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Akiyama Procedure as a Surgical Option for Esophageal Cancer

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Abstract
Background
The purpose of this study is to introduce our experience with the Akiyama procedure as a surgical option for treatment of esophageal cancer in the Mother Theresa Hospital Center of Tirana, Albania. Selection of the suitable site for anastomosis after esophagectomy, whether cervical or thoracic is the key for optimal oncological results. The goal is to minimize recurrence in oncological patients and to avoid complications related to surgery. Controversy still exists among surgeons as the optimal site for anastomosis as well as whether the anastomosis is done manually or with a stapler.
Material and methods
From October 2018 to June 2021, 27 surgical interventions of esophageal cancer were performed in our surgical unit. In 15 patients, subtotal esophagectomy Ivor-Lewis with a mediastinal esophago-gastric anastomosis was performed. In 8 patients, distal esophagectomy and proximal gastrectomy with an abdominal esophago-gastric anastomosis was performed. In 4 patients, subtotal esophagectomy with a cervical esophago-gastric anastomosis, Akiyama procedure was performed. In this study we are evaluating the Akiyama procedure with description of the technique, patient criteria of inclusion, oncological protocol and postoperative care.
Discussion
In our practice we used chemotherapy and radiotherapy as part of a multimodality treatment plan. All of our patients with carcinoma had radiation and chemotherapy prior to surgery. The use of stapler devices in cervical anastomoses in some studies is linked with higher rate of leakage but we consider it a preferential choice of the surgeon. We opted for a one-layer esophagogastric anastomosis in the neck as shown in some studies instead of the two-layer technique because of lower rates of stricture formation. The level of exposure in the cervical route is advantageous in making an accurate anastomosis. In our patients we used the retrosternal space for esophageal replacement to avoid local tumor recurrence in the posterior mediastinum.
Conclusion
As in other cancers there is a mandatory evaluation in congruence to the guidelines in order to each patient have a surgical or adjuvant therapy according to its stage. As per guidelines patients in a T1-2, N0 stage are treated with surgery alone and a close follow up for recurrence and patients in a T3 or N1/M1 stage should be considered for adjuvant therapy prior to surgery. In patients that have extensive disease and are not surgical candidates are considered for chemotherapy and radiation alone. It is advised that the type of surgery performed is the one in which the surgeon is more experienced and has the best outcome in terms of surgical strategy in terms of morbidity and mortality.
Keywords: General surgery, Esophageal cancer, Akiyama procedure, Cervical esophago-gastric anastomosis.
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1. Introduction

Statistical data shows that worldwide esophageal cancer is the eighth most common cancer overall. Being the sixth most common cause of death related to cancer, with an estimated 400 000 deaths in 2012, in percentage 4.9% of deaths from cancer. Statistics also shows that 80% of esopgaheal cancer cases globally occur in less developed countries. The incidence rates in men are more than double compared to women, with a male-to-female ratio of 2.4:1. Esophageal cancer has very poor survival rate (1). Incidence and mortality trends changed considerably across Europe over the last decades, with a difference between sexes and the histological types, the main two types are squamous cell carcinoma and adenocarcinoma. (2)

The rates of mortality and morbidity in operated patients are in decline in recent years due to the improvement of surgical tools and perioperative management. Nevertheless, in comparison with other gastrointestinal cancer surgeries, esophageal cancer surgery has yet higher mortality rates that varies between

3.4–8.3% [3].

The most feared complication is the anastomotic leak, the aetiology of which is connected to various factors such as if the anastomosis location weather is cervical or thoracic, if it is performed in a single or double layer, if it is carried out with the aid of a stapler or done manually, the stage of the tumour, use of radiotherapy or chemotherapy prior to surgery and the serologic levels of haemoglobin and albumin. Studies shows the importance of prognostic factors correlated to the anastomosis such as vascularisation of the remnant esophageal stump, and poor oxygenation of the gastric submucosal tissue due to an insufficient collateral circulation of the submucosae. [10][20]. In congruence with the studies present in literature we evaluated haemoglobin levels and corrected them, as well as administered parenteral nutrition as needed in each of our patients with esopgaheal cancer. In our group, 2 of the patients had a weight loss of 20%, with a mean weight loss value of 10.2 ± 5.1 kg. Various studies shows that the reconstruction after resection is performed usually with the stomach. [4] Using the stomach for the anastomosis has a technical facility of reconstruction by having a sufficient length for substitution of the resected esophagus.

A complication with a high mortality rate, regardless to the anastomosis location, is the necrosis of the gastric stump with a leak of the gastric content that contaminates the anastomotic area. Some studies favour a cervical esophago-gastric anastomosis in comparison to the thoracic anastomosis, in spite of an increased leakage incidence, higher stricture formation and an increased possibility of damaging the recurrent laryngeal nerve. Other authors deny a difference of leakage rates, stricture formation, a dehiscence in the anastomosis site, or an improve of long-term survival. [6][7]

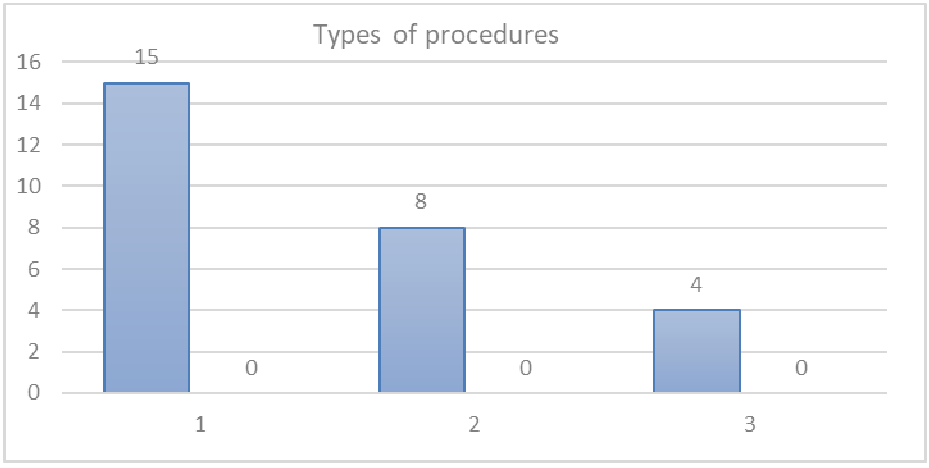
The main focus of studies for esophageal resection is an excursus of the techniques in each specific clinical case. [8] In the present study we have evaluated the results of the Akiyama procedure, the tree incisions technique including a right thoracotomy, with the anastomosis located in the neck.

2. Materials and methods

The time frame of our surgeries is from October 2018 to June 2021, with 27 resections for esophageal cancer performed in The First Surgical Clinic, UHC “Mother Teresa”. In 15 patients, subtotal esophagectomy Ivor-Lewis with a thoracic esophago-gastric anastomosis was performed. In 8 patients, distal esophagectomy and proximal gastrectomy with an abdominal esophago-gastric anastomosis. In 4 patient, subtotal esophagectomy with a cervical esophago-gastric anastomosis (Akiyama Procedure) was performed. It is the first time in the history of Albanian Surgery that this type of surgery is performed.

In this study we are considering just the Akiyama procedure with description of the technique, patient criteria of inclusion, oncology treatment protocol and postoperative care. Every patient had esophago-gastroscopy and histologic analysis of carcinoma prior to surgery. Of the 4 patients undergoing esophagectomy, 1 patient had adenocarcinoma and 3 patients had squamous cell carcinoma. 3 of the patients were male with a median age of 61.75 years as shown in the table below with patient demographic and data.

Graph 1. Types of esophageal procedures performed



Legend: 1) Ivor Lewis procedure, thoracic esophago-gastric anastomosis - 15 cases. 2) Distal esophagectomy - 8 cases, abdominal esophago-gastric anastomosis. 3) Akiyama procedure - 4 cases, cervical anastomosis. From total number of 27 patients.

Table 1. Akiyama procedure patients data

Age	
Mean ± SD	**61.75 ± 6.65**
Range	**52 – 67 aa**
Gender	3
Males	1
Females	
Co-morbidity	
Hypertension	2
Respiratory	1
Pulmonary test function	
Obstructive	1
Normal	3
Chest measures	
(+) positive	3
(–) negative	1

3. Chemotherapy and radiation protocol

As part of our treatment protocol each patient with carcinoma of the esophagus had a feeding jejunostomy and neoadjuvant chemotherapy and radiotherapy treatment prior to surgery. For locally advanced esopghageal cancer the standard treatment is a neoadjuvant chemo-radiotherapy based on meta-analyses and CROSS trial. [23][24][25] It shows an improvement of the negative margin of resection, a better pathologic response and an improvement of long-term survival. In some studies patients having neoadjuvant chemoradiotherapy prior to surgery showed more serious postoperative complications [26] and more deaths not related to cancer progression, but no significant difference on mortality was observed among patients with neoadjuvant chemoradiotherapy in other trials and meta-analysis. [27][28]

Regarding our treatment protocol in collaboration with the Oncology department in UHC “Mother Teresa” Hospital, Tirana, is as follows:

Patients were treated with 3-Dimensional Conformal Radiotherapy (3DCRT) and Intensity Modulated Radiotherapy (IMRT), with a total RT dose 45 Gy (1.8 Gy/fraction) in concomitance with weekly cisplatin 30 mg/m2 in squamous cell carcinoma of the esophagus and with capecitabine 800 mg/m2 in adenocarcinoma of the esophagus.

Patients underwent CT simulation and were treated in the supine position. Patients with lower third thoracic esophagus or EGJ are required to be null per os for at least 3 – 4 hours prior to CT simulation and in each treatment session. The GTVt included primary tumor and GTVn metastatic lymph nodes. Clinical target volume (CTV) and planning target volume (PTV) were contoured according the expert consensus contouring guidelines. [29][30] CTV is created from GTV+ 3 cm expansions in SCC of the esophagus and 5 cm in AC of the esophagus proximally and distally, and 0.5-1 cm radially. PTV is CTV + 1 – 2 cm proximally and distally and 0.5 – 1 cm radially. Patient treatment response was evaluated up to 4 weeks post RT treatment with CT scan and upper endoscopy and planned for the post neoadjuvant surgery.

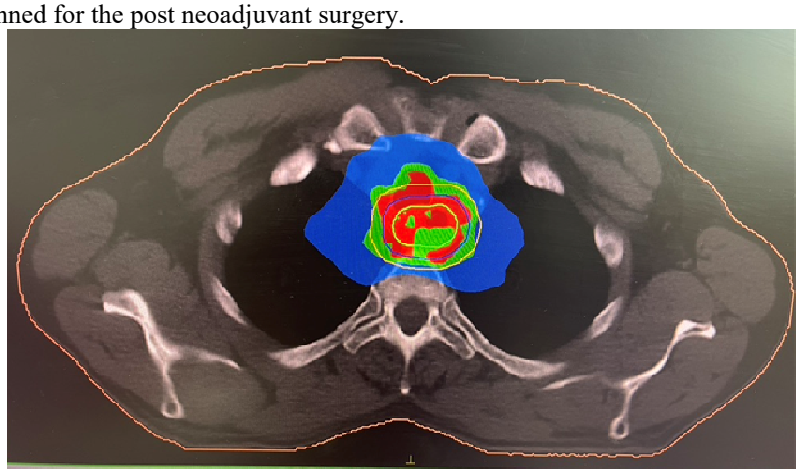


Figure 1. Locally advanced squamous cell carcinoma of upper thoracic esophageal cancer treated with IMRT. Axial CT image of the IMRT treatment planning showing the 100%, 95% and 50% of prescription dose distribution.

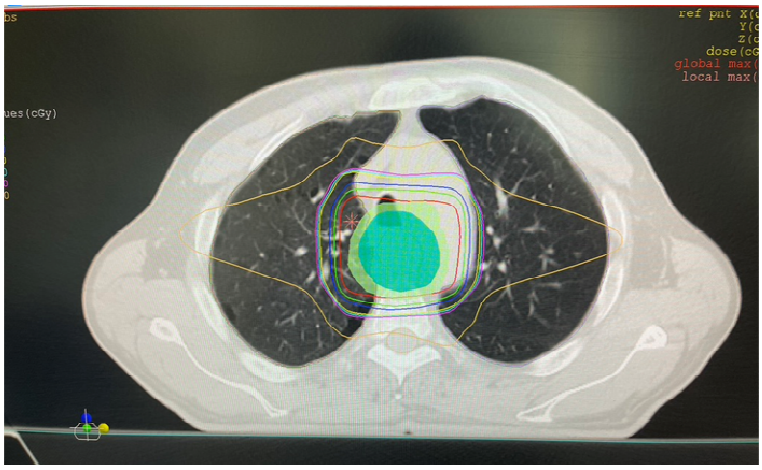


Figure 2. Locally advanced esophageal squamous cell carcinoma of middle esophageal cancer treated with 3DCRT. Axial CT image of the 3DCRT treatment planning showing the isodose distribution.

Our strategy is a combined neoadjuvant and surgery protocol. The pre-operative evaluation included chest röntgenogram, barium swallow with evaluation of the stomach for gastric conduit, and computed tomographic scans of the chest and the abdomen. The inclusion principle for an Akiyama procedure in our patients was cancer of the esophagus for which a tube gastroplasty with the anastomosis located in the neck was considered proper. In each patient a preoperative calculation of the necessary distance from the end of the tumor and the anastomotic locus in the neck was made. Criteria of exclusion included prior gastric resection, presence of a metastases in other organs or locally advanced diffusion of the primary tumour to the adjacent organs. Such patients were opted for chemotherapy and radiation alone.

4. Surgical technique

All surgeries are performed in general anesthesia with the use of a single lung ventilation by using a left-sided double lumen endotracheal tube. After the patient is prepped and draped the surgery starts with a right posterolateral thoracotomy in the fifth intercostal space. Dissection is continued along the mediastinum starting from the diaphragm to the apex of the chest, close to the aorta, the left pleura, the pericardium and towards the superior vena cava, removing fatty tissue, lymph nodes, esophagus and azygos vein. Two drains are positioned in the thorax and the patient is positioned in the supine position. The abdominal phase begins with a midline incision dissecting the fatty tissue and lymph nodes along the superior portion of the abdominal aorta following with dissection near the celiac trunk. Mobilisation of the duodenum and head of pancreas is performed.

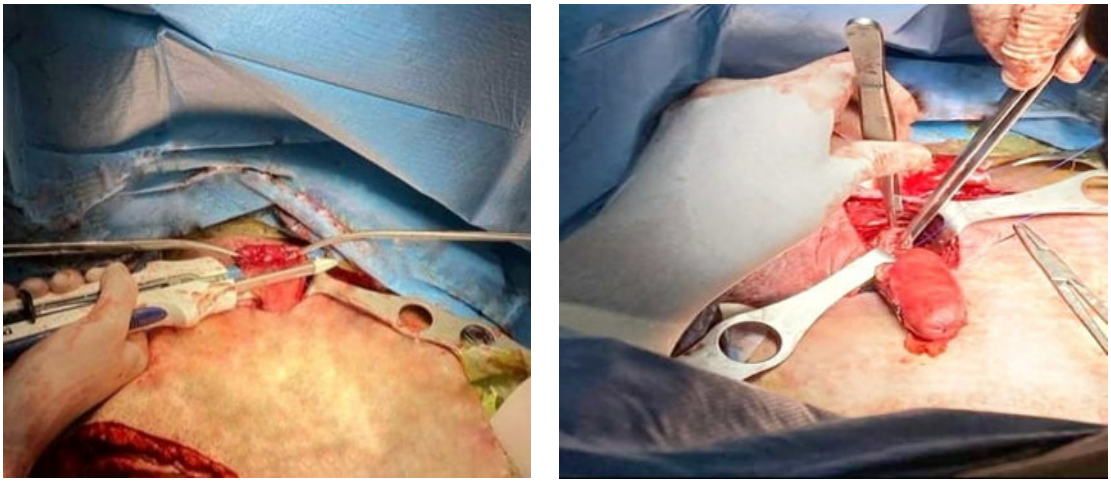


Figure 3. A) Cervical anastomosis using a linear stapler. B) Cervical anastomosis.

Pyloroplasty is performed to avoid reflux of duodenal content. The spleen was not removed in neither of our cases. It follows with creation of a gastric tube with the help of serial linear staplers. The right gastric artery and the gastro-epiploic arteries provide the necessary vascularisation of the conduit created. In order to prevent subsequent vascular compromise of the conduit, a hiatal phrenotomy is done. The cervical phase follows with an incision parallel to the medial part of the left sternocleidomastoid muscle. The gastric tube is gently pushed through the mediastinum and then delivered to the neck. Necessary adjustments of the length are made with

careful calculation of a tension-free end to end anastomosis between the gastric tube and the esophagus using a circular stapler of 25, 28 or 31 mm. The 2 rings from the circular stapler after it was applied were checked for full integrity and are sent to pathology. All 4 patients with carcinoma of the esophagus had tumor-free proximal and distal resection margins as well as tumor free stapler rings after anastomosis.

To check the integrity, the anastomosis is put under saline solution and air is inflated through the nasogastric tube. In the presence of a leak or an incomplete anastomotic ring, the defect is oversewn with an absorbable 4–0 suture. A subtotal esophageal resection is performed with a cervical esophagogastric anastomosis and retrosternal positioning.

As studies shows a complete lymph node excision is mandatory in the mediastinum and in the abdomen despite of tumour anatomic location. Thoracic and abdominal part of the esophagus is resected with excision extended to the cardia and the proximal portion of the greater curvature of the stomach. The greater curvature is involved in the resection not just to form the tubular stump that replaces the esophagus, but also due to the lymph node involvement, intramural vascular spread and possible satellite lymphnodes. We use the right thoracotomy in order to have an optimal exposure and a clear view of the posterior mediastinum. Extension of the resection until the cervical portion of the esophagus is necessary in order to avoid a cancer positive surgical margin. [17] Regarding the lymph node dissection, care must be taken during manipulation close to the right recurrent nerve in dissection of the left para tracheal nodes. Nodes around the ligamentum arteriosum (Botalli) are also dissected because they are occasionally found positive for carcinoma. The lymph nodes in the middle mediastinal area that need dissection are tracheobronchial, paraesophageal, and pulmonary hilar nodes. Lower mediastinal lymph nodes are the paraesophageal and diaphragmatic nodes. Dissection is continued with the paraaortic nodes which are difficult to differ from paraesophageal nodes.

Anatomically the superior gastric lymph nodes are considered the nodes of the lesser curvature of the stomach, nodes of the left gastric artery and the paracardiac nodes which also need dissection. Dissection must be extended also to the lymph nodes of the celiac axis. On the other hand, lymph nodes of the hepato duodenal ligament and of the lienal hilus don't need dissection as they are not involved. Same for the lymph nodes of retro pancreatic and paraaortic location, as they are considered distant stations. Various studies are conducted with the aim of finding a correlation between the location of the tumour and frequency of the positive node stations. For example, in tumors located in the middle esophagus the stations involved are the ones in the mediastinum and in the abdomen. Such studies show that for tumours located in the upper portion of the esophagus the metastasis rate is up to 31.8% of all patients. [32]

Nevertheless, lymph node resection is spite of tumour location complete is mandatory in the mediastinum and abdomen. In the table below is shown an overview of our patients, pre-radiation and therapy and the post-surgical anatomopathological findings. Lymph nodes were found positive in all of the cases. In 2 cases lymph nodes were positive in the superior mediastinum. One case with superior gastric lymph nodes and 2 cases had positive nodes located in the middle mediastinum as shown in the table below. (Table 2)

Table 2. Patient disease stadification and lymph node involvement.

	p-TNM		LN (+) location
Patient 1	pT3N1M0	SCC	1 superior mediastinal
Patient 2	pT3N2M0	SCC	1 superior mediastinal, 1 superior gastric
Patient 3	pT4N1M0	SCC	Middle mediastinal
Patient 4	pT3N1M0	EAC	Middle mediastinal

After appropriate resection and anastomosis surgery follows with drains positioned in the abdominal cavity. The mean operative blood loss in our cases was 550 cc ± 150 cc and two patients received postoperative blood transfusion.

5. Post-operative regimen

Postoperatively the patients are admitted in the Intensive Care Unit. All of our patients received perioperative antibiotics and deep venous thrombosis prophylaxis. After surgery, patients remained intubated overnight. In the fourth postoperative day the thoracic and abdominal drains were removed. Nasogastric tube is placed with its tip just above the pylorus and parenteral nutrition is used for 7 days. Anastomosis integrity and any possible leakage is verified in the seventh postoperative day by x-ray with water soluble contrast per os. No leakage was observed in neither of the patients, and when the nasogastric tube delivered 150 - 200 mL, the patients started fluids, followed by a soft diet. Our protocol continues with a regular diet on the ninth postoperative day. In collaboration with the oncologist and in congruence with the post operatory histopathologic report, all patients were referred to adjuvant chemotherapy and radiotherapy, continued with and a close follow up for possible recurrence. Such following was done biweekly in first month, bimonthly in the following three months, monthly for six months, and every six months thereafter. A gastroscopy was performed in all patients as part of the post operatory follow up and no stricture was shown. With a CT scanning of the chest and barium swallow all patients were studied for possible stenosis. Median range of anastomosis location in the neck varies from 16 - 20

cm from the incisors. Our patients had a hospital stay of 17 ± 2 days (range 17 – 19 days). One patient developed pneumonia that was treated by antibiotics, good oxygen ventilation and nebulizer.

6. Discussion

Surgery in carcinoma of the esophagus as for all cancers, has the primary aim to resolve from the disease and improvement of the overall survival time. The other important complication to avoid is stenosis at the anastomotic site and a proper food intake. The resection and the afterwards reconstruction technique must be cautious to lower the risk related to surgery as a puzzle that has in consideration the patient general condition, tumour location with optimal oncologic resection and the preference and experience of each surgeon. Studies confirm that complete lymph node resection is mandatory in the mediastinum and in the abdomen regardless of the location of the tumour. A surgical strategy is important in order to be oncologically correct. We choose a right thoracotomy to expose the entire mediastinum. Therefore, a trans hiatal esophagectomy was not preferred in our practice. The right thoracotomy has the advantage of an excellent exposure and therefore a clear view of the structures which in turn, minimizes the margins of error. Our practice consists in using the retrosternal space as a safe route for esophageal substitution in order to avoid local tumor recurrence in the posterior mediastinum. For upper esophageal cancer a thoracic anastomosis is not suggested for the deficient mediastinal lymph node excision. [19]

The decision of performing an anastomosis in the neck or a thoracic one is still open to discussion among surgeons. When the anastomosis is located in the neck the surgeon has the possibility to extend the margins of resection with a more common but less dangerous leakage as well as an increased risk of injury of the recurrent laryngeal nerve. In the other hand the anastomosis in the thorax comprehends less esophagus removed with smaller margins of resection and a lower but more threatening leakage rate. The level of exposure in the cervical anastomosis is advantageous in making an accurate anastomosis. [18] In our patients we used the retrosternal space as the space for esophageal replacement in a way to avoid local tumor recurrence in the posterior mediastinum.

The use of stapler devices in cervical anastomosis in some studies is linked with higher rate of leakage but we consider it a preferential choice of the surgeon. Surgeon's individual preference and experience are probably more important than the particular method chosen for anastomosis. [13] We opted for a one-layer esophagogastric anastomosis in the neck as shown in some studies (12) in comparison with the two-layer technique because of lower rates of stricture formation. There is a relation between complications and to the anastomosis site as patients with cervical anastomosis have a major incidence of anastomotic leak or recurrent laryngeal nerve paresis. In the other hand patients with anastomosis located in the thorax may develop pulmonary related complications, a possible chyle leak due to a meticulous lymph node excision, and dumping syndrome.

Bardini and associates [14] found no leakage difference when comparing running and interrupted suturing techniques in single-layer cervical anastomosis. Other studies as the one by Beitler and Urschel [15] showed results from four randomized trials in matching stapled and hand-sewn anastomosis in esophageal cancer with no difference in anastomotic leak incidence (9% and 8%). Anatomically the esophagus' lack of a serosal layer and a fragile outer muscle layer which is possibly linked to the poor ability of holding sutures. This reduced ability in holding a suture may be linked to the higher leakage rate in the running suture technique. [16] In our practice we used chemotherapy and radiotherapy as part of a multimodality treatment plan. All of our patients with carcinoma had radiation and chemotherapy prior to surgery. There has always been a concern among medical community of the possible correlation to complications and the adjuvant therapy prior to surgery but most studies do not support the idea of a negative impact. [21]

7. Conclusion

As in other cancers there is a mandatory evaluation in congruence to the guidelines in order to each patient have a therapy surgical or adjuvant related to stadification. As per guidelines patients in a T1-2N0 stage is treated with surgery alone and a close follow up for recurrence and patients in a T3 or N1/M1 stage should be considered for adjuvant therapy prior to surgery. [22] In patients that have extensive disease and are not surgical candidates are considered for chemotherapy and radiation alone. Therefore, selection of surgical candidates must be accurate in order to minimise the post operative complications. Resection in esophageal carcinoma is generally palliative and rarely curative, ergo the purpose in minimizing morbidity and mortality is more demanding than in other surgeries that have higher survival rate. It is advised that the type of surgery performed is the one in which the surgeon is more experienced and has the best outcome in terms of surgical strategy in terms of morbidity and mortality.

Conflict of interest

The author(s) declare(s) that there is no conflict of interest. The authors alone are responsible for the content and writing of the paper.

Financial disclosure
There is no financial support to this study.

Ethical aspect
Informed consent was obtained from all participants in the study and all procedures were conducted in accordance with the Declaration of Helsinki.

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