verfolgen.

Mit der Analyse unserer Ergebnisse konnten wir zeigen, dass Alter und Gewicht des Patienten zum Zeitpunkt der Operation bestimmend für das Ergebnis der chirurgisch-endoskopischen Behandlung der Choanalatresie sind. Selbst bei einer relativ kleinen Population könnten wir ein logistisches Regressionsmodell anwenden, um mögliche Faktoren zu analysieren. Es konnte für beide Merkmale ein statistisch signifikantes Ergebnis festgestellt werden.
Kinder im jungen Alter bräuchten mehrere Eingriffe , was korrelierte mit dem Gewicht der Patienten.

Die Relevanz des Cut-off-Gewichtes für den Operationserfolg zeigte sich insbesondere bei einem ausschließlich endoskopisch endonasalen Zugang. Dabei konnten wir zeigen, dass sich Patienten unter 3 kg mehr Eingriffen unterziehen müssen, um eine Durchgängigkeit der Choanae zu erreichen.
In dieser Studie haben wir gezeigt, dass erwartungsgemäß ein direkter Zusammenhang zwischen der erreichbaren Größe der Neochoana und dem Gewicht des Patienten besteht, was prognostisch von besonderer Bedeutung ist.
Im Vergleich zu anderen Wunden in der Nase hat sich die Größe als einer der limitierenden Faktoren für den Erfolg beim Erreichen eines offenen Ostiums erwiesen.
Leider konnten wir nicht den Einfluss der Verwendung eines Stents gegenüber keinem Stent auf das Operationsergebnis folgern.
Mit unserer Kohorte konnten wir jedoch einen möglichen Vorteil der Verwendung eines medikamentenfreisetzenden Stents bei der Reduzierung der Anzahl der in Vollnarkose durchgeführten Eingriffe erkennen.
Bei der Analyse der Komplikationen oder des Sicherheitsprofils im Zusammenhang mit der Verwendung von Stents konnten wir zeigen, dass sowohl bei Silikonfolien als auch bei Trachealtuben, die in die Neochoane eingelegt und am Septum fixiert werden, eine Dislokation auftreten kann. Bei diesem Ereignis ist ein weiteres Vorgehen in Vollnarkose zwingend erforderlich.
Wir konnten keine Komplikationen durch die Verwendung eines medikamentenfreisetzenden Stents nachweisen.
Es sind jedoch weitere Studien mit einer größeren Anzahl von Patienten erforderlich, um deren Wirksamkeit und Sicherheit bei der Behandlung zu überprüfen.

Abschließend sind wir überzeugt, dass die Rolle von Kortikosteroiden im Allgemeinen bei der Behandlung der Operationswunde einer Choanalatresie, entweder perioperativ oder postoperativ, weiter untersucht werden muss.

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7. Declaration of Contributions to the Dissertation

The dissertation work was carried out at the University Hospital of Tübingen, Department of Otorhinolaryngology, Head and Neck Surgery under the supervision of PD Dr. med. Sven Becker.

The study was designed in collaboration with Dr. med. Steffen Paasch and PD Dr. med. Sven Becker.

Statistical analysis was carried out after a consultation with the Institute for Biometry by myself.

I confirm that I wrote the manuscript myself (under the supervision of PD Dr. med. Sven Becker) and that any additional sources of information have been duly cited.

Signed_____
Carolina Garcia Rebelo van Schaik

on 2nd. August 2021 in Tübingen

8. Publications

Parts of the dissertation presented here have already appeared in the following publications:

Carolina G. R. van Schaik, Steffen Paasch, Sven Becker, Retrospective study analyzing demographics and intra- and postoperative treatment in the success of surgery of choanal atresia

Accepted for oral presentation in the Congress of the European Rhinologic Society in collaboration with ISIAN and IRS 2021