



POST-OPERATIVE CERVICAL ANASTOMOTIC LEAK IN ESOPHAGEAL CANCER- EXPERIENCE OF A REGIONAL CANCER CENTRE IN SOUTH INDIA.

Oncology

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ABSTRACT

Introduction: Esophageal surgeries have always been considered challenging both in terms of surgical expertise and post operative complications and also its management. Cervical anastomosis between remaining cervical stump and stomach conduit has always been prone for leak given the precarious blood supply of the conduit at the apex.

Aims and Objectives: To identify factors affecting cervical anastomotic leak and its association with postoperative stricture.

Materials and Methods: All 98 patients who underwent esophageal cancer surgery with cervical anastomosis at our institute in the year 2016 were included in the study. Anastomotic leak rates were identified and perioperative factors affecting anastomotic leak were evaluated.

Results: Of the 12 patients (12.24%) who had cervical anastomotic leak, 10 had Clavien Dindo Grade II and 2 had Grade IIIa leak requiring endoscopic procedure. Leak was significantly associated with Increased operative time ($p=0.027$), more number of lymph node extraction ($p=0.014$), increased number of days of ICU stay ($p=0.046$), stapler conduit ($p=0.008$), stapler anastomosis ($p=0.007$), administration of parenteral nutrition ($p=0.018$), recurrent laryngeal nerve palsy ($p=0.007$) and postoperative LRTI ($p=0.0001$). Anastomotic leak however was not significantly associated with stricture formation upon resolution ($p=0.650$). Handsewn anastomosis were associated with increased rates of post operative stricture formation than stapler anastomosis however it was not statistically significant ($p=0.422$).

Conclusion: Significant morbidity is associated with anastomotic leaks in esophageal cancer surgeries. Identification of critical risk factors and refinement of operative techniques can reduce the morbidity caused by this complication.

KEYWORDS

Esophageal cancer, stapler anastomosis, anastomotic leak, stricture.

INTRODUCTION

Incidence of esophageal cancer has been on the rise since last two decades. It ranks sixth among all cancers in mortality.[1] Surgical resection has been the mainstay of operable esophageal cancer however it is a complex procedure with morbidity and mortality rates 23-50% and 2-8% respectively and 9-29% and 2-4% respectively in China where the incidence is highest however not much data is available from the Indian subcontinent.[2] Mortality associated with surgeries for esophageal cancer have declined in recent years due to progress in various techniques, surgical skills, perioperative management and improvement in anesthesia and critical care. Even though many of the complications associated with such a major surgery are not fatal, esophageal cancer surgeries continue to remain a morbid procedure. With the availability of gastrointestinal staplers many centres now prefer stapler neck anastomosis over handsewn anastomosis as it is technically easy and also decreases overall operative time.

Anastomotic leak is one of the most common complications occurring after pulmonary complications following cervical esophagogastric anastomosis.[3] Cervical anastomosis between remnant cervical stump and stomach conduit has always been prone for leak given the precarious blood supply of the conduit at the apex. Stapler anastomosis have been traditionally associated with increased rates of leak when compared to handsewn anastomosis. Fortunately since the anastomosis lies in the neck there is anatomic separation from the spread to mediastinum which would have otherwise caused devastating mediastinitis and sepsis. Nevertheless anastomotic leak is not only morbid for the patient but also increases stress on the already overburdened health care services.

We have tried to audit the cervical anastomotic leak rates and perioperative factors associated with the same at our Regional Cancer center which has high influx of esophageal cancer patients with an average of 90-110 esophageal resections every year.

All 98 patients who underwent esophageal cancer surgery with

cervical anastomosis at our institute in the year 2016 were included in the study. The Objective of our retrospective case control study was to evaluate for anastomotic leak rates after esophageal resection for cancer and its association with perioperative morbidity at our institute.

MATERIALS AND METHODS

Between January 2016 to December 2016, 98 patients underwent Esophageal resection at Kidwai Cancer Institute, Bangalore, India. Patients with cervical esophageal cancer were not part of this analysis as they followed different/non surgical treatment protocols. Both squamous and adenocarcinoma of esophagus along with Siewerts type I and II Gastroesophageal junction (GEJ) tumors were included in the study. Patients were divided into two groups- who had cervical anastomotic leak (Cases) and those who did not (Controls).

Parameters studied in both groups were as follows:

Preoperative parameters: Age, gender, addiction, hemoglobin, serum albumin, neutrophils, length of hospital stay, blood transfusion, endoscopic level of lesion, comorbidities, ASA score, GEJ involvement and neoadjuvant therapy.

Intraoperative parameters: Type of surgery, total blood loss, blood transfusion, intravenous fluids, splenectomy, total operative time, Stapler versus handsewn cervical anastomosis.

Postoperative parameters: Time of extubation, blood transfusion, days of ICU stay, day 1 hemoglobin, day 1 albumin, Feeding Jejunostomy feeds, parenteral nutrition, day of start of oral liquids, conduit necrosis, recurrent laryngeal nerve palsy, pulmonary complications arrhythmia, sepsis, wound infection, chylothorax, total nodes extracted, number of nodes positive, anastomosis leak rates and stricture formation over 1 year of follow up.

Statistical analysis was performed by software SPSS20.0. Chi square test and Mann-Whitney U test correlation was calculated to correlate various clinical parameters with leak rates. Descriptive analysis performed to assess demographic data.

RESULTS

Of the 98 patients, 52 were male (53%) and 45 females (47%) with mean age 54.3 years. Of the 12 patients (12.24%) who had cervical anastomotic leak, 10 had Clavien Dindo Grade II and 2 had Grade IIIa leak requiring endoscopic procedure. There was no mortality recorded in the leak group. 3 patients (3%) died during 30 days of hospital stay (30-day mortality). None of the preoperative parameters were significantly associated with increased anastomotic leak rates. No relation was found between intraoperative blood loss, blood transfusion, intravenous fluids and splenectomy with anastomotic leak. However leak was significantly associated with transhiatal esophagectomy (THE) compared with transthoracic esophagectomy (TTE) and minimally invasive esophagectomy. Increased operative time (p=0.027), more number of lymph node extraction (p=0.014), increased number of days of ICU stay (p=0.046), stapler conduit (p=0.008), stapler anastomosis (p=0.007), administration of parenteral nutrition (p=0.018), recurrent laryngeal nerve palsy (p=0.007) and postoperative LRTI (p=0.0001) were the postoperative parameters significantly associated with anastomotic leak. Anastomotic leak however was not significantly associated with stricture formation upon resolution (p=0.650). Handsewn anastomosis was associated with increased rates of post operative stricture formation than stapler anastomosis however it was not statistically significant (p=0.422). (Table 1,2)

	Post op leak	N	Mean	Std. Deviation	MANN-WHITNEY U TEST	P VALUE
Age	yes	12	54.75	8.635	508.5	0.987
	no	85	53.85	10.410		
FEV1 %	yes	12	72.83	15.859	596.5	0.343
	no	85	77.87	21.754		
Preoperative Hemoglobin	yes	12	13.08	1.443	503	0.938
	no	85	12.75	2.609		
Preoperative Neutrophils	yes	12	6.50	2.236	450.5	0.509
	no	85	6.00	2.012		
Serum Albumin	yes	12	3.92	0.515	559.5	0.412
	no	85	4.02	0.408		
Preoperative Length of hospital stay (Days)	yes	12	14.25	7.473	481	0.75
	no	85	12.91	6.148		
BMI	yes	12	20.33	4.979	536	0.775
	no	85	20.33	4.286		
Operative time (Mins)	yes	12	213.33	45.793	311.5	0.027
	no	85	182.24	55.707		
Intraoperative Blood loss (ml)	yes	12	608.33	189.297	398.5	0.213
	no	85	544.71	196.927		
Blood transfusion preoperative	yes	12	0.00	0.000	576	0.189
	no	85	32	1.082		
Blood transfusion intraoperative	yes	12	75	965	470.5	0.627
	no	85	54	665		
Blood transfusion postoperative	yes	12	50	905	449.5	0.371
	no	85	27	565		
Fluids Intra operative	yes	12	3.33	3.055	576.5	0.458
	no	85	4.35	2.349		
Post operative day 1 Hemoglobin	yes	12	12.50	1.967	0.337	0.054
	no	85	11.81	1.770		
Post operative day 1 albumin	yes	12	2.67	0.492	602	0.187
	no	85	2.86	0.515		
Distal Margin (cm)	yes	12	5.25	2.800	510	1.000
	no	85	5.29	2.712		
Proximal Margin (cm)	yes	12	5.33	2.425	376	0.43
	no	85	4.68	2.479		
Total LN	yes	12	13.29	8.175	733.5	0.014
	no	85	7.58	4.460		
Positive LN	yes	12	1.58	2.314	519.5	0.918
	no	85	1.86	2.573		
Day of Extubation	yes	12	1.67	1.435	436	0.298
	no	85	1.47	2.062		
Number of ICU Stay days	yes	12	7.58	2.778	330	0.046
	no	85	6.11	2.489		
Oral Diet Start Day	yes	12	6.67	1.875	477	0.71
	no	85	6.34	1.600		

Table 1: Association of clinical parameters with cervical anastomotic leak rates.

Surgical and postoperative parameters	Group		Chisquare	p value	
	Case	Control			
Type of surgery	THE	8	52	19.82	0.0001
	TTE	0	19		
	Minimal Invasive	4	14		
Conduit	Handsewn	4	61	7.026	0.008
	Stapler	8	24		
Cervical Anastomosis	Handsewn	6	71	7.223	0.007
	Stapler	6	14		
Parenteral Nutrition	Yes	9	33	5.605	0.018
	No	3	52		
Recurrent Laryngeal Nerve Palsy	Present	11	26	7.157	0.007
	Absent	1	60		
Respiratory Infections	Present	10	26	12.53	0.0001
	Absent	2	59		
Cervical stricture	Present	4	23	0.206	0.65
	Absent	8	62		

Table 2: Association of Surgical and postoperative parameters with anastomotic leak rates

DISCUSSION

Recognition of the influence of intraoperative and postoperative clinical and surgical parameters on the occurrence of anastomotic leak rates after esophagectomy for cancer could contribute to the improvement of intraoperative and postoperative decision making and development of therapeutic approaches.[3]

Increased operative time would subject the patient to extended levels of hypotensive states as demonstrated by Goense et al.[3] In our study too operative time more than 213.3 minutes (p=0.027) were significantly associated with anastomotic leak compared to those surgeries which were completed in lesser time.

Extensive dissection for more number of lymph node retrieval have been associated with both increased rates of recurrent laryngeal nerve palsies and leak rates probably due to increased devascularization of remnant esophageal stump.[4] We found a significant association between leak rates and increased lymph node retrieval and recurrent laryngeal nerve palsy. However which of these factors contributed more to aspiration and respiratory infections would be an difficult to assess.

Use of staplers for esophagogastric anastomosis was associated with increased leak rates in our series. We used linear staplers and performed T shaped anastomosis that might have lead to increased tension between remnant esophagus and gastric conduit. Zielinski et al tried a total mechanical stapled esophagogastric anastomosis using circular staplers with zero leak rates.[5] It seems a technique worth exploring however the technical intraoperative problems associated with its use needs to be considered for placing anastomosis in the neck than its usual use for intrathoracic anastomosis.

Leak rates were high in patients undergoing Transhiatal esophagectomy (p=0.0001) compared to those with transthoracic and minimal invasive esophagectomies. However neck anastomosis in THE does not require thoracotomy and also upon leak it remains well localised in the neck without leading to disastrous mediastinitis and the consequent sepsis. [6]

Leak rates have been traditionally associated with increased stricture formation due to fibrosis upon healing and has been recently upheld by Ahmed Z et al in their review of 524 cases of esophagectomy. Refractory strictures were independently associated with leak and transhiatal esophagectomy.[7] In our case series too we found increased stricture formation following leak rates and transhiatal esophagectomy however they were not statistically significant.

CONCLUSION

Significant morbidity is associated with anastomotic leaks in esophageal cancer surgeries. Identification of critical risk factors and refinement of operative techniques can reduce the morbidity caused by this complication.

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REFERENCES

- Zhang Y. Epidemiology of esophageal cancer. World J Gastroenterol. 2013 Sep 14;19(34):5598-606. doi: 10.3748/wjg.v19.i34.5598. Review. PubMed PMID: 24039351; PubMed Central PMCID: PMC3769895
- Mu J, Gao S, Mao Y, Xue Q, Yuan Z, Li N, Su K, Yang K, Lv F, Qiu B, Liu D, Chen K, Li H, Yan T, Han Y, Du M, Xu R, Wen Z, Wang W, Shi M, Xu Q, Xu S, He J. Open three-stage transthoracic oesophagectomy versus minimally invasive thoraco-laparoscopic oesophagectomy for oesophageal cancer: protocol for a multicentre prospective, open and parallel, randomised controlled trial. BMJ Open. 2015 Nov 17;5(11):e008328. doi: 10.1136/bmjopen-2015-008328. PubMed PMID: 26576807; PubMed Central PMCID: PMC4654388
- Goense L, van Rossum PS, Tromp M, Joore HC, van Dijk D, Kroese AC, Ruurda JP, van Hillegersberg R. Intraoperative and postoperative risk factors for anastomotic leakage and pneumonia after esophagectomy for cancer. Dis Esophagus. 2017 Jan 1;30(1):1-10. doi: 10.1111/dote.12517. PubMed PMID: 27353216.
- Ma GW, Situ DR, Ma QL, Long H, Zhang LJ, Lin P, Rong TH. Three-field vs two-field lymph node dissection for esophageal cancer: a meta-analysis. World J Gastroenterol. 2014 Dec 21;20(47):18022-30. doi: 10.3748/wjg.v20.i47.18022. Review. PubMed PMID: 25548502; PubMed Central PMCID: PMC4273154
- Zielinski J, Jaworski R, Irga-Jaworska N, Haponiuk I, Jaskiewicz J. Total mechanical stapled esophagogastric anastomosis on the neck in esophageal cancer - prevention of postoperative mediastinal complications. Kardiochir Torakochirurgia Pol. 2015 Dec;12(4):318-21. doi: 10.5114/kitp.2015.56781. Epub 2015 Dec 30. PubMed PMID: 26855647; PubMed Central PMCID: PMC4735532.
- Boyle MJ, Franceschi D, Livingstone AS. Transhiatal versus transthoracic esophagectomy: complication and survival rates. Am Surg. 1999 Dec;65(12):1137-41; discussion 1141-2. PubMed PMID: 10597061.
- Ahmed Z, Elliott JA, King S, Donohoe CL, Ravi N, Reynolds JV. Risk Factors for Anastomotic Stricture Post-esophagectomy with a Standardized Sutured Anastomosis. World J Surg. 2017 Feb;41(2):487-497. doi: 10.1007/s00268-016-3746-0. PubMed PMID: 27778075.