Salivary Fistula: Blue Dye Testing as Part of an Algorithm for Early Diagnosis

Kimberley L. Kiong, MMed; Ngian Chye Tan, FRCSEd; Thakshayeni Skanthakumar, BSc; Constance E.H. Teo, FAMS; Khee Chee Soo, FRACS, FACS; Hiang Khoon Tan, PhD, FRCSEd; Elizabeth Roche, BSc; Kaisin Yee, BSc; N. Gopalakrishna Iyer, PhD, FRCSEd

Objective: Orocutaneous and pharyngocutaneous fistula (OPCF) is a debilitating complication of head and neck surgery for squamous cell carcinoma (SCC), resulting in delayed adjuvant treatment and prolonged hospitalization. As yet, there is no established test that can help in prompt and accurate diagnosis of OPCF. This study aims to determine the accuracy of bedside blue dye testing and its role as part of an algorithm for early diagnosis. We also analyze the risk factors predisposing to OPCF.

Study Design: Retrospective cohort study from 2012 to 2014.

Methods: Patients with head and neck SCC who underwent major resection and reconstruction, at risk of OPCF, were included. Results of blue-dye and video-fluoroscopic swallow-studies (VFSS) testing for OPCF were recorded. For the patients that were noted to develop OPCF, the length of time to diagnosis of fistula and subsequent mode of management were examined.

Results: Of the 93 patients in this study, 25 (26.9%) developed OPCF. Advanced T-classification (T3/T4) was the only significant predisposing risk factor (p = 0.013). The sensitivity and specificity of the bedside blue dye testing was found to be 36.4% and 100%, respectively. The test positive patients were diagnosed with OPCF at a median of postoperative day (POD) 9.5 as compared to POD 13 for the test negative patients (p = 0.001). Early diagnosis was associated with faster fistula resolution with treatment.

Conclusion: Blue dye testing is a simple bedside test that can assist in the early diagnosis of OPCF in patients, allowing treatment to be instituted earlier with improved outcomes.

Key Words: Head and neck cancer, head and neck, reconstructive surgery.

Level of Evidence: 3

INTRODUCTION

Orocutaneous and pharyngocutaneous fistula (OPCF) is one of the most debilitating complications of oncologic head and neck surgery. The incidence ranges from 5–65%1,2 and may be difficult to treat. Apart from resulting in delayed adjuvant treatment, prolonged hospitalization, and increased treatment costs, it may also lead to further wound complications and ultimately increased morbidity.3–5

There exists some data on the risk factors that predispose to OPCF but there is limited consensus on the best ways to prevent or manage it. There are studies suggesting that OPCF results from technical issues, primarily from inadequate wound closure,6 while others propose wound breakdown occurs secondary to early and aggressive institution of oral feeding. However, the latter hypothesis is not supported by the notion that there is constant flow of saliva passing through the tract.7 Furthermore, there is a paucity of data on how to diagnose this complication early, apart from relying on the usual clinical signs and symptoms. Intuitively, an early diagnosis can lead to earlier intervention and thereby lessen the impact of this complication on the postoperative recovery of the patient.6 A few studies have looked at radiographic contrast studies for the diagnosis of OPCF, with contrasting results and recommendations.8–10

In this study, the primary aim was to assess a novel method, using bedside blue dye testing in the early diagnosis of OPCF and its influence on the ultimate treatment and healing of the fistula. The secondary objective was to determine risk factors for fistula formation in patients who underwent major resection with or without flap reconstruction for squamous cell carcinoma (SCC) of
the oral cavity, oropharynx, larynx or hypopharynx. With this data, we propose an algorithm to facilitate early diagnosis and intervention of OPCF.

MATERIALS AND METHODS

Medical records of all patients who underwent major resection of the oral cavity, oropharynx, larynx, and hypopharynx for SCC, between 2012 and 2014, were reviewed retrospectively. Inclusion criteria for this study were all patients with squamous cell carcinoma of the upper aerodigestive tract who underwent major resection where there was a significant potential communication between the aerodigestive tract and neck cavity and thus risk of development of OPCF. These included patients with oral cavity or oropharyngeal cancers requiring regional or free flap reconstruction or laryngeal or hypopharyngeal cancers with resection and primary closure of the neopharynx. Exclusion criteria included those who had previous surgery in the head and neck region prior to presenting at our institution and those with limited oral cavity or oropharyngeal cancers that did not require major reconstruction. Demographic data was collected, including patient age, gender, race, comorbidities, tumor site and stage, preoperative radiation therapy (RT) status, margin status, and type of reconstruction. We also reviewed the results of bedside blue dye testing and videofluoroscopic swallow studies (VFSS) that these patients underwent. For the patients that were noted to develop OPCF, the length of time to diagnosis of fistula, subsequent mode of management of the fistula and time to resolution were recorded. This study was approved by the Singhealth Centralized Institutional Review Board (CIRB 2015/2441).

All surgeries were performed by Head and Neck surgeons at our institution. The decision for the method of reconstruction was jointly made by the resection and reconstructive surgeons, and generally determined by nature and size of the defect. The reconstructive options included primary closure, pectoralis major pedicled flap, latissimus dorsi pedicled flap, gastric pull-up (pedicled), free radial forearm flap, free anterolateral thigh flap, and free fibula flap. All patients were given prophylactic antibiotic therapy for a minimum of 7 days after initial surgery.

The bedside blue test was conducted as follows: 1 ml of blue food dye (Permitted color E133) was diluted in 30 ml of water. This was fed to the patient via spoon/syringe in small boluses of 5–10 ml. The patient would be instructed to hold the bolus in the mouth for 5 seconds initially, then instructed to swallow. The patient would then be monitored for 24 hours, looking for blue dye in the drains or skin suture lines, which would signify a positive test result (Fig. 1). This would be performed at any time after postoperative day (POD) 5, at the discretion of the surgeon. An early blue dye test was defined as one performed on POD 12 or less.

A VFSS was also performed in some patients to assess for leak or aspiration. In this study, water soluble contrast was orally administered to the patient in the erect position. Antero-posterior and lateral serial radiographs were taken to image the bolus as it passed into the esophagus. A positive test was taken as one with pooling of contrast in the neck or communication of a contrast filled tract to the skin of the neck.

The diagnosis of OPCF was made on the confirmation of saliva leakage from a definite tract between the digestive tract and skin of the neck. Once the diagnosis was made, either clinically or with the assistance of the above-mentioned tests, these patients were started initially on vacuum assisted closure (VAC) therapy. If the fistula did not close despite a period of conservative treatment or it was felt that it was unlikely for the defect to heal spontaneously, the patient would undergo surgery. The latter could either be primary closure of the fistula or using a second flap.

The incidence of OPCF was determined by looking at the number of patients who developed fistula from the entire cohort of patients analyzed. The potential prognostic factors of age (≤60 or >60), diabetes mellitus, previous radiotherapy of the head and neck, previous surgery in the head and neck region, surgical margin status, type of flap (regional/pedicled vs. free), and T stage (T1/T2 versus T3/T4) were analyzed with two-tailed Fisher’s exact test.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of early blue dye test and VFSS were calculated from the group of patients that had the respective tests performed. For the outcome of fistula patients, statistical analysis was performed with the two tailed Students t-test for quantitative data and the Fisher’s exact test. A p value of <0.05 was taken to be significant. All statistical analyses were performed on SPSS version 23.0.0 (IBM, Armonk, New York).

RESULTS

A total of 93 patients were deemed suitable and included in this study. Clinic-pathologic and treatment details are summarized in Table I. The median age was 61 (27–83), with 69 (74.2%) male patients. Majority presented with SCC of the oral cavity (63.4%), with the remainder being fairly equally divided between oropharyngeal, laryngeal, and hypopharyngeal SCC. Almost two-thirds (61.3%) of patients had locally advanced (T4) tumors. Twenty patients (21.5%) had radiotherapy of the head and neck region at some point before surgery. Seventeen patients (18.3%) underwent primary closure of the surgical defect, 39 patients (41.9%) had local, regional or pedicled flap closure, 36 patients (38.7%) had free flap reconstruction, and one patient (1.1%) had a combined free flap and regional flap reconstruction.

The incidence of OPCF was 26.9% (25/93) in our study. The median time to diagnosis of OPCF was 11 days (range 5–32). Analyzing factors that potentially affect the development of OPCF, only advanced T stage (T3/T4) was a significant risk factor (p = 0.013) (Table II).

The early blue dye test, performed at between 5 to 12 days post-operation, was performed in 83 patients (89.2%) and a fistula was detected in eight patients. The
sensitivity of this test was found to be 36.4% and specificity 100%. The PPV was 100% and NPV was 81.3% (Table III). The remaining patients did not undergo the early blue dye testing for various reasons such as poor medical fitness of the patient, or surgeon-decision to delay testing.

A VFSS was performed in 21 patients (22.6%), with a sensitivity of 42.9%, specificity of 100%, PPV of 100%, and NPV of 83.3% (Table IV).

Of the 25 patients who developed OPCF, 13 (52%) resolved with conservative management while 12 (48%) underwent some form of surgery to assist in closure of the fistula. For these two management strategies, the median time to resolution of the fistula was 18 (16–168) days and 91 (11–369) days, respectively.

Looking at this same cohort who developed OPCF, eight tested positive on early blue dye testing while 11 patients tested negative. Six patients did not have the early blue dye test performed within 12 days of operation. Comparing the group who was diagnosed early with positive blue dye test versus the group that either tested negative or did not have the test performed, the test positive patients were diagnosed with OPCF at a median of POD 9.5 as compared to POD 13 for the test negative patients, which was statistically significant (p = 0.001) (Table V). Two patients in the test positive group required surgical closure while 10 in the test negative group required surgical closure (p = 0.202). The median time to resolution of OPCF was 40 (16–329) days and 76.5 (14–369) days for the test positive and test negative groups, respectively.

### TABLE I. Demographics.

| Demographic data                        | All patients (n = 93) |
|-----------------------------------------|----------------------|
| Median age                              | 61                   |
| Gender                                  | n (%/range)          |
| Male                                    | 69 (74.2)            |
| Female                                  | 24 (25.8)            |
| Site                                    |                      |
| Oral cavity                             | 57 (61.3)            |
| Oropharynx                              | 9 (9.7)              |
| Larynx                                  | 15 (16.1)            |
| Hypopharynx                             | 12 (12.9)            |
| pT stage                                |                      |
| T1                                      | 13 (14.0)            |
| T2                                      | 11 (11.8)            |
| T3                                      | 12 (12.9)            |
| T4                                      | 57 (61.3)            |
| Previous radiotherapy                   |                      |
| Yes                                     | 20 (21.5)            |
| No                                      | 73 (78.5)            |
| Type of reconstruction                  |                      |
| Primary closure                         | 17 (18.3)            |
| Local flap                              | 5 (5.4)              |
| Pectoralis major                        | 24 (25.8)            |
| Latissimus dorsi                        | 3 (3.2)              |
| Gastric pull-up                         | 7 (7.5)              |
| Free radial forearm flap                | 13 (14.0)            |
| Free ALT flap                           | 16 (17.2)            |
| Free fibula flap                        | 7 (7.5)              |
| Combined free ALT and PM flap           | 1 (1.1)              |
| Presence of fistula                     |                      |
| Salivary fistula                        | 25 (26.9)            |
| No salivary fistula                     | 68 (73.1)            |
| Median time to diagnosis of fistula (days) | 11 (5–32)           |
| Management of fistula                   |                      |
| Conservative management                 | 13 (52)              |
| Surgical without flap                   | 2 (8)                |
| Surgical with flap                      | 10 (40)              |
| Median time to resolution of fistula (days) |                  |
| Conservative                            | 18 (16–168)          |
| Surgical (with or without flap)         | 91 (29–369)          |

### TABLE II. Factors Affecting Salivary Leak Rate.

| Factors                        | Presence of leak (n = 25) | Absence of leak (n = 68) | p-value |
|-------------------------------|---------------------------|--------------------------|---------|
| Age                           | 60                        | 30 (44.1)                | 0.195   |
| >60                           | 10 (40)                   | 38 (55.9)                |         |
| Diabetes                      |                           |                          |         |
| Presence                      | 6 (24)                    | 13 (19.1)                | 0.448   |
| Absence                       | 19 (76)                   | 55 (80.9)                |         |
| RT                            |                           |                          |         |
| Previous RT                   | 6 (24)                    | 15 (22.1)                | 0.707   |
| No previous RT                | 19 (76)                   | 53 (77.9)                |         |
| Previous surgery              |                           |                          |         |
| Presence                      | 3 (12)                    | 6 (8.8)                  | 0.371   |
| Absence                       | 22 (88)                   | 62 (91.2)                |         |
| Margins                       |                           |                          |         |
| Positive/close                | 4 (16)                    | 20 (29.4)                | 0.165   |
| Clear                         | 21 (84)                   | 48 (70.6)                |         |
| Flap (n = 79)*                |                           |                          |         |
| Regional/pedicled             | 9 (47.4)                  | 33 (55)                  | 0.692   |
| Free                          | 10 (52.6)                 | 27 (45)                  |         |
| T stage                       |                           |                          |         |
| T1/T2                         | 2 (8)                     | 22 (32.4)                | 0.013   |
| T3/T4                         | 23 (92)                   | 46 (67.6)                |         |

*Reconstruction for initial surgery only.

### TABLE III. Sensitivity and Specificity of Early Blue Dye Test.

| Blue dye (<12 days) | Leak | Absence of leak | Total |
|---------------------|------|-----------------|-------|
| Test positive       | 8    | 0               | 8     |
| Test negative       | 14   | 61              | 75    |
| Total               | 22   | 61              | 83    |

Sensitivity 36.4.
Specificity 100.
PPV 100.
NPV 81.3.
TABLE IV. Sensitivity and Specificity of VFSS.

| VFSS (<21 days) | Leak | Absence of leak | Total |
|----------------|------|-----------------|-------|
| Test positive  | 3    | 0               | 3     |
| Test negative  | 4    | 20              | 24    |

Sensitivity 42.9, Specificity 100, PPV 100, NPV 83.3.

DISCUSSION

OPCF is a dreaded complication that results in prolonged hospital stay, debilitation and compromises oncologic outcomes. The incidence varies greatly depending on the cohort, and the incidence of 26.9% reported here falls within the published range. One of the major issues with patients who develop OPCF is the delay in subsequent progress to normalcy and adjuvant therapy if needed. In these patients, oral intake is limited and patients require complex dressings and wound care often in an inpatient setting, resulting in significant deconditioning. Our focus in this study was thus to assess the usefulness of blue dye testing in early diagnosis of OPCF and the potential improved outcomes of faster healing with conservative strategies where possible.

Traditionally, many surgeons have empirically delayed feeding patients till the seventh to tenth postoperative day in an attempt to decrease the OPCF rate, which may even be delayed till the 14th postoperative day in patients with previous irradiation. Apart from clinical parameters, some surgeons employ various radiological studies to assess for the presence of salivary leak or impending fistula. Giordano et al. conducted routine postoperative barium swallows on POD 7 in his series of post-laryngectomy patients and concluded that barium swallows were effective in decreasing hospitalization stay without an increase in fistula rate, as the patients were fed immediately after a negative barium swallow. White et al. tested 79.2% of his cohort of post-laryngectomy patients with a gastrograftin esophagram and found that the test had a sensitivity of 26% and a specificity of 94%. They concluded that it was beneficial to test patients at high risk for fistula formation with imaging before initiating oral intake. Moses et al. tested 38 post-laryngectomy patients with cinepharyngoesophagram and made the similar recommendation that there was benefit in performing this imaging if the patient had clinical signs and symptoms of impending fistula. As with VFSS performed in our institution, these require additional radiation exposure and are subject to interpretation by radiologists. In fact, the study by Cordeiro et al. found that the sensitivity of barium swallow was revised from 45 to 63% on subsequent review of the images by a single experienced radiologist. Analyzing drain amylase levels has varied results, with some reporting a significant difference in levels between patients who develop OPCF and those who do not. However, a study looking at the sensitivity and specificity of drain amylase levels >4000 IU/L on day 1 reported 59% and 64%, respectively, which is still not ideal.

As such, our institution employs early blue dye testing as a simple and useful adjunct to clinical assessment in detecting the presence of OPCF. This test can be done as a bedside procedure with little to no additional cost and can also be repeated multiple times to improve its accuracy. As leak from the neck suture lines and drains are easily identifiable by any observer, there is no chance of a false positive result (as seen in our data). In all cases, there was no debate among the surgeons and observers as to whether the test was positive or negative. A positive test result is also quickly apparent within 24 hours, with blue dye seen staining the neck or drain output (Fig. 1). The ease of application of blue dye testing explains its established use in testing for leaks either intra- or postoperatively in many types of surgeries where there is potential for leakage at an anastomotic site. Kapila et al. recommend methylene blue testing in patients post esophagectomy as it is inexpensive and widely available. As the dye used is widely used as food coloring, there have been no documented major side effects or contraindications. To our knowledge, this study is the first to look at the use of blue dye to assess for OPCF in head and neck SCC patients post resection and reconstruction. Its use is also widely applicable to most types of head and neck resection and reconstruction where the potential OPCF site is below the salivary line. As such, we have not limited its usage to laryngeal or hypopharyngeal reconstructions as the other studies have. Although there is yet no gold standard test for salivary fistula to compare against, our reported sensitivity and specificity of 36.4 and 100%, respectively does not fall short of the current radiological studies, although caution should be used for negative tests especially if there is a strong index of suspicion for an impending OPCF. In such cases, the blue dye test can be easily repeated on subsequent days.

TABLE V. Outcomes for Patients Diagnosed with OPCF

| Outcomes                        | Early blue dye test positive (n = 8) | Early blue dye test negative/ not performed (n = 17) | p-value |
|---------------------------------|-------------------------------------|-----------------------------------------------------|---------|
| Median POD of diagnosis         | 9.5 (6–11)                          | 13 (7–32)                                           | 0.001   |
| Conservative management         | 6                                   | 7                                                   | 0.202   |
| Surgical closure                | 2                                   | 10                                                  |         |
| Median time to closure of fistula (days) | 40 (16–329)                         | 76.5 (14–369)                                       | 0.629   |
Importantly, patients with a positive blue test are diagnosed at a median of POD 9.5 as opposed to POD 13 for test negative patient, allowing for treatment to be instituted earlier. As Friedman et al. have found, an earlier diagnosis tends to result in earlier healing and discharge from hospital. Healing time is an important outcome measure that has a great impact on other measures such as costs incurred and patient satisfaction. Although the time required for healing involves a multitude of factors, we believe that the earlier diagnosis has a crucial role to play in our finding that patients who test positive in the early blue dye test show resolution of their fistula at a median time of 40 days as compared to those fistula patients who are not diagnosed with the early blue dye test, with a median healing time of 76.5 days. Although this result did not reach statistical significance, it may be attributed to the small numbers in the group. It is difficult to estimate the sample size required to prove significance in the comparison of time to fistula closure, given that each case of OPCF tends to be unique in terms of size, location, healing rate, management options and superimposed complications such as infection or carotid blowout, resulting in a wide variation of fistula closure times.

In our study, advanced T-classification appears to be the only significant risk factor for the development of OPCF. This is probably a surrogate for the size and complexity of the defect post-resection, consequently reflecting the extent of reconstruction. In particular, we did not identify preoperative radiotherapy as a risk factor for OPCF, as has been reported in a number of studies. The lack of factors found to be of significance is likely due to the small sample size. Sample size estimation indicates that our study is underpowered and our numbers are too small to detect a statistically significant difference. However, with regards to preoperative radiotherapy being a factor in the development of OPCF, it is important to note that the above mentioned studies did not take into account the radiation dose, type, and interval between RT and surgery. Also, some studies have reported a decrease in OPCF rates in irradiated patients in the recent years due to improvement in dose delivery techniques and better tissue sparing of the surrounding uninvolved tissues. Indeed, the patients in this study who were irradiated prior to treatment all received intensity modulated radiation therapy (IMRT), which has superior normal tissue sparing compared to more traditional two-dimensional techniques, and hence may mitigate the effects of radiation on wound healing and hence, development of OPCF.

In accordance with our results, we have developed an algorithm that we believe will help in early diagnosis of OPCF patients (Fig. 2) and ultimately a better outcome for all head and neck SCC patients undergoing resection and reconstruction. In view of the low sensitivity of the blue dye test, it would have been ideal to perform a more sensitive test as an initial screening tool before the blue dye test. However, due to the retrospective nature of this study and the lack of a gold standard test to compare against, we were unable to include another form of testing into our proposed algorithm.

Fig. 2. Proposed algorithm for early diagnosis of OPCF.
It is imperative that the algorithm takes into account the surgeon’s index of suspicion of fistula. This should be based on the clinical signs and symptoms of the patient (including postoperative fever, wound swelling, erythema, and tenderness), the potential risk factors for OPCF, and the difficulty of flap inset and wound closure. For example, fever and tachycardia in a patient with increasing neck swelling and tenderness, on a background of technically difficult surgery and flap inset would constitute a patient with a high suspicion of leak and would warrant, based on our algorithm, repeated blue dye tests even if the first is negative. On the other hand, an afebrile patient with straightforward surgery, no underlying potential risk factors, and no neck signs would be one of low suspicion for leak and a single negative blue dye test would suffice. As previously mentioned, making an early diagnosis of salivary fistula is rarely easy or straightforward and there is no gold standard test that is highly sensitive or specific. As such, we remain reliant on a combination of clinical acumen and imperfect tests to make the diagnosis as early as possible.

We also recommend repeating the blue dye test in more difficult or suspicious cases as we have found that in the patients who initially tested negative for the early blue dye test, eight patients subsequently went on to test positive when the test was repeated at a range of POD 8–30. Although VFSS seems to be a slightly more sensitive test such as drain amylase levels as part of initial evaluation, it is a safe, and easy to carry out that it is nearly considered a component of bedside clinical examination in our institution. Another study limitation is its retrospective quality and thus no fixed protocol for administering the blue dye test. However, this does not affect its usability and generalizability as a test. In reality, factors such as a patient’s medical condition would also affect a clinician’s decision to time different tests. With this initial data, it would be useful to design a prospective trial based a proposed algorithm, with the inclusion of a potentially more sensitive test such as drain amylase levels as part of initial screening prior to the blue dye test. From there, we can perform further analysis into secondary outcomes such as length of hospital stay and expenses.

**CONCLUSION**

Fistula formation post head and neck resection and reconstruction is a dreaded complication. Despite the fact that it is one of the more common complications, there is still not yet a gold standard test or reliable method of early diagnosis. Early blue dye testing appears to be valuable in the diagnosis of oro/pharyngocutaneous fistula, with the additional advantage of being low in cost and easily administered. With earlier diagnosis, there can be earlier intervention with all its attendant improved outcomes.

**CONFLICT OF INTEREST**

The authors declare that they have no conflict of interest.

**BIBLIOGRAPHY**

1. Redaelli de Zinis LO, Ferrari L, Tomenzoli D, et al. Postlaryngectomy pharyngocutaneous fistula: incidence, predisposing factors, and therapy. *Head Neck* 1999;21:131–138.
2. Weber BS, Berkley BA, Forastiere A, et al. Outcome of salvage total laryngectomy following organ preservation therapy: The Radiation Therapy Oncology Group trial 91-11. *Arch Otolaryngol Head Neck Surg* 2003;129:44–49.
3. Parkh SR, Irish JC, Curran AJ, et al. Pharyngocutaneous fistula in laryngectomy patients: The Toronto Hospital experience. *J Otolaryngol* 1998;27:136–140.
4. Qureshi SS, Chaturvedi P, Pai PS, et al. A prospective study of pharyngocutaneous fistulas following total laryngectomy. *J Cancer Res Ther* 2005;1:51–56.
5. Saki N, Nikahdagh S, Kazemi M. Pharyngocutaneous fistula after laryngectomy: incidence, predisposing factors, and outcome. *Arch Iran Med* 2008;11:314–317.
6. Friedman M, Venkatesan TK, Yakovlev A, Lim JW, Tanyeri H, Caldarelli DD. Early detection and treatment of postoperative pharyngocutaneous fistula. *Otolaryngol Head Neck Surg* 1999;121:378.
7. Saydam L, Kalciloglu T, Kiralay A. Early oral feeding following total laryngectomy. *Am J Otolaryngol* 2002;23:277–281.
8. Cordiero PG, Shah K, Santamaria E, Gillies MJ, Singh B, Shah J. Barium swallows after free jejunal transfer: Should they be performed routinely? *Plast Reconstr Surg* 1999;103:1167–1175.
9. Moses BL, Eisele DW, Jones B. Radiologic assessment of the early postoperative total laryngectomy patient. *Laryngoscope* 1993;103:1157–1160.
10. White RN, Golden B, Sweeney L, Carroll WR, Magnuson JS, Rosenthal EL. Assessment and incidence of salivary leak following laryngectomy. *Laryngoscope* 2012;122:1796–1799.
11. Tian B, Khoa D, Tay AC, et al. Management of urorcutaneous fistulas using a vacuum-assisted closure system. *Head Neck* 2014;36:873–881.
12. Makite AA, Irish J, Guille PJ. Pharyngocutaneous fistula. *Curr Opin Otolaryngol Head Neck Surg* 2003;11:78–84.
13. Johansen LV, Overgaard J, Elbrend O. Pharyngo-cutaneous fistulae after laryngectomy: incidence, predisposing factors, and outcome. *Arch Otolaryngology* 1984;92:19–23.
14. Aydogan LB, Kiroglu M, Tuncer U, Boylu L. The wound amylace concentration in the prediction of pharyngocutaneous fistula. *Otolaryngol Head Neck Surg* 2003;129:414–416.
15. Kasapoglu F, Ozmen OA, Coskun H, Erisen L, Onart S. Evaluation of amylase levels in the neck drainage and serum for early diagnosis of the pharyngocutaneous fistula. *Kulak Burun Bogaz Ihtis Derg* 2009;19:67–70.
16. Morton RP, Mehanna H, Hall FT, McVor NP. Prediction of pharyngocutaneous fistulas after laryngectomy. *Otolaryngol Head Neck Surg* 2007;136:846–849.
17. Kapila S, Rozen WM, Huang T, Wu T, Fairbank S. Determining between chyle leak and anastomotic leak after esophageal reconstruction: The utility of methylene blue dye. *Laryngoscope* 2012;122:779–800.
18. Vincensini JA, Kumpulainen E, Hirsikoski P, Johansson RT, Kosma VM. The incidence and etiology of postlaryngectomy pharyngocutaneous fistula. *Head Neck* 2001;23:29–33.
19. Galli J, De Corso E, Volante M, Almadori G, Paludetti G. Postlaryngectomy pharyngocutaneous fistula: incidence, predisposing factors, and therapy. *Otolaryngol Head Neck Surg* 2005;133:689–694.
20. Whitely E, Ball J. Statistics review 4: Sample size calculations. *Crit Care* 2002;6:335–341.
21. Gandly I, Patel S, Matsuo J, et al. Postoperative complications of salvage total laryngectomy. *Cancer* 2005;103:2073–2081.

Laryngoscope Investigative Otolaryngology 2: December 2017
Kiong et al.: Blue Dye Testing for Salivary Fistula

368