Incidence and management of cervical anastomotic leak after transhiatal esophagectomy for cancer esophagus

Authors
Hakeem Zubair Ashraf*, Nadeem Ul Nazeer, Farooq A Ganie, Syed Abdul Wahid, Haroon Rashid Naqshi, Mohammad Yaqoob Khan, Abdul Majeed Dar, Mohammad Akbar Bhat
Department of CVTS, Sher-i-Kashmir Institute of Medical Sciences (SKIMS) Soura, Srinagar, Kashmir, India, 190011
*Corresponding Author
Dr Hakeem Zubair Ashraf (MCh.)

Abstract
Background: The incidence of cervical anastomotic leak after transhiatal esophagectomy for carcinoma esophagus has traditionally been high at around 20%. The severity ranges from asymptomatic minor defects to more fulminant leaks causing sepsis and multi organ failure. Surgery is still the mainstay of treatment. Squamous cell carcinoma forms the dominant histology worldwide with adenocarcinoma showing an upward trend. We sought to determine the incidence and management of cervical esophageal leaks after esophagectomy for cancer of esophagus in our centre.

Material and Methods: Between January 2012 to December 2015, 143 patients with cancer of esophagus were operated all of whom underwent transhiatal esophagectomy. All patients had surgical resection chosen as primary treatment. Gut continuity was restored by using a stomach tube. A preoperative histopathology of lesion was carried out to determine the type of tumor. A contrast computer tomography (CT) scan of chest and abdomen helped establish the extent of growth. A methylene blue test was done followed by a contrast conray swallow. Patients were categorised in early and late leak group with each group having patients with mild, moderate and severe leak.

Results: Of 143 patients, 17 had cervical anastomotic leak of which 12 were males and 5 females. Twenty nine percent had early and 71% late leak. Ten patients had mild, 6 moderate and 1 severe leak. The patient with severe leak died on 11th postoperative day. Of remaining 16 leaked patients, methylene blue and conray swallow together detected the leaks, all of which healed by conservative measures. Patients in cervical leak group had stricture rate of 29%.

Conclusion: Cervical leaks after esophagectomy remain a significant morbidity. The need for conservative treatment and surgical intervention should be carefully weighed as per severity of leak and general condition of the patient. Postoperative optimization of nutritional status and through appraisal of surgical wounds helps to prevent and identify leaks earlier.

Keywords: Esophageal cancer, Transhiatal esophagectomy, Cervical anastomotic leak, Incidence, Management.

Introduction
Esophagogastric anastomotic leaks are the most feared surgical complications following resection of esophageal cancers and are a significant cause of morbidity and mortality. Various factors implicated include technique of anastomosis, type of conduit, location of anastomosis, single or double layered
anastomosis, manual or mechanical anastomosis, the stage of the tumour, additional chemoradiation used and nutritional status\(^1,2\). Decreased blood supply of the gastric conduit and faulty surgical technique still remain the most important predisposing factors\(^3\). A final conclusion whether manual or mechanical anastomosis is better has not yet reached to any consensus\(^4,5\). Traditionally cervical anastomoses are said to have high leakage and stenosis rate and low mortality as compared to thoracic anastomosis\(^6,7\). The severity of the leaks range from asymptomatic and minor anastomotic defects to more fulminant leaks causing systemic sepsis and multiorgan failure\(^3\). Despite decreasing trend in incidence throughout the world for the last few decades\(^8\), they are still a significant factor responsible for morbidity and mortality. Surgery is still the mainstay of treatment for resectable esophageal cancer with a five-year survival rates as high as 40% to 50% achieved after curative resection in specialized centers\(^9\). Various biological factors adversely effect the success of surgical management of esophageal cancers. Lack of serosa and a rich network of vertically and transversely placed submucosal lymphatic network accounts for frequent extension of this tumor to regional and distant lymph nodes irrespective of the tumor location in the esophagus\(^10\). Squamous cell carcinoma forms the dominant histology worldwide with more commonly involving the mid and upper two-third of esophagus. However adenocarcinoma has been showing an upward trend involving the lower third of esophagus.

We sought to determine the incidence and management of cervical esophageal leaks after esophagectomy for cancer of esophagus in our centre.

**Material and Methods**

Between January 2012 to December 2015, 143 patients with cancer of esophagus were operated in our department all of whom underwent transhiatal esophagectomy. Surgery was the primary treatment and none received any neoadjuvant chemoradiation. Only those patients in whom gut continuity was restored by using a stomach tube were selected for the study. Patients were thoroughly evaluated preoperatively for general physical condition, nutritional and cardiopulmonary status. A preoperative esophagogastrroduodenoscopy and histopathology of lesion was carried out to determine the type of tumor. A contrast computer tomography of chest and abdomen helped establish the extent of growth and relation to surrounding structures. The procedure of transhiatal esophagectomy involves one supraumbilical midline incision from xiphisternum and another neck incision without opening the thorax. The stomach is mobilized on a right gastroepiploic artery pedicle. Left gastric and short gastric arteries are sacrificed and thorough lymph node dissection is done. The crura of the esophageal hiatus are then widened and blunt finger dissection of thoracic esophagus away from surrounding thoracic structures is done. The cervical incision is given in the lower part of the neck medial to left sternocleidomastoid muscle. The cervical esophagus is identified and separated from trachea and surrounding structures. The specimen is then excised including upper one third of stomach, lower esophageal sphincter, whole of thoracic esophagus along with the growth and distal part of cervical esophagus. A tube is constructed from the remaining part of the stomach that is taken up retrosternally in posterior mediastinum and anastomosed with the cervical esophageal stump in single layer using 2-0 vicryl. All anastomoses were hand sewn. All patients had feeding jejunostomy done and a Ryle’s tube placed across the anastomosis. Digital dilatation of Pylorus was done in all cases. A right chest drain was put as a routine and left drain was put in case of
pleural breach on left side. An abdominal drain in the region of the hiatus was also put along with a corrugated neck drain in the region of esophagogastric anastomosis. Feeding in all patients was started on 2\textsuperscript{nd} postoperative day through feeding jejunostomy. A methylene blue test was done on 7\textsuperscript{th} postoperative day followed by a contrast conray swallow the next day. In patients who did not have any evidence of anatomic leak, the nasogastric tubes were removed on the day of barium contrast study and patients started on oral feeds initially with plain water and gradually allowed solid foods. The thoracic and abdominal tubes were removed second day after oral intake (10\textsuperscript{th} postoperative day). In patients were there was a suspicion of excessive soaking through the neck drain or features of mediastinitis or sepsis after 3\textsuperscript{rd} postoperative day but prior to the 7\textsuperscript{th} postoperative day, the methylene blue test was performed earlier. Any extravasation of the methylene blue dye through drains or contrast on conray swallow constituted the definition of anastomotic leak. Once diagnosed with a leak and based on the time of appearance patients were categorised into Group 1 (early leak…within 7 days) and Group 2 (late leak…after 7 days). Each group had patients further separated into three sub groups:

a. Mild leak -- extravasation of only a streak of dye and contrast or minimal amount of oral liquids without solids.

b. Moderate leak -- extravasation of considerable quantity of dye and contrast or considerable amount of oral liquids with solids.

c. Severe leak-- extravasation of whole of dye and contrast or most of oral intake along with features of mediastinitis and sepsis.

In all the patients with mild leak, the nasogastric tube was removed on seventh day and patients started on small quantities of oral semisolid diet only. Feeding jejunostomy however was continued. A repeat methylene blue test and conray contrast was done ten days after initial contrast study. In all the patients, the leak healed with conservative measures. Moderate leak patients were put on a conservative regimen of nil per orally and feeding jejunostomy for next fifteen days after detection of leak and a repeat methylene blue test followed by contrast study was done. The patient with severe leak was subjected to surgical closure as soon as detected. This patient had contents from cervical leak that trickled down into the thorax causing pleuritis and mediastinitis. Right posterolateral thoracotomy in fifth intercostal space was done, thoracic cavity thoroughly washed and cleaned. The patient had disruption of the gastroesophageal anastomotic line causing leak. The cervical incision was opened and necessary debridement was done followed by re-anastomosis of gastric stump with remanant esophagus.

All the patients during their immediate postoperative period were maintained on a strict nutritional regimen to prevent any mineral or electrolyte imbalance. Adequate enteral feeding of carbohydrates, fats and proteins was maintained through feeding jejunostomy or naso enteral tube, besides regular albumin and multivitamin infusion to aid in healing. With the gradual increase in oral feeds from liquids to solids, the jejunostomy feeds were stopped and patients encouraged to take orally. Jejunostomy tube was kept in situ for 6 weeks after discharge. All patients were then referred to medical oncology for postoperative chemoradiation.

**Results**

The clinical data of patients involved in study is given in Table 1.

Of the 143 patients, 61% were males and 39% females with a male to female ratio of 1.6 : 1. The age of patients ranged from 45 years to 78 years with a mean age of 57.76 ± 12.2 years. Thirty one percent of the tumours were located in upper third of thoracic esophagus,
61% in middle third of thoracic esophagus and 8% in abdominal esophagus and GE junction. Seventy six percent of patients had squamous cell carcinoma, 24% had adenocarcinoma of the esophagus. Seventy two percent of the patients belonged to TNM stage III and 22% to stage II [Table 1] Fifty eight percent of our patients gave history of some weight loss. Considering loss of 10% of body weight in last six months as significant, 36% patients had a mean loss of 6.24 kg with a range of 5 to 7.5 kg . Mean haemoglobin was 13gm% with a range of 10 to 15 gm% while mean serum albumin level was 3.34mg/dl. All patients were evaluated for pulmonary functions and mean FEV$_1$ 2.25 L was observed Mean hospital stay of patients was 13.25 ± 3.5 days.

Of the 143 patients operated, seventeen patients (12%) had cervical anastomotic leak. The characteristics of all patients with cervical anastomotic leak is given in Table 2. Out of 17 patients, twelve were males and 5 females. Twenty nine percent had early and 71% late leak. Ten patients had mild, 6 moderate and 1 severe leak. All patients except one with severe leak were managed conservatively. The patient with severe leak underwent reexploration, necrotic gastric anastomotic line excised, Kocherization of duodenum done to gain length of stomach tube and reanastomosis done in neck. However the patient died on 11th post operative day.

Assessed 3 months after discharge, 5 patients in cervical anastomotic leak group and 21 in non leak group developed anastomotic strictures and needed on an average of 3 sessions of dilatations. There were 6 deaths in our study. One of the patients who died belonged to cervical anastomosis leak group. The patient died on 11th postoperative day due to severe mediastinitis and sepsis. The other 5 mortalities belonged to the non leak group. Out of these patients, two had ventilator related complications and died within 10 days postoperatively and three died due to unrelated sudden cardiac event

### Table 1: Clinical Data of patients involved in study.

| S No. | Characteristic                        | Total No. | Percentage |
|-------|--------------------------------------|-----------|------------|
| 1.    | Total No. of patients operated       | 143       |            |
|       | Males                                | 87        | (61%)      |
|       | Females                              | 56        | (39%)      |
| 2.    | Age range                            | 45 – 78 years |          |
|       | Mean age                             | 57.76 ± 12.2 |          |
| 3.    | Location of tumor                    |           |            |
|       | Upper third of thoracic esophagus    | 44        | (31%)      |
|       | Middle third of thoracic esophagus   | 88        | (61%)      |
|       | Abdominal esophagus and GE junction  | 11        | (8%)       |
| 4.    | Tumor Pathology                      |           |            |
|       | Squamous cell carcinoma              | 109       | (76%)      |
|       | Adenocarcinoma                       | 34        | (24%)      |
| 5.    | Mean Haemoglobin                     | 13gm%     |            |
| 6.    | Mean FEV$_1$                         | 2.25L     |            |
| 7.    | Mean serum albumin                   | 3.34gm/dl |            |
| 8.    | Tumour Stage                         |           |            |
|       | I                                    | 1         | (0.69%)    |
|       | II                                   | 32        | (22.3%)    |
|       | III                                  | 103       | (72%)      |
|       | IV                                   | 7         | (5%)       |
| 9.    | Mean hospital stay                   | 13.25 ± 3.5 days |          |
Table 2 Characteristics of patients with cervical leak

|   | Characteristics                          | Number | Percentage |
|---|------------------------------------------|--------|------------|
| 1 | No. of patients leaked                    | 17     |            |
|   | Males                                    | 12     | (71%)      |
|   | Females                                  | 5      | (29%)      |
| 2 | Time of leak                              |        |            |
|   | Early                                    | 5      | (29%)      |
|   | Late                                     | 12     | (71%)      |
| 3 | Severity                                 |        |            |
|   | Mild                                     | 10     | (58.8%)    |
|   | Moderate                                 | 6      | (35.29%)   |
|   | Severe                                   | 1      | (5.88%)    |
| 4 | Pathology                                |        |            |
|   | Squamous cell carcinoma                  | 13     | (76%)      |
|   | Adenocarcinoma                           | 4      | (24%)      |
| 5 | Detection of leak                        |        |            |
|   | Methylene blue and Conray                | 11     | (64.7%)    |
|   | Methylene blue only                      | 3      | (17.6%)    |
|   | Conray only                              | 2      | (11.7%)    |
|   | Endoscopy                                | 1      | (5.8%)     |
| 6 | Mortality in cervical leak group         | 1      | (5.8%)     |

Discussion

Esophagogastric anastomotic leaks continue to be a significant cause of morbidity and mortality after esophagectomy. The incidence of cervical anastomotic leak after THE for carcinoma esophagus has traditionally been high at around 20%\(^{(1,11,12)}\). Some series report anastomotic leak rate of around 13%\(^{(13)}\) to 10%\(^{(14)}\) but these included patients with benign esophageal disease and transthoracic anastomosis. Our study reported an incidence of 12% for patients with carcinoma esophagus which could be due to our series having majority of tumors resected had a tumor free margins and also due to improved surgical techniques. Earlier studies with high incidence of leak had majority of cancers reported in stage III and above\(^{(1)}\). Despite straightforward management the long-term consequences of cervical leaks cannot be ignored. Leaks may be due to conduit ischemia and technical errors, or a combination of the two\(^{(15)}\) ranging clinically from asymptomatic fistulae to those causing systemic sepsis thereby betraying any standard management protocol. Despite improvements in surgical results over last couple of decades, they constitute a significant complication\(^{(8)}\). Earlier thought to be less lethal\(^{(3)}\), cervical leaks were found to be as morbid as those complicating thoracic anastomoses\(^{(15)}\). Though constructed in the neck it may leak into the mediastinum or pleural space\(^{(16,17)}\) with attendant morbidity and mortality. One of our patients with cervical leak had contents gravitating into the mediastinum and died due to severe mediastinitis. Time of leak has a profound effect on the overall outcome of the surgery. Leaks that manifest in first 7 days are more likely to be severe, need reoperation, cause complications and even death\(^{(3,6,15)}\). Diagnosis of the anastomotic leak as early as possible is of paramount importance. Thorough clinical and biochemical examination and daily inspection of wound sites and drains should be carried...
out. Any suspicion of excessive drainage or features suggestive of sepsis should prompt investigation to look for any leak. Alteration in cardiac rate and rhythm especially first time atrial fibrillation is often the first and only indicator of anastomotic insufficiency. Early symptoms of sepsis may be as inconsequential as persisting pain and minor changes in neurological status, such as reduced compliance. Bed side methylene blue test, conray swallow, oral contrast CT radiography and endoscopy have all been used to diagnose and identify leaks. In our series, patient with severe leak had objective evidence of anastomotic leak in form of excessive drainage through neck and chest drains and features of sepsis and mediastinitis. Out of the rest 16 patients, methylene blue and conray swallow together detected leaks in 11 patients, Methylene blue only in 3, conray swallow only in 2 and Endoscopy in 1.

Despite refinement in anastomotic techniques and postoperative management as many as one-third of cervical anastomotic leaks result in stricture formation as healing occurs. Reported incidences of anastomotic strictures have varied from 10 to 31%. Of late the use of PPI and the development of better and safer dilatation techniques resulted in a major decrease in morbidity caused by these strictures. In our series the overall stricture formation was around 19%, with patients in cervical leak group having stricture rate of 29% while those in non leak group having a stricture rate of 17%. These are consistent with that reported in literature. Multiple endoscopic dilatations in those surviving have reported good functional outcome with considerable decrease in postoperative dysphagia. The surviving patients continue to be on our 3 monthly follow up.

In conclusion though considerable improvements in technique and management have been made, cervical leaks still remain a significant morbidity with manifestations ranging from subtle fistulae to life threatening sepsis. The need for conservative treatment and surgical intervention should be carefully weighed as per severity of leak and general condition of the patient. Postoperative optimization of nutritional status and through appraisal of surgical wounds helps to prevent and identify leaks earlier. Contrast radiography though a cardinal investigation might not detect leak in all cases in isolation. We therefore recommend combination of bed side methylene blue test and contrast radiography with esophagoscopy reserved if both the investigations together cannot detect leak. We also found that in mild leaks as described by us, continuation of semisolid diet does not adversely affect healing provided distal passage is patent.

Conflict of interest - None

References
1. Abbas Tabatabai, Mozaffar Hashemi, Gholamreza Mohajeri, Mojtaba Ahmadinejad, Ishfaq Abass Khan, Saeid Haghdani: Incidence and risk factors predisposing anastomotic leak after transhiatal esophagectomy. Annals of thoracic medicine 2009, Vol 4 ,Issue 4 :197-200.
2. Orringer MB, Marshall B, Iannettoni MD. Eliminating the cervical esophagogastric anastomotic leak with a side-to-side stapled anastomosis. J Thorac Cardiovasc Surg 2000;119: 277-88.
3. Urschel JD. Esophagogastronomy anastomotic leaks complicating esophagectomy: A review.Am J Surg 1995;169: 634-40.
4. Law S, Fok M, Chu KM, Wong J.Comparison of hand-sewn and stapled esophagogastric anastomosis after Esophageal resection for cancer:A prospective randomized controlled trial. Ann Surg 1997;226: 169-73.
5. Valverde A, Hay JM, Fingerhut A, Elhadad A. Manual versus mechanical
esophagogastric anastomosis after resection for carcinoma: A controlled trial. French Associations for Surgical Research. Surgery 1996;120: 476-83.

6. Pierie JP, de Graaf PW, van Vroonhoven TJ, Obertop H. Healing of the cervical esophagogastrostomy. J Am Coll Surg 1999;188: 448-54.

7. Giuli R, Gignoux M. Treatment of carcinoma of the esophagus: Retrospective study of 2,400 patients. Ann Surg 1980;192: 44-52.

8. Lerut T, Coosemans W, Decker G, De Leyn P, Nafteux P, van Raemdonck D. Anastomotic complications after esophagectomy. Dig Surg 2002; 19: 92–8.

9. Michael Hünerbein, Christian Stroszczynski, Kurt T. Moesta, Peter M. Schlag. Treatment of Thoracic Anastomotic Leaks After Esophagectomy With Self-expanding Plastic Stents. Ann Surg. 2004 Nov; 240(5): 801–807.

10. American Joint Committee on Cancer. AJCC Cancer Staging Handbook. Philadelphia: Lippincott-Raven, 1998:67.

11. Hankins JR, Attar S, Coughlin TR, et al. Carcinoma of the esophagus: a comparison of the results of transhiatal versus transthoracic resection. Ann Thorac Surg. 1989;47:700–705.

12. Vigneswaran WT, Trastek VF, Pairolero PC, et al:Transhiatal esophagectomy for carcinoma of the esophagus. Ann Thorac Surg. 1993; 56:838–844.

13. Orringer MB, Marshall B, Iannettoni MD: Transhiatal esophagectomy: clinical experience and refinements. Ann Surg 1999;230: 392-400

14. Briel JW, Tamhankar AP, Hagen JA, De Meester SR, Johansson J, Choustoulakis E, et al. Prevalence and risk factors for ischemia, leak and stricture of esophageal anastomosis: Gastric pull-up versus colon interposition. J Am Coll Surg. 2004;198:536–41.

15. Khaled Alanezi, John D. Urschel. Mortality Secondary to Esophageal Anastomotic Leak. Ann Thorac Cardiovasc Surg 2004; Vol. 10, No. 2.

16. Iannettoni MD, Whyte RI, Orringer MB. Catastrophic complications of the cervical esophagogastric anastomosis. J Thorac Cardiovasc Surg 1995; 110: 1493–501.

17. Bardini R, Bonavina L, Asolati M, Narne S, Peracchia A. Surgical treatment of cervical anastomotic leaks following esophageal reconstruction. Int Surg 1987; 72: 163–5.

18. Stippel DL, Taylan C, Schröder W, Beckurts KT, Holscher AH. Supraventricular tachyarrhythmia as early Indicator of a complicated course after esophagectomy. Dis Esophagus 2005; 18: 267–73.

19. Wolf Arif Mardin, Daniel Palmes & Matthias Bruewer. Current concepts in the management of leakages after esophagectomy. Thoracic Cancer 2012;3: 117–124.

20. Juntang Guo, Xiangyang Chu, Yang Liu, Naikang Zhou, Yongfu Ma; Chaoyang Liang. Choice of therapeutic strategies in intrathoracic anastomotic leak following esophagectomy. World Journal of Surgical Oncology 2014 12 : 402.

21. Dewar L, Gelfand G, Finley RJ, et al: Factors affecting cervical anastomotic leak and stricture formation following esophagogastrectomy and gastric tube interposition. Am J Surg 1992:163:484-489.

22. Gandhi SK, Naunheim KS: Complications of transhiatal esophagectomy. Chest Surg Clin N Am 1997; 7:601-610.