

## An Insight Into Pharyngeal Closure Techniques During A Laryngectomy- Can We Minimize Pharyngocutaneous Fistulas?

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### Abstract

In this age of Chemoradiation for carcinoma of laryngopharynx, post-operative pharyngocutaneous fistula (PCF) is has become quite common. It results in significant morbidity and prolonged patient stay. Although conservative management is the mainstay of its treatment, it causes tremendous psychological impact on the patient due to repeated visits to hospital, in ability to take oral feeds, social stigma because of neck wound. We have explored literature to present various risk factors associated with this complication and how to treat it. The technique of pharyngeal closure during a laryngectomy surgery has an important role in preventing a pharyngocutaneous fistula. All surgeons dealing with laryngopharyngeal malignancies need to know the available evidence and described techniques in literature to minimize the incidence of post-operative fistulae. We present to you an extensive literature review regarding pharyngoplasty techniques.

**Key Words:** pharyngocutaneous fistula, pharyngoplasty, laryngectomy, pharyngeal closure.

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### I. Pharyngocutaneous Fistula (PCF) - Incidence, Risk Factors And Prognostication

Most common surgical complication of total laryngectomy is pharyngocutaneous fistula with an incidence of around 10-30%. (1-9) Concurrent chemoradiation became stand of care for organ preservation after the Intergroup Radiation Therapy Oncology Group Study (RTOG 91-11), its 10 year follow-up also strengthens the same. (10,11) Total laryngectomy has been increasingly restricted to extensive extra laryngeal disease, cartilage erosion and reserved for salvage setting for persistent and recurrent disease. Major wound complication rates in salvage laryngectomees according to RTOG 91-11 data is around 59% to 64% of patients, with pharyngocutaneous fistulas in atleast 30%. (11) To address this problem non-irradiated vascularized tissue flaps were used in literature with significant benefits. Guimaraes et al (12) conducted a systematic review on efficacy of prophylactic use of pectoralis major muscle flap for prevention of PCF in salvage laryngectomy setting. He included 12 retrospective studies with a total study population of 253 and meta-analysis showed significant risk difference between pectoralis flap group and control group. When techniques of interposition of flap are compared between onlay and inseting technique, although no significant difference in fistula rates were found, onlay technique seemed superior to inseting technique because in-setting further increases the length of suture line, increasing the chance of potential fistula formation and onlay reinforces the standard pharyngoplasty closure. (12,13) When free flaps are compared to regional flaps in closure of pharyngeal defects in salvage setting, Pateletal multi institutional retrospective study of 359 patients showed superiority of pectoralis major (15% fistula rate) to free flaps (25% fistula rate). This can be attributed to unreliable blood supply to the periphery of free flaps. (13) Hyaluronan content is higher in deep fascia surrounding pectoralis major muscle which further accelerates wound healing. (14,15)

There is an ample amount of evidence regarding the incidence, risk factors and outcomes of this troublesome complication. In recent literature three systematic reviews and meta-analyses were published studying the risk factors associated with PCF, the findings are summarized in Table 1. (2,3,9)

Author	Year	Type of study	Risk factors
Liang (3)	2015	systematic review and Meta-analysis (16 studies)	Tumour subsite, T stage (T1-2 stage and T3-4 stage was 11.7% and 16.5%), previous radiotherapy, postoperative hemoglobin <12.5mg/dl, margin status
Dedivitis(9)	2015	systematic review	COPD, previous hemoglobin <12.5g/dL,

		(63 studies)	blood transfusion requirement, previous radiotherapy or chemoradiotherapy, supraglottic tumor subsite, hypopharyngeal tumor site, advanced primary tumors, positive surgical margins and the performance of neck dissection (regardless the type).
Wang(2)	2019	systematic review and Meta-analysis (52 studies)	Age, smoking, COPD, CAD, T-stage, previous radiotherapy, preoperative albumin, preoperative hemoglobin, tumor site, and treatment method.

There is a strong link between inflammation and fistula formation, this aspect is under evaluation to determine tissue markers and prognosticators. Koobetal(16) studied parameters like body temperature, pain, C-reactive protein (CRP) and leucocytes and tissue markers like bradykinin 1 receptor (B1-R), bradykinin 2 receptor (B2-R), and vascular endothelial growth factor receptor 2 (VEGF-R2) in a retrospective study of 182 patients and found that high bradykinin 1 receptor expression in the tumor samples correlated with postoperative fistulas. B1-R membrane-bound score  $\geq 5$  or a VEGF-R2 endothelial score  $\geq 5$  vessel/fov should be categorized as high-risk patients for PCF development Persistently elevated CRP( $\geq 6.1$  mg/dl) and leukocyte levels ( $\geq 8.3$  G/l) beyond the 6th postoperative day were also risk factors.

PCF has variable morbidity from patient to patient ranging from increased hospital stay, discomfort, delayed functional recovery, late postoperative strictures to more morbid conditions like carotid blowout. Horgan and Dedo(17) has defined major fistula as the one lasting more than 8 weeks or requiring surgical treatment. A more recent definition for major PCF was given by Casasayasetal(6) as the one lasting more than one month or needs surgical treatment or leads to death. The importance of maintaining total treatment package time within 100 days is pivotal for survival advantage.(18)National Comprehensive Cancer Network guidelines (NCCN) recommends initiating radiation therapy within 6 weeks of surgery.(19,20) However in PCF context there is paucity of literature regarding its impact on survival. Kim etal studied 232 patients and found a significant difference in 5 year DFS rates between patient with and without fistulas.(21)

### **Management and surgical repair of PCF**

Most fistulas present 7–11 days after surgery and it is a preventable complication. Controversy still prevails around prevention of pharyngo-cutaneous fistulas. It is a general agreement that fistulas usually respond to conservative treatment strategies like early aspiration of collection, exteriorization and lateralization, antibiotic cover. 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; enteral feeding must be started; hemodynamics must be optimized; infections must be treated and comorbid must be controlled. Conventional wound dressings with appropriate debridement and lateralization of fistulous tracts is the dictum for conservative management. A variety of dressing materials have been tried like hydrocolloid products, hydrogel, silver coated and honey impregnated products. They are not cost effective and would be useful only in small fistulas with less saliva output. More recently vacuum (negative pressure) assisted dressings made its way into management of PCF. It has an advantage of promoting granulation in highly exudative wounds and at the same time can be combined with other products to add antimicrobial effects. Disadvantages of vacuum assisted dressing would be the need for customized moulds to achieve an airtight seal and need for training/expertise in the wound care team.(22)Systematic review by Fu-Yu Lin of 9 studies with 122 head and neck wounds negative pressure wound therapy adopting a continuous pressure of around 125 mm Hg achieved fistula closure rates between 78% and 100%. Definitive recommendations based on this data cannot be made because of the studies included provide low level of evidence with lot of heterogeneity.(23) Asher etal described a novel way of designing and utilizing an intraluminal negative pressure wound therapy system combined with a vascular flap and successfully closed some difficult fistulae. Such intraluminal negative suction would divert saliva from not reaching the suture line and eventually aid in healing.(24)Few surgeons advocate routine use of salivary bypass tubes in laryngectomy patients, a recent systematic review suggested a low level evidence (three retrospective case-control trials and six case series) in reducing the incidence of fistula rates.(25)

Hyperbaric oxygen therapy (HBOT) can also be considered when other conventional treatments have failed and in recurrent fistulae. A Cochrane review published in 2016 validated the utilization of HBOT in difficult to heal wounds and osteoradionecrosis.(26) HBOT improves oxygen tension in tissue, promotes angiogenesis and increases free radical bactericidal activity. There are few studies in literature supporting the role of HBOT in head and neck wounds.(27–29)

Appropriate time for reintroduction of oral feeding is still not established. Aswanietal(30) in a prospective study compared early oral feeding (7<sup>th</sup> to 10<sup>th</sup> postoperative day) to delayed oral feeding, has found no significant difference between early feeding and fistula rates, reduction of length of hospital stay and reduced financial costs. Meta-analysis of 6 studies as a part of Aswanietal(30) study also establishes no significant difference in fistula rates between early and late reintroduction of oral feeds.

Appropriate time for surgical intervention is also not well defined in literature. Surgical intervention is generally considered after failure of all conservative measures in common practice. McLean et al(31) demonstrated that the mean time to spontaneous fistula closure in the irradiated group is 50 days vs 24 days in non-irradiated group. Few surgeons prefer early surgical intervention in view of not missing the window for adjuvant radiation, prevent scarring and fibrosis and prevent the existing defect to become larger in size. Iteld and Yu suggested early repair within 3 to 28 days for PCF larger than 5 mm(32). Casasayasetal suggested that 4 weeks is the critical cutoff point to consider for surgery, as they observed that PCF lasting more than 4 weeks will rarely heal completely with conservative measures.(6)

## **II. Pharyngoplasty Techniques**

### **1. Suture pharyngoplasty**

Basics of intestinal mucosal closure techniques, Inversion vs eversion were described way back in early 1800's by Astley Cooper, and in 1812 by Travers, they inculcated eversion techniques into gastrointestinal surgery.(33) In 1826 Lembert described the now widely used technique of serosa to serosa approximation.(34)

Surgical method is designed to patient's tumour stage, physical condition and expected postoperative quality of life. Need for primary pharyngoplasty or patch/ circumferential depends on width, quality of remnant pharyngeal mucosa and previous radiotherapy. Regarding how much of remnant pharyngeal mucosa would yield a primary closure without postoperative swallowing dysfunction, Hui etal(35) study on 52 patients showed the narrowest width to achieve the above would be 1.5 cm of relaxed and 2.5 cm of stretched mucosa. Surgeon's expertise on closure techniques also has an impact on postoperative fistula rates. Although meta-analyses didn't attain a statistical significance(2,3,9) between suturing technique and fistula rate, this area has paucity of literature and needs to be emphasized in further studies. Aries etal(36) performed a meta-analysis of 4 studies with a total of 417 patients, comparing manual and mechanical closures of pharyngeal mucosa. Surgical stapler group had reduction in absolute risk by 15% of fistula (IC95% 0.02 a 0.28; p=0.02; I2=66%), reduced operative time (reduction by 80 minutes), shorter hospital stay (by 6 days) and early initiation of oral feeds (by 8 day difference). Regardless the technique used favourable outcomes can be attained by creating a tension free suture line, attaining a water tight closure with preserved viability of the mucosa.

Superiority of horizontal closure with interrupted inverting sutures to a T shaped closure in view of fistula rates was described by Jatin shah(37). He also emphasized that the weakest point of 'Y' or 'T' closure was the three pointer.(38) Stell and Cooney (39) has stressed the importance of vertical closure. Qureshi etal(40) in prospective study of pharyngocutaneous fistulas investigating relation to type of closure(T,Y,vertical), technique of closure( full thickness interrupted, submucosal interrupted, submucosal continuous), suture material (silk,vicryl) did not show any statistically significant correlation. Soyluetal(41) when comparing vicryl and catgut suture materials, showed a statistically significant reduction of complication rates in vicryl group, this may be explained by less inflammatory, stronger and longer half-life properties of vicryl. Govindasamyetal(42) has shown the superiority of horizontal closure compared to 'T' shaped closure. Barton(43) in 1982 has described a double 'V' advancement mucosal flaps technique for primary pharyngoplasty which gave successful swallowing results even with 4 mm remnant mucosa, this technique is seldom practiced now. Hakseveretal(44) has devised a new modified continuous Connell suture technique named 'Zipper suture' for easy inversion of mucosal edges and reduced fistula rates. Two layer(extra mucosal ,serosal) vs three layer (extra mucosal ,serosal and muscular) suturing technique comparison showed less rates of fistulae in three layered technique but reduced voice outcomes with tracheo-esophageal puncture prosthesis.(45)

### **2. Stapler pharyngoplasty**

The first mechanical device usage was reported by Henroz in 1826 with an eversion technique, but it was less explored due to strong evidence provided by Lempert's study.(34) Only after studies by Galluzzi and Ravitch there was acceptance towards mechanical stapler in American surgeons.(46,47) Many retrospective and prospective case series are available in literature which advice the ease of mechanical closure and reduced postoperative fistula rates.(4,48-53) Felipe T Aries published a systematic review in 2013 which included 417 patients, showed an absolute risk reduction of pharyngocutaneous fistula by 15% (95% confidence interval [CI], 0.02-0.28; p ¼ .02; I2 ¼ 66%), there was also a significant improvement in operative time, early postoperative feeding in stapler group.(36) Recently technique using magnifying endoscopy with Narrow band imaging to assist linear stapler closure, in such way triple check of mucosal edges would be possible.(54)

### **3. Others**

Augmentation of the pharyngoplasty defect was done in literature using various range of free and regional flaps. A study by Sherif G Ibrahim on sternocleidomastoid muscle augmentation did not reduce the incidence of postoperative fistula.(55) Bilateral infrahyoid muscle, myofascial and myoperichondrial flaps have also been described to augment closure of pharynx.(56) Vascularized and non- irradiated tissue transferred in to

a post radiation salvage laryngectomy field is a surgical norm followed these days. The efficacy of Pectoralis major muscle flap for augmentation of pharyngoplasty in salvage laryngectomy setting was explored in systematic review by Andre Vicente Guimaraes in 2015, he analysed 12 studies and found that the prophylactic use of pectoralis muscle decreased the incidence of fistulas.(12) Lattissimusdorsimyocutaneous flap also has a similar reduced fistula rate as pectoralis flap.(57) In circumferential defects the use of free flaps is of utmost significance to reconstruct large defects, defects with cutaneous resection and extensive soft tissue resection. Anterolateral thigh flap, radial artery forearm flap, free jejunum etc. are widely described in literature.(58)

When it comes to novel techniques use of acellular dermal matrices, tissue adhesives, decellularised human amnion / chorion grafts have been in research. A recently published systematic review on the use of acellular dermal matrices in pharyngoplasty by A Hui compared 11 studies with 170 cases came to a conclusion that although efficacy has been achieved by various studies, the evidence is still poor to make it a standard of care. When tissue adhesives like platelet rich plasma, fibrin adhesive and protein-based albumin glutaraldehyde were compared against controls, although positive results were obtained, there was no statistically significant reduction in postoperative fistulas.(59) Decellularized and lyophilized human amnion/chorion membrane grafts showed positive results in fistula repair.(60)

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