Chapter

Pharyngocutaneous Fistulas Following Total Laryngectomy

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Abstract

Total laryngectomy is still the final therapeutic solution in cases of locally advanced laryngeal cancer, as well as in cases of therapeutic failure of organ-sparing surgery or radiation therapy. Following excision of the larynx, the remaining pharynx is reconstructed to obtain continuity of the upper digestive tract. One of the most common complications in these patients, despite constant refinement of the procedure, is the development of a pharyngo-cutaneous fistula. These fistulas prolong hospital stay and often require a second surgical procedure, increasing morbidity and cost for the patient, while diminishing his quality of life. Some risk-factors have been identified, but only some may be corrected before surgery to lower this risk. Managing the fistula once present depends on multiple factors, essential being the size of the fistula as well as the position and concomitant factors, with options ranging from conservative measures to aggressive reconstructive surgery with local miocutaneous flaps. Modern vocal rehabilitation with T.E.P. (tracheo-esophageal puncture) and vocal prosthesis placement presents a new challenge – because of the risk of developing a tracheo-esophageal fistula, with an even higher risk for the patient because of tracheal aspiration. Understanding healing mechanisms of these structures is key to proper management of this complication.

Keywords: fistula, laryngectomy, TEP, vocal rehabilitation, Head & Neck surgery, Wound healing

1. Introduction

Although a well-known technique, having been around from 1873 when Prof. Billroth of Vienna recorded the first procedure, total laryngectomy was constantly refined seeking to improve surgical outcome. Today, narrow-field and wide-field total laryngectomy are combined with partial pharyngectomy and neck dissection to obtain good results following surgery – regarding disease-free survival of patients as well as a good quality-of-life (especially when it comes to speech and swallowing) [1–3].

After the larynx is removed, in the anterior part of the hypopharynx, there is always a resulting defect. This lack of substance is caused by the shared anatomy of the larynx and pharynx. Because most laryngeal neoplasia that warrants a total laryngectomy is usually a locally advanced disease, and the glottis and supraglottic regions are the most frequent regions involved in the disease process, there is often an extension of the neoplasia to the adjacent hypopharynx. This requires an extended resection of the diseased pharynx – a total laryngectomy with a partial pharyngectomy.

After completing the resection, reconstruction of the area uses the principle of separation of the respiratory and digestive tracts. Thus, a permanent tracheostomy is performed by anchoring the subglottic tracheal end to the skin in the suprasternal notch and the remaining pharynx is sutured around a naso-gastric feeding tube and usually covered with the prelaryngeal muscle layers (when available). This is called a three-layer closure – with the pharynx being the first layer, the prelaryngeal strap muscles the second layer and the cervical skin the third [4]. Depending on the size and shape of the resulting pharyngeal defect, primary closure by suturing of the pharyngeal margins may be done in a horizontal pattern or by a T shape pattern. (**Figure 1**) The horizontal closure, when feasible, offers the best healing chance and has the lowest risk of development of a pharyngeal fistula. The T shape closure has more stitching, and the tips of the 2 vertical pharyngeal tranches which form the upper part of the T have the least vascularization, which make them more susceptible to necrosis and therefore a salivary leak, which may progress towards fistula formation.

There are multiple types of suturing techniques used to close the pharynx. Choosing a closure type often depends on the size of the defect to be closed, as well as the surgeon's personal preference. The only recommendation, which every student in Otorhinolaryngology learns from compulsory surgery textbooks is that an inverting suture should be used, similar to sutures used in digestive surgery [4].

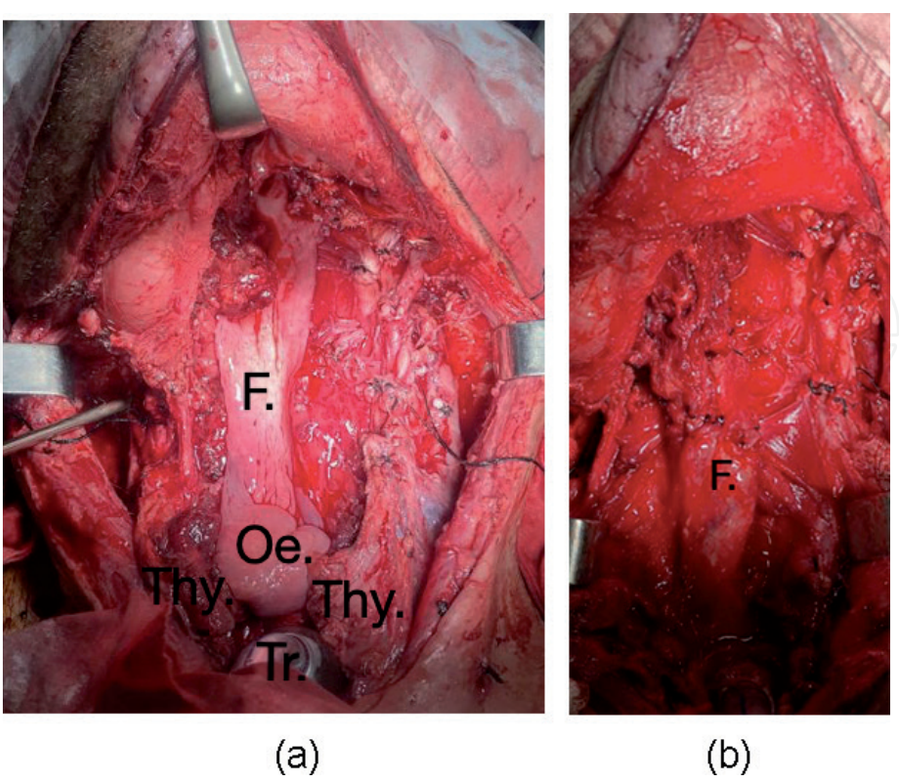

Figure 1.
Pharyngeal closure following total laryngectomy – Left (a): before suturing; Right (b): T-shaped pharyngoraphy on a naso-gastric feeding tube. Legend: F – pharynx, Tr. – trachea, Thy. – thyroid lobes, Oe – Oesophagus.

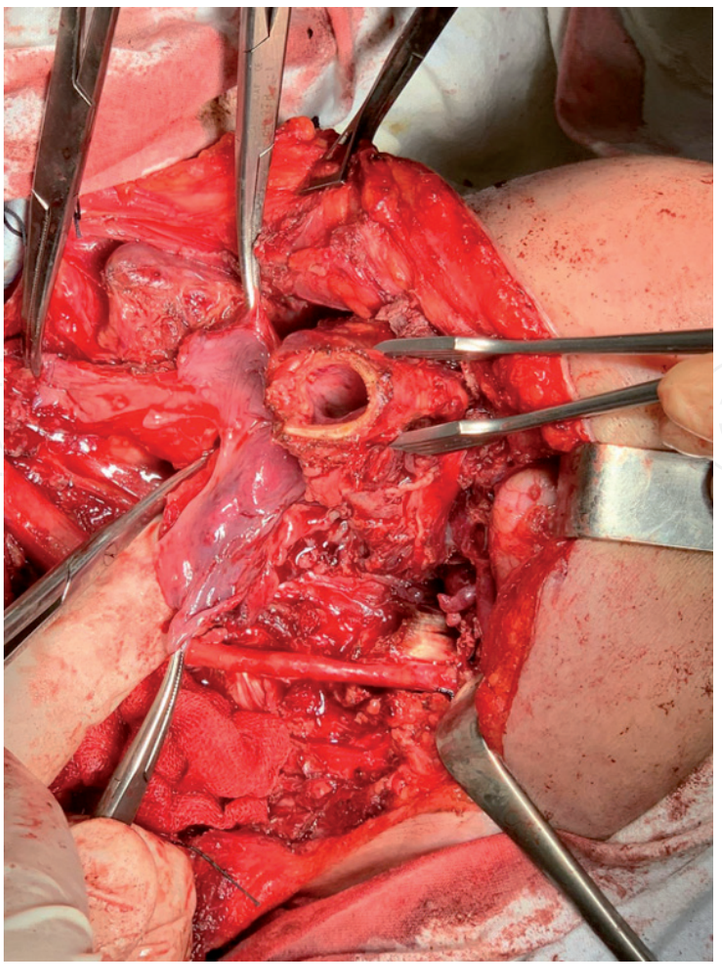

Figure 2.
Resulting defect following total laryngectomy "en bloc" with right thyroid lobe, large segment of pharynx as well as right side prelaryngeal muscle and skin. The resulting defect made primary reconstruction impossible – a local pedicled miocutaneous flap was used.

The most frequent type of suture used is the Connell suture, which is a continuous (running) inverting suture. The needle is passed parallel to the incision line, through all the layers of the pharynx, and out on the same side, after which it runs perpendicular to the incision line to the opposite side, where it passes in similar fashion. Some authors use variations of this suture, but there is not a consensus yet on a superior technique of suturing [5].

In cases of locally advanced tumours, where surgical excision extends to the pharynx, the resulting pharyngeal defect often makes primary closure impossible. (**Figure 2**) Such cases warrant a second, reconstructive step to obtain surgical healing, such as using a local miocutaneous pedicled flap (pectoralis major or latissimus dorsi).

After wound healing – deglution is possible by oral intake, and respiration will always remain through the tracheostomy. Advances in speech rehabilitation made tracheoesophageal fistulisation with vocal prosthesis placement the gold-standard for vocal rehabilitation after total laryngectomy, assuring the possibility for adequate communication even without the larynx.

2. Surgical healing mechanism

As with most tissue injuries, after sectioning the pharyngeal wall through all three layers and then reapproximating them to close the resulting pharyngostoma,

the healing mechanism is activated by way of inflammation, angiogenesis, migration and proliferation of fibroblasts, scar formation and subsequent connective tissue remodelling [6]. Following the surgeon's cut, the surface of the resected pharynx forms blood clots. These contain trapped red blood cells, as well as fibrin, fibronectin and complement components. Clots not only act a bleeding preventing mechanism, but also as a matrix for cells that are attracted by cytokines, chemokines and growth factors released in the area. Release of VEGF (vascular endothelial growth factor) permits increased blood vessel permeability – with subsequent inflammation and oedema. Within 24 hours from the injury, neutrophils migrate to the area and enter the local injury site by way of the blood clot matrix, to contribute to healing by releasing proteolytic enzymes. These enzymes clear debris and destroy bacteria. Between 24 and 72 hours after injury, granulation tissue is formed, by proliferating fibroblasts and vascular endothelial cells. This type of tissue has special properties, because of the high vascular permeability of new endothelial cells. This granulation tissue progressively fills all the injury space, and by 5 to 7 days the entire wound area is filled by this new tissue and neovascularization is maximal [7, 8]. Chemokines and different growth factors that are released by macrophages and neutrophils attract fibroblasts, which usually colonize the wound area in the first two days after injury. Macrophages stimulate the fibroblasts to produce IL-6 as well as epithelial growth factors, which in turn leads to epithelial cell proliferation and subsequent epithelization of the wound. During the second week after injury, the oedema, vascularity and lymphocytic infiltrate subside, and the granulation tissue scaffolding is replaced by dense collagen fibres, spindle-cell fibroblasts and other extracellular matrix components [6]. These collagen fibres are responsible for the tensile strength of the repaired wound. Shear resistance is only about 10% of normal tissue at 7 days following injury. It increases at a fast pace during the following 4 weeks, only to plateau around 70-80% of the normal tissue strength. It is of great importance to note that a repaired wound never acquires the same resistance as normal tissue [6].

3. Fistula formation – predisposing factors

One of the most important aspects in pharyngocutaneous fistulas is the lack of understanding on how the different risk factors affect and potentially cause this complications. Several factors are widely accepted as risk factors in developing a pharyngocutaneous fistula like concomitant or preexisting radiotherapy or chemotherapy, the extension and localization of the tumor – which invariably affects how large the resulting pharyngeal excision will be, the surgical technique (if a deficient surgical closure is performed – either by incorrect approximation of the tissues or improper suturing) used or septic complications of the wound (rarely encountered currently due to antibiotic therapy preoperatively as well as postoperatively). (**Figure 3**) Other lesser-known risk factors include preexisting comorbidities like diabetes, low hemoglobin and albumin levels, liver conditions and malnutrition as well as GERD (gastro-esophageal reflux disease).

What is highly specific about the pharyngeal segment following total laryngectomy is that it is permanently, since day 1 of surgery, in contact with saliva as well as the microbiota of the oral cavity. The chemical composition of saliva is known for its antibacterial and mucosal protection properties, however the mucin content as well as proteases in its composition are often inefficient to prevent even dental plaque formation. Modern studies aimed to use saliva as a diagnostic tool showed however that the proteases are very active and protein cleaving is a dynamic and fast-paced process, with protein degradation being a challenge for developing

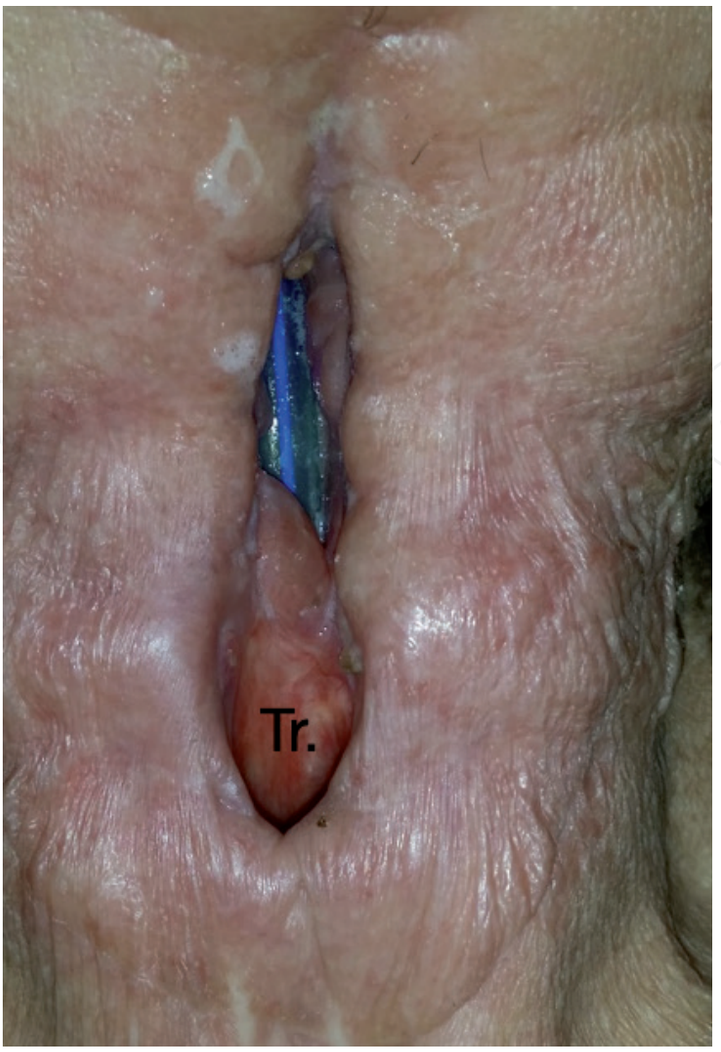

Figure 3.
Large midline pharyngocutaneous and pharyngotracheal fistula following total laryngectomy and radiation therapy. A nasogastric feeding tube is visibile through the fistula orifice, just above the tracheostomy (Tr.)

reliable diagnostic tests [9]. This may factor in the decision to use a salivary bypass tube after total laryngectomy (a Montgomery tube). Some authors reported favorable results using this method [10] – but the small sample size of the study groups, as well as a lack of uniform inclusion criteria and patient distribution resulted in results that were not statistically significant [11, 12].

GERD is another factor which is demonstrated to elevate the risk of fistula formation. Studies have shown that after total laryngectomy, because of upper oesophageal sphincter impairment, patients have elevated acidity and pepsin levels at this level [13, 14]. This affects pharyngeal wound healing – with a higher incidence of fistula formation. Studies showed that postoperative antisecretory and antiacid medication lower the risk for fistula formation after total laryngectomy [15, 16].

The extent of pharyngeal resection – and consequent pharyngeal tissue remaining for pharyngeal closure is one of the factors influencing the rate of postoperative fistula formation. This is probably due to tension around the suture lines, as well as postoperative tension generated by swallowing when resuming oral feeding [17]. Another factor, this time linked to the quality of remaining pharyngeal tissues, is radiation therapy. Salvage surgery, a term coined to describe surgery following other therapies of curative intent that failed (in cases of larynx cancer usually radiation therapy and conservative surgery), has a much higher rate of postoperative complications, including pharyngocutaneous fistulas [18]. In this aspect, radiation

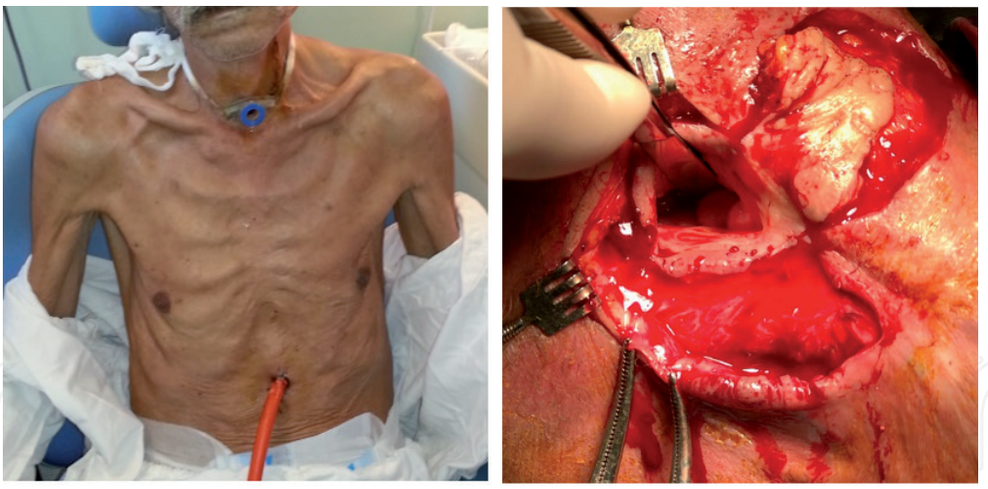

Figure 4.
Malnourished patient suffering from neoplasia of the larynx and hypopharynx. Left (a): Tracheostomy and gastrostomy – before surgical treatment. Right (b): Postoperative lateral cervical fistula – intraoperative aspect showing the diameter of the fistula, as well as the metaplasia of the epithelium of the fistula tract.

therapy is considered the main risk factor for complications because of the changes it produces in the irradiated tissues, and as important is the interval between radiation therapy and salvage surgery. Surgery in the first year after radiation therapy presents a significant higher risk for fistula formation, risk that decreases yearly after the first one [19]. Also demonstrated to present a higher risk of pharyngocutaneous fistula formation is concomitant bilateral neck dissection [20].

Systemic factors that influence wound healing, with regard to pharyngocutaneous fistula formation following total laryngectomy are linked to malnutrition and protein deficit (**Figure 4**). Studies showed that laryngeal cancer in itself negatively influences the nutritional status of patients, oftentimes patients presenting with malnutrition on diagnosis of laryngeal or pharyngo-laryngeal neoplasia [21]. Regarding pharyngocutaneous fistula formation after total laryngectomy, available data demonstrates that malnutrition (**Figure 6**) and protein deficiency (measured by albumin and prealbumin levels), is an independent risk factor. Current medical thought process encourages correcting malnutrition in the perioperative period to lower the risk of fistula formation [22].

4. Management of pharyngocutaneous fistulas

If present, managing pharyngo-cutaneous fistulas is important because their persistence can lead to increased hospital visits, a longer hospital stay and increased time for the surgical wound to heal and can prolong the time from surgery to oncological treatment. It can also have severe complication like aspiration pneumonia or carotid blowout. Although self limiting in most cases, it poses some important complications and sequelae like vessel ruptures or aspirative pneumonia if it is not resolved [23].

4.1 Conservative treatment

Conservative treatment is usually considered the first option for pharyngocutaneous fistulas. The first step in assuring a chance for spontaneous healing of the fistula is to bypass the fistula by ceasing oral feeding. This is done by either placing

a naso-gastric feeding tube (which is usually kept for a limited time) or by parenteral feeding. Conservative measures consist of medical therapy with antibiotics and anti-inflammatory drugs. Daily wound care is also an important aspect with the need for fluid drainage from the fistula, local cleaning and the removal of necrotic tissues if they are present. In the same time the comorbidities of the patient must be addressed for example diabetes and hemodynamic parameters of the patient must be optimized [3] especially hemoglobin and albumin levels [4]. Applying pressure dressing above the fistula has also been seen traditionally as an important routine for daily management of the pharyngocutaneous fistula. However, traditional simple dressings are not suited for fistulas due to high output of saliva and exudate. They act more as a stopgap, so that the saliva and exudate does not come out, rather it stagnates along the fistula canal. The current concept is to move away from the simple wound dressing and use modern dressings like hydrocolloid, hydrogel or silver coated dressings [24, 25]. Sterilizing the fistula from within has also been used by different authors with substances like 0,25% acetic acid by mouth [26]. Another important aspect is the nutritional status of the patient prior and after surgery. Usually head and neck cancer patient are malnourished long time before surgery is even considered and this nutritional status is seen as a risk factor for developing complications like fistulas. Immunonutrition is a process that can modulate the immune system with certain nutrients like arginine, glutamine, omega 3 fatty acids and nucleotides, that can lead to an improvement of protein synthesis. Although not universally accepted, there is evidence that preoperative immunonutrition may lower the risk of developing fistulas [27]. Literature reviews demonstrated decreased hospital stay by an average of at least 3.5 days, but the mechanism by which this was achieved is still unclear [28]. Casas-Rodero et al. demonstrated that immunonutrition by itself did not improve fistula rate, but in the group where nutritional support was administered concomitant with immunoenhanced products the best results were obtained [29].

4.2 Negative pressure wound therapy

Negative pressure wound therapy represents a dressing process in which subatmospheric pressure is applied to the wound in a continuous or intermittent way. By decreasing local tissue swelling, improving blood flow and removing excess fluid it can trigger intracellular signals that may increase the rate of cell division and promotes the formation of granulation tissue transforming the wound into a closed controlled environment with a better management of secretions [30]. In recent years this method of wound dressing has been increasingly used by head and neck surgeons to manage pharyngocutaneous fistulas with good results. It can be used even on large size fistulas and can reduce the size and even heal the fistula. It comes with some contraindications like the presence of necrotic tissues and important wound infection that cannot be controlled. Another important aspect is the cost of this system and the accessibility of it for the patient that develop fistulas [31].

Despite being a complicated site with the presence of the tracheostomy tube which can make it difficult to maintain everything airtight negative wound pressure therapy has proven to be an effective alternative treatment for pharyngocutaneous fistula as a first line or in cases where fistulas persist after surgical revisions [32].

4.3 Hyperbaric oxygen therapy

Hyperbaric oxygen therapy involves breathing 100% oxygen in a pressurized environment with increased atmospheric pressure. Initially used for treating

decompression sickness and carbon monoxide poisoning it has proven to be also effective in treating gangrene and wounds. This therapy promotes angiogenesis and cellular synthesis. The literature available on the use of hyperbaric oxygen therapy consists mostly of studies on chronic wounds such as diabetic ulcers and venous ulcers. A Cochrane database literature review demonstrated that a large part of studies had bias issues, but most had similar results, positive short-term impact on wound healing, with statistically non-significant long-term improvement [33] Published data regarding its use in treating pharyncocutaneous fistulas is scarce. Some results look promising ranging from 87,5% -100% fistula closure [34]. The drawbacks of this therapy despite the promising results are the high cost and the availability of such pressurized rooms.

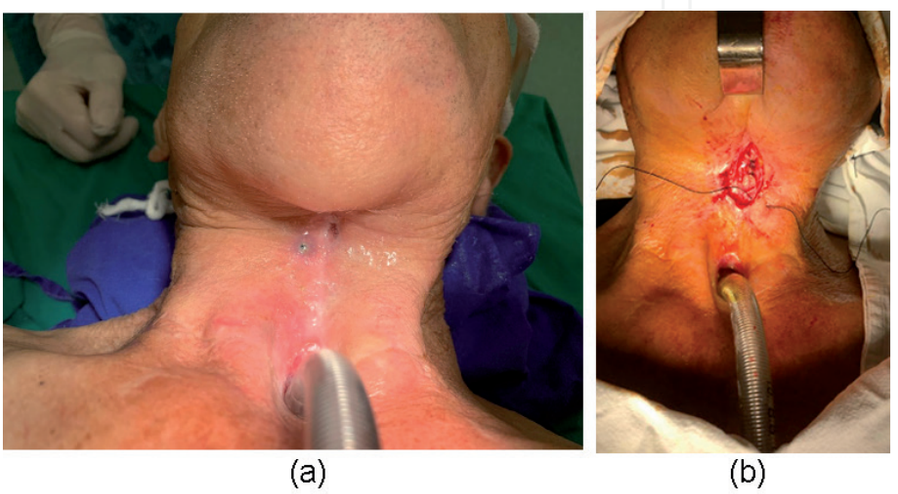

Figure 5.
(Up - a) Midline submandibular fistula following total laryngectomy. (Right - b) Closure of the fistula after resections of margins and 3 plane suturing – pharyngeal mucosa, platysma muscle, skin.

Figure 6.
Midline medium diameter (12 mm) pharyngocutaneous fistula following total laryngectomy and radiation therapy.

4.4 Surgical management

All pharyngo-cutaneous fistulas should be promptly treated, but the urgency as well as aggressiveness of the therapeutic response should be adapted to the size of the fistula, the potential for complications (e.g.: carotid blowout by salivary erosion), the underlying conditions of the patient, and the impact the fistula has on the patient's quality of life. For example: a small, midline fistula orifice, with little to no exudate that appeared during or immediately after radiation therapy in an otherwise healthy individual poses no immediate risk for complications and is easily tolerated by the patient with little to no impact on his quality of life, and has a large

Figure 7.
Surgical closure using two opposing miocutaneous rotation flaps from the sternocleidomastoid muscle and overlying skin. 2 safety sutures placed to prevent head extension and tensioning of the wound.

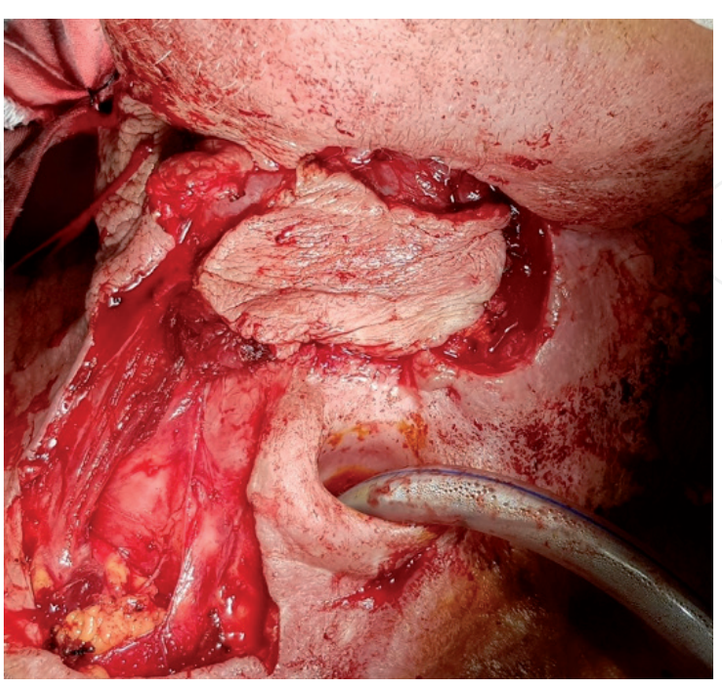

Figure 8.
Closure of a large midline pharyngocutaneous fistula after total laryngectomy. Translation of a miocutaneous pectoralis major flap to cover de defect.

chance for spontaneous healing, which makes it ideal for conservative treatment. Unfortunately, in head and neck cancer surgery most cases of fistulas developing after laryngectomy are not so straightforward to treat and require surgical interventions. A universal set of recommendations does not exist, but basic surgical principles should be tailored and applied to each case depending on each patient's characteristics and the surgeon's preference and experience. These principles state that for small diameter orifices, closure by margin resection and two plane suturing is usually sufficient (**Figure 5**).

Larger defects require interposition of a muscle layer – usually from a local source by way of a pedicled flap. One of the closest available flaps is the sternocleidomastoid muscle, however oftentimes the skin or even the muscle has modifications following neck dissection or/and radiation, which make it not ideal for dissection and manipulation. When available, the SCM pedicled flap is an ideal solution to close small to medium midline or paramedian fistulas (**Figures 6** and **7**).

The workhorse of cervical defect reconstructions, therefore including pharyngocutaneous fistula closure, is the pectoralis major miocutaneous pedicled flap. Because of the size of the muscle, the arterial supply (the pectoral artery is situated in the upper-lateral quadrant of the muscle, ideal for translation towards superior and medial) as well as the subcutaneous fatty tissue, this is ideal for closing large and deep fistulas or pharyngostomas [35] (**Figure 8**). Unbiased data regarding surgical closure methods is hard to obtain, because there is a great deal of variation between surgeons and centres, however some studies shown that use of the pectoralis major flap is the most morbidity prone technique, with a high rate of complications (bleeding, flap dehiscence, recurrent fistula, carotid blowout), but it remains the most used method (**Figures 9** and **10**) [36].

Figure 9.
Final postoperative aspect of closure of an anterior pharyngocutaneous fistula using a pectoral miocutaneous flap. Notice the hair follicules on the flap skin – different from normal cervical skin.

Figure 10.
Postoperative aspect of patient with necrosis of the miocutaneous pectoral flap. After muscle tissue necrosis – large pharyngostomy, with abundant salivary leakage, as well as exposure of the underlying carotid vessels (whitish contour parallel to the NG feeding tube) with great risk of carotid blowout.

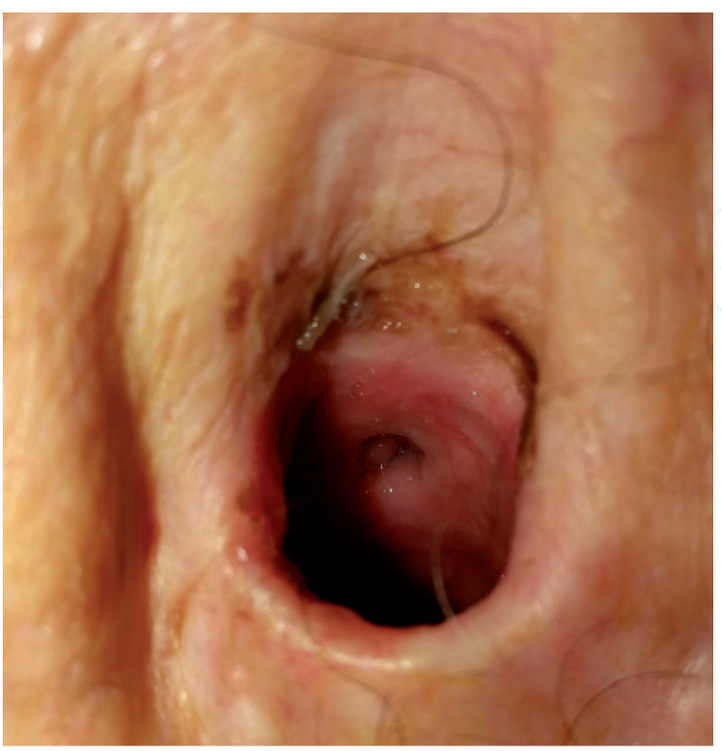

Figure 11.
Tracheoesophageal puncture orifice – enlarged, with spontaneous expulsion of vocal prosthesis. Small granulation tissue visible through opening.

Temporoparietal fascia flap is a new addition to the increasing techniques of fistula repair and is based on the temporoparietal branch of the superficial temporalis artery. One advantage of this flap is that the pedicle is safe from radiotherapy damage but its disadvantages of pedicle length and size of flap can limit its use [37].

In recent years the need for minimal invasive surgeries has grown and endoscopic techniques have been developed to lower comorbidities, complications and try to lower hospital stay. Endoscopic techniques for fistula repair have been developed but have some limitations depending on the size of the fistula and the condition of the surrounding tissues (like the platysma muscle and the accessibility of the fistula transorally) [38].

4.5 Free flaps

Free flaps are used when proximal tissues are unavailable or cannot offer epithelial surface for the repair of the fistula. The advantages of free flaps are that the donor site is far from the primary wound and therefore safe from infection and have not been irradiated. The important limitation of using free flaps is the availability of neck vessels for anastomosis (especially in cases of previous radical neck dissection with ligation of internal jugular vein) [39]. The most common free flap used is the radial forearm flap and anterior thigh flap. Other free flaps that can be used are jejunal flap and latissimus dorsi flap. Another relative disadvantage of using free flaps is the significant longer operating time needed – with harvesting and implantation taking longer than using local pedicled flaps, as well as sometimes requiring two surgical teams [39].

5. Particular case: tracheoesophageal puncture vocal rehabilitation – fistula enlargement and management

One particular situation of fistula formation is in cases of vocal rehabilitation using tracheo-esophageal fistulization with vocal prosthesis implant. In these cases, a fistula is made by the surgeon, between the trachea and the upper cervical esophagus through the posterior tracheal wall right at the level of the tracheostomy. In this iatrogenic fistula the surgeon inserts a vocal prosthesis – basically a two-flanged device with a lumen that has a unidirectional valve. This is placed so as to permit air from the trachea to pass through towards the pharynx, but not so as to allow food and liquids to pass from the pharynx. This method permits a higher quality esophageal speech and is currently the gold-standard method for vocal rehabilitation following total laryngectomy and has been for the last 30 years [40]. However, long term studies showed that a number of complications may arise in these patients. The hardest to treat is enlargement of the fistula. This is currently linked to local factors, such as acid reflux in the upper esophageal and pharyngeal areas [41], as well as inflammation of the tissues surrounding the prosthesis – inflammation which in turn is caused by the biofilm that forms on the body and flanges of the device [42]. Once enlargement begins (**Figure 11**), one of the first signs will be leakage around the prosthesis, with coughing especially during drinking. Salivary leakage and micro aspiration are potentially very harmful, because of the risk of aspiration pneumonia, which may endanger the patient's life. Methods to treat fistula enlargement vary from using larger and larger diameter flanges, to surgically closing the fistula using a local muscle flap (usually sternocleidomastoid) and after surgical healing refistulization in a different site. Some patients however after such complications abandon this technique of vocal

rehabilitation altogether and opt for other methods of communication (esophageal speech or an electric larynx) [43, 44].

6. Conclusions

Following total laryngectomy, some anatomical and functional modifications of the cervical region and especially of the pharynx and upper cervical esophagus are important for the consequent evolution of the laryngectomee. Wound healing follows the same basic principles as everywhere else in the human body, but this region presents a series of particular elements. Understanding the importance of not just the quantity of the remaining pharyngeal tissue and the pharyngeal closure technique but equally the quality of said tissues (affected by recent previous radiation therapy and malnutrition) and the intrinsic factors that influence local healing (bacterial colonization, gastro-esophageal acid reflux) – is paramount to micro-managing each total laryngectomy case, in order to decrease the risk of developing a pharyngo-cutaneous fistula. Once formed, fistulas are treated by a multitude of techniques, from conservative to radical surgical plastic reconstructions using local or distant free miocutaneous flaps. Either way, treatment of fistulas is always a more expensive and higher-risk procedure than preventing fistula formation. A particular case is vocal rehabilitation of the laryngectomees, by way of iatrogenic tracheo-esophageal fistula formation with vocal prosthesis placement. In this case, managing the fistula orifice presents another set of challenges, the goal being to maintain fistula patency without granulation tissue formation and without orifice enlargement, so as to maintain patency and prevent leakage or expulsion/aspiration of the prosthesis. The same intrinsic factors – biofilm formation and GERD have been established as risk factors for complications regarding the size of the fistula orifice.

Conflict of interest - disclosure

The authors declare that there are no conflicts of interests among them. All authors have contributed equally and would like to thank their colleagues for the considerable work and support.

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