

A prospective study of pharyngocutaneous fistulas following total laryngectomy

ABSTRACT

Pharyngocutaneous (PC) fistula is a common complication following laryngectomy. It leads to increased morbidity, delay in adjuvant treatment, prolonged hospitalization and an increase in treatment costs. Although a number of factors that result in PC fistula have been described, there is still no agreement on the most significant factors. We undertook a prospective study to critically analyze PC fistula and its association with various tumors, patient and treatment related factors. This was a prospective study that included 143 patients who underwent laryngeal surgery for squamous cell carcinoma of the larynx and pyriform sinus. Use of pectoralis major myocutaneous flap to reconstruct the neopharynx, primary disease in pyriform and extensive soft tissue infiltration were significantly associated with PC fistula. Prior treatment (radiotherapy and chemotherapy), type of closure (T closure, Y closure and vertical closure), Layers of closure (full thickness interrupted, submucosal interrupted, submucosal continuous) type of suture material (silk, vicryl), age, sex, stage, preoperative tracheostomy, cut margin status, pre/postoperative hemoglobin and experience of surgeons did not relate significantly.

Key words: Pharyngocutaneous fistula, total laryngectomy, morbidity

INTRODUCTION

The development of a pharyngocutaneous fistula (PCF) is the most common and troublesome post-operative complication following laryngectomy. Its occurrence leads to increased morbidity, delay in adjuvant treatment, prolonged hospitalization and an increase in treatment costs. The reported incidence of PCF is extremely variable in the literature, ranging from 5% to 65%.^[1-3] A rate between 13 and 25%^[4-23] has been often reported and only few reports had a rate of less than 10%.^[3,24-27] Although a number of factors that result in PCF have been described, there is still no agreement on the most significant factors. We undertook a prospective study to critically analyze PC fistula and its association with various tumors, patient and treatment related factors.

MATERIALS AND METHODS

This was a prospective study that included all patients who underwent laryngeal surgery for squamous cell carcinoma of the larynx and pyriform sinus between January 2003 to December 2004. A total of 143 laryngectomies were performed during this period. All the patients had similar pre-operative/post-operative care. We studied all the previously reported factors that could influence fistula formation such as - age, sex, site of primary, T stage, extent of nodal dissection, soft tissue infiltration, prior treatment (ra-

diotherapy), type of closure (T closure, Y closure and vertical closure), technique of closure (full thickness interrupted, submucosal interrupted, submucosal continuous) suture material (silk, vicryl), preoperative tracheostomy, cut margin status, serum hemoglobin and albumin level, experience of surgeons (consultant Vs residents).

RESULTS

Two third (67%) of the patients had hypopharyngeal cancers and one third were laryngeal cancers. Of the 143 laryngectomies, 130 required total laryngectomy with or without partial pharyngectomy and 13 underwent near total laryngectomy. One hundred and five (73%) patients had primary closure of the mucosa, 18 patients required pectoralis major myocutaneous flap for neopharynx augmentation and 7 patients required a gastric pull-up. Table 1 enlists the common complications encountered in our study.

The overall fistula rate was 23% (33/143) but 14% in patients with primary closure. (Table 2) Of 18 patients who underwent pectoralis major myocutaneous flap for neopharynx reconstruction two third witnessed a PC fistula. There was no PC fistula in patients who underwent neopharynx reconstruction with gastric pull up (7/143). Majority of leaks manifested within first 2 weeks (25/33) and most appeared in the lateral part of the suture line (29/33). In most patients (27/33) the fistula healed with conservative man-

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Table 1: Complications following total laryngectomy

Complication	Number (n=143)	Percentage
Fistula	33	23
Hemorrhage	8	5
Flap Necrosis	8	5
Metabolic problem	4	2.5
Hypocalcemia	4	2.5
Wound Infection	9	6
Others	8	5

Table 2: Type of Surgery vis-à-vis rates of Pharyngocutaneous fistula

Type of surgery	Percentage
Larynx	11
Primary closure-Pyriform	19
Near Total Laryngectomy	38
Total Laryngectomy with Patch PMMC	66
Total Laryngectomy with Patch PMMC	66

agement alone. The conservative management involved adequate drainage, neck compression and frequent dressings. In patients with evidence of infection, suitable antibiotics were used. Half of these fistulas healed within 14 days and 3/4th healed within 4 weeks. Eighteen percent of the patients (6/33) required surgical intervention by way of a myocutaneous flap for control of PC fistula. All these patients had undergone primary mucosal closure at the time of laryngectomy. The indications of were hemorrhage in 4 patients and high output fistula in 2. Following the leak, these patients required PMMC flap to cover the exposed neck vessels and to close the mucosal dehiscence. Interestingly, the PMMC did not completely stop leakage in any of these patients. It only reduced the salivary output of the fistula and probably prevented a vascular catastrophe common in such patients. 80% patients were discharged within first 2 weeks of the index surgery. Oral feeds could be initiated in nearly 2/3rd of these patients in first 2 weeks. Average hospital stay in the patients having PCF was 27 days. Three patients (9%) could not undergo planned adjuvant radiotherapy because of the leak.

Amongst the various possible contributory factors, reconstructions, primary disease in pyriform and extensive soft tissue infiltration were significantly associated with PC fistula. (Table 3) Prior treatment (radiotherapy and chemotherapy), type of closure (T closure, Y closure and vertical closure), layers of closure (full thickness interrupted, submucosal interrupted, submucosal continuous) type of suture material (silk, vicryl), age, sex, stage, preoperative tracheostomy, cut margin status, pre/post-operative hemoglobin and experience of surgeons did not relate significantly.

DISCUSSION

Even though much controversy still surrounds the prevention of pharyngocutaneous fistulas, it is generally agreed that most fistulas respond well to conservative manage-

Table 3: Summary of factors influencing pharyngocutaneous fistula formation

Parameter	Significance
Reconstruction	Significant (<i>P</i> < 0.05)
Soft tissue infiltration	Significant (<i>P</i> < 0.05)
Hypopharyngeal disease	Significant (<i>P</i> < 0.05)
Consultant vs Resident	Not Significant (<i>P</i> > 0.05)
Types of Suture	Not Significant (<i>P</i> > 0.05)
Prior RT	Not Significant (<i>P</i> > 0.05)
Type of Closure	Not Significant (<i>P</i> > 0.05)
Prior Tracheostomy	Not Significant (<i>P</i> > 0.05)
Extent of nodal dissection	Not Significant (<i>P</i> > 0.05)
T stage	Not Significant (<i>P</i> > 0.05)
Cut margins	Not Significant (<i>P</i> > 0.05)
Serum Hemoglobin	Not Significant (<i>P</i> > 0.05)

ment: figures between 60% and 80% are commonly reported.^[10,11,14,17,19,28,29] Two third of our fistulas also healed with conservative management. The differences appear to be mainly related to previous radiotherapy: spontaneous closure was achieved in 44% to 82% of previously treated patients^[11,17,19] versus 80% to 95% of patients who had not been previously treated.^[17,20,26-28] Local wound care (drainage, local antiseptic, removal of necrotic tissue, curettage of the fistulous borders and tract and pressure dressing above the flaps) should be associated with introduction of the feeding tube and administration of general antibiotics, if signs of local infection are present.^[30] In contrast a curious conservative approach was adopted by Fradis et al.^[23] Reinsertion of the nasogastric tube for fluid intake, oral feeding for solid foods and suspension of antibiotic therapy favored, in their patients, granulation tissue formation and spontaneous closure of the fistula. Even though surgical repair has been performed after more than 3 months of conservative treatment,^[5,7,13,26] but if closure of the fistula is not obtained in a month with medical management, it is not wise to wait any longer and surgery should be planned.^[30] Cure of infection is an important prerequisite for a successful outcome. Many surgical options are available,^[4,13,31-38] and the choice of the surgical technique should be dictated by the diameter of the fistula and previous radiation history. Along with direct suture or local flaps, the favored reconstructive methods are deltopectoral and pectoralis major myocutaneous flaps^[5,7,10,11,13,14] In recent years, reconstruction with free flaps such as the radial forearm and jejunal has gained some popularity.^[36-40] None of our patients who had undergone free jejunal flap for pharynx reconstruction witnessed PCF. The observation in our study suggests that though PMMC in patients having fistula, reduces the salivary output, does not totally stop it. Probably it gives a vascular cover to the exposed neck vessels and prevents a vascular catastrophe.

The type of surgery is one of the less controversial predisposing factors for fistula development in the literature, and extended laryngectomy invariably carries a higher incidence of fistulization by a factor of two or more.^[5,10-13,24,29] Resec-

tion of large amount of pharyngeal mucosa leads to closure made under tension. These wound are more prone for break down and formation of PCF.^[41] In our study, the pyriform disease appeared significantly associated with PCF because of the above mentioned reasons. A pyriform primary necessitates partial pharyngectomy along with total laryngectomy. Since 2/3rd of our patients have advanced pyriform disease, our average leak rate (25%) may appear very high. The leak rate dropped to half (11%) the average rate (25%) when patients underwent laryngectomy alone.

Many authors believe that delayed oral feeding reduces fistula formation after laryngectomy as there is no stress on the suture line due to feeding. In our study, three fourth (75% and 25/33) of our patients had leak in less than 2 weeks i.e. before the oral feed was initiated in them. A poll conducted by Boyce and Meyers^[20] revealed that 84.5% of the practicing head and neck surgeons wait at least 7 days to feed their patients after laryngectomy, and only 2.8% feed at 4 days or before. However, there is little evidence to support the view that the timing of oral feeding influences fistula formation following laryngectomy, and in most cases, PCF had developed before the patients received any oral feeding. Most authors^[20,21,42,43] no longer consider delayed oral feeding necessary until after the seventh postoperative day unless fever, wound erythema, swelling, or continuous elevated drainage (which raise the suspicion of an impending fistula) is present. A few authors did not even adopt the nasogastric tube and instead started oral feeding on the first^[22] or the third^[27] postoperative day. Moses et al^[21] reported a lower incidence of fistula in the group of patients who resumed feeding on postoperative day 7, whereas it was much higher in patients who did so after 7 days. Aprigaliano^[27] reported a 9% fistula rate without use of nasogastric tube and oral feeding on postoperative day 3.

Numerous patient related factors have been studied for their role in causation of PCF. Patients requiring a tracheostomy prior to surgery are at increased risk of developing a PCF.^[13] It is probably due to contamination and the higher T stage. This did not happen in our study. Few other authors have reported similar experience where prior tracheostomy was not found to be a risk factor for PCF.^[44,45]

Pre/postoperative hemoglobin level lower than 12.5 g/dL have been associated with PCF.^[28,30] Zinis et al^[30] found a nine fold increase in the risk of PCF. Horgan et al^[13] also found a rise in the number of fistulas in patients with hemoglobin values less than 11.5 g/dl. Postoperative anemia is a consequence of high intraoperative blood loss and can be compared to the need for intraoperative transfusion which significantly increased the incidence of PCF from 7% to 28% in the report by Hier et al.^[14] On the other hand preoperative hemoglobin has not been found to be a significant risk factor.^[41] We did find such a relation in our study. May be the

sample size was inadequate to reach to such a conclusion in our study.

The anesthesiologic risk which is mainly an index of concomitant diseases was associated with a 19% fistula rate compared to 4% in patients without concomitant diseases.^[26] This view is also supported by Horgan et al^[13] and Cavalot et al.^[45] Conversely Zinis et al^[30] did not found concomitant diseases to be predictive of fistula formation. Age, sex, smoking, alcohol, preoperative hemoglobin, Karnofsky performance status, body mass index have not been considered as significant factors increasing the risk of PCF.^[41] We had similar findings in our study too.

The role of previous radiotherapy has been extensively reported in the literature. Grau et al^[46] in a large series of 472 patients undergoing salvage laryngectomy after radiotherapy reported a PCF rate of 21%. Numerous authors have also found significant correlation with radiotherapy and PCF^[4,8-10,26,27,29,41,45] but at the same time some authors have also reported no correlation with radiotherapy.^[11,14,15,23-25,30] In our subset of 13 patients who had prior RT before laryngectomy, there was no significant increase in fistula rate. As regards to the time between radiotherapy and surgery some authors did not find any significant correlation.^[13,47] However, Hier et al^[14] stated that preoperative radiation appears to be a risk factor if surgery is performed within 3 months. This could probably due to the vasculitis which develops after radiotherapy and increases the risk of infection. Vasculitis generally subsides within 3 months. Briant^[48] in contrast stated that if surgery after radiotherapy is performed within 3 months the complications were comparable between radiotherapy and surgery alone control group. Also the fistulas appear earlier and the sizes are significantly larger in patients with preoperative radiotherapy than in patients with no pre-operative irradiation.^[41] Bresson et al^[2] and Briant^[48] found the fistulas to be more serious and associated with higher mortality rates in patients who had fistulas develop after radiotherapy than in a purely surgical group of patients. In our study, majority (11/13) of the fistulas in the post radiation laryngectomy group stopped by conservative treatment and 2 required PMMC. The incidence of fistulas was significantly increased in patients who received cobalt/roentgen treatment compared with those who had been treated with photons in a few studies.^[6,41] Photons have the advantage of sparing the subcutaneous tissue during irradiation.^[41] Dedo et al^[49] identified a RT dose of more than 30 Gy as a contributing factor, but Virtaneimi et al^[41] did not find the dose and height of radiation field as important for causing PCF. McCombe et al^[9] also noted a prolonged hospital stay (112 vs. 28 days) and increased requirement of surgical closure of PCF in patients with preoperative radical RT.

In the literature, T closure is reported as another risk factor for PCF formation.^[1,50] According to Shah et al^[51] the weak-

est point was the three-point junction, if “T” or “Y-shaped” closure was performed. This further stresses the importance of the vertical line repair, which was also stressed by Stell et al.^[4] Soylu et al^[44] demonstrated a statistically significant difference in the formation of PCF between vicryl and catgut groups, in favor of vicryl. Vicryl has unique properties when compared with catgut, in that it is much stronger, is less inflammatory, and has a longer half-life. It is believed that low PCF rate with vicryl can be explained by these properties.^[44] We did not have any such experience in our study.

Association of neck dissection with fistula development is controversial.^[13,50] In one study the incidence of PCF is reported to be increased from 11.3% to 17.5% when neck dissection is combined with total laryngectomy.^[13] Whereas some authors have reported a lower rate of PCF in patients who had accompanying neck dissection.^[44] In our study the neck dissection did not have significant correlation with PCF.

Advancing tumor stage has been considered as a risk factor for PCF by some authors^[7,44,52] however, at the same time Hier,^[14] Cavalot^[45] and Lavelle et al^[28] did not find this to be significant. We found that advanced T stage alone did not contribute to fistula formation unless it was associated with extensive soft tissue infiltration.

Virtaneimi et al^[41] noted supraglottic tumors had significantly more leak than glottic tumors. They attributed this due to extension of the supraglottic tumors either to the vallecula or the pyriform sinus, consequently requiring excision of large amount of pharyngeal mucosa and resulting in closures performed under tension. In our study the leak rate was higher in patients with pyriform primary.

Histological infiltration of the surgical margins were found to be statistically significant in the development of PCF by Markou et al,^[53] however at the same time this did not had impact on the local tumor recurrence in their follow-ups. Only 3 of our patients had tumor at the cut margin and none had PCF.

Various studies have been conducted to predict fistula as early as possible. Some of these studies have managed to diagnose PCF within an average of 5 to 10 days.^[21,26] Krouse and Metson^[3] noted the presence of a sinus tract 2 cm or longer on barium swallow as a predictor of a postlaryngectomy PCF. Friedman et al^[54] studied the fever ($\geq 101.5^{\circ}$ F) in the first 48 hours after the surgery as an indicator of PCF and suggested that fever was an excellent tool for early identification of PCF. The relevance of wound amylase concentration for early detection of PCF has been shown in many studies. An increase in the wound amylase concentrations can be a useful marker in the early identification of PCF, thus leading to early rehabilitation.^[55-57] We routinely do not employ any of the above techniques to detect

or diagnose fistula. Our diagnosis of fistula is clinical based on factors such as – skin flap edema, neck erythema, salivary leak etc.

Much controversy also surrounds the management of laryngectomized patients in preventing pharyngocutaneous fistula. Smith et al^[58] demonstrated a significant decreased incidence of PCF by the routine addition of a pectoralis major myogenous flap to cover the pharyngeal defect. They also noted a substantial and dramatic reduction in patient’s morbidity and mortality and reduction in hospital stay, with major financial savings to the health care system. Righini et al^[59] also confirmed the advantage of pectoralis myogenous flap in post radiotherapy laryngectomy in a selected group of patients (with diabetes mellitus, history of vascular disease or poor nutritional status). Prophylactic antibiotic therapy is generally recommended. A modification of the antimicrobial prophylaxis with the addition of metronidazole, electively used against anaerobes, was suggested by Innes et al^[60] and systematically adopted by Cousins et al^[16] and Johansen et al,^[47] all of whom obtained a significant drop in the fistulization rate. Seikaly and Park^[42] proposed a gastroesophageal reflux prophylaxis with continuous drip tube feeding for the first 3 postoperative days and ranitidine and metoclopramide hydrochloride given intravenously for 7 days. No fistula and a significant reduction in mean hospitalization was observed in the group of patients treated with the protocol. Most authors do not routinely perform radiographic studies, others always conduct a contrast study because it can decrease the fistula rate,^[42,61] still others recommend the study only in patients with an increased risk of PCF (previous radiotherapy, neck dissection, pharyngolaryngectomy)^[62]

CONCLUSION

We encountered higher incidence of PC fistula because majority of the patients had cancers of the pyriform sinus, extensive soft tissue infiltration and significant proportion of them required PMMC reconstruction of the neopharynx. Subset analysis of patients with localized larynx cancers showed 11% leak rate. On the contrary, whenever extensive hypopharynx involvement necessitated removal of large areas of pharynx, leak rate increased by 6 folds. Patients who had reconstruction, though had higher leak, did not have vascular catastrophe and their leak were contained by conservative management. All 4 patients who developed post operative hemorrhage with PCF did not have PMMC reconstruction up front and required it at the time of re-exploration. Though, all these patients continued to have salivary fistula, the volume of the saliva markedly reduced and none of these patients had re-bleed. All other parameters such as - age, sex, nodal dissection, prior treatment (radiotherapy and/or chemotherapy), type of closure, Layers of closure, type of suture material, preoperative tracheostomy, cut margin status, pre/postoperative hemoglobin,

experience of surgeons did not relate significantly correlate with PCF.

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