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Risk factors of pharyngocutaneous fistula following total laryngectomy

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Abstract

Background: Total laryngectomy is the procedure of removing the entire laryngeal structure. The purpose of this study was to analyze the risk factors for postoperative total pharyngocutaneous fistula.

Methods: This was a retrospective study using medical record data with cross-sectional design. This research was conducted at Dr. Soetomo Surabaya, Indonesia from January 1, 2016 to December 31, 2018.

Results: The prevalence of pharyngocutaneous fistula was 14 patients (17.07%) of 82 patients with laryngeal carcinoma. Age factors ($p = 0.243$), sex ($p = 1.000$), previous smoking history ($p = 0.506$), history of type 2 diabetes mellitus ($p = 1.000$), histopathology ($p = 0.076$), stage ($p = 1.000$), tumor location ($p = 0.183$), incision technique ($p = 0.924$), preoperative hemoglobin levels ($p = 0.669$), and preoperative albumin levels ($p = 1.00$) were not found to be significantly associated with complications of pharyngocutaneous fistula. However, there was a significant relationship between neck dissection and pharyngocutaneous fistula complications ($p = 0.023$, OR = 6.8, 95% CI 1.373 - 33.867). Patients with neck dissection had the possibility to experience complications of pharyngocutaneous fistula 6.8 times higher compared to those without neck dissection.

Conclusion: There is a relationship between neck dissection and pharyngocutaneous fistula complications.

Keywords: total laryngectomy, pharyngocutaneous fistula, risk factors

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INTRODUCTION

Cancer has become a global burden because of the aging, increased adoption of cancer-causing behaviors particularly smoking and exposure to triggering factors, such as chemicals, radiations, unhealthy eating habits, and a sedentary lifestyle (Nasution et al. 2018). Mortality due to neoplasms remained at the second place between 1990 and 2017 (Fitzmaurice et al. 2019). Cancer also affects economic-social consequences and disability for individuals (Razak et al. 2018; Tsiring et al. 2019). Current advances in diagnosis and therapy can support cancer survivors so they can survive longer (Suhardin et al. 2016). More than half of cancer patients are treated with chemotherapy, a cancer treatment using chemicals or drugs for local cancer and metastasis (Haseeb et al., 2020). Chemotherapy is usually combined with surgery or radiotherapy (Sari et al. 2019).

One type of cancer that can cause disability is laryngeal carcinoma (Fitzmaurice et al. 2019). Laryngeal carcinoma is a malignancy in the larynx affecting the glottis, supraglottis, and subglottis (Indiyana et al. 2016). Total laryngectomy is the procedure of removing the entire laryngeal structure, starting from the upper limit of

the epiglottis and os hioid to the lower limit of the tracheal ring. Total laryngectomy is performed on residual laryngeal tumors of T3, T4 and T1/T2 stages or failure of radiation therapy (Dhingra et al. 2014). Total laryngectomy can lead to various complications, such as pharyngocutaneous fistula, flap infection, and stoma stenosis with an impact on the morbidity and quality of life of the patient. Thus, longer hospital treatment is needed (Maharjan et al. 2010, Rassekh et al. 2010, Reddy et al. 2012).

Fistula is an abnormal connection between the surfaces of two epithelium. Pharyngocutaneous fistula is the fistula track between pharyngeal mucosa and neck or cervical skin around the surgical suture or the area around the stoma due to failure of wound healing that causes salivary leakage (Luo, 2020). The prevalence of pharyngocutaneous fistulas varies between 5% to 65%. The incidence of fistulas is usually found around 4-7 days postoperatively (Nitassi et al. 2016, Sabri 2010). Some risk factors for these complications include age,

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preoperative hemoglobin levels, preoperative albumin levels, length of surgery, neck dissection, amount of bleeding, stage, tumor location, preoperative tracheotomy, skin incision techniques, and esophageal suturing techniques (Nitassi et al. 2016). Complications of total laryngectomy can increase morbidity, high costs, a longer healing period, and cause permanent disability (Shah et al., 2016). For this reason, surgical wound care plays an essential role in the process of wound healing and prevention of pharyngocutaneous fistulas (Sabri 2010). Proper treatment of cancer can make it easier for the healing process (Deliana et al. 2019). The purpose of this study was to analyze the risk factors for post-laryngectomy pharyngocutaneous fistula at Dr. Soetomo Hospital, Surabaya, from January 1, 2016 to December 31, 2018.

METHODS

This type of research is a descriptive-analytic retrospective approach using central medical record data and One-Stop Oncology Polyclinic of Dr. Soetomo Hospital, Surabaya, Indonesia with cross-sectional design. The study population was all patients with laryngeal carcinoma who had undergone total laryngectomy surgery in the Department of Otorhinolaryngology-Head and Neck Surgery, Oncology Division from January 1, 2016 to December 31, 2018. The study sample was all patients with pharyngocutaneous fistula after total laryngectomy surgery who met the inclusion criteria. Inclusion criteria were patients with a complete medical record and had never undergone preoperative chemoradiotherapy.

The data recorded included basic data in the form of gender, age. Clinical data included smoking history, history of diabetes mellitus, stage, histopathology, tumor location, skin incision technique, neck dissection. Laboratory data included preoperative hemoglobin levels, preoperative albumin levels. Data obtained in this study were then performed statistical tests to determine the relationship of risk factors with pharyngocutaneous fistula using Chi-square, Kruskal-Wallis, Mann Whitney, and Fisher Exact. If there is a significance value (p) <0.05 , it is followed by a multivariate logistic regression test to test whether the probability of a pharyngocutaneous fistula can be predicted from risk factors.

Ethical clearance was approved by the Research Ethics Committee for the Research and Development Sector of Dr. Soetomo Hospital, Surabaya, in October 2019.

RESULTS

From January 1, 2016 to December 31, 2018, there were 82 patients with laryngeal carcinoma who underwent total laryngectomy surgery. However, only 61 patients had complete medical record data and had not

received chemoradiotherapy. The prevalence of pharyngocutaneous fistula was 14 patients (17.07%) of 82 patients with laryngeal carcinoma, while non-fistula was 47 patients (57.31%).

Table 1 presents that age ($p = 0.243$), sex ($p = 1.000$), previous smoking history ($p = 0.506$), history of type 2 diabetes ($p = 1.000$), histopathology ($p = 0.076$), stage ($p = 1.000$), tumor location ($p = 0.183$), incision technique ($p = 0.924$), preoperative hemoglobin levels ($p = 0.669$), and preoperative albumin levels ($p = 1.00$) did not show a significant relationship with complications of pharyngocutaneous fistula. However, a significant relationship was found between neck dissection and pharyngocutaneous fistula complications ($p = 0.023$, OR = 6.8, 95% CI 1.373 - 33.867). Patients with neck dissection had the possibility to experience complications of pharyngocutaneous fistula 6.8 times higher compared to those without get neck dissection (Sittisom, 2020). OR >1 can also be concluded that neck dissection increases the risk of fistula complications.

DISCUSSION

Risk factors investigated in this study included age, sex, smoking history, history of diabetes mellitus, histopathology, stage, location of tumor, skin incision technique, preoperative hemoglobin level, preoperative albumin level, and neck dissection. The results showed that only risk factors for neck dissection have a significant relationship with the onset of complications of post-laryngectomy pharyngocutaneous fistula. Meanwhile, other researchers observed several risk factors, such as preoperative tracheotomy, esophageal suturing techniques, and history of preoperative radiotherapy with varied variable results (Cecatto et al. 2014, Nitassi et al. 2016, Sabri 2010; Chang, & Kim, 2018).

This study shows that neck dissection has a significant relationship with pharyngocutaneous fistula complications. This is in accordance with previous studies revealing that the incidence of fistula increased by 11.3% -17.5% during total laryngectomy surgery accompanied by neck dissection (Qureshi et al. 2005). Other studies have also found neck dissection as a risk factor for pharyngocutaneous fistula complications in total laryngectomy accompanied by bilateral neck dissection compared to unilateral neck dissection or no dissection. Neck dissection can lead to a longer duration of surgery, wider tissue defects, reduced normal residual mucosa and disrupt blood flow and lymphatic system circulation (Basheeth et al. 2014). Large tumors (T3 or T4), neck dissection and, partial resection of the pharyngeal wall during surgery may be needed, making pharyngeal closure difficult. Large surgical wound defects also cause tissue pressure and will reduce microcirculation (Jefferson 2014). If the remaining pharyngeal mucosa is insufficient for closure, the risk of

Table 1. Description and analysis of risk factors

Characteristics	Fistula		p
	No (n= 47) n (%)	Yes (n = 14) n (%)	
Age (year) ^a	56.38±11.43	52.36±12.06	0.243
Sex ^b			
Male	42 (89.36)	13 (92.86)	1.000
Female	5 (10.63)	1 (7.14)	
Smoking ^b			
No	12 (25.53)	5 (35.71)	0.506
Yes	35 (74.47)	9 (64.29)	
Diabetes Mellitus ^b			
No	43 (91.49)	13 (92.86)	1.000
Yes	4 (8.51)	1 (7.14)	
Histopathology ^c			
SCC Keratin invasive	0 (0)	2 (14.29)	0.076
SCC is well differentiated	23 (48.94)	6 (42.86)	
SCC is moderately differentiated	19 (40.43)	5 (35.71)	
SCC is poorly differentiated	5 (10.64)	1 (7.14)	
Stages ^b			
3	5 (10.64)	1 (7.14)	1.000
4	42 (89.36)	13 (92.86)	
Location of Tumor ^c			
Supraglottis	4 (8.51)	0 (0)	0.183
Supraglottis-glottis	16 (34.04)	2 (14.29)	
Supraglottis-subglottis	14 (29.79)	4 (28.57)	
Glottis	8 (17.02)	4 (28.57)	
Glottis-subglottis	5 (10.64)	3 (21.43)	
Subglottis	0 (0)	1 (7.14)	
Skin Incision Techniques ^d			
U incision	45 (95.74)	14 (100)	0.924
Y incision	2 (4.26)	0 (0)	
Pre-opb Hb ^d			
<11.5 mg/dl	22 (46.81)	5 (35.71)	0.669
≥11.5 mg/dl	25 (53.19)	9 (64.29)	
Pre-op albumin ^d			
<3.5 mg/dl	18 (38.30)	5 (35.71)	1.000
≥ 3.5 mg/dl	29 (61.70)	9 (64.29)	
Neck Dissection ^d			
No	25 (53.19)	2 (14.29)	0.023
Yes	22 (46.81)	12 (85.71)	

SCC: squamous cell carcinomas a: Mann Whitney; b: Fisher exact; c: Kruskal wallis; d: Chi-square

defects around the wound suture and healing process will increase (Papazoglou et al. 1994). This is in contrast to some studies with a total sample of 2200 from review articles showing that neck dissection had no significant relationship with pharyngocutaneous fistulas (Cecatto et al. 2014).

Neck dissection often done in this study was radical modification of type 2 and type 3 neck dissection, a procedure performed by performing neck dissection of lymph node tissue on one side of the neck (level I to V) raised to enbloc, maintaining the accessory nerve and jugular veins internal (type 2), and accompanied by maintenance of the structure of the sternocleidomastoid muscle for type 3 (Medina 2014). Also, patients undergo laryngectomy surgery (with or without neck dissection) then receive chemoradiotherapy due to the queue on chemotherapy and radiotherapy itself. Thus, most total laryngectomy operations accompanied by neck dissection aim to eliminate primary carcinoma metastasis in the larynx and prevent a recurrence. This is different if radiotherapy is done before laryngectomy surgery because of a good neck mass response so that it can be considered about the decision to do neck dissection.

Other risk factors in this study that statistically did not have a significant relationship with the emergence of pharyngocutaneous fistula complications were age, sex, smoking history, history of diabetes mellitus, histopathology, staging, tumor location, skin incision techniques, preoperative hemoglobin levels, preoperative albumin levels and duration of the operation. This study did not involve patients undergoing chemoradiotherapy before total laryngectomy surgery was performed because of the long queues at the radiotherapy department of Dr. Soetomo Hospital. Thus, all samples of this study received operative therapy first then chemoradiotherapy. Preoperative radiotherapy is a risk factor for pharyngocutaneous fistula. In the initial phase, during radiotherapy, cells divide and die regularly and quickly, causing acute toxic effects such as dermatitis or mucositis. The second or subsequent phase, injury to cells due to the effects of radiotherapy, is a microvascular tissue disorder, such as subintimal fibrosis, endarteritis, and thrombus formation. This results in tissue becoming hypovascular, hypocellular, and hypoxic. This radiotherapy effect can last 6 months, even during the patient's life. Thus, if total laryngectomy is performed, it will disrupt the wound healing process,

and ultimately increase the risk of postoperative complications (Paydarfar et al. 2006).

Symptoms that appear if a post-laryngectomy total fistula is formed is the flow of saliva or food through the sidelines of the surgical wound suture. Examination by pressing the area around the suspected fistula results in the appearance of the saliva flow. Experts argue that delaying oral feeding will reduce the incidence of fistula. This is because the stress level of esophageal sutures after total laryngectomy is much reduced. Delay oral feeding by providing nutrition through a nasogastric tube (NGT), maintained for 7-10 days after total laryngectomy to prevent fistula. Postoperative vomiting can trigger damage to the esophageal suture, while postoperative patients often experience nausea due to anesthesia. Therefore, the administration of anti-emetic injection drugs (metoclopramide) and gastric drugs (ranitidine) is needed for the initial three days after surgery (Qureshi et al. 2005). Fever on the first postoperative day is prognostic in the development of fistula. Some studies find a high correlation between fever that develops in the first 48 hours and fistula formation. Thus, early intervention (before the third postoperative day) decreases morbidity and duration of hospitalization (Galli et al. 2005).

Surgical wound care plays an important role in the process of wound healing and prevention of pharyngocutaneous fistulas. The drain hose must be observed every 8 hours to ensure it works well to prevent the formation of hematomas and infections. Signs of infected incision wounds that must be considered, such as redness, urine, and wet. Good postoperative oral hygiene is very important to control infection and prevent bad breath. Pharyngocutaneous fistulas can occur in the area of the surgical incision, most often in the first week after surgery. Per its location, pharyngocutaneous and orocutaneous fistulas are the most common fistulas in patients with extensive resection (Irfandy et al. 2015, Sabri 2010).

Based on the way of healing, pharyngocutaneous fistula can be divided into two groups. The first group is

small fistulas that can heal spontaneously with the treatment of intensive wounds. Administration of antibiotics, septic wound closure, minimal debridement, and feeding through nasogastric tubes with surveillance of nutritional status in patients allow secondary fistula healing within a month or more. The second group is a large fistula characterized by the extent of the skin over the fistula lost and delicate from the mucosa (Myers 2008). The remaining tumor and the possibility of recurrence need to be considered when the fistula does not close secondary. Large fistulas can close through secondary healing, but in cases of exposure to major blood vessels, surgical procedures with a flap need to be performed. Surgical closure with a flap is recommended for blood vessel protection, infection control, and facilitating postoperative adjuvant therapy (Cecatto et al. 2014).

The limitation of this study is that the cross-sectional design is challenging to assess the cause and effect relationship because the measurement of disease events and exposure to risk factors are observed at one-time point at the same time. Most of the risk factors studied are natural factors of the patient. In contrast, the emergence of pharyngocutaneous fistula complications requires the role of many factors such as suturing techniques esophagus, preoperative tracheotomy, and amount of bleeding. The study period was limited to 3 years due to limited medical record data so that the sample size was fulfilled based on period rather than on statistical calculations.

CONCLUSION

The results obtained a significant relationship between risk factors for neck dissection with pharyngocutaneous fistula complications with an OR of 6.8. Patients with neck dissection have the possibility to experience complications of pharyngocutaneous fistula 6.8 times higher compared to those who do not get neck dissection. Meanwhile, other risk factors do not have a significant relationship with pharyngocutaneous fistulas.

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