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Morbus Menière: Were the last 50 years of molecular biological research fruitless for Menière's disease?

Raphael Richard Ciuman

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Abstract

After discovering an inner ear hemorrhage, Prosper Menière ascribed disease to the inner ear for the first time. Since that time, a lot of efforts have been made to determine the pathophysiologic causes of the classical symptoms sensorineural hearing loss, vertigo attacks, tinnitus and ear fullness. According to its express pattern Menière's disease may appear as classical and

atypical disease. In the last decades, huge advances have taken place in biochemical and physiological research and in pathophysiological understanding of the inner ear and its diseases. This encloses stimulus perception and conduction, regulation of inner-ear fluid homeostasis and inner ear diseases with underlying genetics. Menière's disease pathophysiologic correlate is an endolymphatic hydrops which is characterized by changes of inner ear homeostasis with its parameters volume, concentration, osmolality and pressure of the endolymph. Hormones, autonomous system and the immunsystem together with purinergic, adrenergic and muscarinic receptors, steroids, vasopressin, atrial natriuretic peptide and aquaporin channels regulate inner ear homeostasis. Consequently, general diagnostics comprise a magnetic resonance imaging with gadolinium, vestibular diagnostics and tone audiometry. Standard therapy for acute inner ear symptoms is limited to cortisone infusions together with a rheologic agent or a radical scavenger. For acute vertigo attacks and for the mainstay therapy antivertiginous pharmaceuticals are given. In severe cases destruction of the vestibular hair cells by ototoxic antibiotics, endolymphatic sac surgery or neurectomy of the vestibular nerve might be necessary. Certainly, in research there is a move from simple pharmaceutical therapy forward to nanoparticle-based, genetic-based and stem cell therapy.

Key words: Menière; Hearing loss; Vertigo; Tinnitus; Endolymphatic hydrops; Stem cell; Genetic-therapy; Nanoparticles

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Core tip: Morbus Menière has become the reference type of inner ear disease. It may express all kind of inner ear symptoms at once, but appears as atypical disease as well. There have been immense achievements in physiologic and biochemical understanding for the inner ear, various inner ear diseases in general and Menière's disease specifically. Pathophysiologic

understanding, ongoing research and therapeutic options for Menière's disease are described and discussed.

Ciuman RR. Morbus Menière: Were the last 50 years of molecular biological research fruitless for Menière's disease? *World J Otorhinolaryngol* 2015; 5(4): 90-92 Available from: URL: <http://www.wjgnet.com/2218-6247/full/v5/i4/90.htm> DOI: <http://dx.doi.org/10.5319/wjo.v5.i4.90>

Not holding the answer back, the response has to be "Yes" from a therapeutic understanding. But the last decades of molecular biological research involved immense achievements in pathophysiologic understanding for various inner ear diseases and underlied biochemical mechanisms that are valuable points of attachments for future nanoparticle-based and stem cell therapy.

Prosper Menière's description of an inner ear disease after performed dissection in a haemorrhagic ear in 1861^[1], was the first ascription of disease to the inner ear and since then Morbus Menière has become the reference type of inner ear disease. It may express all kind of inner ear symptoms at once, but appears as atypical disease just as often. The classic express pattern is only found in 7%-30% initially, in 40%-50% cochlear precede vestibular symptoms and in 20%-50% the disease manifests *vice versa*^[2]. Correlations with migraine and psychiatric patterns like anxiety and depression are typical, all the more than course and progress can't be foreseen. In addition, Menière's-like symptoms can be caused by various diseases like high jugular bulb, displacement of the venous sinus, and irregularities in the labyrinth system and its draining veins^[3] occur as well as affection of the efferent system^[4].

Endolymphatic hydrops as pathophysiologic correlate was described by Hallpike *et al*^[5] and Yamakawa^[6] simultaneously in 1938. It is characterised by changes of inner-ear homeostasis and its parameters volume, concentration, osmolarity and pressure of the endolymph. Potassium, as the major charge carrier for sensory transduction, and endolymph volume increase, followed by loss of stereociliary cross-links, with concomitant disarray of the outer hair cell stereociliary bundles and possible membrane rupture of the endolymphatic spaces, mixing perilymph with endolymph^[7]. Hormones, autonomous system and the immunsystem together with purinergic, adrenergic and muscarinic receptors, steroids, vasopressin, atrial natriuretic peptide and aquaporin channels regulate the inner ear homeostasis^[8-10]. Besides, cranial venous insufficiency might play an additive role as it correlates with Menière's disease and venous obstruction serves as an animal model for endolymphatic hydrops. Other animal models comprise an obstruction of the endolymphatic system, an obliteration of the endolymphatic sac that shows fibrosis in later disease stages of Menière disease, or immunmodulation by antigen challenge to

the endolymphatic sac. In recent years, endolymphatic hydrops in animal models triggered by vasopressin or its derivatives (ADH = antidiuretic hormone, AVP = arginine vasopressin, DDAVP = one trade name of desmopressin) have become more popular. They block the fluid absorption and increase the potassium secretion and its gradient along the length of the cochlea. Consequently, hormones responsible for inner ear homeostasis, aquaporin channels and ion channels represent the first therapeutic options for nanoparticle-based or genetic-based therapy.

Specific and comprised diagnostics may be necessary in the individual case, but the general test battery can be reduced to vestibular diagnostics like calorics and vestibular evoked myogenic potentials and to tone audiometry with the Klockhoff test (glycerol, furosemide), which results in an potassium increase in the endolymphatic spaces, and an improved hearing perception during the state of fluctuating hearing loss. A magnetic resonance imaging (MRI) with gadolinium should be performed to depict the endolymphatic hydrops and for exclusion. Imaging protocols were developed by Naganawa *et al*^[11]. The degree of endolymphatic hydrops in an MRI is correlated with cochlear and vestibular symptoms. It seems that all patients with classical symptoms have an endolymphatic hydrops, but not vice versa, as not all patients with hydrops show symptoms.

Currently, the preventive therapeutic options are limited to antivertiginous pharmaceuticals like cinnarizine and betahistine as mainstay therapy for vertigo control, which reduce number and intensity of vertigo episodes. Standard therapy for acute inner ear symptoms are cortisone infusions together with a rheologic agent, and radical savengers can be added to the therapy regimen what shows improved hearing outcome. In severe cases destruction of the vestibular hair cells by ototoxic antibiotics might be necessary showing in a metaanalysis a complete vertigo control in about 75% and substantial vertigo control in about 90%^[12]. Endolymphatic sac surgery or neurectomy of the vestibular nerve are used when chemical ablation of the vestibular organ fails. As the vestibular organ is four times more vulnerable to gentamicin than the cochlea, transtympanic application of gentamicin has become the most used intervention. Every diagnostic and therapeutic intervention has to be accompanied by a detailed counseling as the patients are disturbed and anxious by the dramatic kind of attacks.

Certainly, in research there is a move from simple pharmaceutical therapy for inner ear disease forward to nanoparticle-based, genetic-based and stem cell therapy. It is now already 10 years, when the first gene-therapy-mediated recovery of hearing loss in animals was reported in 2005^[13]. Due to the anatomical characteristics of the inner ear with bony isolation and the blood-inner ear barrier better understanding and therapeutic options in Menière's disease will go hand in hand with inner ear therapy in general.

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Management of post-operative fistula in head and neck surgery: Sweeping it under the carpet?

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Abstract

The most dreaded complication in head and neck

surgery is the development of fistula. Fistulas are common and devastating. The prevalence and the risk factors that contribute to fistula formation after head and neck procedures were discussed briefly. The main goal of this manuscript is to discuss current management of head and neck fistula. We believed that the best management strategy for head and neck fistulas is prevention. We recommend a holistic preventive approach during the perioperative period. The roles of different types of wound products and hyperbaric oxygen therapy were also discussed and highlighted. We also discussed the operative repair of fistulas, which relies on the tenet of providing well-vascularized tissue to an area of poor wound healing. Most often, the surgeon's preference and range of operative skills dictate the timing and the type of repair. We highlighted the use of the pectoralis major, a well-known flap, as well as a novel technique in the surgical repair of complex, difficult-to-heal head and neck fistula.

Key words: Orocutaneous fistula; Pharyngocutaneous fistula; Fistula; Head and neck surgery; Head and neck surgery complications; Carotid blowout

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Core tip: Fistulas after head and neck surgery is the most dreaded complication for good reasons: they are common, they occur in the sickest group of patients, and they are devastating physically and psychologically. The best treatment for fistulas is prevention. We discussed in details steps that can be taken to optimize patients and to reduce the risk of fistula formation. As we discussed up-to-date evidence on the conservative and surgical managements of fistula, we highlighted areas that need improvements and benefit from further researches.

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DEFINITION AND PREVALENCE OF FISTULA

The most significant complication in oncologic surgery of the head and neck is the development of fistula. Fistula is an aberrant connection between two epithelial surfaces that permitting the passage of fluids and secretions. Most fistulas in the head and neck (H and N) are external fistulas in which the fistulas drain onto the skin. This article will focus on the two types of fistula that arise as complications after head and neck surgery: Orocuteaneous (OCF) and pharyngocuteaneous fistula (PCF). Besides from the anatomical differences, these two types of fistula share many common features in their epidemiology, risk factors, morbidity and managements and thus, will be discussed together.

In high-quality series of patients undergoing total laryngectomy (TL), a highly standardized head and neck operation, the rate of fistula was reported from 3% to 65%^[1-5]. The true mean was between 10%-40% according to a meta-analysis by Paydarfar and Birkmeyer. In hypopharyngectomy, where the surgical approach is more diverse owing much to the multitude of flap options, the frequency of fistula distributed widely. Fistula developed in 43% to 59% hypopharyngeal defect closed with a radial forearm flap^[6]. The fistula rate for hypopharyngeal defect closed with an anterolateral thigh flap was reported favorably at 0%-9%^[7-9]. A recent retrospective study looking at 368 consecutive cases of reconstruction using jejunal free flap from 1977 to 2010 revealed an overall fistula rate of 8.2%^[10]. Collectively, with the increasing use of concurrent chemo RT as first line treatment, more and more H and N cancer patients present with high risks of developing fistulas postoperatively^[11,12]. While the frequency of fistula may vary, its morbidity is uniformly damaging. In the immediate postoperative period, when the fistula tract involves and exposes the carotid to the enzymatic action of saliva, patient is at an increased risk of devastating carotid blowout. In a subgroup analysis with matched pair control group, Upile *et al*^[13], reported a pre-blowout salivary fistula in all patients with carotid artery rupture. Furthermore, fistula prolongs functional recovery of oral intake and speech, increases hospitalization time and cost. More importantly, fistula delays the initiation of adjuvant therapy^[14]. The total treatment package time of surgery and postoperative radiotherapy (RT) of < 100 d was shown to improve local control and overall survival^[15]. However, whether fistula formation affects survival rate remains unclear. A recent retrospective study of 217 patients in the Netherlands found no statistical difference in the survival rate in patients with PCF vs

patients without PCF^[16]. In contrast, a recent study of 232 patients underwent surgery for HNSCC at Asan Medical Center, South Korea reported decreased disease-free survivals and decreased overall survival in patients who developed fistula^[17]. Last but not least, abnormal tissue granulation and wound contracture due to the presence of fistula may contribute to late complication such as the development of stricture in as high as 50% of patients^[18].

RISK FACTORS AND PREVENTION

Given the significant morbidity and sequelae of fistula formation, the best management calls for prevention. Unfortunately, the 21st century head and neck surgeons are more likely to face patients with multiple comorbidities and operate on irradiated tissues than ever before^[11,12]. Both historical and recent data have repeatedly demonstrated that preoperative RT significantly increases the risk of fistula formation^[1,2,19-24]. In a study of 177 patients, McLean *et al*^[25] demonstrated that the mean time to spontaneous fistula closure in the irradiated group is 50 d vs 24 d in non-irradiated group. Unsurprisingly, there is a dose dependent effect with a fistula percentage reported at 43% in patients who received more than 60 Gy to the neck compared to 25% in patients who received < 60 Gy^[26]. Irradiated patients are also more likely to fail conservative management for their fistula. The risk of fistula formation does not differ whether the patient received RT less than or more than three months prior to surgery^[20]. This finding supports the theory that irradiated tissue is chronically hypoxic, hypoperfused, and hypocellular^[27]. Concurrent chemotherapy further increases the risk of fistula^[28] as well as concurrent neck dissection^[20]. In a study of 110 patients undergoing salvage laryngectomy, the rate of PCF is as high as 57.2% in patients with neck dissection vs 13.4% in patients without neck dissection^[29].

Another well-established risk factor exposing patient to fistula formation is the presence of surgical site infection (SSI). A recent series of 504 free flap head and neck reconstruction analyzed the oral microbiome found in SSI post head and neck surgery. Remarkably, 40% of patients colonized with MRSA developed an SSI. Moreover, this series also showed that normal oral microbiota is only found in 25% of wound culture. Gram-negative bacilli are found in 44% of wound cultures, MRSA in 20% and MSSA in 16%^[30]. MRSA was shown to be associated with higher postoperative fistula formation^[31,32]. More recently, a small study established MRSA as the causative agent of PCF following laryngectomy^[33]. Poor oral hygiene is also a significant factor for the development of wound complications postop in a prospective study of 186 H and N patients^[34]. Patients are two times more likely to have an SSI, dehiscence and fistula when they experienced perioperative weight loss^[35]. Incidence of PCF after TL is also significantly higher in patients with lower albumin level^[16]. Besides poor nutritional status,

other predictive factors for fistula formation have also been identified: Preoperative hypothyroidism, tumor site and stage, prior tracheostomy, low perioperative hemoglobin, perioperative blood transfusion, concurrent neck dissection in salvage surgery, and duration of surgery^[16,20,34,36-38]. Interestingly, in the above studies, systemic comorbid, with the exception of hypothyroidism, was not found to be a major risk factor. While the heterogeneity for the analyzed population is certainly implicated, perhaps a more intuitive answer lies in the fact that irradiated tissue is so hypoxic, hypoperfused and hypocellular that it is not possible to observe the consequences of the added insults from systemic illness.

In summary, the risk factors that predispose the patient to fistula formation have been well described in the literature. Certainly, there is extensive interplay and overlap between these risk factors; for instance, concurrent neck dissection may predispose the patient to fistula formation due to the increased blood lost, increased operative time and extensive dissection. Some risk factors are outside the surgeon's ability to influence; however, we maintain that the best treatment of fistula is prevention. Indeed, at every stage of patient care whether pre-, intra-, or post-operatively, there are measures that can help us avoid this dreaded complication.

Preoperative preventive measures

Firstly, the indication and extend of surgery must be carefully reviewed. Especially in the salvage setting when there are multiple risk factors at play, the decision for neck dissection in a node-negative neck must be considered judiciously. Concurrent neck dissection, as previously mentioned, increases the risk of fistula development. Recent data that recommend against concurrent neck dissection begin to emerge, although they suffer from small sample size, selection bias, and are limited to laryngeal tumor^[29,39]. At this time junction, the negative predictive value of CT-PET is not high enough to safely guide conservative management. Novel techniques such as MRI-PET or diffusion-weighted MRI, have shown good sensitivity and specificity but further data are needed in this field. Another surgical consideration to be made at this time is deciding on how to close the defect. A thorough discussion about flap choice is beyond the scope of this paper. However, we would like to offer a caveat that whilst the desire to choose a flap with the lowest fistula rate is strong, long-term morbidity, such as stricture, must also be put in contention. For example, while the fistula rate for ALT flap and jejunal flap for a circumferential hypopharyngeal defect were reported to be less than 10% in several series^[7-10,40], objective assessment by esophagoscope and esophagram showed that jejunal flap had a much lower stricture rate than compare to ALT flap^[41]. The jejunal flap is a superior choice for patients with good long-term prognoses. Finally, another consideration is whether to use or not to use a prophylactic flap to reinforce the suture line.

Incorporation of well-vascularized and healthy tissue into an anastomosis that is at high risk of breakdown can theoretically improve wound healing. Recent and robust data support prophylactic flap reconstruction. A recent multisite retrospective review of closure technique in 359 patients showed reduced overall complications and fistula in patients who received vascularized tissue^[42]. Another systematic review of 591 patients by Paleri *et al*^[43] reported a consistent lower rate of PCF across the 7 studies when vascularized tissue is used to buttress the anastomosis. Thus, if the procedure is within the surgeon's operative range and the patient can tolerate the added anesthesia time, a prophylactic flap should be considered^[43].

Once the scope of surgery has been decided, nutrition status should be assessed and optimized early, since this requires the most amount of time to adjust. Malnutrition is a hallmark of head and neck cancer patient due to a combination of factors: Lifetime of tobacco and alcohol abuse, cancer biology, and dysphagia. A multidisciplinary approach with a speech therapist, a dietician and a nursing coordinator should be a matter of course. The timeless study done by Haydock *et al*^[44] in 1987 reported remarkably better wound healing when nutritional status was improved at least one week preoperatively. Additionally, the question of preoperative gastrostomy placement may emerge, especially if the patient requires adjuvant therapy at a later stage. Although gastrostomy has a good safety profile^[45], the usefulness of prophylaxis gastrostomy is hotly debated due largely to the lack of randomized control trials (RCT) comparing different modes of enteral feedings^[46]. Some data suggest that the nutritional status appeared to be the same between prophylaxis G-tube, reactive G-tube and nasogastric tube and that a large proportion of prophylaxis G-tube was unused and unnecessary^[45,47,48]. On the other hand, newer data suggest that patients benefit from prophylactic G-tube and experienced a lower rate of complications overall^[49-51]. Thus, given the lack of consensus, we recommend a case-by-case consideration, a multidisciplinary approach and thorough patient counseling to this contentious issue of G-tube placement. However, two things are clear: Firstly, enteral feeding is superior to parenteral feeding and secondly, percutaneous endoscopic gastrostomy (PEG) is safer than radiologically inserted gastrostomy^[52]. Complication rate of PEG in patients with H and N cancer is the same as patients with other pathologies requiring PEG^[52]. Lastly, G-tube has been shown to aid closure of PCF in multiple series^[53-56] and thus should be strongly considered once a fistula has developed.

As with any other major surgeries, attention should be directed to optimize the patient's psychological and physiological states. Of note, thyroid function should be tested and titrated for correction. This is especially important in patients undergoing salvage surgery and patients who are severely hypoalbuminemic. Previous RT may have damaged the thyroid and a hypoalbuminemia

Table 1 We suggested the above preoperative considerations to reduce the risk of fistula formation: Level of evidence and references are included where applicable

Preoperative considerations	Level of evidence	Ref.
Extend of surgery		
Concurrent neck dissection	III	[29]
Sentinel lymph node biopsy	II	[75]
Extend of resection	-	-
Choice of flap		
Short-term vs long-term complications	-	-
Use of prophylactic flap	III	[42,43]
Nutrition		
For prophylactic gastrostomy	II, III	[45-48]
Against prophylactic gastrostomy	II, III	[49-51]
PEG is preferred over RIG	II	[52]
Improve preoperative nutritional status	-	-
Optimization of comorbidities		
Treat comorbidities (hypothyroidism, diabetes, anemia)	-	-
MRSA decolonization	III	[58,59]
Antibiotics prophylaxis	III	[60]
Dental care	IV	[62]

PEG: Percutaneous endoscopic gastrostomy; RIG: Radiologically inserted gastrostomy.

state may alter the metabolism of largely protein-bound tyrosine. It is critical to titrate tyrosine as soon as possible because of its long half-life.

A recent survey of antibiotic prophylaxis choice in the United Kingdom showed that there is little consensus and evidence-based practice on choice and duration of antibiotic prophylaxis in patients undergoing laryngectomy^[57]. For reason previously discussed, we strongly recommend MRSA decolonization. MRSA decolonization has been shown to reduce the risk of SSIs in patients undergoing head and neck operations^[58,59]. Evidence also support a short course of prophylaxis antibiotic targeting Gram-negative bacilli and MSSA such as ampicillin/sulbactam within an hour of incision^[60]. Paradoxically, antimicrobial prophylaxis exceeding 48 h increases the risk of SSI^[61]. An experienced dentist, practicing as part of the multidisciplinary team, should prescribe mouthwash, perform simple restorative procedures to the teeth including calculi removal as well as remove seriously damaged teeth or teeth that is within the operative field^[62] (Table 1).

Intraoperative preventive measures

Although radiation can obliterate tissue planes and render tissues fibrotic, every attempt should be made to strictly obey the Halstedian principles of meticulous dissection and gentle tissue handling. Suture materials and charred tissues from excessive electrocautery are considered foreign bodies and must be limited as much as possible. To this end, modern energy devices may theoretically help reduce the risks of SSIs and fistula formation; additionally, one study suggested that

ultrasound-based energy scalpel creates less collateral endothelial damage during vascular dissection, which theoretically improves flap survivability and thus, decreases fistula formation. However, initial data show no difference in fistula frequency^[63,64]. Use of mechanical staple is also controversial with conflicting evidence: some series, including a systematic review, reported decreased PCF incidence^[65,66]; however, a recent series from John Hopkins H and N unit described an overwhelmingly increased rate of PCF when mechanical staple was used^[38].

Technology is also permitting a new and minimally invasive protocol to achieve goal-directed volume expansion in head and neck surgery to optimize hemodynamics^[67]. Traditionally, intraoperative goal-directed volume expansion is achieved with an esophageal Doppler ultrasound, which is difficult in major head and neck resection. Intraoperative cardiac output (CO) monitoring and optimization have been shown to shorten postoperative stay and reduce complications in different types of major surgeries^[68-70]. Unfortunately, as recent as 2012, in the United Kingdom, only 9% of head and neck units routinely monitor CO intraoperatively^[71]. Certainly, this is an area where further researches, adoption of new technology, and improvements are needed.

Another area in which further researches and adaptation are needed is the application of sentinel lymph node biopsy (SLNB) in a clinically negative neck. SLNB may reduce unnecessary neck dissection, amount of blood lost, and operative time, all of which are aforementioned risk factors for fistula formation. From a prospective series of 59 patients with T1/T2 oral squamous cell carcinoma undergoing SLNB, a NPV of 97.5% was reported^[39]. Other series, including a multicenter prospective trial, have also reported excellent outcomes of SLNB for oral cancer^[72,73] even for a previously treated neck^[74]. A recent meta-analysis of 23 studies reported the sensitivity and negative predictive value of SLNB as 95% and 96%, respectively. Although 82.4% of the data are comprised of oral cavity tumors, the authors concluded that SLNB is worth considering in laryngeal, hypopharyngeal and oropharyngeal tumors^[75]. Thus, with the growing body of evidence and the desire to avoid unnecessary neck dissection and its associated risks, the impetus is shifting toward applying SLNB more regularly.

Postoperative preventive measures

Prevention of infection, early enteral feeding, and adequate tissue perfusion in the immediate post-operative period are important protective factors against fistula formation. Since most SSIs develop more than 1 wk postoperatively^[30], theoretically, patients may benefit from a short pulse of prophylactic antibiotics during this period. Nutrition is of paramount importance to combat the postoperative catabolic state. Although Hb < 12.6 is a known RF for fistula development, we do

not suggest routine transfusion to keep Hb above this threshold. A more rational approach is to maintain stable hemodynamic to maintain adequate tissue oxygen tension. IV Iron with or without rHuEPO has been shown to reduce transfusion requirements in surgical patients^[76] and may be a useful adjunct in head and neck cancer patients. We also recommend aggressive prophylaxis against post-operative nausea and vomiting although the evidence that post-operative vomiting increases the risk of post-operative fistula is rather limited^[77]. Attention to oral hygiene is often neglected during this stage, partly due to poor patient compliance but also difficulty in execution. The healthcare team should be vigilant and take measures include frequent suctioning, chlorhexidine gargling, mechanical cleaning of the oral cavity with gauze and cotton buds and even oscillating electric toothbrush to minimize the risk of gingivitis, mucositis, SSIs, and fistulas^[62].

NON-SURGICAL MANAGEMENT OF FISTULA

The mainstay of conservative management of OCF and PCF is wound care with frequent wound inspections and application of wound products. The goal of conservative management of fistula is to promote healing by secondary intention. Thus, a holistic approach must be commenced prior to any attempt at addressing the fistula itself: Necrotic tissues must be debrided; infections must be treated; enteral feeding must be started; hemodynamics must be optimized and comorbid must be controlled. We also suggest paying attention to the care of peristomal skin integrity because macerated and infected skin will eventually lead to ulceration and ultimately enlargement of the fistula. To this end, prior to applying wound products and topical agents, a patient allergy history must be reviewed because the development of contact dermatitis will preclude the wound from healing and the fistula from closing.

Conventional, simple wound dressing by applying gauze soaked in solutions such as saline, water, chlorhexidine or Dakin's solution is usually not appropriate in the setting of fistula due to the high and constant output of both saliva and exudate. Furthermore, conventional dressing requires constant dressing change, which is especially time consuming in an already very difficult and complex 3-dimensional wound. Unsurprisingly, no data on simple wound dressing in the head and neck setting was found on PubMed Central. Other surgical specialties are also moving away from using simple, wet-to-dry dressing due to its nonselective mechanical debridement^[78]. Modern wound dressings were invented with the aim of absorbing exudates while providing a matrix upon which granulation can take place as well as enhance the principles of moist wound healing^[79,80]. Hydrocolloid (HC) dressings come in a form of a polyurethane film or foam combined with a gel-forming agent. These products include Granuflex® (ConvaTec,

United States), Tegaserb® (3M Healthcare, United Kingdom), etc. Although these products are good at achieving moist wound healing by promoting uniform and robust granulation^[80], their utility in managing head and neck fistula is again restricted by their limited capacity to absorb exudate. Even in less exudative wounds such as leg ulcers or burnt wounds, the range of exudate between 4-12 g/10 cm² per 24 h^[81,82] is already beyond the capacity of most hydrocolloid dressings, which can absorb about 10 g/10 cm² per 24 h^[83]. Although an old study, there has been no newer evidence on this topic since this study. In our anecdotal experience, a combined output of exudates and saliva in most PCF or OCF will overwhelm the absorbent capacity of even the newest hydrocolloid dressing. Thus, HC is only applicable when the fistula output can be controlled or diverted. Another area where hydrocolloid dressings have shown promise in the head and neck setting is when it was applied to defect with exposed bones prior to skin grafts^[84]. Last but not least, the use of hydrocolloids dressing is further hampered by their restricted conformability, malodor that could confuse assessment of infection and further reduce quality of life^[85].

Another alternative to hydrocolloid products are the hydrogel products. They share a common basic structure of absorbent polymers such as alginate, starch, pectins, or sodium carboxymethylcellulose and water. Examples of hydrogel products are Intrasite Gel® (Smith and Nephew Medical, United States), Granugel® (ConvaTec, United States), Nugel® (Johnson and Johnson Medical, United States). These products have improved absorbent capacity due to their absorbent polymer component. In fact, a retrospective study of 47 head and neck cancer patients with wound complications and fistula in France showed improved wound healing with a mean of 33.53 d in the group using seaweed-based products vs 72.94 d in the control group^[86]. Theoretically, the efficacy of intense absorbent wound product can be improved with antimicrobial properties. This can be achieved with nanosilver-impregnated dressings^[87] or with honey-coated bandage^[88]. Despite its established popularity in treating wound dehiscence in abdominal surgery, there is little evidence of silver-based dressing use in head and neck wound. The utility and effectiveness of silver dressings in the treatment of chronic wounds have been established in several studies and a meta-analysis^[89]. However, what was not mentioned in this meta-analysis is the cost. In a recent study of wounds rated to have healing potential between 7 to 21 d, the cost of Aquacel® Ag was 4814.08 Euro's vs a cost of 13249.46 Euro's for Acticoat^[90,91]. Perhaps the dearth of data regarding silver-based dressing in the management of head and neck fistula is down to cost. A more affordable alternative may be readily available in the form of honey-based wound products. Although we were not able to find any trial comparing silver-coated dressing to honey-coated dressing to other forms of dressing in the H and N setting, an RCT

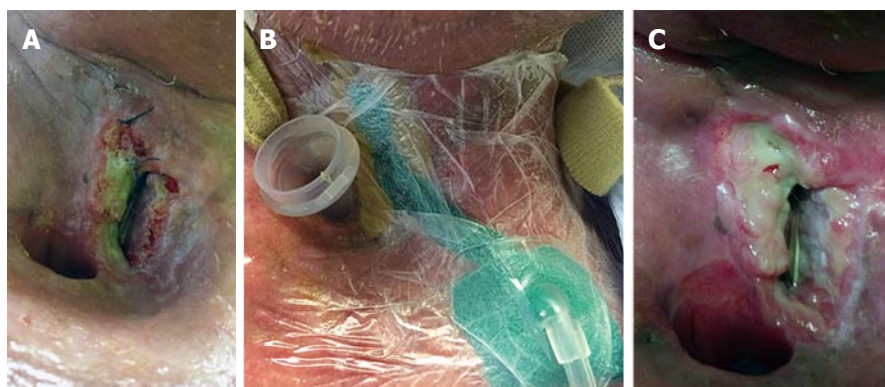


Figure 1 Negative pressure wound therapy dressing applied at a challenging location for a peristomal fistula using a combination of hydrogum dental paste and medical silicone. A: A parastomal fistula in a patient with a hypopharyngeal SCC status post pharyngolaryngectomy with Provox prosthesis, bilateral modified radical neck dissection, end tracheostomy, and pectoralis major flap; B: A negative pressure wound therapy (NPWT) dressing applied over the parastomal fistula using medical silicone and dental pasting (not shown); C: Wound inspection of fistula after 1 wk of NPWT shows improved granulating tissue. Patient also reported improved quality of life with the fistula being properly drained with little to no odor.

in Denmark compared honey-coated bandage to silver-coated bandage in treatment of malignant wounds of the breast and showed no difference between the two regiments. Patients in both group reported improve satisfaction with quality of life (QOL) and the wound size also reduced significantly^[92]. The reduction in size is encouraging because these are malignant wounds, which the law of nature forbids from healing. It is important to point out that the antimicrobial effect of honey can be 11-fold higher than compared to application of sugar solutions due to enzymatic activities of compounds such as bee defensin-1 in addition to osmotic effects^[92]. Honey-impregnation also has the added benefits of anti-odor, anti-exudation, and analgesia^[93]. Anecdotal experience from France and Britain described positive and promising results in treating a series of 3000 non-healing surgical wound dehiscence a salivary fistulas with topical and regular oral ingestion of honey several times a day^[94]. Despite initial enthusiasm, a recent Cochrane review failed to find clear benefits of honey as a topical treatment^[95]. Given the safety of honey-based wound therapy, the readiness availability and affordability of honey, we believe that the application of honey-based wound products to H and N wound in general and H and N fistula in particular worth further researches, especially in the forms of prospective, randomized controlled trials. Other forms of affordable antimicrobial dressing such as the recently reported hydrogel product with polyvinyl alcohol, polyvinylpyrrolidone and seaweed formulation^[96] warrant further investigation and application in our specialty.

Negative pressure wound therapy (NPWT) in treating complex wound and fistula in H and N surgery is in vogue. Regrettably, head and neck surgeons joined the party rather late. In the early 90's, NPWT was first reported by Fleischmann *et al*^[97] in the treatment of open fracture; only until 2005, the first successful application of NPWT in 23 H and N patients was reported by Rosenthal *et al*^[98]. Of note, four PCFs were treated with the mean duration of treatment of

6.25 d. Three of these four patients had previous RT. Other series followed and quickly validated the utility of NPWT in managing H and N wounds, including combat wounds^[99-103]. A result of meta-analysis in 2011 firmly placed NPWT as an integral modality of modern wound treatments^[104]. Even for wounds with high levels of complexity such as wounds with great vessel exposure, or peristomal application, NPWT is efficacious and safe with a reported complication rate of 3.5%^[105] (Table 2).

During the early days, applications of NPWT were plaque with difficulties in applying the device to a 3-dimensional wound in a topographically complex area. Communication between the aerodigestive tract and the skin adds another layer of immense complexity when NPWT is attempted in treating fistulas. Intriguing solutions have been described in the literature recently. Honey can also be used as an adjunct to maintain airtightness for NPWT^[95]. Medical silicone can bolster and form an airtight seal in a leaking NPWT dressing^[106]. Our own data supported the use of hydrogum dental paste to form an airtight seal for NPWT treatment of OCF^[102]. NPWT for PCF can be further complicated by the proximity of the tracheostomy site. Figure 1 illustrates a NPWT dressing applied at a challenging location for a peristomal fistula using a combination of hydrogum dental paste and medical silicone. Other options exist. In their series, Loaec *et al*^[103] describes the use of a Tulle Gras (Smith and Nephew, Australia) to maintain air-tightness. Counter-incision can also be used to divert the fistula away from the tracheostomy with great effectiveness^[104]. Intraluminal negative pressure dressing, which allows intraoperative and prophylactic placement of NPWT, has also shown great potentials^[106]. Certainly, the intraluminal device itself is intriguing; but the possibility of using NPWT as a prophylaxis against fistula in high risks patients merits further attention. Additionally, reported success of adjunct combination of other wound products such as silver, octenidine, and Dakin's solution with NPWT in treatment of chronic, difficult-to-heal wounds^[107-109] justify future application

Table 2 Advantages and disadvantages of dressings used in management of post-operative head and neck fistula

Wound products	Advantages	Disadvantages
Simple wet-to-dry/wet-to-moist dressing	Affordable Readily available	Require frequent changes, sometimes multiple times a day Cannot be used when wound is high output or exudative
Hydrocolloid based	No special training/dedicate wound nurse Provide microdebridement Maintain moist wound bed Promote granulation and epithelization Readily available Evidence supported use on bone	Traumatize tissue and disrupt granulation Limited absorbent capacity Malodorous Rigid form factor made it difficult to apply; limited use in wound with deep tracts, undermining May irritate/dessicate perifistular skin
Hydrogel based	May be applied to moderately exudative wound Easy to remove, can be changed daily Maintain moist wound bed Promote granulation and epithelization Mildly analgesic	May adhere to wound bed and cause pain when removed May not work in highly exudative/high output wound May irritate/macerate perifistular skin Malodorous Require secondary dressing
Silver-coated	Provide autolytic debridement Proven anti-microbial efficacy and decreases bioburden Promote granulation and epithelization May be applied to highly exudative wound	Costly Different silver products have different properties; no reliable evidence supporting one product over another May cause discoloration or dermatitis of perifistular skin
Honey-impregnated	Can be changed every other day or longer depends on need Affordable Anti-odor Anti-microbial Mildly analgesic Moisturize and maintain perifistular skin	Conflicting evidence Only one brand formally approved for Medical use: Medihoney™ (United States) Different honey from different bees and/or flower species have different efficacy
Negative wound pressure therapy	May be applied to highly exudative wound Little data on safety profile and side effects, especially in diabetic Proven efficacy Promote granulation Promote vascularization Can be used in highly exudative wound Can be combined with other products (Dakin's solution, octanidine...) to add anti-microbial effect	Technically challenged to achieve airtight seal, especially when fistula is in communication with the aerodigestive tract May require bedside procedure to divert fistula if near tracheostomy Moderate cost Controversy surrounding use directly on vessels Require experience/training and dedicated wound team Dressing change can be painful to patients

of these products in the HandN setting (Figure 1).

In our experience, hyperbaric oxygen therapy is used when we are unable to take the patients back to theatre, when other conventional treatments have failed, and our back is against the wall. The cost is nearly prohibitive; and the treatment regime, cumbersome. Despite these drawbacks, HBOT has a long and successful history of usage in managing complicated H and N wounds. The first study in 1973 reported complete healing in all four patients with fistulas and wound infections after undergoing HBOT. Remarkably, a landmark RCT in 1993 investigated prophylactic HBOT in high-risk patients showed significantly fewer wound-related complications in the HBOT group: 11% dehiscence in HBOT vs 48% in control group, 6% infection in HBOT vs 24% in control group^[110]. Subsequent trials investigating the utilities of HBOT prophylaxis also showed improved QOL, improved wound healing, and survivability of skin grafts and free flaps^[27,111]. Moreover, a comprehensive review by Feldmeier *et al*^[112] dismissed concern of HBOT enhancing the rate of tumor growth, clearing the way for future use in a prophylactic setting prior to resection. Many other studies reported improved healing in patients with radionecrosis of the larynx, mandible, or

soft tissue after undergoing HBOT^[113-115]. HBOT has been shown to improve wound healings and facilitate fistula closure in H and N wounds that failed to respond to conventional therapies^[116-118]. The therapeutic effect of HBOT is three-pronged. HBOT improves the oxygen tension in tissue, promotes angiogenesis and cellular synthesis, and generates oxygen free radicals that are important in oxygen-dependent killing of bacteria. Although there are data that dispute the use of HBOT in treating complicated H and N wounds, most notably, the prospective RCT by Annane *et al*^[118] that showed no difference in wound healings between the HBOT group and the placebo group of pressurized Nitrogen, a Cochrane review in 2012 validated the overall favorable outcome of HBOT in difficult-to-heal wound^[119]. Finally, data from patients with osteoradionecrosis undergoing HBOT prior to surgery may support the use of HBOT as a bridge prior to surgical repair of the fistula.

We also would like to point out that there might exist a psychosocial benefit to the act of changing dressing and tending to the wound of H and N patients. Psychosocial support offered during dressing changes in breast patients with stubborn malignant wounds have been shown to improve the women's sense of well-being and self-confidence^[91]. H and N cancer and

surgical treatment for H and N cancer significant alter the physical appearance and patient's body image, not unlike what happen to women receiving treatment for breast cancer. Arguably, the development of a devastating complication such as fistula puts the patient at a higher risk for psychosocial issues. Unfortunately, unlike breast cancer, researches in body image and psychosocial issues in H and N cancer patients are lacking and have only started gaining minor tractions recently^[120]. Until further evidence become available, we maintain that wound inspection and wound dressing change provide the unique opportunity for the health care providers to deliver much needed psychosocial care, especially when the patients are suffering from a complication as devastating as fistula.

SURGICAL MANAGEMENT OF FISTULA

Once conservative management failed to promote healing, surgical repair is required. The timing for the surgical management of postoperative fistula is worth considering. The common practice is to defer surgery until conservative treatment options have been exhausted. However, conventional surgical wisdoms support early repair to avoid scarring and fibrosis. Iteld and Yu also recommended early surgical repair within 3 to 28 d for PFC larger than 5 mm and in patients with high risk factors. Late surgical repair also runs the risk of allowing the fistula to convert a small defect into a larger one that requires extensive reconstruction^[121]. The obvious downside to early surgical repair is the lack of time given for the wound to heal. We are unable to find further evidence on the optimal timing of surgical intervention. Thus, due to the lack of evidence, timing of surgery remains a matter of surgeon's and also, patient's discretion, with a caveat that fistula is unlikely to close with conservative management after 4-8 wk^[122].

The choice of flap in H and N surgery is ever expanding. It is beyond the scope of this paper to discuss each flap in details and its potential benefits in preventing and/or treating fistula. We however would like to call attention to some very new data that could help guide future practice and research. The Pectoralis Major (PM) flap, which was and still is a workhorse in H and N reconstruction, was previously shown to reliably decrease the rate of fistula formation^[123,124]. However, newer data reported an interesting observation: although PM flap was associated with increased incidence of PCF, PCFs reinforced by PM flap were less severe^[38]. The authors in this study suggest that this result might have been confounded due to the concurrent use of mechanical stapled device; however, this suggests that with evolving epidemiology and surgical practices, it is necessary to review old-timed practice. In contrast, a very recent study from Taiwan, describing a unique double-layer design in the surgical treatment of large, complex fistula, offered a new direction in flap design. Double-layer techniques have been described with successful results in the

past^[125,126]. However, this newer design is structurally more secured, requires less local tissue to be available to create the double layers, and is compatible with a variety of flaps^[127]. The long-term outcome of this new technique was also reported as favorable, with a mean follow up of 28 mo. In conclusion, in the surgical repair of fistula, from the time of surgery to the type of surgery, much depend on the preference of the surgeon. While it is important to continue the surgical tradition of innovation, the surgical management of H and N fistula demands future researches in revising and standardizing practice.

CONCLUSION

Fistula of the H and N is dreaded for good reasons: They are common, they occur in the sickest group of patients, and they are devastating physically and psychologically. But perhaps, the most dreaded part about managing this complication is the lack of consensus and well-defined guidelines. We are armed with a myriad of wound products, treatment options, and choices of flap; yet, as we have described above, many crucial questions remain unanswered. Unfortunately, at the time of writing, to the best of the authors' knowledge, there is no risk stratification system to predict fistula formation in surgery of the H and N. A scoring system of risk factors is a foundation upon which our specialty can start designing trials with well-defined populations and good controls to objectively compare treatment modalities and outcomes. Until such a stratification system exists, the crack in our collective knowledge in the optimal prevention and treatment of fistula will continue to exist. Without knowing what is the best treatment and when is the best time to apply it, postoperative H and N fistula will continue to be swept under the carpet of novel wound products, and innovative surgical techniques.

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Observational Study

Diagnosis and management of laryngeal cleft: A single centre experience and a novel endoscopic technique

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Abstract

AIM: To examine the presentation, diagnosis and outcomes of patients with laryngeal cleft.

METHODS: An 18 mo (from mid-2012 to 2013) prospective longitudinal study was performed at the Barts Children's and Royal London Hospital, a tertiary referral centre. Chart review was performed for all patients including data extraction of demographics, outpatient clinic review documentation, speech therapy findings, medication list, operative findings alongside technique and follow up. A systematic review of contemporary English medical literature was also reviewed to compare series. The study was approved and registered by the hospital clinical governance and audit board. Biostatistician review was not required.

RESULTS: Twenty-two children aged 1 to 72 mo (mean age 23.5 mo) with a 7:4 male-female ratio. Twenty had Benjamin-Evans type 1 clefts and 2 had a type 2 cleft. All were symptomatic despite medical management including anti-reflux therapy. Patients presented with dyspnoea (81%), feeding difficulty (63%), stridor (54%) and recurrent pneumonia (36%). Several patients had concomitant aerodigestive abnormalities including 7 with laryngomalacia, 4 subglottic stenosis, 2 subglottic webs and 1 tracheo-oesophageal fistula. To date, 18 patients have undergone endoscopic repair, all of whom have shown radiological and/or clinical signs of improvement. All endoscopic repairs were performed with the novel use of a Negus knot pusher, with Baby Benjamin rigid suspension, to more reliably and easily suture at depth.

CONCLUSION: This is a significant single unit series demonstrating the strong association of laryngeal cleft with combined aerodigestive symptoms and other laryngeal abnormalities. Endoscopic management of type 1 and 2 laryngeal clefts is successful. We recommend the use of a Negus knot pusher to facilitate endoscopic repair.

Key words: Laryngeal cleft; Endoscopic; Pediatric; Dyspnea; Aspiration; Stridor

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Core tip: Laryngeal cleft is a rare laryngo-tracheal wall abnormality. Patients may present with laryngeal or respiratory symptoms. A high index of suspicion is required. A multi-disciplinary team, including speech therapy and otorhinolaryngology, is required to manage these patients. Endoscopic surgical repair is increasingly the gold standard for symptomatic patients. We propose the use of the Negus knot pusher to facilitate endoscopic repair procedures.

Yalamachili S, Virk JS, Bajaj Y. Diagnosis and management of laryngeal cleft: A single centre experience and a novel endoscopic technique. *World J Otorhinolaryngol* 2015; 5(4): 105-109 Available from: URL: <http://www.wjgnet.com/2218-6247/full/v5/i4/105.htm> DOI: <http://dx.doi.org/10.5319/wjo.v5.i4.105>

INTRODUCTION

Laryngeal cleft is a congenital malformation that results in an abnormal communication between the oesophagus and larynotracheal complex. It is a rare disease, slightly more common in males, affecting approximately 1:10000 live births, constituting 1% of congenital laryngeal malformations^[1-3]. However, there has been an increased prevalence in more recent literature due, in part, to increased diagnosis of latent and asymptomatic cases^[4-8].

Laryngeal clefts occur due to an absence of fusion of the posterior cricoid lamina and in some cases, the tracheoesophageal septum. Histopathological investigations suggest deformities of the posterior cricoid lamina and alterations in muscle differentiation of the inter- and crico-arytenoid muscles. As a result, laryngeal cleft is typically associated with other malformations, particularly those of the digestive tract^[2-4,6,9].

There are a number of classification systems but the most commonly employed is that which Benjamin *et al*^[10] described in 1989, with Type 1-4 clefts depending on their length. Symptoms correlate with the extent of the cleft and may be laryngeal, in the form of stridor, swallowing difficulties, aspiration, cough or hoarse cry, or respiratory, such as dyspnoea, cyanosis and recurrent lower respiratory tract infections. There are also known associations with reflux disease and syndromes including CHARGE, Pallister Hall, VACTERL and OPTIZ G^[3].

The aim of this study was to present and analyse a prospective series of laryngeal cleft patients at a single tertiary referral centre.

MATERIALS AND METHODS

An 18 mo (mid-2012 to 2013) prospective longitudinal

Table 1 Review of literature

Ref.	Year	Number ¹	Grading of laryngeal cleft	Type of repair	Pro-spective	Level of evidence
Yalamachili <i>et al</i>	2015	18 (22)	16 grade 1; 2 grade 2	18 endoscopic	Yes	IV
Ojha ^[2]	2014	27 (42)	27 grade 1	27 endoscopic	No	IV
Thiel <i>et al</i> ^[6]	2011	12	6 grade 1; 5 grade 2; 1 grade 3	3 endoscopic; 2 open	No	IV
Cohen <i>et al</i> ^[19]	2011	16	16 grade 1	16 injection laryngoplasty	No	IV
Broomfield <i>et al</i> ^[7]	2011	7	3 grade 2; 4 grade 3	7 endoscopic	No	IV
Rahbar <i>et al</i> ^[18]	2009	49 (74)	28 grade 1; 21 grade 2	49 endoscopic	No	IV
Rahbar <i>et al</i> ^[17]	2006	22	3 grade 1; 10 grade 2; 9 grade 3	6 endoscopic; 16 open	No	IV
Chien <i>et al</i> ^[8]	2006	16 (20)	16 grade 1	16 endoscopic	Yes	IV
Kubba <i>et al</i> ^[16]	2005	35	35 grade 1-3	Variable	No	IV
Watters <i>et al</i> ^[21]	2003	8 (12)	8 grade 1	8 endoscopic	No	IV
Kennedy <i>et al</i> ^[15]	2000	8	8 grade 1	8 gelfoam	No	IV
Glossop <i>et al</i> ^[22]	1984	6 (10)	6 grade 2-4	Variable	No	IV

¹x(y) refers to x operated and y total cases (*i.e.*, y-x managed conservatively).

study was performed at the Barts Children's and Royal London Hospital. Chart review was performed for all patients. A systematic review of contemporary English medical literature was also reviewed to compare series (Table 1). The study was approved and registered by the hospital clinical governance and audit board. Biostatistician review was not required.

RESULTS

Twenty-two patients were identified with an age range of 1 to 72 mo (mean 23.5 mo) and 7:4 male to female ratio. All patients were symptomatic despite full medical management including anti-reflux therapy. Twenty patients had type 1 clefts with the remaining 2 diagnosed with type 2 laryngeal cleft.

The main referral sources were general or family practitioners (45%) and hospital paediatricians (36%), with the remainder from the paediatric intensive care service. The commonest presenting symptoms were dyspnoea (81%), feeding difficulty (63%), stridor (54%) and recurrent pneumonia (36%). Co-pathologies were noted in 14 patients (64%) including 7 with laryngomalacia (32%), 4 subglottic stenosis (18%), 2 subglottic web (9%), 1 tracheoesophageal fistula (4.5%).

All patients underwent speech and language team assessment with penetration or aspiration demonstrated on video fluoroscopy ($n = 18$) unless speech therapy

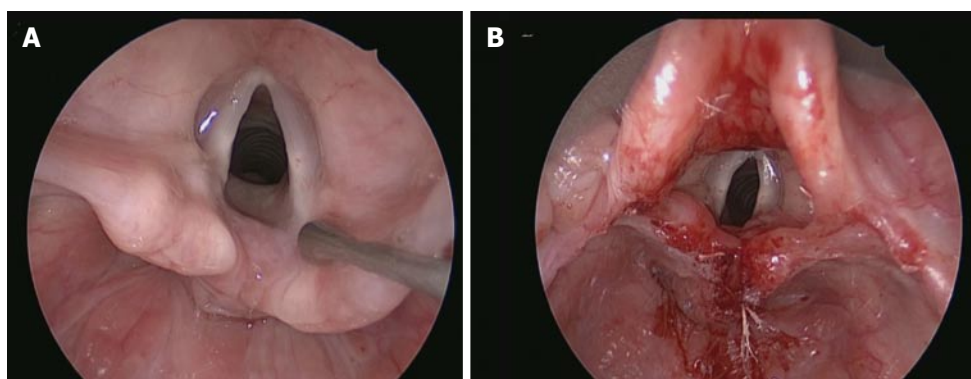


Figure 1 Endoscopic view. A: Type 1 Laryngeal cleft; B: Endoscopic repair.

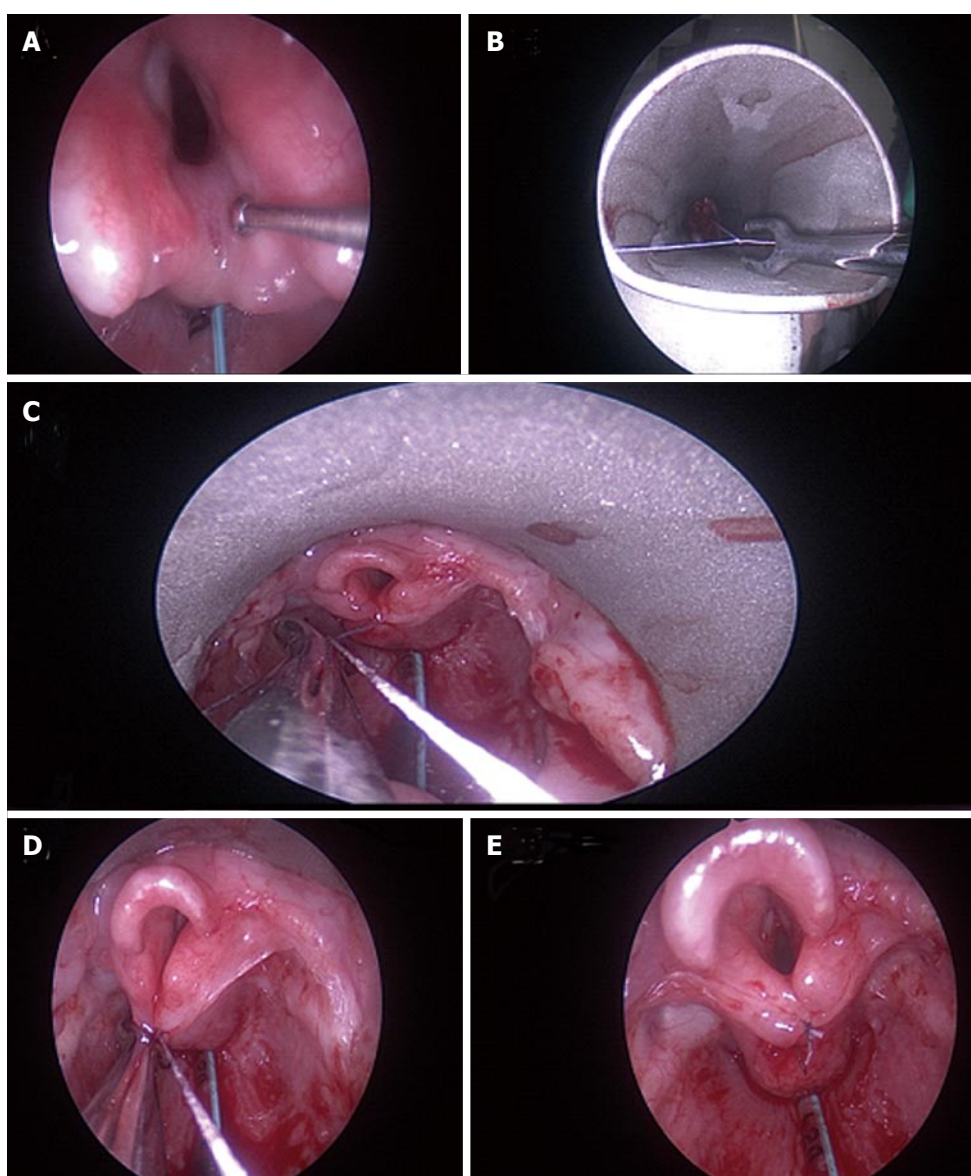


Figure 2 Novel endoscopic suture technique. A: Type 1 Laryngeal cleft; B: Baby Benjamin suspension with Negus knot pusher and suture in situ; C, D: Squaring of knot at depth with more reliability and ease; E: Post-operative result.

deemed the swallow too unsafe to proceed ($n = 4$). At the time of chart review, 18 children had subsequently undergone surgical endoscopic laryngeal cleft repair

(Figure 1).

All patients underwent our standard departmental anaesthetic induction with spontaneous ventilation. All

endoscopic repairs were performed with Baby Benjamin laryngoscope in suspension. We employed the novel use of a Negus knot pusher with an absorbable suture to facilitate ease and reliability of squaring of knots and closure. This produced excellent intraoperative and postoperative outcomes (Figure 2).

DISCUSSION

Laryngeal cleft is rare disorder for which a high index of suspicion is required, across a number of specialities from intensivists, family practitioners, paediatricians and otolaryngologists due to wide variety of presenting symptoms, as highlighted by our results^[1,8,11]. This is a significant single unit series demonstrating the strong association of laryngeal cleft with combined upper aerodigestive tract symptoms and other laryngeal abnormalities. All patients in this series either underwent or are due to undergo endoscopic cleft repair as they remain symptomatic despite maximal medical and speech therapy including anti-reflux medications.

This series represents one of the largest prospective analyses (Table 1) of laryngeal clefts in recent literature and highlights the importance of the symptom profile of children presenting with this abnormality alongside associated findings and successful endoscopic management. In our series, the proportion of males was less than published in the literature^[3]. In addition, the rate of tracheoesophageal fistula in our series (4.5%) was much lower than typically expected (10%-20%) from the literature^[2,4,8,12]. This may reflect referral patterns and our local population.

Management options for laryngeal cleft are myriad ranging from conservative/medical management (including reflux treatment, prevention of pulmonary complications, thickened feeds) to early surgery to prevent complications and where conservative therapies have failed. Viable surgical options incorporate endoscopic surgical repair and external approaches, with anterior (or less commonly, lateral) cervical approaches for more significant clefts^[1-3]. Other techniques such as injection laryngoplasty, gel foam, laser repair and cartilage grafts have also been attempted^[5,6,13-19]. There is however an increasing trend, like in our series, towards endoscopic approaches^[1,2,11].

We note a growth in absolute numbers of referrals from paediatric respiratory and intensivist colleagues. This trend may be in part due to a rise in awareness locally but may also reflect a wider trend in greater prevalence due to a greater cohort of premature babies being supported through infancy. This pattern might in turn correspond to the increased prevalence reported in recent literature^[1,2,4,8,12,20]. We propose to continue to monitor the growing influx into the paediatric airway service at our centre with particular respect to laryngeal clefts and report further trends in presentation and outcomes in the management of these children.

In conclusion, a high index of suspicion and a multi-disciplinary team, including speech therapy and

otolaryngology, is required to manage these patients. Endoscopic surgical repair is increasingly the gold standard for symptomatic patients with laryngeal cleft, particularly of types 1-2. We recommend the use of the Negus knot pusher to facilitate endoscopic repair.

COMMENTS

Background

The main objective of this study was to analyse the laryngeal cleft patients at a tertiary referral centre, in terms of presentation, diagnosis, management and outcomes.

Research frontiers

This is one of the largest single unit series of laryngeal cleft patients.

Innovations and breakthroughs

This endoscopic repair technique is previously unpublished.

Applications

The authors recommend their technique to add to the armamentarium of paediatric otorhinolaryngologists.

Peer-review

This is a paper reporting the diagnosis and management of laryngeal cleft. The subjects for this investigation included 22 children. A novel endoscopic technique is a main point of this paper.

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