

# Management of Complications of Radical Esophagectomy

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**Abstract** The aim of this article is to describe management of complications of radical esophagectomy and to present outcome analysis of prospective study done on patients who underwent radical esophagectomy with 3FLND in our institution. The data analysis and results of our study and its comparison with current literature suggests that improvement in anaesthesia delivery, proper patient selection, refinements in surgical techniques and improved perioperative care are associated with decreased complication rates, morbidity and mortality thereby improving outcome in terms of overall survival with decreased rate of loco regional recurrence.

**Keywords** Radical esophagectomy · 3 field lymphadenectomy · Complications

## Abbreviations

SS Sanjay Sharma  
RLN Recurrent Laryngeal Nerve  
ICU Intensive Care Unit

## Introduction

Globally esophageal cancer is the eight most common malignancy and sixth most common fatal with approximately 4,60,000 new diagnosis and >3,80,000 deaths annually [1]. In a disease where many deaths occur as new cases reported, thorough search has been and is being done in recent years

to offer optimal therapeutic interventional strategy for its management. The advances in technology combined with understanding of genomics and biology of esophageal cancer has allowed introduction of era of multimodality treatment. Despite these advances, a radical three field esophagectomy for most patients remains the mainstay as primary curative option for localised resectable esophageal cancers or as secondary to achieve R0 resection after down staging disease with neo adjuvant chemo therapy or after chemo radiation to confirm pathologic response at primary tumor and nodal level and to eradicate residual disease [2].

Radical esophagectomy is a demanding operation which in combination with unfavourable patient state (poor nutrition and severe co morbidities) presents an extreme burden on patient organism with high demand on whole surgical team. Though morbidity and mortality has decreased significantly in recent years, complications of surgery remain which may have fatal consequences for patients if not diagnosed and adequately treated in time.

The aim of this article is to describe management of complications of radical esophagectomy and to present outcome analysis of prospective study done on patients who underwent radical esophagectomy with 3FLND in our institution. The data analysis and results of our study and its comparison with current literature suggests that improvement in anaesthesia delivery, proper patient selection, refinements in surgical techniques and improved perioperative care are associated with decreased complication rates, morbidity and mortality thereby improving outcome in terms of overall survival with decreased rate of loco regional recurrence.

## Complications

Radical esophagectomy is a technically complex resection and reconstruction operation where margin of error is less. It is not surprising that even today many centres have increased associated complication rates. The complications are in Table 1.

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**Table 1** Complications of radical esophagectomy

Medical		Surgical	
Major	Minor	Major	Minor
<b>Respiratory</b>			
- Aspiration pneumonia	- Arrhythmias	- Anastomotic leaks	- wound infection
- Broncho pneumonia	- Psychiatric	- Conduit necrosis	- Effusion
- Respiratory failure	- Urinary tract infection	- Chyle (Thoracic duct) leak	- Pneumothorax
- ARDS	- Infective diarrhoea	- RLN palsy	- Delayed emptying
		- Bleeding	- Feeding tube related
		- Gastrointestinal	- collection (intra-abdominal)
		- Intra thoracic	
		- Gastro bronchial fistula	
		- Injury to tracheo bronchial tree	
		- Tumor rupture & contamination	
		- Strictures	
<b>Cardiac</b>			
Myocardial infarction			
Unstable angina			
- Thromboembolism			

Complication of radical esophagectomy can be broadly classified as intra or post-operative, immediate or delayed, minor or major, medical or surgical. Major surgical complications include anastomotic leak, conduit necrosis, thoracic duct leak, recurrent laryngeal nerve (RLN), bleeding (gastro intestinal, intra thoracic), injury to tracheo bronchial tree, tumour rupture and contamination. Minor surgical complications include wound infection, effusion, pneumothorax, intra abdominal collection or feeding tube related. Delayed surgical complications include strictures and delayed emptying. Major medical complications include respiratory (aspiration pneumonia, broncho pneumonia, respiratory failure, ARDS), cardiac (Myocardial infarction, unstable angina), thromboembolism, hepatic dysfunction/failure, renal dysfunction/failure and sepsis. Minor medical complications include arrhythmias, psychiatric, urinary tract infection or infective diarrhoea. Overall postoperatively most common complications are respiratory (pneumonia, aspiration), followed by conduit related (leak, necrosis) and cardiac (primarily atrial fibrillation). Some of these complications occur as a consequence of specific intraoperative events like thoracic duct injury, Recurrent Laryngeal Nerve injury, a technically compromised anastomosis and excessive bleeding.

## Material and Methods

At Tata Memorial hospital initially and later at Asian Institute of Oncology, we have been performing radical 3 field esophagectomies for over a decade and have developed technique

and expertise with a considerable reduction in mortality and morbidity and improved survival in a highly selected group of patients. A prospective study was initiated in 1997 where we choose 335 patients for evaluation. Tumors of gastro esophageal junction were excluded. Nine patients were inoperable and excluded from study. Rest 326 patients underwent radical 3 field esophagectomy with lymphadenectomy. After a learning curve the techniques and methods were modified, thus patients were divided into 3 time periods—Period I (1997 August–2000 December) included 106 patients, Period II (2001 Jan–2003 Dec) 90 patients, Period III (2004 Jan–2012 Dec) 139 patients. (Table 2)

A standard evaluation and staging protocol was followed which included routine blood test (complete haemogram, coagulation profile, renal and liver function test), contrast enhanced CT scan chest and upper abdomen, upper GI were done in all cases, endoscopy and biopsy, 2D echocardiography

**Table 2** Three field esophagectomy 1997–2010 (AIO-SS)

Pathological stage	Period I	Period II	Period III	Overall
T1N0	3	5	4	12
T2N0	6	8	16	30
T3N0	12	15	28	55
T2N1	18	10	15	43
T3N1	54	45	52	151
T4N1/2	7	5	7	19
Tx/T1S/N1 or 2	0	0	6	6
Inoperable	6	2	1	9

and pulmonary function test. Endoscopic ultra sonography was done in selected patients to assess local invasion and periesophageal nodes. In patients having lesions proximal to carina bronchoscopy was done. In bulky lesions with nodes, PET scan was done to assess extent of disease and response to neo adjuvant chemotherapy. Borderline cases with cardiopulmonary comorbidity were subjected to radionuclide (stress thallium) test. For better case selection modified TMH (SS) risk factor analysis was used as Scoring System and applied in all cases (Table 3).

Neo adjuvant chemo therapy was given to locally advance esophageal cancers (6 % patients in period I, 10 % in period II and 20 % in period III). Before surgery cardiac, pulmonary and nutritional status was optimised by spirometry, physiotherapy, nebulisation and nutritional supplements if required.

All the patients were approached surgically by classical right posterior lateral thoracotomy. In period II and III, emphasis was on preservation of azygous vein, bronchial artery and thoracic duct was ligated in all cases except patients with poor liver functions.

Enbloc resection with meticulous dissection was done to avoid blood loss, injury to RLN, tracheobronchial and thoracic duct. Abdomen and neck were approached by upper midline and left supraclavicular incisions respectively. Bilateral cervical lymph node dissection was done In lesions patients with lesion proximal to carina. In all cases stomach tube was fashioned as a conduit using NTLC 55 linear cutter staplers. Handsewn end to side two layered esophago gastric anastomosis was done in neck. The proximal end of stomach tube was wrapped anteriorly to cervical esophagus (SS technique). Patients were kept post operatively in ICU and extubated after 24 to 48 h. Feeding jejunostomy was done in all and feeds started on 1st post op day and increased gradually. The patients nutritional status was ensured by means of enteral and if required parenteral nutrition. On 7th post op day, gastro griffin swallow was performed to rule out anastomotic leaks.

Predominant histology was squamous cell carcinoma and less commonly adenocarcinoma. Final histopathology revealed 65 %–70 % cases in late stage II and early stage III. Approximately 72 % patients had positive nodal disease on pathological examination (Table 3). The study had minimal follow up of 15 months and mean follow up up to 85 months

## Data Analysis and Results

The incidence of mortality, morbidity, complication rates and loco regional recurrences were compared in 3 time periods (Table 4). It was observed that period III was associated with no mortality, minimal morbidity and decreased risk of complications with leak rates decreasing from 5 % in period I to 0 % in period III, pulmonary complications from 22 % to 9.5 %, loco regional recurrence from 12 % to 4 % and thoracic duct leaks from 3 % to 0 %. The preventive measures like bronchial artery preservation, thoracic duct ligation, opting for neo adjuvant chemotherapy for locally advanced esophageal cancers were done more frequently in period III which had impact on outcome (Table 5). The mortality and morbidity of our study was compared with other studies in literature. The pulmonary complications and leak rates were less as compared to others (Table 6). The loco regional recurrence rate and overall survival was also compared with other studies. The overall survival in our series is 55.6 %, 41 % in node +ve and 87 % in node negative patients (Table 6).

## Discussion

Radical esophagectomy with lymphadenectomy inspite of being a technically challenging surgery, lately there has been a significant improvement in post esophagectomy results in comparison with past. In a selected literature review of the 122 series from 1953 to 1978 by Earlam &

**Table 3** CA esophagus-SS modified risk factor analysis

Organ	Function test	Risk classes	Points	Relevant findings
Lung	PFT (FVC, PaO <sub>2</sub> , FEV <sub>1</sub> )	Normal	1	FVC>90 % 2 PaO <sub>2</sub> 70 mmhg
		Increased	2	FVC<90 % 1PaO <sub>2</sub> 70 mmhg
		High	3	FVC<90 % PaO <sub>2</sub> 70 mmhg
Heart	Cardiac	Normal	1	No apparent cardiac risk
		Increased	2	Increased risk
		Pari clinic opinion	High	3
Liver	Serum parameters	Normal	1	
		Increased	2	
		High	3	
General	Karlofsky index	Normal	1	>80 %, Good co-operation
		Increased	2	=80 %. Bad co-operation
		High	3	<80 %, Bad co-operation

**Table 4** Morbidity, mortality, complication rate in 3 FRE 1997–2010

Events	Period I (100)	Period II (88)	Period III (138)	Overall (326)
Mortality	6 %	2.2 %	0 %	2.75 %
Loco regional recurrence	12 %	6.4 %	4.1 %	9.7 %
Leak	5 %	2.2 %	0 %	2.4 %
Pulmonary	22 %	20 %	9.5 %	16 %
Tracheostomy	10 %	8 %	8 %	8.2 %
Blood loss	550 ml	220 ml	200 ml	360 ml
Strictures	8 %	5.7 %	1.3 %	5.3 %
Post op hemorrhage	2 %	0 %	0.7 %	0.9 %
Thoracic duct leak	3 %	0 %	0 %	0.9 %

Cunha—Melo in 1980's, the average mortality was 33 % [3]. Based on current literary references the mortality rate now is within 1.0–5.8 % and morbidity 17.9 to 58 % with a considerable improvement in overall survival and decreased loco regional recurrences [4]. The reasons for improved results are—(A) Improvement in preoperative risk assessment, patient selection and advances in preoperative staging and imaging. (B) Standardisation and refinements of surgical techniques and (C) Improvement in post-operative care and pain management. The data results from our study and other recent studies have shown that specific measures when taken preoperatively, intra operatively and post-operatively have improved results.

### Preoperative Measures

The focus has to be on better case selection. Preoperatively risk factors have to be taken into account to reduce morbidity and mortality as has been shown by Siewert. We have modified the assessment to a modified TMH (SS) risk scoring system (Table 7). This has reduced our morbidity considerably in patients with low and intermediate scores. Patients with high scores have been treated with other modalities rather than surgery.

Preoperatively various patient factors need optimisation which have been implicated to increase cardio pulmonary morbidities. These include advancing age, history of smoking, diabetes, cirrhosis, poor LFT'S (FEV1 < 65 %), poor

nutritional status, pre-existing lung diseases (COPD or infection). Measures taken are optimisation of comorbidities, nutritionally replenish patient, cessation of smoking, adequate hydration and antibiotics. Preoperative chest physiotherapy and incentive spirometry is the key. Bulky locally advanced diseases especially above tracheal bifunction have more chance of RLN injury and may require some form of neo adjuvant therapy before definitive surgery.

### Intra Operative Measures

There are various principles and measures taken to reduce morbidity and mortality and improve results. The most important pre requisite is effective synchronisation and jelling of team members with good anticipation. Secondly good anaesthesia delivery with epidural catheter placement and single lung ventilation. Thirdly standardisation of surgical techniques and principles—Aim should be monobloc meticulous R0 resection safeguarding RLN, bronchial artery with end to side esophago gastric anastomosis. The monobloc R0 resection prevents tumor implantation and decreases loco regional recurrence rates [5]. R+ resections have been shown to have bad prognosis and thus avoided. Meticulous dissection in surgical planes leads to decreased blood loss and thereby decreased rate of transfusions. Increased blood loss has been shown to be associated with an increased incidence of pulmonary complication and hospital deaths after esophagectomy [6].

Preservation of bronchial artery & RLN helps in decreasing pulmonary complications. We generally tend to preserve azygous vein and bronchial artery which lies beneath it. RLN should be dissected meticulously by avoiding traction, compression, blunt dissection and use of bipolar cautery preferred to avoid thermal injury. The principles of anastomosis followed are—end to side, between two vascular ends, mucosa involved, tension free, no redundancy and effective decompression. This reduces technically chance of leak. The transposed

**Table 5** Preventive measures in 3 FRE 1997–2010

Preventive measures	Period I (100)	Period II (88)	Period III (138)	Overall (327)
Bronchial artery preservation	NIL	78	130	208
Thoracic duct ligation	–	All	108	–
Pre-operative chemotherapy	6 %	10 %	20 % (27)	13 %

**Table 6** The mortality and morbidity of our study was compared with other studies in literature

Study	Mortality	Morbidity			
		Pulmonary	RLN Palsy	Leak	Tracheostomy
Aikyam 1994	2 %	31 %	10 %	0 %	–
Fujita et al. 1995	2 %	6 %	70 %	11 %	21 %
Kato 1991	2.6 %	9 %	14 %	33 %	–
Nishi Hara 1998	3.1 %	19 %	56 %	6 %	53 %
Altorki 2002	15 %	26 %	9 %	11 %	4 %
Ando 2000	1.7 %	22 %	–	13 %	–
Verba et al. 2012 -		20 %	10.6 %	6.6 %	–
Nakamura et al. 2008	3.3 %	19.6 %	1.6 %	9.2 %	–
Sharma et al. 2010	2.75 %	16 %	12.5 %	2.4 %	8.2 %

gastric conduit should reach neck in a tension free manner with proper lie to avoid ischemia of the conduit. There should be minimal handling of lung to reduce risk of post-operative atelectasis or pressure on heart to avoid arrhythmias. Avoid traction injury gently by handling of vessels arising from aorta and supplying esophagus. Use of harmonic and metal clips eases the job. We ligate thoracic duct in all patients except if deranged LFT's or comorbid patients. Proper feeding jejunostomy and placement of drains should be done.

### Post Operative Measures

The patient after surgery needs to be properly oxygenated and put on elective ventilation for 12–24 h. To avoid pulmonary events aim is to prevent fluid overload and thus JT feeds are started within 24 h and increased gradually. Early ambulation, bronchial toileting, intense physiotherapy, prophylactic anti-coagulant therapy, proper antibiotics, analgesics are the key. Retained secretions or vocal cord palsy may require repeated bronchoscopies or tracheostomy. Post-operative pain control by epidural analgesia has significantly improved outcome. Patients should be monitored on daily basis for any signs of complications like anastomotic leaks, chyle leaks, sepsis, thromboembolism, conduit necrosis.

**Table 7** LRR & OS after radical 3F esophagectomy

Study	Patients	Locoregional recurrence	Survival
Akiyama et al.	210	11.4 %	53 %
Lerut et al.	38	17.6 %	45 %
Fujita et al.	90	30 %	54 %
Sharma et al.	326	9.7 %	55.6 %
Altorki et al.	80	9.7 %	51 %

### Management of Post Operative Complications

#### Pulmonary Complications

Respiratory complications variably defined as atelectasis, pneumonia, aspiration pneumonitis, ARDS, pulmonary thromboembolism and respiratory insufficiency are the most common post-operative complications after radical esophagectomy [7]. The incidence of pulmonary complications ranges from 17 % to 50 % in literature (21 % at MSKCC, Siewert et al. 22.9 %, Baba et al. 23.6 %, Vrba et al. 20 %, Mariette 19.3 %, Ott et al. 44.4 %, Nakamura et al. 19.6 %) [8–10]. Published literature confirms that pulmonary complications are most often associated with post-operative mortality. Rizk et al. at MSKCC reported that if patients had pneumonia as one of their complications, the mortality rate was 18 % vs 1.8 % if they did not [11]. Atkinson et al. reported 3.8 % mortality due to pulmonary complications in 379 patients who underwent radical esophagectomy with dominating cause being pneumonia in 54 %, subsequent respiratory failure due to pneumonia was cause of death in 81 % [12]. Proper patient selection, pre and post-operative pulmonary care (physiotherapy, incentive spirometry) and intra-operative measures (bronchial artery preservation, handling lung with care) help to minimise the risk for pulmonary complications after radical esophagectomy. ARDS and respiratory insufficiency may require prolonged orotracheal intubation or transient post-operative tracheostomy. Multiple selective bronchoscopic aspirations (toileting) along with good antibiotic coverage are required in aspiration pneumonitis. Pulmonary thromboembolism warrants diagnosis by CT angiography or ventilation perfusion lung scan, Doppler studies to rule out DVT of lower limbs and effective treatment with thrombolytic therapy.



## Anastomotic Leaks

Anastomotic leaks are less common than respiratory complications, but their impact is potentially more severe. The average leak rate in literature is between 8 and 155 [13]. Rizk et al. investigated surgical complications in 510 patients between 1996 and 2001 showing that there was increased mortality rate (12 %) in patients who had leak compared with 4 % who did not [14]. Nakamura et al. reported 9.2 % leak rates in 184 patients operated between 1991 and 2000 [15]. At MSKCC anastomotic leak rate is 14.2 % During perioperative period presence of anastomotic leak is associated with other complications including respiratory, cardiac, infectious, renal and thrombotic. Anastomotic leaks can be smaller or large (output based), subclinical (detected by contrast study only) or clinically apparent with increased foul saliva in neck drain, neck wound inflammation or collection. Major leaks present within first 5 days with severe sepsis. Patients can have unexplained tachycardia, arrhythmias, flushed face, effusion, hydropneumothorax, breathlessness with decreased oxygen saturation and may require inotropic or ventilator support. Minor leaks are usually after 7–8 days and usually present with neck wound sepsis, collection, effusion.

High index of suspicion, timely diagnosis and appropriate intervention is the key in management. Patient with small leak with good performance status are managed conservatively with nil by mouth, IV fluids, nasogastric tube drainage, antibiotics, USGOR CT guided drainage of septic foci or collection, chest physiotherapy to keep lungs up, high protein enteral feeding or TPN. Serial contrast study (gastrograffin or CT scan) and endoscopy by experienced gastroenterologist are required. If leaks are major with associated deterioration of general condition (sepsis) immediate re-exploration is done. Esophagectomy and gastrostomy is done after dismantling anastomosis completely followed by second stage coloplasty or jejunal interposition.

## Conduit Necrosis/Gangrene

One serious complication which may have fatal consequences is necrosis of the transposition. Wholly described necrosis of transposition in 0.8 % in sample of 710 patients [16]. The most common cause of necrosis is ischemia which is more frequent in coloplasty than gastroplasty. This was confirmed by Moorehead and Wong in a sample of 760 patients who underwent radical esophagectomy. Gastroplasty ischemia was described in 0.5 %, in case jejunal interposition in 11.3 % and with coloplasty in 13.3 % [17]. Necrosis of transposition is characterised by a total alteration of state of patient (unexplained tachycardia, respiratory failure, increase in inflammatory factors and increased lactate). Patient may die to septic shock if not managed properly. The diagnosis is made endoscopically and by surgical

revision. If confirmed extirpation of the transposition is indicated with a cervical esophagostomy and a feeding jejunostomy. In second phase, reconstruction of gastro intestinal tract by means of coloplasty is performed.

## Thoracic Duct Leak

It usually occurs in bulky mid esophageal lesions or surgery post chemo radiation where anatomical planes are distorted. The reported incidence of thoracic duct leak in literature varies from 2 to 10 % [18]. The diagnosis of chyle leak is subjective and diagnostic criteria may vary. A milky appearance of the drainage fluid is often the initial clue. If euteral feed is restricted drainage fluid becomes clear or decreases. The drainage can be evaluated for characteristics such as triglyceride (>110 mg/dl), presence of that, specific gravity cholesterol : Triglyceride ratio, alkaline pH, lymphocyte count and identification of chylomicrons upon lipoprotein electrophoresis. Some opt for methylene blue test or adding either to fluid which becomes clear. The chyle leak can be minor or major. Most of the leaks heal spontaneously on conservative treatment. Goal of nutritional therapy is to decrease production of chyle fluid, replace fluid and electrolytes (as patient is kept on nil by mouth) and maintain or replete nutritional status and prevent malnutrition. Fat free diet, medium chain triglycerides (MCT) are often recommended as they are absorbed directly across mucosa into portal system and doesn't require transport via lymphatic system. Patient may require TPN also. In major leaks (>1 l output/day for 5 days) or persistent leak for >2 weeks, re-exploration is required. With dry field and sharp pair of eyes, surgeon identifies thoracic duct and ligates it juxta to aortain lower thoracic areas.

## Recurrent Laryngeal Nerve Palsy

The literature on paresis of RLN varies between 4 % (Nagel et al.) and 67 % (Nishimaki) [19]. Left RLN injury is more frequent than right. RLN injury can be temporary or permanent. Temporary RLN injury usually recovers spontaneously within 2–3 months with compensation of opposite vocal cord. Permanent RLN injury may require medialisation of cord by Teflon injection or thyroplasty.

## Conclusion

Radical esophagectomy with 3 FLND is a formidable operation with potential to improve survival and decrease loco regional recurrences. The complications of radical esophagectomy must be identified and treated in time. The advanced in pre-operative diagnostic staging and patient selection, good

instruments, good team work (anaesthetist, surgeon, Nurses, ICU), good knowledge of fluid and electrolytes, refinements in surgical techniques have considerably decreased complication rates. A considerable progress has been made to manage complications of radical esophagectomy.

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