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ORIGINAL ARTICLE

Pharyngocutaneous Fistula Following Primary and Salvage Laryngectomy: Aetiology and Predictive Factors

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Abstract Laryngeal cancer treatment is often wrought with challenges, pharyngocutaneous fistula formation (PCF) in patients undergoing either primary or salvage laryngectomy for laryngeal and hypopharyngeal for squamous cell carcinoma is an important one. We aimed to study the factors before and at the surgery that are associated with PCF formation in a South Indian tertiary care hospital. A retrospective chart review of 127 patients who underwent total laryngectomy (TL) between May 2014 and April 2019 at our centre were done. Data was collected, including patient age and gender, comorbidities (Diabetes mellitus, COPD and hypothyroidism), smoking, tumor stage and site, prior tracheostomy, prior radiation, concurrent neck dissection and type of pharyngoplasty, Preoperative hemoglobin and albumin levels, surgical margin status and development of a PCF was also done. Further details specific to the development of a PCF were recorded for that subset of patients including the length of time to fistula, mode of closure, time of closure and modality of management. The overall incidence of PCF was 16.5% (21 of 127 patients), and the median time from TL to the diagnosis of PCF was 6 days (range, 3–20 days). The analysis was done separately for laryngectomies without any pharyngeal reconstruction (112/127 patients). In patients treated with a primary TL, the incidence of PCF was 12.20% (10 of 82) and 26.66% (8 of 30) after salvage TL. Subset analysis for type of pharyngoplasty repair showed 12% (15/127) underwent different types of vascularised/muscular flap for smaller residual pharyngeal mucosa, of which 20% (3/15) developed PCF and one patient developed haematoma needing exploration and re-suturing. The predictive factors for PCF were hypopharynx cancer ($P < 0.05$), surgical margin positivity ($P < 0.0001$), female gender ($P < 0.05$), absence of prior tracheostomy ($P < 0.05$) and tumor extension into pyriform sinus mucosa ($P < 0.05$). Preoperative patient factors of gender and site of primary along with histological margin positivity and extension of tumor to the pyriform sinus mucosa were significant risk factors for PCF formation. Pre-Op radiotherapy remains a strong clinical suspicion but not statistically significant.

Keywords Pharyngocutaneous fistula · Predictive factor · Radiotherapy · Total laryngectomy · Salvage laryngectomy

Abbreviations

PCF	Pharyngocutaneous fistula
OR	Odds Ratio
CI	Confident interval
TL	Total laryngectomy
RT	Radiation therapy
CTRT	Chemotherapy and radiation therapy
COPD	Chronic obstructive pulmonary disease
TNM	Tumor node metastasis system
POD	Postoperative day
PO	Postoperative
SCC	Squamous cell carcinoma

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Introduction

Laryngeal cancer in the Indian subcontinent is on the rise, due to increased use of tobacco products especially smoking [1, 2]. Its incidence has been reported to be 1.26–8.18 per 100,000 populations and the five-year survival rate for cancer larynx in India is approximately 28%. Hence, still carries a poor prognosis in these patients in comparison to other Asian countries such as China, South Korea, and Singapore [3].

Advanced stage laryngeal and hypopharyngeal cancers require a dual- modality of treatment in the form of surgery followed by adjuvant radiation. Surgery for advanced laryngeal cancers is total laryngectomy with partial pharyngectomy and neck dissection. In the current era of organ preservation, majority of the laryngectomies are done as a salvage procedure in patients with recurrent or residual tumor following curative chemoradiation [4]. This often is reported as a cause for major complications after surgery, which include wound complications (PCF or Nonfistulous complications such as cellulitis, neck abscess and incisional wound dehiscence), hematoma, chyle leak, seroma, pneumonia and rarely death. Prolonged hospital stay and readmission rates are significantly high with wound complications contributing towards poor patient morbidity and outcomes [5, 6].

Pharyngocutaneous fistula (PCF) is one of the most common surgical complications following total laryngectomy [7]. PCF occurs when there is a failure in the pharyngeal repair resulting in an abnormal communication between the pharynx and skin through which saliva leaks. PCF is associated with longer hospital stays, delays in adjuvant therapy, and poor quality of life for patients [7, 8]. The incidence of this complication has often been quoted as anywhere between 3 and 65% [7]. The incidence of PCF is high in salvage laryngectomies as compared to a primary total laryngectomy, due to the impaired healing characteristics of irradiated tissues. Reported PCF incidence rates in salvage laryngectomies vary between 14% and 61% [9, 10].

Many factors have been described in the literature as predisposing factors for fistula formation such as preoperative radiotherapy, preoperative tracheostomy, presence of systemic diseases, tumor stage, surgical technique, concurrent neck dissection, suture material used for pharyngeal reconstruction, positive surgical margins, preoperative and postoperative hemoglobin levels and nutritional status [11–13]. There is considerable controversy over the risk factors associated with these complications. It is essential to understand the risk factors in salvage surgeries post organ preservation therapy as there is a high incidence of PCF in this group. Moreover, there is a paucity of literature on this complication in the South Indian sub-continent; hence, there is a need for studying the factors both preoperatively and at the surgery that are associated with PCF formation to improve our patient care and cancer treatment.

Materials and Methods

Study Design and Patients

A retrospective study with prospective analysis of 127 patients diagnosed with laryngeal or hypopharyngeal squamous cell carcinoma who underwent a primary or salvage total laryngectomy in tertiary care hospital in South India from May 2014 to April 2019. Institutional review board (IRB) permission was obtained and patients who underwent pharyngeal reconstruction with regional or free flap (15 patients) were studied separately. International Union Against Cancer (UICC) TNM system was followed for staging and all primary tumors were squamous cell carcinomas (SCC) with various degrees of differentiation. Factors predisposing PCF formation were evaluated, including age, gender, smoking and alcohol intake, preoperative tracheostomy, previous radiotherapy, concurrent neck dissection, tumor stage, presence of systemic diseases (Diabetes, COPD and Hypothyroidism), preoperative hemoglobin and albumin levels, surgical margin status, and the respective incidences of the variables in patients who developed PCF and without PCF in the postoperative period.

Surgical Technique

Total Laryngectomy with partial Pharyngectomy was the procedure of choice for SCC with extension to the hypopharynx or for primary hypopharyngeal malignancy. Surgeries were performed or supervised by senior surgeons with extensive experience in oncological laryngeal surgery. Surgical technique and postoperative care were generally standardized. Primary Pharyngeal reconstruction was performed in two layers, mucosal and muscular, closure of the pharynx was carried out in a vertical manner, mucosa inverting with a continuous alternate interlocking technique using Vicryl (polyglactin) sutures.

Some of the patients with tumour extending into hypopharynx or primary in the hypopharynx needing a larger pharyngeal mucosa excision were left with very little healthy pharyngeal mucosa for repair. The lengths varied from 10 mm to 35 mm and they were treated with an additional vascularised/muscular flap, this was predominantly Pectoralis Major Myo-cutaneous flap (PMMC) as a patch or a tube. Postoperative care included standard neck wound care for 7 days following which skin sutures were

removed on the seventh PO day in primary surgery and tenth day for salvage laryngectomy. Nasogastric feeding was commenced on the first postoperative day and oral feeding started between the 7–10th post-operative day. Post-operative voice rehabilitation was done on patients opting for primary tracheoesophageal puncture and prosthesis inserted during surgery or a nasogastric tube was inserted through the puncture site for a latter placement of prosthesis post operatively on the 10th day.

Diagnostic Criteria and Treatment Protocol

Diagnosis of a pharyngocutaneous fistula (Fig. 1a) was based on clinical factors like skin flap oedema, neck skin erythema, salivary leak etc. and salivary amylase levels was done to confirm the PCF was done in suspected chyle leak along with the triglyceride's levels.

Initial treatment of PCF was conservative, consisting of medical treatment with culture-based antibiotics, anti-inflammatory drugs, suspension of oral feeding with nasogastric tube feeding and daily local antiseptic medication. Daily compressive Sterile dressing after debridement of necrotic tissue, drainage of collected fluids from the fistulous tract, and local wound cleaning with normal saline solution was routinely done for 4 weeks PO for spontaneous closure to occur (Fig. 1b, c). Surgical closure was performed if the PCF did not spontaneously resolve in 28 days (Fig. 1d).

Statistical Analysis

Descriptive statistics for continuous variables like Age, Pre op Haemoglobin level, Pre op Albumin level, etc. were expressed as mean values ± the standard deviation (SD) (median and interquartile range can be used for variables having skewed distributions). All categorical variables like Gender, Diagnosis, Neck dissection etc. were represented as numbers and percentages.

Independent T test (for normal distribution) or Mann–Whitney U test (skewed distribution) was used for

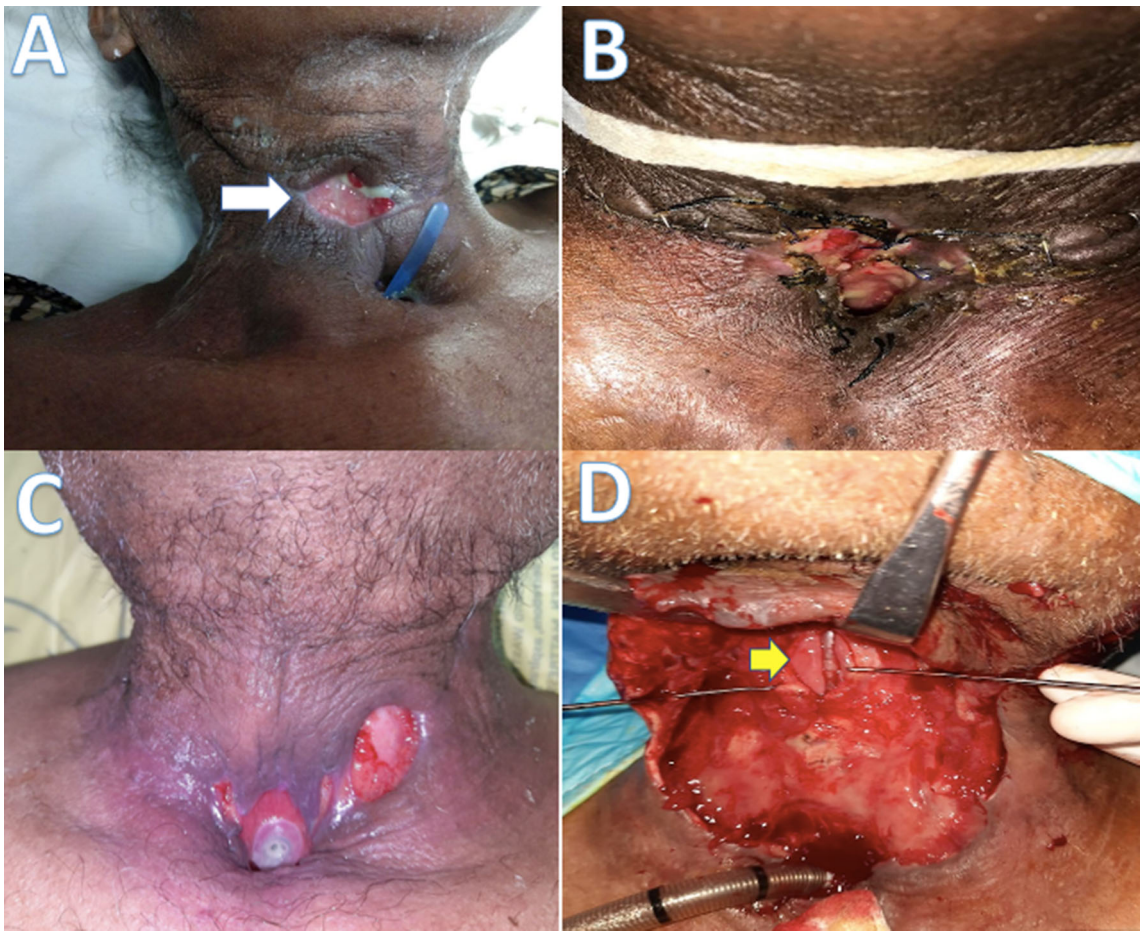

Fig. 1 Legend: Pictures representing different stages of Pharyngocutaneus fistula (PCF) formation during post operative period after Total Laryngectomy, **a** spontaneous healing after primary surgery (white arrow), **b** spontaneous healing after salvage surgery, **c** Non healing fistula after salvage surgery, **d** Intra-op picture showing the pharyngeal leak area (yellow arrow)

continuous variables to compare between PCF and Non-PCF. A Chi square test was performed for comparing categorical variables between two groups (PCF and Non-PCF). The Logistic regression model was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) for PCF development. Statistical significance was defined at $P < 0.05$. Data were analysed using STATA 16.0 software.

Results

Patient and Tumor Details

In the total of 127 patients, 15 patients had a pharyngeal reconstruction with vascularized muscle flap and these patients were excluded from the analysis to avoid bias. Of the 112 patients studied, 103 (91.96%) were men and 09 women (8.04%), with a mean age at the time of TL of 58.07 years (range, 30–86 years). The index tumor was located in the larynx in 75 patients (75, 67%; 25 supraglottic, 49 glottic and 01 subglottic), and in the hypopharynx in 37 patients (33.03%). Table 1 shows a detailed overview of patient and tumor characteristics.

Pharyngocutaneous Fistula (PCF)

The overall incidence of PCF during the PO period was 16% (18 of 112 patients), and the median time from TL to the diagnosis of PCF was 6 days (range 3–20 days). In patients treated with a primary TL, the incidence of PCF was 12.20% (10 of 82) and 26.66% (8 of 30) after salvage TL.

14 of these 18 patients (77.77%) could be treated conservatively, and in 4 (22.22%) surgically closed. 2 out of 10 patients in primary laryngectomy and 2 out of 8 patients in salvage laryngectomy were required additional surgical treatment for PCF repair in the form of regional flap reconstruction (Fig. 2). Only one patient who underwent salvage laryngectomy had a flap related complication which required another additional surgical procedure. One patient with PCF in the salvage group died due to myocardial infarction on POD 20 (not related to PCF).

PCF Predictive Factors

The following variables were included in the univariate analysis to identify possible predictive factors for PCF: Age and gender, smoking and drinking habits, preoperative tracheostomy, prior radiotherapy, concurrent neck dissection, tumor stage, systemic diseases (Diabetes, COPD and Hypothyroidism), Preoperative hemoglobin and albumin levels, and surgical margin status (Table 2).

Preoperative Factors

In our series, 4 out of 9 (44.44%) female patients developed PCF. Female patients are high risk and they are 5 times increased risk of developing PCF formation

Table 1 Patient and tumor characteristics

Variable	Mean ± SD/N (%)
Age	58.07 ± 10.66
Gender	
Male	103 (91.96)
Female	09 (8.04)
Site of origin tumor	
Supraglottis	25 (22.32)
Glottis	49 (43.75)
Subglottis	01 (0.89)
Hypopharynx	37 (33.04)
T stage	
T2	04 (3.57)
T3	21 (18.75)
T4	87 (77.67)
N stage	
N0	57 (50.89)
N1	15 (13.39)
N2	37 (33.03)
N3	03 (2.67)

Fig. 2 PCF management

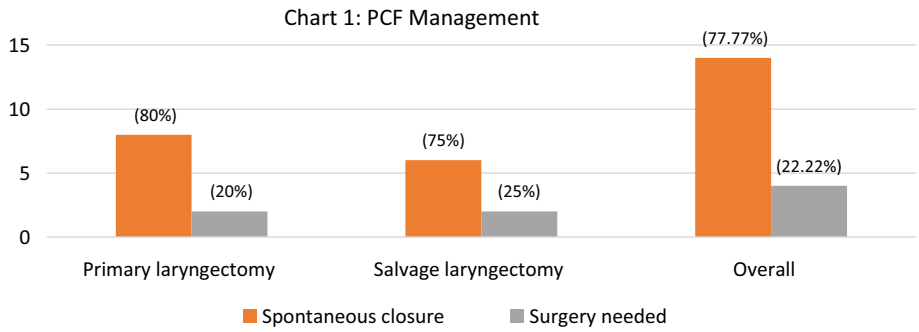

Table 2 Univariate analysis of predictive factors

Variable	PCF (N = 18) n (%)	Non-PCF (N = 94) n (%)	*p* value	OR (95% CI)
Gender			0.026*	
Male	14 (77.78)	89 (94.68)		5.09 (1.22, 21.26)
Female	4 (22.22)	5 (5.32)		1
Co morbidities			0.265	
Yes	8 (44.44)	29 (30.85)		0.55 (0.19,1.55)
No	10 (55.56)	65 (69.15)		1
Smoking			0.265	
Yes	10 (55.56)	65 (69.15)		1.79 (0.64, 5.01)
No	8 (44.44)	29 (30.85)		1
Pre-Op radiation	8(44.44)	22(23.40)	0.071	2.62 (0.92, 7.44)
Yes	10(55.56)	72(76.60)		1
No				
Pre-Op Tracheostomy			**0.04***	
Yes	2 (11.11)	36 (38.30)		0.20 (0.04, 0.93)
No	16 (88.89)	58 (61.70)		1
Pre-Op Haemoglobin (g/dL)			0.826	
Less than 12.5	7 (38.89)	34 (36.17)		1.12 (0.39, 3.16)
Greater than 12.5	11 (61.11)	60 (63.83)		1
Pre-Op Albumin (g/dL)			0.515	
Less than 3.5	1 (5.56)	10 (10.64)		0.49 (0.06, 4.12)
More than 3.5	17 (94.44)	84 (89.36)		1
Concurrent Neck dissection			0.618	
Yes	13 (72.22)	72 (77.66)		0.79 (0.25, 2.48)
No	5 (27.78)	21 (22.34)		1
Neck dissection			0.726	
Bilateral	03 (23.08)	20 (27.78)		0.78 (0.19, 3.13)
Unilateral	10 (76.92)	52 (72.22)		1
Duration between RT and surgery				
Less than 6 months	0 (0.00)	6 (27.27)	–	–
More than 6 months	8 (100.00)	16 (72.73)		

*Statistically significant results

compared to male population {OR 5.09 (CI 1.22–21.26)} this was found to be statistically significant ($P < 0.05$). The chance of PCF formation was less with the patient who already had a tracheostomy in the preoperative period. The presence of Pre-operative tracheostomy somehow decreased PCF formation ($P < 0.05$). But the association

with PCF formation is weaker {OR 0.20 (CI 0.04–0.93)}. Conversely, there were no statistically significant differences between the fistula and the non-fistula groups with regard to age, smoking, drinking habits, concurrent neck dissection, systemic diseases, previous radiotherapy, pre op hemoglobin and albumin levels. The duration of pre-operative radiotherapy and the time of surgery does not show any significance in association with PCF formation.

Tumour Factors

In our series, 10 out of 37 (27%) patients with carcinoma hypopharynx had PCF in the PO period as compared to 8 out of 75 (10.6%) patients with carcinoma of the larynx. The chance of PCF formation was statically high ($P < 0.05$) with carcinoma hypopharynx and there was 3 times more risk of developing PCF in comparison to patients with carcinoma larynx {OR 3.10 (CI 1.1–8.7)}. Positive surgical margin in histopathology showed a statistically significant ($P- < 0.001$) increase in PCF formation as compared to other risk factors 12 out of 29 (41.3%) patients. There was a 9 times higher risk of PCF formation with positive surgical margin as compared to patients with negative surgical margins.

Tumor with the involvement of pyriform sinus region irrespective of primary origin (26%) had significantly ($P < 0.05$) more PCF formation as compared to tumor confined to the larynx (9%). Pyriform sinus involvement increased the chances of PCF formation by 3 times. The advanced stage of disease at surgery does not show any association of PCF formation when compared to lower stage disease (*P*-0.624). Hypopharyngeal tumor, positive surgical margin and tumor involving pyriform sinus mucosa were all significantly associated with the development of the fistula (55.55% vs 28.72%, 66.66% vs 18.08% and 66.66% vs 36.17%) respectively (Table 3).

Pharyngoplasty

Of the entire cohort 12%(15/127) of patients underwent different types of vascularised/muscular flap for pharyngeal repair due to a smaller residual pharyngeal mucosa of length varying between 1 and 3.5 cm, of which 3 (20%) developed PCF and one patient developed haematoma (suspected Internal Jugular vein rupture) needing exploration and re-suturing. None of these patients had any delay in receiving RT subsequently. Of these 73% (9/11-Primary, 2/11-Salvage) were treated for Ca Hypopharynx and 27% (1/4-Primary and 3/4 salvage) were treated for Ca Larynx. The majority (67%) were treated with patch PMMC and rest either a Tube PMMC or on lay muscle patch.

Discussion

This study aimed to establish the role of risk factors in the aetiology of PCF formation after total laryngectomy. A significant relationship was found between PCF development and hypopharyngeal primary tumors positive surgical margin as well as tumor involving the pyriform sinus mucosa. It is paramount to understand the risk factors associated with an increased likelihood of PCF formation so as to provide early and aggressive pre and peri-operative care. PCF continues to cause significant morbidity, including salivary leakage, prolonged hospitalization, swallowing difficulty, delayed initiation of adjuvant therapy, increased cost of treatment and potentially fatal complications such as carotid artery blowout [14].

Earlier studies report a variable incidence of PCFs after total laryngectomy, ranging from 3% to 65%, with an average time of appearance of 10 days post op [7]. Our observation of 18(16%) fistulas in a cohort of 112 patients and a mean time of incidence being 6 days (range 3–20 days) and this is consistent with the mean values reported in the literature. As expected, the PCF incidence is lower for primary TL (12.20%) than for salvage TL (26.66%), the higher incidences for the "salvage" procedure being in line with the literature [15].

The use of organ-preserving treatments such as Radiation therapy and Chemoradiation therapy for advanced laryngeal and hypopharyngeal cancer is increasingly recommended, TL increasingly becoming a salvage procedure if such treatment fails or due to loco-regional recurrence [16]. Thus, the incidence of complications such as PCF after TL are a well-known consequence of surgery in irradiated patients, and this is likely to increase in the near future. In our series, pre-operative radiation therapy patients had a high incidence of PCF as compared to the primary group, but this was not statistically significant p = 0.071(OR 2.62, CI 0.92–7.44). Salvage laryngectomy patient predicted to have 2.6 times more risk of developing PCF than primary laryngectomy patient. With respect to the role of RT, several studies reported a higher incidence of PCF in patients treated with radiotherapy before TL, whereas our study reported that RT prior to TL had no influence [17, 18]. This could be due to the sample size (30 patients) in the study population who underwent salvage TL. Based on our clinical experiences, there seems to a trend in RT having a role in the formation of a PCF (26.66%) and surgical and post-surgical management should be dealt with additional care.

In our study, the hypopharyngeal primary tumor appeared to be significantly associated with PCF (27%) with 10 out of 37 patients developing PCF as compared to 8 out of 75 (10%) patients with laryngeal primary tumor (*P*-0.028) (OR 3.10, CI

Table 3 Tumour site and stage association with PCF formation

Variables	PCF (N = 18) n (%)	Non-PCF(N = 94) n (%)	P value	OR (95% CI)
Diagnosis				1
Ca Larynx	8 (44.44)	67 (71.27)	**0.028***	3.10 (1.11, 8.70)
Ca hypopharynx	10(55.55)	27(28.72)		
Stage IV A				
YES	13 (72.22)	74 (78.72)	0.624	0.70 (0.22, 2.20)
NO	5 (27.78)	20 (21.28)		1
Surgical margin positivity				
YES	12 (66.66)	17 (18.08)	**<0.001***	9.06 (2.97, 27.54)
NO	6 (33.33)	77 (81.91)		1
Pyriform involvement				
YES	12 (66.66)	34 (36.17)	**0.020***	3.53 (1.21, 10.25)
NO	6 (33.33)	60 (63.83)		1

*Statistically significant results

1.1–8.7). The literature explains the high incidence of PCF in hypopharyngeal malignancies as being due to the resection of large amounts of pharyngeal mucosa leads to the pharyngeal closure made under tension. The closure of this wound under heavy tension makes it more prone to break down leading to the formation of PCF [19]. No randomized studies are available as of now to give a clear cut guideline for the assessment of the minimum amount of pharyngeal mucosa that would be required to reconstruct a neopharynx without tension. The general recommendation is that, unstretched pharyngeal mucosa of more than 2.5 cm to 4 cm is sufficient to reconstruct the neopharynx in primary surgeries but adequate data in salvage surgery is still lacking [20, 21]. The critical problem in primary surgery would be a neopharyngeal stricture following adjuvant radiotherapy apart from inadequacy in swallowing and speech following a tight pharyngeal closure after a primary and salvage surgery. Our institutional policy of neopharyngeal reconstruction with patch regional or free flap reconstruction if the remnant relaxed pharyngeal mucosa after laryngectomy is less than 3.5 cm to prevent the above-mentioned complications. Patients with pyriform sinus involvement irrespective of the site of the tumor developed PCF(*P*-0.020) in our cohort. They were 3.5 times more risk of developing PCF than without the involvement of pyriform sinus mucosa. The use of Vascularised/Muscular flap gave adequate muscle cover and vascular supply to the healing neo-pharynx and prevented PCF formation but statistically not significant.

A systematic review by Ji Wang Liang et al. noted that the histological infiltrations of the surgical margins were found to be statistically significant in the development of PCF [8]. We found a similar pattern in our study where 12 out of 18 patients had positive surgical margin compared to 17 out of 94 patients (*P*- < 0.001). 8 out of 10 patients (80%) and 4 out of 8 patients (50%) had a positive surgical margin in the primary and salvage groups respectively. All the primary laryngectomy patients had adjuvant radiotherapy and only 3 had concurrent chemotherapy. 4 patients in the salvage group had a tumor recurrence whereas only 2 patients in the primary group had a tumor recurrence in 1 year follow up. Our study shows that PCF with a positive surgical margin in salvage surgeries invariably causes local tumor recurrence. Histological infiltration of the surgical margins was found to be statistically significant in the development of PCF by Markou et al., however, at the same time, this did not had an impact on the local tumor recurrence in their follow-ups. Even though this study showed the significant correlation of positive surgical margins with PCF formation, 94% of patients who had PCF were treated by conservative management alone or with the minor procedures under local anaesthesia [27].

We find it difficult to understand that patients from the primary surgery group with positive surgical margins who had developed PCF were healed by conservative management instead of the formation of a malignant fistula. But we reported the results as they were and considered the following explanation, which could be as a result of multiple factors. First, the tissue shrinkage phenomenon on surgical margins is a strong possibility and could be a false positive margin, because on table surgical resection margins were done as per guidelines. This would be evaluated thoroughly in the future [28]. Second, pathologically positive margins because of occult microscopic margins,

finger extensions or islands of tumor that extend beyond the clinically visible and palpable tumor. Even though histologically positive, clinical significance on complications and disease recurrence needs to be evaluated [29]. Third, tumor differentiation might be low, and closure could have happened by granulation tissue formation from the surrounding area [30]. Finally, as mentioned in the discussion earlier, factors such as intraoperative closure technique, the experience of the surgeon might play a role along with margin positivity.

Association of neck dissection with fistula development is controversial, Basheeth et al., reported that neck dissection is a risk factor for PCF based on the argument that neck dissection disrupts local blood supply which engenders hypo vascularity and increases the chance of infection [22]. Our study showed that the relationship between neck dissection and PCF was not statistically significant ($P = 0.408$). For all primary stage IV laryngeal carcinomas, it is the standard institutional protocol to perform an ipsilateral neck dissection even for an N0 neck. Thus, neck dissection as an independent risk factor for PCF needs to be studied in more detail. However, it is plausible that a bilateral neck dissection could be the cause of a PCF because of the disruption of the blood supply on both sides of the neck. We did not find any significant impact on unilateral and bilateral neck dissection on the development of PCF. (P-0.726).

Preoperative hemoglobin and albumin levels reflect the nutritional status of the body. Some studies have verified that postoperative hemoglobin and albumin were the risk factors for PCF [10, 23, 24]. Our study does not show such findings, the reasons could be the nature of the study population and most of our patients had carcinoma of the larynx. Dysphagia and nutritional deficiency are usually more common with carcinoma of the hypopharynx rather than carcinoma larynx.

Other factors like age, gender, prior tracheostomy, prior radiotherapy, smoking and comorbidities like diabetes and hypothyroidism are associated with PCF formation [12, 14]. We did not find any association of the above factors in our study although this study shows female gender is an important risk factor. But due to the lesser number of female patients in our study the possibility of the risk factor might be erroneous. Smoking is considered a strong risk factor but was not significant in our study. In our subset of 30 patients who had prior radiotherapy before laryngectomy, there was no significant increase in the fistula rate. As regards to the time between radiotherapy and surgery some authors did not find any significant correlation [19]. William J. Scotton et al. reported that the acute biological effects of radiation continue for 2–3 months after RT treatment, leading to impaired wound healing and an increased risk of infection which leads to a higher chance for PCF formation [25]. In contrast, our study showed that PCF formation is more in the group where the time duration between prior radiotherapy and surgery was more than 6 months. This could be due to tissue fibrosis and disturbances in the local blood circulation caused by radiation therapy. Most of the PCF described in the literature in the past are more with cobalt radiotherapy and this was an independent risk factor for PCF. The standard of pre and perioperative care to the prior RT patients has been improved. Improved newer radiotherapy techniques and careful attention to prior radiotherapy patients leads to lower the incidence of PCF among salvage surgeries now [17, 25].

A growing number of studies have suggested that systemic diseases, including lung disease, cardiopathy, and diabetes mellitus, could also increase the incidence of PCF [7, 10]. However, in our study, the results indicate that diabetes mellitus was not a risk factor for PCF ($P = 0.26$). Prior tracheostomy may be the cause of postoperative infection because the secondary infection often occurs in the tracheal orifice after tracheotomy, which communicates with the surgical field during total laryngectomy, thus leading to wound infection and increased incidence of PCF. But in most of the other studies, there was no relationship between preoperative tracheotomy and PCF [22, 26]. In contrast, we have found that the absence of tracheostomy may predispose to PCF formation or prior tracheostomy has a protective effect on PCF formation. We could not find any reason for this finding probably it could be due to a smaller study population.

Most of the patients with PCF were as diagnosed before starting oral feeds (median—6 days). We do not do contrast studies for the diagnosis of a PCF nor do we do biochemical analysis routinely. Some studies showed the usefulness of these markers for early identification of PCF [31]. We believe that a clinical assessment is much valuable than the biochemical analysis. Much controversy exists surrounding the management of PCF and we routinely treat our patients conservatively as mentioned earlier. It is always wise to plan surgical management in case conservative treatment fails after a month of conservative management. In our study, all the primary laryngectomy patients who had a PCF healed spontaneously by conservative management without any additional surgical procedure irrespective of the tumor site. 2 out of 8 patients (25%) in the salvage group had additional surgery in the form of PMMC patch pharyngoplasty and Deltopectoral flap for skin cover. We routinely use regional flaps such as Pectoralis muscle flap and deltopectoral flap for the repair of PCF. Many studies have described the use of vascularised muscle flaps as a reinforcement or as an onlay patch over the pharyngeal closure to prevent the incidence of PCF in both primary as well as salvage surgery [9, 32].

The limitations of this study include the fact that it is a retrospective chart review and does not include the other described risk factors such as BMI, nasogastric tube placement in the pre-operative period, TEP puncture, type of pharyngeal closure, blood transfusion, the experience of surgeons and post-operative hemoglobin. The PCF is a multifactorial problem and no independent risk factor has been described so far hence it is advisable to look for other common risk factors that have been strongly associated with PCF formation. In a developing country with low socioeconomic status, nutrition deficit is quite common and could be the leading cause of healing defects postoperatively and hence more importance should be given to the preoperative nutritional status of the patient.

Conclusion

Hypopharyngeal primary tumor, histological margin positivity, absence of prior tracheostomy and extension of tumor in pyriform sinus mucosa are significant risk factors of PCF formation. Prior radiotherapy showed a strong clinical significance even though it is statistically insignificant. Most PCF heal by conservative management and vascularised muscle flap has a promising role in preventing the PCF formation.

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