COMPARISON OF RADIONUCLIDE SCAN AND CONVENTIONAL CONTRAST STUDY IN DETECTION OF ESOPHAGEAL ANASTOMOTIC LEAKS – A PROSPECTIVE STUDY

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DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT OF THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY FOR THE DEGREE OF M.S. BRANCH I - GENERAL SURGERY EXAMINATION TO BE HELD IN MARCH-2007

<u>Certificate</u>

This is to certify that **“Comparison of radionuclide scan and conventional contrast study in detection of esophageal anastomotic leaks – a prospective study”**, which is being submitted as thesis requirement for M.S. Degree Branch I – General Surgery examination of the Dr. M.G.R. Medical University of Tamil Nadu, is a bonafide work of the candidate – **Dr. Sujith Varghese Thomas**.

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Certificate

This is to certify that the topic entitled **"Comparison of radionuclide scan and conventional contrast study in detection of esophageal anastomotic leaks – a prospective study"** is a bonafide work done by **Dr. Sujith Varghese Thomas**, post graduate in General Surgery of Christian Medical College, Vellore. This work has been carried under my guidance and supervision in partial fulfillment of the regulation of Dr. M.G.R. Medical University of Tamil Nadu for Master of Surgery- Branch I (General Surgery) examination to be held in February 2007.

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CONTENTS

1. INTRODUCTION AND JUSTIFICATION

Esophageal resection and reconstruction remain a major therapeutic challenge for surgeons involved in the care of patients with benign and malignant disease of esophagus. Despite major advances in postoperative care, operative mortality rates worldwide remain high. Much of the operative mortality is related to complications of anastomotic leak.

In a majority of esophageal surgeries, the anastomosis involves another segment of the esophagus, stomach, jejunum or colon. Anastomoses in operations of the stomach like total gastrectomy or proximal gastrectomy also involve the esophagus.

One of the commonest complications encountered in patients after the above operations are an anastomotic leak. These leaks can lead to severe morbidity, increased hospital stay and cost and increased mortality. The crucial factors in the management of anastomotic leak are to recognize it earlier even at a sub clinical stage and act accordingly. Conservative management like delaying oral feeds and drainage techniques can be employed. However, rapidly progressing clinical scenario mandates aggressive approach.

Contrast esophagography is the investigation of choice for detecting sub clinical anastomotic leaks when done from 7^{th} to 10^{th} postoperative days. Barium or water soluble contrasts are being used for the same. Our institution routinely performs thin barium contrast studies between the 7^{th} to 10^{th} postoperative day. Due to its hygroscopic property, water soluble contrast agents causes dilution of the contrast, thereby decreasing its sensitivity and specificity. Barium is more sensitive than water soluble contrast agents but is known to cause complications such as barium peritonitis and can interfere with repeat scans. Moreover, various studies show that the numbers of false negatives are high.

Technetium scans are being used for diagnosis and evaluation of esophageal motility disorders and gastroesophageal reflux disease. There is no data of its use in detection of sub clinical anastomotic leaks in current literature. This study is to evaluate the diagnostic efficacy of technetium scans in detecting sub clinical leaks in comparison to barium contrast studies. It also aims at evaluating the reliability, limitations, disadvantages and complications of a Technetium sulphocolloid scan.

2. AIMS OF THE STUDY

To evaluate the diagnostic efficacy and feasibility of Technetium sulphocolloid scans in comparison to esophageal contrast studies in diagnosis of sub clinical anastomotic leaks following esophageal anastomosis.

3. OBJECTIVES OF THE STUDY

1. To prospectively evaluate the feasibility of technetium sulphocolloid studies in the diagnosis of sub clinical anastomotic leaks.

2. To quantify the agreement that technetium sulphocolloid scans have with contrast studies in diagnosis of sub clinical anastomotic leaks.

3. To evaluate advantages and disadvantages of technetium sulphocolloid studies in terms of reliability, patient acceptance and cost in comparison to contrast studies.

4. To characterize Tc-99m sulphocolloid scan findings that would describe a sub clinical anastomotic leak.

5. To correlate patient dependant surgical factors with development of anastomotic leaks.

4.1 Microstructural anatomy of esophagus

The esophagus is a mucosa-lined muscular tube that lacks a serosa and is surrounded by a layer of loose fibroalveolar adventitia. Beneath the adventitia is a layer of longitudinal muscle, overlying an inner layer of circular muscle. Between the two muscular layers is a thin intramuscular septum of connective tissue that contains the blood vessels and ganglion cells (Auerbach plexus). Both the longitudinal and circular muscle layer of the upper third of the esophagus are striated whereas the layers of the lower third are smooth. The fatty and relatively thick submucosa permits considerable mobility of the esophageal mucosa[1]. The submucosa contains

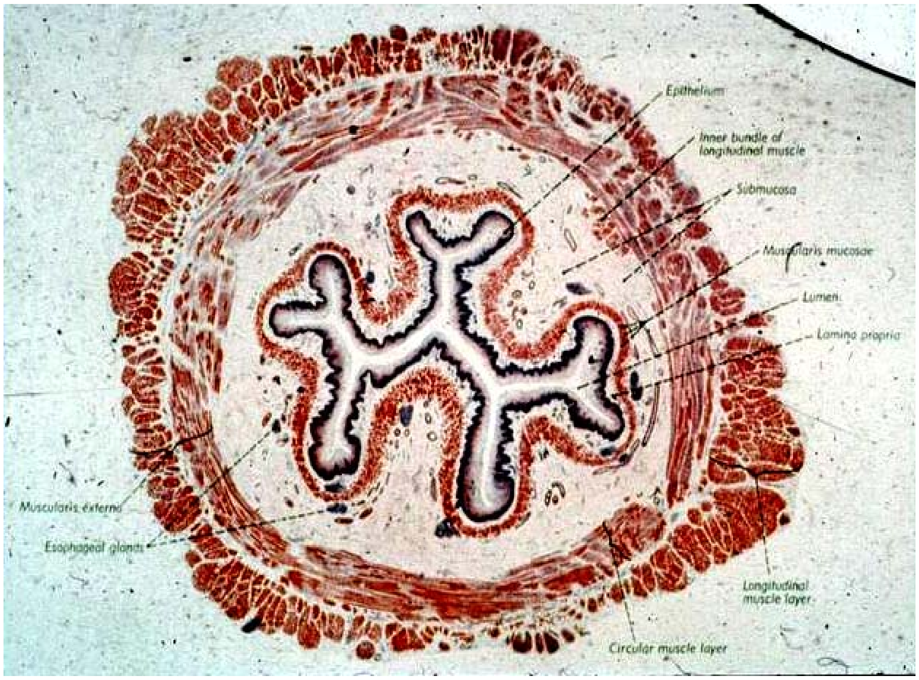

Fig 4.1 Histology of esophagus

the mucous glands, blood vessels, the Meissner neural plexus and an extensive lymphatic network. The esophageal mucosa consists of squamous epithelium except for the distal 1 to 2 cm, which is junctional columnar epithelium. Occasionally, ectopic gastric mucosa may be found throughout the length of the esophagus[2]

4.2 Blood supply and venous drainage of esophagus

Esophagus is supplied by numerous segmental arteries, all of which contribute to the extensive capillary network. The cervical esophagus receives blood from the superior thyroid artery as well as the inferior thyroid artery of the thyrocervical trunk, with both sides communicating through collateral vessels.

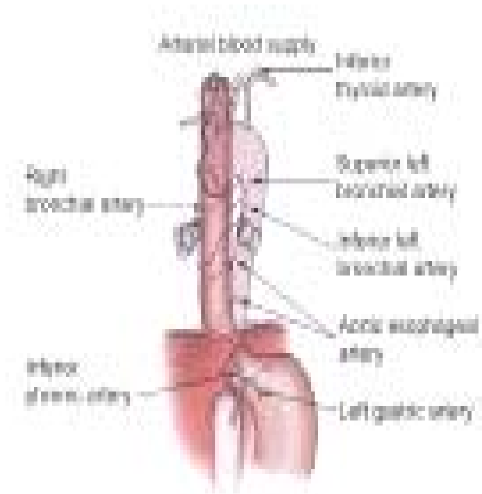

Fig 4.2 Arterial blood supply of esophagus

The major blood supply of the thoracic esophagus is from four to six aortic esophageal arteries, supplemented by collateral vessels from the inferior thyroid, intercostal and bronchial, inferior phrenic and left gastric arteries[2]. The aortic esophageal arteries terminate in fine capillary networks before they actually penetrate the esophageal muscle layer. After penetrating and supplying the muscle layers of the esophagus, the esophageal capillary network runs longitudinally in the submucosa. Therefore, the mucosa receives poor blood supply. This entails that rough handling or wide mobilization of the esophagus may imperil its blood supply, especially over its main extent where the aortic branches are distributed in a segmental manner[3]. They are slender, tenuous vessels and this makes it possible to mobilize the intrathoracic esophagus by blind digital dissection from the suprasternal notch above and from the esophageal hiatus below during certain cases of esophagectomy[3].

The veins of the cervical esophagus drain into the inferior thyroid vein and then, the brachiocephalic veins. The veins in the left side of the thoracic esophagus drain into the brachiocephalic vein via the left hemiazygous system. On the right side, the drainage is through the azygous system into the superior vena cava. At the cardio esophageal junction, venous drainage of the esophagus may be into the coronary, splenic, retroperitoneal and inferior phrenic veins which connect with the portal and caval systems. In portal hypertension, the cardio esophageal junction is the site of esophageal varices[2].

Anastomosis of the esophagus to any other part of the gastrointestinal tract such as stomach, small bowel or colon is prone to leakage from the suture line. This is because of its poor mucosal blood supply, the absence of a serosal covering and the friability of the mucosal layers[2]. It is particularly important to include the mucosal layer in suturing the esophagus. Most surgeons use an ‘all-coats’ interrupted suture when anastomosing the esophagus[3].

4.3 Esophageal operations

Esophageal operations are some of the most major procedures of the gastrointestinal tract. The postoperative morbidity and mortality rates remain high in spite of the advance in perioperative and postoperative care. The mortality rates are as high as 8%.

Esophageal carcinoma continues to be challenge to the surgeon and oncologist in treatment. The classical presentation is one of progressively increasing dysphagia, initially to solids and later to liquids, associated with loss of weight and appetite. Advanced cases may also present with hematemesis, hoarseness of voice and metastatic symptoms. Diagnosis is made by esophagoscopy and endoscopic biopsy. As with most other malignant conditions, there are 3 modalities of treatment – surgery, chemotherapy or radiotherapy; however, despite numerous clinical trials, no treatment modality has proved superior. In the absence of metastatic disease, an esophagectomy can be performed in patients who are able to tolerate the procedure. A gastric pull-up is the preferred technique of reconstruction unless the stomach is extensively involved with tumor. In advanced disease, only palliative therapy is indicated which include chemoradiotherapy or procedures like esophageal dilatation or stenting.

The definitive surgeries for esophageal carcinoma involve esophageal resection with restoration of esophageal continuity. Factors such as general debility, malnutrition, cardiac risk, multisystem dysfunction, liver failure, infection, invasion of a vital structure or metastatic disease influences the outcome of treatment and chances of tolerating a surgical procedure[4]. At best, only 50% of patients are eligible for a curative resection at presentation[5]. The lymphatic drainage is extensive, both within the esophageal wall and in the surrounding mediastinal tissues. As a result, longitudinal spread of the esophageal carcinoma may be extensive and tumors may be multicentric. Tumor recurs at the resection margin in 10% of patients who have had a 6 to 8 cm margin of normal esophagus removed. Since 1970, the reported 5-year survival rates for patients undergoing esophagectomy have risen from 10% to 15% to a high of 35%. This is secondary to refinements in surgical techniques and risk management, improved anesthesia and critical care management and an emphasis on nutrition by enteral or parenteral routes[6]. Despite these improvements in surgical outcome, the overall survival rates for carcinoma esophagus has changed little.

There are four types of esophagectomy (transthoracic, enbloc, transhiatal and video-assisted), with no particular technique shown to have any survival advantage.

In transhiatal esophagectomy, the entire thoracic esophagus is dissected through a widened hiatus and reconstructed with the stomach anastomosed to the remaining cervical esophagus above the level of the clavicles. The overall in-hospital mortality for transhiatal esophagectomy is 5.7% versus 9.2% for transthoracic esophagectomy with no significant difference in 3 and 5-year survival[7]. Advocates of transhiatal esophagectomy report a low operative mortality of 2 to 8% and a low anastomotic leak rate of 5 to 7.9%[8,9]. Orringer and coauthors[10] reviewed their 22 year experience with transhiatal esophagectomy in 1085 patients. They reported hospital mortality of 4% an average blood loss of less than 700 ml. Anastomotic leak occurred in 13% of patients. A modified technique of reconstructing the GI tract by switching to side to side staple esophagogastric anastomosis has reduced the leak rate to less than 3%[11].

The advantages of the transhiatal esophagectomy approach is that include (1) a thoracotomy is avoided (2) an intrathoracic esophageal anastomosis is avoided (if a cervical esophagogastric anastomotic leak does occur, it is easily drained and rarely causes mediastinitis or fatal complications) and (3) no intraabdominal or intrathoracic gastrointestinal suture lines are present. The surgical stapler is used to fashion a gastric tube from the stomach and the stomach is pulled up through the posterior mediastinum and is anastomosed (hand sewn or stapled) to the cervical esophagus[12].

Critics of transhiatal esophagectomy object to the limited exposure afforded by the hiatus to the intrathoracic esophagus. The limited exposure potentially increases the risk of uncontrolled hemorrhage by injury to the azygos vein, the pulmonary veins or the aortic arch and precludes a complete mediastinal lymph node dissection for purposes of staging and potential cure. A review of the literature with a meta-analysis, however, has shown that operative blood loss is significantly less during transhiatal than transthoracic esophagectomy[7]. Contraindications include evidence of tumor invasion of the pericardium, aorta or tracheo-bronchial tree[13]. Pulmonary complications are more common in transthoracic. Transhiatal cervical anastomosis predisposes to a higher rate of leaks (13.6% for transhiatal versus 7.2% for transthoracic). However, majority of leaks are detected by postoperative barium swallows and resolve spontaneously[7]. Side-to-side stapler technique for the anastomosis decreases the incidence of leaks. Decreased traction on recurrent laryngeal nerve decreases incidence of hoarseness. Other complications include wound infection, pneumothorax, esophageal stricture and delayed gastric emptying[12].

Transthoracic esophagectomy may be performed via the following incisions – left or right thoraco-abdominal incision, separate posterolateral thoracic incision and abdominal incision (Ivor-Lewis esophagectomy) and cervical, posterolateral thoracic and abdominal incision (Mckeown's esophagectomy). A transthoracic surgery allows complete lymph node dissection under direct vision and complete resection of tumor mass and adjacent tissue staging of patient is better, however with possibly higher perioperative morbidity. Unfortunately, a combined thoracic and abdominal operation in a debilitated patient may lead to respiratory insufficiency, resulting from postoperative incisional pain and an inability to breathe deeply that requires prolonged mechanical ventilatory assistance. This increases mortality due to increased risk of ARDS[14]. Although disruption of an intrathoracic esophageal anastomosis is reported less frequently than a cervical anastomotic leak from a transhiatal esophagectomy, the consequences, including mediastinitis and sepsis, are fatal in up to 40% of patients. The operative mortality varies significantly depending on the centre, ranging from 14% to 2.2%[13].

En Bloc esophagectomy involves radical resection of esophagus and lymph nodes along with an envelope of normal tissue, spleen, celiac nodes, posterior pericardium, azygos vein, thoracic duct and adjacent diaphragm. With this aggressive surgery, operative mortality ranges from

5.1% to 11%, and is not significantly different from the other approaches[15]. The two major complications are the same- anastomotic leaks and respiratory complications. With this technique, the 5-year survival rate is 40 to 55 %[16]. 44 patients with transmural adenocarcinoma who underwent enbloc esophagectomy had an overall actuarial 5-year survival of 26%, with the presence and number of lymph node metastasis, the most important predictors of survival[16].

Thoracoscopic esophagectomy has 3 stages: the first is in the thoracoscopic dissection of the thoracic esophagus. The second is the laparoscopic mobilization of the intended gastric conduit and the third is the cervical anastomosis. Studies reporting on thoracoscopic esophagectomy have indicated an operative mortality between 0 and 13.5%. The morbidity has been reported to be 27 to 55%. Major causes of complications include respiratory disorders, anastomotic leak, chylothorax and laryngeal nerve injury[4]. Although, technically feasible, the success of thoracoscopic esophagectomy is highly dependant on the experience of the surgeon with no current technique considered standard. Thoracoscopic esophagectomy has not been shown to reduce the length of hospitalization or complications relative to open surgical procedures. Randomized trials with longer follow up are required to fully evaluate the procedure[12].

After portion of the esophagus is removed or after complete esophagectomy, a conduit must be established for alimentary continuity. The stomach, colon and jejunum have all been successfully used as esophageal substitutes, most often using the posterior mediastinum or retrosternal routes. The stomach is the conduit of choice because of ease in mobilization and rich blood supply. A higher incidence of mortality is noted with the use of the colon because of the necessity for three anastomosis eg. Coloesophagostomy, colojejunostomy and colocolostomy. The colon is used if the patient has undergone a partial or total gastrectomy previously or if the tumor involves the stomach to preclude a 5 cm margin. Jejunal loops can also be used but their limited vascular supply restricts mobility and length[12].

Another esophageal pathology that requires major esophageal surgery is caustic injury to the esophagus. Initial management is usually conservative but many of these patients present at a later date with stricture of the esophagus and in most cases the stomach is also affected. The treatment of choice is esophageal dilatations but if there are more than 2 failed dilatations, the probability of further dilatations being helpful, is very minimal. The alternative management plan for these patients is a colon bypass either via a substernal tunnel or via the posterior mediastinum using side-to-side anastomosis between the cervical esophagus and left or right colon. Such patients are seen to have a low nutritional status because of their limitation in oral feeds. Anastomotic leakage is the most common complication in the postoperative period[1].

Carcinoma stomach involving the fundus and the GE junction require a total gastrectomy with esophagojejunal anastomosis. A Roux-en-Y loop of jejunum is commonly used for this anastomosis. This part of the esophagus due to its proximity to the highly vascular stomach is a well vascularised anastomosis and therefore the overall incidence of leak is only 7.5%[17].

4.4 Classification of fistulae

A new classification of anastomotic fistulas of esophagojejunostomy after total extended gastrectomy for advanced gastric carcinoma is presented. In a group of 230 consecutive patients submitted to total gastrectomy within a 10-year period, there were 20 patients with Type I fistula (8.8%) and 18 cases with Type II (7.8%). Type I or subclinical fistula corresponded to a local leakage around the anastomosis, with no septic complications, which heals with prolongation of enteral feeding up to 20 days after surgery. The mortality rate was 5% in this group. Type II or clinical leakage corresponded to patients with early septic manifestations after surgery, in whom the methylene blue test was positive, that is, immediate appearance of the stain in any drain was observed after oral ingestion, confirmed by radiological studies. The mortality rate in this group was 78%. Resuturing of the fistula was a complete failure. Cervical lateral esophagostomy produced complete healing in two cases. Parenteral and enteral feeding, antibiotics and successful surgical drainage are measured that can provide good results in these cases[18].

4.5 Anastomotic leak

The overall incidence of anastomotic leaks after esophagectomy ranges from 12% to 30% as according to several studies. This wide range shows the involvement perioperative and intra-operative factors that play a role in the development of anastomotic leaks. The pre operative factors include presence of other co morbidities[19], poor nutritional status, low hematocrit and neoadjuvant chemotherapy[19]. Intraoperative factors include conduit ischaemia[19], experience of the surgeon[20], cervical anastomosis[21], estimated blood loss per milliliter[21], the anastomosis being performed via a retrosternal or subcutaneous route as opposed to an intrathoracic route[22], the use of colonic interposition as opposed to gastric pedicle[22], performing a manual anastomosis as opposed to a mechanical anastomosis[22] and employing an end to end anastomosis as opposed to an end to side anastomosis using a mechanical technique[22].Using stapled anastomosis, microvascular technique, a staged operation based on the preoperative risk analysis, and improvement in pre- and postoperative management, the incidence of anastomotic leakage could be decreased from 35% to 14%, and hospital mortality, from 9% to 2%. The occurrence of ARDS in the postoperative period was associated with increased chance of anastomotic leak[21]. The use of thoracic epidural analgesia and early nutritional rehabilitation were shown to decrease the incidence of anastomotic leakage.

According to Wormuth et al, average rates of ischemic complications for stomach, colon, and jejunum are 3.2%, 5.1%, and 4.2%, respectively. Most reports that compare outcomes using different esophageal conduits demonstrate similar findings'. Davis and colleagues compared results with colon versus gastric conduit esophageal reconstruction. They found that operative mortality, anastomotic leaks, and conduit ischemia rates were all lower for the stomach than for the colon. Specifically, ischemia of the stomach conduit was 0.5%, compared with 2.4% for the colon conduit. Moorehead and Wong, in a large series of 760 esophagectomy patients in whom the stomach, colon, or jejunum was used for reconstruction, demonstrated that the stomach had the lowest incidence of conduit ischemia

(1%), followed by jejunum (11.3%), then colon (13.3%). Some of the factors they identified as correlating with the risk of ischemia include length of conduit, technique of stomach graft preparation, whether anastomosis is in the neck or chest, and route of passage of the conduit[23].

Mansour and colleagues compared their results using bowel interposition (either colon or jejunum) to reconstruct the resected esophagus. The authors report an overall mortality of 5.9%, and 3% conduit ischemia. All ischemia was noted in the colon conduits harvested from the left side. No ischemic complications were noted from jejunal segments.

Anastomotic leaks can be divided according to the level of the leaks into 3 types – cervical, thoracic or mediastinal and abdominal. Of these, cervical anastomotic leaks are the most common but are easily detected and managed. Thoracic leaks are less common but have very high incidence of morbidity and mortality. Abdominal leaks are very rare in esophageal surgeries when compared to cervical and thoracic.

Cervical anastomotic leaks presents with disruption of the cervical wound and obvious discharge along with fistula formation. There may be initially a fluctuant swelling at the region of the leak. This can be confirmed by giving some water and observing for an increase in the volume of discharge or an increase in the size of the swelling. Patient may also have mild fever, leucocytosis, dysphagia or sticking sensation at the throat.

After completion of a cervical esophageal anastomosis, the neck wound is closed loosely in with only four or five 4-0 sutures over a

1/4th inch Penrose drain placed adjacent to the anastomosis. If an anastomotic leak does occur, the neck wound is opened at the bed side in its entirety and gentle wound packing with gauze is initiated. The size of the leak can be estimated by having the patient drink water and evaluating the amount that escapes from the neck wound with a disposable bedside suction catheter. Generally, within several days of opening the wound, the drainage diminishes considerably and the patient may resume oral intake while maintaining steady gentle pressure over the wound to occlude the fistula. Passage of tapered Maloney dilators (Nos 40 and 46) at the bedside during the first week after drainage of the cervical fistula ensures that no element of obstruction from either local edema or spasm contributes to continued drainage of fistula. Passage of esophageal dilator before the fistula has closed does not damage the anastomosis further and in fact is followed by total closure of the fistula in 2 to 5 days. More than 98% of cervical esophagogastric anastomotic leaks are small and respond to the open drainage and packing as described. The majority of cervical anastomotic leaks heal spontaneously by 2 to 3 weeks. A small proportion, however, are associated with catastrophic complications – major gastric tip necrosis necessitating take down of the anastomosis, construction of cervical esophagostomy and resection of nonviable stomach; vertebral body osteomyelitis; epidural abscess with resultant paraplegia; pulmonary micro abscesses from internal jugular vein abscess; and tracheooesophagogastric anastomotic fistula[12].

When disruption of an intrathoracic esophageal anastomosis occurs during the first 10 days after operation, the clinical picture is quite characteristic. The typical symptoms of mediastinitis (fever, chest pain, tachycardia, tachypneoa, respiratory distress, peripheral cyanosis, vasoconstriction, hypertension and shock) associated with a chest Xray that demonstrated hydrothorax or pneumothorax suggest the diagnosis. This should nonetheless be documented with a contrast study. An occasional small (less than one cm), contained, closed anastomotic leak detected on routine postoperative barium swallow in an otherwise asymptomatic patient may require no treatment. In most cases however, anastomotic disruption warrant immediate re-exploration, irrigation of the chest and mediastinum, repair of the fistula if possible and chest tube drainage. A localized anastomotic leak with viable adjacent tissue may be amenable to direct suture repair. Reinforcement with a pedicled anterior mediastinal fat or intercostal muscle flap, pleura or omentum should be carried out. Decompression of stomach with nasogastric tube, placement of a jejunostomy tube for nutritional support and appropriate antibiotics complete the therapy. A barium swallow examination should be performed 10 days later to be certain that healing has occurred, and the chest tube should be removed before this time. If breakdown of the anastomosis occurs again, the goal is to establish a controlled esophago-pleural cutaneous fistula. It may be necessary to perform a rib resection in order to position a large bore drainage tube adjacent to the fistula and ensure that all drainage from the esophageal leak can flow freely out of the chest. Gastric contents that are aspirated through the nasogastric tube can be returned to the alimentary tract through the jejunostomy tube to minimize electrolyte imbalance and to simplify fluid and electrolyte replacement[12].

If on re-exploration of the chest, for a disrupted esophageal anastomosis, extensive local necrosis of the tissue with a major anastomotic dehiscence is found, there is little recourse but to take down the anastomosis, resect the nonviable stomach, and return it to the abdomen. Only nonviable distal esophagus should be resected. The proximal end of the divided intrathoracic esophagus, however, should not be oversewn and left in the infected mediastinum while a diverting lateral cervical esophagostomy is carried out. Disruption of the intrathoracic esophageal suture line is not only likely but if subsequent reconstruction is possible, management of the remaining segment of intrathoracic esophagus presents a considerable technical problem. The best alternative is to circumferentially mobilize the esophagus well into the neck through the thoracic incision and after the thoracotomy is closed, turn the patient supine and construct a formal end esophagostomy. As indicated earlier, the submucosal collateral circulation of the esophagus is excellent and most of the length of the thoracic esophagus will remain viable so long as at least one inferior thyroid artery remains intact. Therefore, after delivering the divided thoracic esophagus out of the neck incision, viable esophagus should not be discarded to “tailor” the remaining esophagus for a standard cervical esophagostomy. Rather, the maximum length of remaining esophagus should be preserved to facilitate later reconstruction. This is achieved by developing a subcutaneous tunnel on the anterior chest wall and constructing an anterior thoracic esophagostomy. An esophagostomy stoma placed on the relatively flat upper anterior chest wall is much more easily cared for by the patient because a stomal appliance is more readily adapted to this location than to the usual site of a standard cervical esophagostomy. A feeding jejunostomy is, of course, required until later esophageal reconstruction can be performed[12].

When colon or jejunum has been used to replace the esophagus and necrosis of the graft is documented at re-exploration for anastomotic leak, there is similarly little recourse but to remove the nonviable graft and insert a feeding tube. If the patient survives the sequelae of the mediastinal sepsis, later reconstruction can be considered.

Abdominal leaks are intermediate in their presentation. They may present at a later date than intrathoracic leaks. These may produce a peritonitis–like picture with fever, abdominal pain, guarding and tenderness. X-ray may show gas under the diaphragm. The incidence of these type of leaks are much less when compared to the other two and are associated with total gastrectomies and esophageal surgeries with anastomosis near the gastroesophageal junction.

Page et al reviewed retrospectively 23 patients who developed anastomotic leakage, out of 389 patients undergoing oesophagectomy with gastric interposition. The presentation, diagnosis, and treatment of the leaks, and patient outcomes were analysed. Leaks occurred from 3 to 23 (median=7.5) days after surgery. Clinical features included fever (57%), leucocytosis (52%), dysphagia (4%), coughing bile (4%), wound infection (13%), pneumothorax (35%), pleural effusion (70%) and septicaemia (70%). All but one leak was due to variable degree of gastric tip necrosis. Surgical treatment (resection of necrotic stomach and either immediate or staged re-anastomosis, or end-esophageal exteriorisation) was the primary treatment in 17 patients of whom 15 survived to discharge. Two out of the 6 patients treated non-surgically died. Gastric tip necrosis was by far the most common cause[24].

Esophageal anastomotic leak is a potentially life threatening complication of esophagectomy and esophagogastrectomy. Alanezi et al reviewed 307 patients undergoing esophagectomy and esophagogastrectomy for benign or malignant disease over a 10-year period (1989-1999), who developed esophageal anastomotic leaks, were reviewed. Twenty-three (7.5%) developed esophageal anastomotic leaks. Eight of these patients (35%) died. Factors predictive of death included age (died, 72.8+/-8.3 years; survived, 65.3+/-8.8 years; p=0.063), location of anastomosis (cervical, 3/9 died; thoracic, 5/14 died; p=0.91), leak presentation (clinical, 6/12 died; contrast study, 2/11 died; p=0.11), time of leak (<7 days, 3/5 died; > or =7 days, 5/18 died; p=0.18), presence of gastric necrosis (necrosis, 3/3 died; no necrosis, 5/20 died; p=0.019), and treatment (surgical, 4/4 died; conservative, 4/19 died; p=0.005). Gastric necrosis is an important predictor of subsequent death. Advanced age, early postoperative (<7 days) leakage, and clinically apparent signs of leakage may be predictive of death but these factors did not reach statistical significance in this study[25].

The management of anastomotic leakage of the oesophago-jejunostomy after total gastrectomy for gastric carcinoma was reviewed in a retrospective study done by Lang H and Piso P et al. Over a 30-year period, a total of 1114 oesophago-jejunostomies were performed during total gastrectomy for gastric cancer. In 83 cases (7.5%) in this series, a leak of the oesophago-jejunostomy was diagnosed. Frequency of anastomotic leakage was independent of the type of reconstruction and of surgical radicality. Management was conservative in 58 cases (69.9%), with placement of a naso-jejunal tube along the anastomoses and with percutaneous drainage of intraabdominal abscesses. In 25 patients re-operation with resuturing of the anastomoses or surgical drainage of an abscess was performed. Mortality was 11/58 (19%) after conservative treatment of the anastomotic leakage and 16/25 (64%) after re-operation. It was concluded that conservative management with a naso-intestinal tube and percutaneous drainage of intraabdominal abscesses is a realistic line of management for anastomotic leaks. Re-operation results in a high morbidity and should only be considered when conservative management does not succeed[17].

<u>4.6 Anastomotic stricture</u>

Although management of cervical anastomotic leak is usually conservative, the long term sequelae of a cervical leak are significant. As many as 50% of cervicoesophagogastric anastomotic leaks result in an anastomotic stricture as healing occurs and this represents an unsatisfactory outcome of an operation that is intended to provide comfortable swallowing. The implications are similar in patients who survive an intrathoracic anastomotic leak. In their collective review of 46,692 patients undergoing an esophagectomy for cancer, Mueller and associates[26] reported that the incidence of anastomotic leakage with an intrathoracic esophagogastric anastomosis was not significantly different for a one-layer(12%) versus a 2-layer(12%) anastomosis. There was also no difference for an anastomosis that was performed manually(11%) versus one performed with an EEA surgical stapler. On the other hand, in a series of 580 esophageal anastomoses, Fok et al[27] found that a single layer manually sewn anastomosis was associated with a 5% incidence of leak compared with 3.8% in those with a circular stapled technique(p=0.69). However, stapled anastomosis were associated with a higher number of strictures.

In reviewing the complications of transhiatal esophagectomy in 1,353 patients, Kataria et al[28] reported a mean incidence of cervical anastomotic leak of 15% and the same number (15%) of patients developed anastomotic strictures. In a series reported by Dewar et al[29], a 17% incidence of anastomotic leak and 31% incidence of anastomotic stricture in 169 patients undergoing a cervical esophagogastric anastomosis There was statistical significance between anastomotic stricture and a prior anastomotic leak(P=0.001). In a review of 131 patients undergoing a transhiatal esophagectomy for carcinoma, the Mayo Clinic group reported a 25% incidence of cervical leaks[30]. In another collective review, cervical anastomotic leaks occurred in 5 to 26% of patients undergoing a transhiatal esophagectomy with cervical esophagogastric anastomosis. Of this, a series of 10 to 15% of the patients developed anastomotic strictures[31]. Anastomotic leak rate averaged 13% in the more than 1000 transhiatal esophagectomy patients at the University of Michigan, and nearly half of these patients developed subsequent anastomotic strictures[10]. The prevention of an anastomotic leak is the key to a successful outcome in these patients. According to recent published data, side to side stapled cervical esophagogastric anastomosis has been associated with an anastomotic leak rate of less than 3%. This has dramatically reduced the need for late postoperative anastomotic dilatations in patients.

From each of the above studies, it becomes clear that many leaks lead to anastomotic strictures causing the same symptom that he presented with.

4.7 Diagnosis of subclinical anastomotic leaks

The diagnosis of anastomotic leaks still poses a diagnostic challenge in itself. Anastomotic leaks are one of the most common complication contributing to a major part of the mortality and morbidity esophageal operations. Clinically obvious leaks do not require further studies for confirmation. But subclinical anastomotic leaks need a routine screening test done. Subclinical anastomotic leaks, if not diagnosed, can progress to a clinical leak. Moreover, the subclinical leaks that do not progress into clinically evident leaks may develop anastomotic strictures.

Esophageal conduit necrosis is an uncommon but disastrous complication of esophageal surgery. Careful selection of patients for surgery, preoperative evaluation of the proposed conduit, and meticulous operative technique are the best defenses against conduit ischemia. Postoperatively, surgeons should have a high index of suspicion for this complication. Unexplained tachycardia, respiratory failure, leukocytosis, or any evidence for graft or anastomotic leak should prompt a search for conduit ischemia. The diagnosis is made by contrast esophagography, endoscopy, or direct operative inspection[23].

Contrast esophagography is done routinely in many centres including ours from the 7th to 10th postoperative day. A negative study indicates start of oral feeds. If a subclinical leak is reported, the patient is either managed conservatively or a decision for aggressive management, as mentioned earlier, is considered. Contrast esophagography can be done either with barium suspension or water soluble contrast agent.

4.7.1 Barium contrast media

The first known study of GI tract involved stomach of a guinea pig using lead acetate. Subsequently, various studies were done using bismuth subnitrites which were useful in showing the anatomical details of the GI tract but the reduction of subnitrite into nitrate produced severe long term toxicity. It was then that barium studies became popular and till today, barium contrast is being used for most of radiological contrast studies.

The ideal characteristics of the barium contrast media used are the following. The barium suspension must be dense yet flow readily. It must not be too fluid or it drains too quickly, leaves too thin a coat on the mucosa and is poorly recorded on the radiograph. The suspension is somewhat thixotropic so that barium remains suspended when agitation or stirring is stopped. The yield point must be low so that the suspension flows readily under the influence of gravity. Any cake at the bottom of the suspension must form slowly and resuspend easily. It should not foam and should coat the mucosa evenly without artifacts. It must adhere and remain firmly attached to the damp mucosal wall for a considerable length of time. It must form mucosal coating films that accommodate themselves to extensive dimensional films without cracking. These films must remain flexible and even must resist the formation of weak points. Surface defects must level themselves out. The suspension, as it coats the mucosa, must not drag and flow too slowly or it increases the radiation burden on the patient and the radiologist. It must be non toxic. The suspension must do all this at large and varying ranges of pH and patient hydration. It must do all of the above in the presence of flocculating substances such as sodium chloride, mucin and blood and in other difficult extremes of patient's internal environment[32]

The barium ion is highly toxic. Hecht claims that the oral intake by human adults of more than 3 mg /kg body weight of soluble barium salts may be considered harmful. However, barium sulphate is very poorly soluble in water. Barium causes a constipating tendency for all patients. When ingested in a toxic dose, the soluble barium salts result in a relatively acute muscular paralysis and lead to death. Patients with barium toxicity may present with hypertensive uropathy unresponsive to phentolamine. There is profound muscle weakness associated with hypokalemia[33]. The erythrocyte potassium level is increased because of intracellular movement of potassium. Sulfhaemoglobin may be present. Involvement of muscles of respiration can produce a respiratory acidosis. Therapy consists of aggressive intravenous administration of potassium, marked diuresis to help clear barium and where necessary, ventilation assistance[32].

Other important complications include bowel perforation, barium peritonitis or barium intravasation. Barium may enter the peri-intestinal tissues[34], resulting in extensive fibrosis and barium granuloma formation. Perforation can be difficult to detect during fluoroscopy. Contrast medium can spread throughout the peritoneal cavity or be localized in the pelvis. Mortality from colonic perforation during a barium enema is probably over 50%. The morbidity and mortality depend on the amount of contrast in the peritoneal cavity. Barium sulphate and stool are more toxic as a combination than either alone[35]. However, even sterile barium sulphate in the peritoneal cavity of dogs, produce hemorrhagic peritonitis. The long term sequel of barium sulfate peritonitis[36] include extensive bowel adhesions and barium sulfate granulomas. Ureteral obstruction has been reported. There is dense fibrosis around the barium sulfate particles. The granulomas may contain large cells with refringent granules of barium sulphate in the cytoplasm. Some of the barium sulphate can enter the lymphatics. Another potential complication is barium intravasation[37]. This may occur anywhere due to gastrointestinal ulceration. Most of the reported cases with intravastion died[32].

4.7.2 Water soluble contrast medium-

Water soluble contrast was introduced for the examination of the GI tract in 1955. It became unpopular after it was shown by Nelson and colleagues that it causes dehydration especially in infants. Vest and Margulis reported in 1962 on the advantages of water soluble contrast agents in differentiating between adynamic ileus and mechanical small bowel obstruction, particularly in the postoperative patients. Presently, most radiologists as well as studies agree that water soluble contrast agents are the contrast media of choice in demonstrating the site of perforation of the GI tract and for injecting sinus tracts which may connect with the general peritoneal cavity[32].

In patients with suspected perforation as well as in those with peritonitis, subphrenic abscesses or other post surgical complicatons, there is a need for a contrast medium which will not produce more adhesions or aggravate the peritonitis should the medium leaks into the peritoneal cavity. In patients with postoperative complications of an ischaemic or obstructive nature, it is imperative to outline rapidly the GI tract and determine whether immediate surgical intervention is necessary or whether there is time to observe the patient without endangering his life. The oral use of Barium sulphate in these patients usually implies a protracted procedure[32].

Under certain conditions, water soluble iodine containing contrast media have advantages over barium sulfate because barium sulfate is used as a suspension and is therefore, osmotically inert, whereas water soluble contrast media are hyperosmolar solutions. Barium permits excellent radiographic detail and in the presence of normal small bowel motility, permits unequivocal as well as specific diagnoses. However, if there is an adynamic ileus present, the progress of barium is very slow. The barium sulfate which spills into the peritoneal cavity produces a fibrotic reaction, resulting in avascular adhesions which may envelop and shield bacteria in small abscesses from contact with blood borne antibiotics. Water soluble contrast media are hyperosmolar and therefore draw interstitial fluid across the intestinal mucosa into the lumen. The intestinal content thus increases in volume which stimulates the peristaltic activity. Water soluble contrast media thus act as saline cathartics in speeding up passage, but in the course are diluted[38]. This prevents the specific diagnoses beyond the mere statement of whether there is or is not a complete or partial small bowel obstruction.

Indications for the use of water soluble contrast media are

(1) Mechanical obstruction- in very ill patients and in postoperative patients who have adynamic ileus with partial small bowel obstruction.

(2) Demonstration of leaks from the GI tract[39,40,41].
(3) Small bowel study in the presence of large bowel obstruction- to avoid the danger of inspissation of barium proximal tot he large bowel obstruction.
(4) Demonstration of stab wounds, sinuses ad fistulas.

About 100 ml of undiluted Gastrograffin are used if the patient has to swallow the contrast material. The objectionable taste of the contrast material is somewhat improved, as Gastrograffin contains a flavoring agent. If a nasogastric tube is in place, it is advisable to inject sodium diatrizoate (Hypaque) through it. This is mixed from powder to a concentration of 40%. In cases of perforation, the examination is monitored under fluoroscopy to prevent massive filling of the peritoneal cavity with hyperosmolar contrast medium. Sodium diatrizoate (Hypaque) is less costly and as it does not contain a flavoring agent, it is less likely to produce local tissue reaction than Gastrograffin[32].

Dangers and contraindications of water soluble contrast media include the following: Water soluble contrast medium draw interstitial fluid into the intestinal lumen, thus speeding up the examination but diminishing demonstration of detail because of dilution. If hypovolemia is present, oral administration of water soluble media may result in shock and possibly, death, particularly in infants, children, the aged and the very ill. All patients who are hypovolemic, particularly those enumerated above, should be carefully followed for their electrolyte status. Should an oral study with water soluble contrast be necessary in this type of patient, fluid and electrolyte replacement therapy must be instituted. Progressive dilution of the contrast medium as it approaches the site of obstruction, particularly in the distal small bowel, further diminishes detail. Water soluble contrast media can be used in the study of possible esophageal perforations. It should be remembered that if an esophagobronchial fistula exists, serious complications may result from aspiration of water soluble hyperosmolar contrast medium. Pulmonary edema occurs, and if both lungs are affected, the results may be fatal[42]. Tracheoesophageal fistulae usually present clinical manifestations of cough with ingestion of liquids. This clinical symptom should preclude the use of water soluble contrast media. Small amounts of barium sulphate carefully monitored by fluoroscopy would be the approach of choice. For the same reasons it is not appropriate to use water soluble contrast media in the study of esophageal atresia with or without tracheoesophageal fistulas.

According to Tirnaksiz et al, out of the 39 leaks reported from aqueous contrast studies that occurred of the 489 cases in a series, only 17 developed clinical leaks. 25 patients who had normal swallow study developed a clinical anastomotic leak. There were therefore 22 (4.7%) false positive and 25 (5.4%) false negative results. The specificity was 94.7, the sensitivity, 40.4% and false negative error rate of 59.5%. Aspiration of the contrast agent was noted on fluoroscopy in 30 (6.5%) patients. Only 2 (0.4%) patients developed aqueous contrast agent-caused aspiration pneumonia[43].

Radiological contrast studies remain the most accepted diagnostic tool for sub clinical anastomotic leaks after esophageal surgeries. But it is debatable if it is the ideal investigation. In the study reported by Page et al[24] on 23 patients, who developed leaks following esophageal surgery, contrast swallow showed leakage in only 14 (61%) patients, whereas esophagoscopy confirmed all the leaks. They concluded that diagnosis of anastomotic leakage after esophagectomy is difficult due to its variable presentation and the unreliability of contrast swallow. In another study by Alanezi et al[25], four of 23 (17%) patients who had leaks had seemingly normal postoperative contrast studies. These studies indicate the low sensitivity of contrast studies in diagnosing sub clinical anastomotic leaks, thereby emphasizing the need to search for better diagnostic tools.

4.8 NUCLEAR MEDICINE IMAGING

Unstable atoms or nuclides which release energy to reach a stable state are called radionuclide or radioisotopes. Radioactivity refers to the rearrangement process that takes place within an excited nucleus. There are four types of radioactive decay which are of interest in nuclear medicine - alpha decay, beta decay, electron capture and isomeric transition. Most radionuclides used in nuclear imaging and therapy are manmade. They are produced by bombarding stable nuclei with neutrons or protons, which converts stable nuclei into excited ones which then undergo radioactive decay[44].

The rate of decay is constant for each radionuclide. The decay constant is the probability of a disintegration per unit time and per atom. Isotope decay is usually characterized by the half life (t 1/2). The half life is the time required to reach one half of the amount present at an initial time t0. The activity of a sample of radioactive material refers to the number of disintegrations per unit time. The activity present at any time, therefore, depends on the decay constant and the number of undecayed atoms present. One curie (Ci) was defined as 3.7 x 10^10 disintegrations per second. This was thought to be the number of disintegrations in 1g of radium. Since curies was such a large number, activities used in nuclear medicine were frequently given in milliecuries (mCi). The basic SI unit of activity is becquerel. 1 becquerel corresponds to 1 disintegration per second[44].

4.8.1 Imaging equipment

Scintillation camera, which is the detector most commonly used in nuclear imaging, uses a sodium iodide (NaI) crystal. When a sodium iodide crystal is struck by a photon of X- or gamma-rays, it scintillates or gives off energy as a flash of light. In a NaI crystal, an energized electron will fluoresce, as it relaxes to a ground state. This results in emission of visible blue light. The amount of light produced in a scintillation is proportional to the energy deposited in the crystal by the incident photon. By measuring the amplitude of each flash of light, one can select photons of specific energies. This relationship between the energy of a gamma ray and the amount of light produced is critical to the production of good quality nuclear medicine images.

An array of electronic photomultiplier tubes (PMTs) detect the light produced in the NaI crystal. Each PMT generates a signal with an amplitude proportional to the amount of light which is thus a measure of the energy of the incident photon. The actual distribution of radioactivity in the body, as seen by the crystal is ultimately determined by a collimator placed in front of

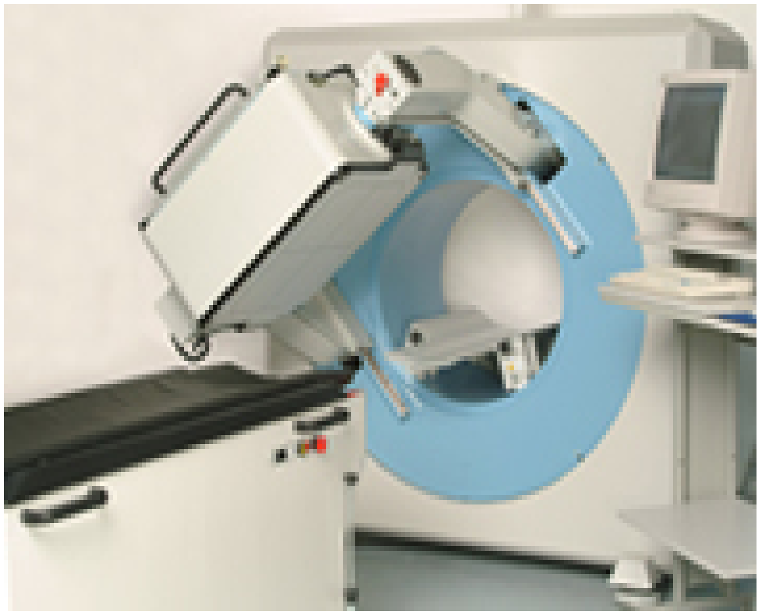

Fig 4.3 Gamma camera

the crystal. The collimator's function is similar to that of a lens of a camera focusing light rays onto a film. Photons which arrive at an angle to the crystal will not penetrate the collimator. Spatial resolution (which is a measure of the precision of locating the source of gamma rays) is best if the collimator is close to the source. Collimators are usually made of lead and its performance is determined by the number of channels and holes, the hole diameter, the length of each channel and the septal thickness. Collimators for low isotopes can be very efficient because the septa are very thin and more holes with smaller diameter can be used.

The speed at which a scintillating camera can count incident photons is determined by the electronics of the camera as well as the properties of the NaI crystal. The ‘dead time’ of a detector is that time during which the system cannot respond to an incident photon. It is also referred to as the resolving time and the time that must separate two events for the system to recognize them. Most cameras today have 'dead times' in the range of 1.5 -

2.0 microseconds, giving maximum count rates of 50,000 - 60,000 counts per second[44].

4.8.2 Imaging methods

A wide variety of diagnostic imaging methods are used in nuclear imaging- static, whole body, dynamic, SPECT and positron emission tomography (PET).

Static imaging is the acquisition of a single image of a particular structure. This image can be thought of as a snapshot of the radiopharmaceutical distribution within a part of the body. Static images are obtained in various orientations around a particular structure to demonstrate all aspects of that structure. Low radiopharmaceutical activity levels are used to minimize radiation exposure to the patients. Because of these low activity levels, images must be acquired for a preset time or a minimum number of counts or radioactive emissions. This time frame may vary from a few seconds to several minutes to acquire 100,000 to more than 1 million counts. Generally, it takes 30 seconds to 5 minutes to obtain a sufficient number of counts to produce a satisfactory image.

Whole body imaging uses a specially designed moving detector system to produce an image of the entire body or large body section. In this type of imaging, the gamma camera collects data as it passes over the body. These are used primarily for whole body scans, whole body tumor or abscess imaging and other clinical and research applications.

Dynamic images display the distribution of a particular radiopharmaceutical over a specific time period. A dynamic or 'flow' study of a particular structure is generally used to evaluate blood perfusion to the tissue. This can be thought of sequential or time lapse images. Images may be acquired and displayed in time sequences as short as one-tenth of a second to longer than 10 minutes per image. Dynamic imaging is commonly used for first pass cardiac studies, hepatobiliary studies and gastric emptying studies.

SPECT produces images similar to those obtained by CT or MRI in that a computer creates thin slices through a particular organ. This imaging technique has proved very beneficial for delineating small lesions within tissues and can be used on virtually any structure or organ.

PET imaging uses positron emissions from particular radionuclides to produce detailed functional images within the body. PET is unique in that its images are of blood flow or metabolic processes at the cellular level rather than the conventional anatomic images produced by X-ray, CT, MRI or even SPECT[44].

4.8.3 Radiopharmaceuticals

A radiopharmaceutical is a radioactive substance, which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. Radiopharmaceuticals can be subdivided into therapeutic and diagnostic agents. Therapeutic agents are used to deliver particulate radiation for the destruction of tissues or cells. Common examples are P-32 and I-131. Diagnostic radiopharmaceuticals are gamma emitting or positron emitting radionuclides used for imaging a specific organ system or for evaluation of a physiological process. Use in humans is regulated by Governmental agencies which impose strict guidelines for their safe and effective use in therapy and diagnosis.

The radionuclide determines the radiation dose to the patient, as well as the imaging properties needed by the detection system. Large numbers of emitted photons are needed for accurate temporal and spatial localisation of a radiopharmaceutical. Short lived isotopes which can be given in large doses to yield high count rates over a relatively short period of time are desirable so that the count rates are high, yet with a total body radiation. While it is desirable for an isotope to have the shortest practical half life, this must be compatible with the half time of the physiological process being studied. Any isotope which decays away before the completion of the biological process under study would obviously be of little clinical use. The energy of emitted gamma ray is also important for detection by a scintillating cameras. Gamma rays from 75 - 300 keV are most suitable for imaging with conventional scintillating cameras[44].

Historically, iodine has played an important role in nuclear imaging. The major disadvantage of iodine is that none of its isotopes are ideally suited for routine nuclear imaging. So they have been replaced by Tc-99m or In-111. Tc-99 and In-111 can be subdivided into metal-essential and metal-tagged agents. Metal tagged agents use radio nuclides to trace the distribution pattern of the unlabelled material. The attachment of the radio nuclides to these compounds does not alter the normal distribution of these compounds. Metal-essential agents, however, require the metal to be complexed by the ligand in order to achieve the desired tracer localization.

Metal tagged agents:

Proteins:	Monoclonal antibodies
	Plasma proteins
	Human serum albumin
Colloids:	Sulfur colloid
	Microaggregated albumin
	Macroaggregated albumin
Cells:	RBCs
	WBCs

Metal essential agents :

Brain perfusion:	Hexamethyl-propyleneamine oxime
Myocardial:	Isonitriles
Renal:	DTPA
	Mercaptoacetyl triglycine
	Glucoheptonate
	Dimercapto succinic acid
Hepatobiliary:	Imino diacetates
	Pyridoxylidiene glutamate

4.8.4 Tc-99 radiopharmaceutical agents

Tc-99 is utilized for the vast majority of all nuclear imaging and is obtained as a daughter product of molybdenum-99. Mo-99 has a 67-hour half life and decays 86% of time to the metastable state of Tc-99m and 14% of the time directly to Tc-99. Tc-99m has a 6.02 hour half life and decays to Tc-99 with the emission of a 140-keV gamma emission and lack of particulate radiation.

The problems associated with Tc-99m sulfur colloid are :
(1)High quantities of carrier Tc-99 may increase the concentration of free pertechnetate in a reconstituted kit. (2)An improper pH during preparation may degrade Tc-99m sulfocolloid yielding free pertechnetate. (3)Aluminium may form a precipitate with Tc-99m sulfocolloid with the resulting particles lodging in the pulmonary capillaries causing lung visualization. (4)Sulphocolloid particle size is dependant on heating time. The size may increase if the kit is heated longer than the recommended time with potential lung visualization. If heated for less time particle size decreases with alterations in the liver to spleen ratios. (5)Particle size of Tc-99m sulfocolloid may change after reconstitution due to agglomeration of particles in vivo[44].

Tc-99m is safe with regard to radiation hazard especially because of its short half life.

4.8.5 Esophageal transit scintigraphy

The movement of a swallowed bolus through the esophagus is defined as esophageal transit whereas emptying from the esophagus of material which has been refluxed is defined as clearance. Radionuclide scans are useful in screening patients with suspected esophageal motility disorders as well as for monitoring response to treatment.

The single swallow technique uses multiple regions of interest to characterize the progression of the esophageal bolus following a single supine swallow of 250 mCi of Tc-99m sulphur colloid in 10 ml of water. Images are recorded on the gamma computer system at a 0.4 second/ frame rate for upto 60 seconds. In multiple swallow tests by Tolin, 150-300 mCi of Tc-99m sulphur colloid in 15 ml of water is ingested as a single swallow in the supine position and followed by dry swallows at 15 sec intervals up to 10 min. These esophageal transit studies have been used in the evaluation of esophageal disorders like achalasia cardia, diffuse esophageal spasm, nutcracker esophagus, oculopharyngeal muscular dystrophy, reflux esophagitis, gastroesophageal reflux, Barrett's esophagus, hiatal hernias, pharyngoesophageal diverticulum, and malignant tumors of the esophagus are included. These scans have not been reported to be used for the purpose of detecting anastomotic leaks in postoperative patients[44].

4.9 RADIATION PROTECTION

After exposure to high doses of radiation, a number of early responses may appear. A whole-body radiation dose in excess of 200 rad (2mGy) can result in death within weeks. Partial body irradiation to any organ or tissue can cause atrophy and dysfunction. A whole body radiation of as low as 25 rad (250 mGy), may produce measurable hematological depression.

These early responses result from high doses of radiation rarely experienced in diagnostic radiology. Such effects are called deterministic. The principle concern today is for late effects of radiation exposure. These effects are called stochastic. The incidence of response is dose related and there is no dose threshold. Such effects of low dose radiation exposures may not occur for years and they fall into genetic or somatic categories.

4.9.1 Radiation units

When an X-ray tube is energized, X-rays are emitted in a collimated beam and this beam ionizes the air through which it passes. This effect is called exposure. The unit of exposure is roentgen(R) (conventional) and C/kg or Gy (SI unit). 1 R = 10 mGy. When the radiation exposure occurs, the resulting ionization deposit is in the air or in the patient who has been exposed to. This is the absorbed dose and it is measured in rad. One rad is equivalent to depositing 100 erg of energy in each gram of tissue. The SI unit of absorbed dose is the gray and 1 Gy = 100 rad = 1 J/kg. If the irradiated object is a radiation worker or the public, then the radiation dose results in a dose equivalent. The dose equivalent is measured in rem (radiation equivalent man) and 1 rem = 100 erg/g. The SI unit of dose equivalent is the sievert (Sv) and 1 Sv = 1 J/kg. When a medical physicist evaluates the performance of an x-ray imaging system, the radiation intensity is expressed in mR/milliampere-seconds at a given kilovolt[45].

4.9.2 Medical radiation dose and exposure

Various factors like the type of equipment, technique employed, model of machine, whether radiographic or fluoroscopy and the X-ray intensity, all put together determine the radiation dose to the patient as well as the radiographer. Patient dose during fluoroscopy is difficult to estimate because the X-ray beam is modulated and moves during the examination. Fluoroscopes have X-ray intensity limited by regulation to 10 R/min at the tabletop. Experience has shown that, when operated at approximately 90kVp, most fluoroscopes produce tabletop exposure of approximately 4 R/min. Radiographic x-ray intensity varies directly with the mAs, with the square kVp and inversely as the square of the distance from the source. A good approximation of X-ray intensity during radiography is 5 mR/mAs at 80 cm source-to-skin distance(SSD)[45].

The dose received by patients during diagnostic radiological examination is usually expressed in one of the 3 ways: entrance skin exposure (ESE), organ dose or fetal dose. Organ dose and fetal dose cannot be measured but has to be calculated. The ESE of the patient during any radiographic examination can be measured directly or estimated by various techniques. Too low a radiation exposure is as hazardous as excessive radiation exposure because an inadequate image is produced making diagnosis less precise and needing repeat radiographic examinations. The range of acceptable ESEs for selected radiographic examinations in mR are as follows:

Chest(PA)	10 to 25
Skull (lat)	105 to 240
Abdomen (AP)	375 to 700
Retrograde pyelogram	475 to 830
Cervical spine (AP)	35 to 165
Thoracic spine(AP)	295 to 485
Extremity	10 to 330
Dental (bite-wing & peri-apical)	230 to 425

Damilakis J et al estimated the average patient dose and risks associated with upper gastrointestinal contrast studies from data collected from 25 studies done on infants. The cases were divided into 2 groups – Group 1 including 12 infants ranging from 0.5 to 5.9 months and Group 2 including 13 infants aging from 6 months to 15 months. The mean total fluoroscopy time was 1.26 and 1.62 min for groups 1 and 2, respectively. The average effective dose was 1.6 mSv for group 1 and 1.9 mSv for group 2. The risk of cancer attributable to the radiation exposure associated with a typical UGIC study was found to be up to 3 per 10 000 infants undergoing an UGIC examination. The mean radiation dose absorbed by the hands of comforters was 47 microGy. In conclusion, radiation dose values associated with UGIC examinations carried out to infants are not low and should be minimized as much as possible[46].

In yet another study done by Delichas MG et al on 41 barium meal and 42 barium enemas, mean total DAP values were found to be 25 +/- 11 Gy cm2 for BM and 60 +/- 35 Gy cm2 for BE examinations, whereas the estimated mean values of effective dose were 8.6 +/- 4.0 and 24 +/- 16 mSv respectively. DAP to effective dose conversion coefficients were estimated to be 0.34 mSv per Gy cm2 for BM and 0.41 mSv per Gy cm2 for BE[47]. Other studies also report the increased radiation hazards involved in upper GI contrast studies[48,49].

4.9.3 Radiation safety in nuclear medicine

The radiation protection measures in nuclear medicine are different from the general radiation safety measures used for diagnostic radiography. The radio nuclides employed in nuclear medicine are in liquid, solid or gaseous form. Because of the nature of radioactive decay, these radio nuclides continue to emit radiation after administration. Therefore, special precautions are required.

In general, the quantities of radioactive tracers used in nuclear medicine present no significant hazard. Nonetheless, care must be taken to reduce unnecessary exposure. The handling and administering of diagnostic doses to patients warrants the use of gloves and a lead syringe shield, especially effective for reduction of exposure to hands and fingers during patient injection. But Tc-99m, the most commonly used radionuclide, due to tits short half life has almost negligible radiation hazard when administered at low dose. Only at high doses does it become hazardous but that too for a short period of time.

The radiation safety in Technetium agents have been mainly studied in breast sentinel node biopsies. According to a study done by Strattmann et al, 21 patients were injected with 0.7 to 1.1 mCi of technetium sulphur colloid1.5 to 3 hours before a sentinel lymph node biopsy. They concluded that radiation exposure to operating room personnel, pathologists, and operative equipment during a breast sentinel node biopsy using Tc99m is minimal. A primary surgeon can perform 2,190 hours, a scrub nurse 33,333 hours, and a pathologist 14,705 hours of procedural work before surpassing Occupational Safety and Health Administration limits. Operative instruments, pathology slides, and cryostat machines do not require special handling. All lumpectomy specimens should be stored for decontamination until the dose rate equals background levels[50].

5. Methodology

This study aimed at exploring the diagnostic feasibility and efficacy of nuclear images in the detection of postoperative sub clinical anastomotic leak.

5.1 Patients

Cases for the study were selected according to a set of inclusion and exclusion criteria. They were as follows:

5.1.1 Inclusion criteria:

- All patients undergoing the following operations, irrespective of age or sex, were included for the study.

  # Esophagectomy with reconstruction – Transhiatal, transthoracic (Ivor- Lewis, McKeown's), en bloc esophagectomy.

  # Substernal colon bypass with or without esophageal resection

  # Total gastrectomy

  # Proximal gastrectomy

5.1.2 Exclusion criteria:

1. All patients who are clinically unstable and may not be able to tolerate both the studies as according to the surgeon's judgment.
2. Patients with clinically obvious leaks.
3. Patients in whom both the studies could not done to completion.

5.2 Methods

A pilot study was done on 5 patients to explore the feasibility of the study and also to standardize the vehicle, dose, volume and timing of the Technetium studies. 2 patients underwent esophagectomy and 3 underwent total gastrectomy. Technetium sulphocolloid and Technetium-DTPA were tried as radionuclide agents. It was decided to use Technetium sulphocolloid scans for reasons of superior quality. Milk and sterile water were tried as vehicles. Since sterile water was more physiological and safer for a patient in the postoperative period, it was decided to use plain water as the vehicle for radionuclide. The dose of radionuclide was standardized at 5 mCi per patient with a volume of vehicle ranging from 30-100 ml.

Since there were no similar studies recorded in literature, it was decided to have a sample size of 40 based on an estimate of the number of patients that can be studied in the time period of the study. After the detailed research plan was laid down, approval was obtained from the Department of Upper Gastrointestinal Surgery unit and the fluid research committee. The study extended for a period of 18 months from March, 2005 to August, 2006

All patients who underwent the operations listed in the inclusion criteria were selected for the study after obtaining informed consent. Selected preoperative, intraoperative and postoperative data as mentioned in the proforma were collected for each patient. Patients who satisfied the exclusion criteria during the course of the study were taken off the study.

Technetium sulphocolloid scans were undertaken on the 8^{th} postoperative day and barium meal studies on the 9^{th} postoperative day. The patients were interviewed after the procedures and a discomfort analogue score was obtained from each patient. The score was a subjective score measured on an ordinal scale and displayed the level of discomfort experienced by the patient during the study. The highest possible score was 10 and it expressed the maximum discomfort the patient could imagine. The lowest score was 0 which described the state in which consumption of the study solution was comparable to what the patient considered as effortless as drinking potable water. The scans were reported independently by the nuclear medicine physician and the radiologist respectively. Technetium scan reports were not used for decision on further management. All decisions regarding further management of patient was done on the basis of report of the barium study.

5.2.1 Technetium sulphocolloid studies

Technetium sulphocolloid scans were planned for the after noon of the 8^{th} postoperative day. Just prior to the procedure, patient was given a test feed of about 15 ml of plain water. If the patient tolerated the test feed, he was taken for the scan.

Sterile water was used as the vehicle of radioactive material. 30-100 ml of sterile water with 5 mCi of Technetium was prepared and the patient was instructed to drink the liquid while images were taken with gamma cameras. Initially, dynamic images were taken as 5-second frames for 5 min. Patient took the next swallow in a supine position and 5-second frames were taken for 5 min. Similar static images are taken for ½ hour in antero-posterior and lateral views. A delayed study was done if the nuclear medicine physician wanted further clarifications on the previous images.. Images were stored and analyzed with the help of computers. The final report was reported by the Head of the Nuclear Medicine Department. The report gave details of the appearance of the images as well as about the presence or absence of anastomotic leaks. This report was not used for further decisions on management but only for study purposes.

5.2.2 Radiological contrast study:

Contrast esophagography was planned for the morning of the 9^{th} postoperative day. Thin barium was used as the contrast agent. No procedural restrictions were placed. The images were analyzed and reported by the radiologist as routinely done. Further decisions on management were based on the report.

5.3 Data analysis

Data obtained from the study was tabulated and analyzed with the help of the Department of Community Medicine and Biostatistics and the results are presented in the next section.

6.Data Analysis

6.1 PATIENT PROFILE

6.1.1 Number of cases enrolled

51 cases were enrolled into the study of which 13 cases were excluded from the study due to the various exclusion criteria. The reasons for exclusion form the study were as follows.

1. Patients who were clinically unstable during the time of the tests – 4 patients.
2. Patients who developed clinically detectable leaks prior to the imaging – 5 patients.
3. Patients who could not complete either one of the study due to patient related factors -1 patient (Barium induced vomiting).
4. Patients who could not complete either one of the study due to technical reasons- 2 patients.

6.1.2 Age – sex distribution of patients

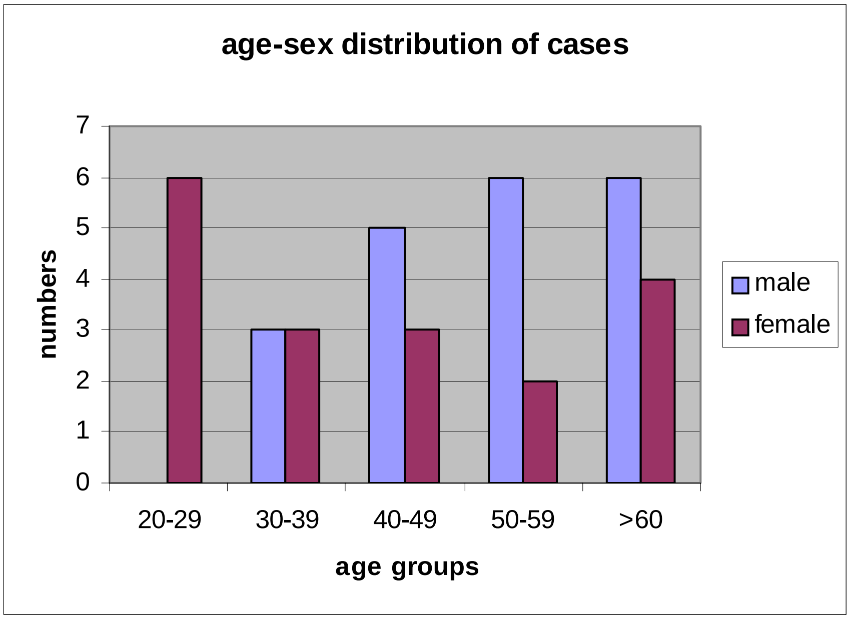

Figure 6.1: Age-sex distribution of patients in the study

Of the 38 cases were studied, there were 20 males and 18 females. The age-sex distribution of the studied population has been depicted. The above bar diagram shows that female cases were predominant in the younger age group and as age increases male cases predominate. This is probably due to the higher incidence of benign corrosive acid strictures in the female younger age group.

6.1.3 Clinical presentation profile in patients

The common symptoms with which the patients presented with are depicted in the picture below.

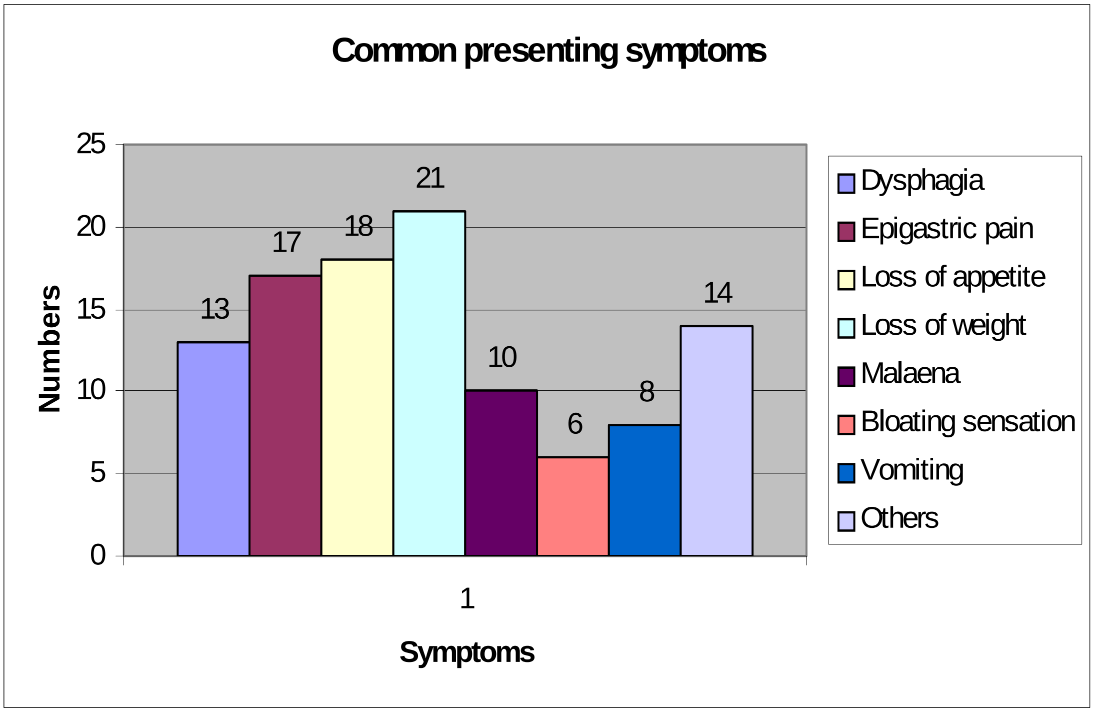

Figure 6.2: Common presenting complaints of patients in the study

The most common symptom among the 38 cases studied was loss of weight. Other important symptoms were loss of appetite, epigastric pain, dysphagia and vomiting. Some of the minor symptoms that were included under the heading of ‘others’ were hematemesis, odynophagia, generalized weakness, early satiety and regurgitation.

6.1.4 Duration of symptoms

The duration of the first symptom was tabulated and depicted in the bar diagram:

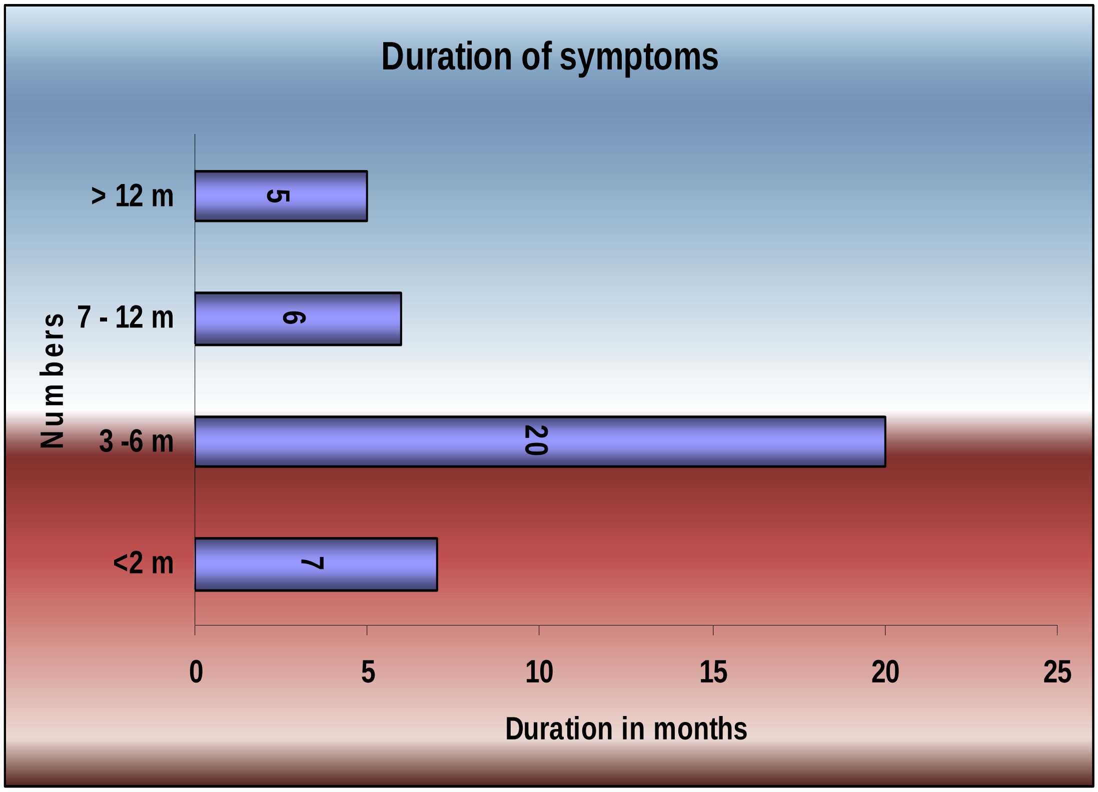

Figure 6.3: Duration of the first symptom (months)

The duration of the first symptom ranged from 1 month to 48 months. The mean was 8.79 months. In 20 of the 38 cases, the duration of the first symptom was in the range of 3 to 6 months.

6.1.5 Personal and past history

8 patients (21.1%) had history of smoking. 4 patients (10.5%) were known diabetics at the time of study while 3 patients (7.5%) were known hypertensives. The other co-morbidities that were also associated in the patients in the study were tuberculosis(1), thyroid disorders(2), dyslipidemia(3), situs inversus(1) and chronic renal failure(1).

Only one out of the 38 patients had a history of previous radiotherapy while 4 patients had history of previous chemotherapy. 9 patients of the 38 cases had history of previous operation. 4 of these 9 patients had esophagogastric operations while another 4 patients had other GI operations.

Analysis done to identify any associations between history of smoking, previous radiotherapy and chemotherapy did not reveal any significant associations.

Other variables

Variable	Mean	Standard deviation	Significant association with leak
BMI	20.69	1.4	Nil
Hemoglobin	10.6 gm%	2.2	Nil
S. albumin	3.8 mg%	0.58	Nil

Table 6.1

The height and weight of all the patients were tabulated and the body mass index was calculated according to the formula:

$$BMI = Weight (kg) / Height^2 (cm)$$

The normal BMI of the general population was between 22 and 25. BMI of the study patients ranged from 15.6 to 26.0 with a mean of 20.69 and a mode of 21.7. 42% of patients had a BMI between 18.0 and 21.9 while 74.5% of patients had a low BMI. This was in agreement to the fact that loss of weight was the predominant presenting symptom in a majority of the study patients.

The blood investigations that were analyzed were hemoglobin and Serum albumin. Hb values were in the range of 5.4 to 15.6 with a mean of 10.6 gm% (SD- 2.2). The mean serum albumin value was 3.8 mg% (SD-0.58) while the values ranged from 2.3 to 4.9. Any association between these variables to the development of anastomotic leaks according to barium study was tested by the chi square test and found to be not significant.

6.2 PROFILE OF MANAGEMENT

6.2.1 Types of Surgery done

Surgery done	**Number**
Ivor Lewis esophagectomy	2
McKeown’s esophagectomy	2
Total gastrectomy	31
Substernal colon bypass	2
Distal esophagectomy + proximal esophagectomy	1

Table 6.2: Types of surgery done for study patients

The majority of cases in the study underwent total gastrectomy. This is because the number of esophageal resections was relatively low and some of the cases who underwent esophagectomy fell into the exclusion criteria due to early clinical leaks

6.2.2 Histopathology

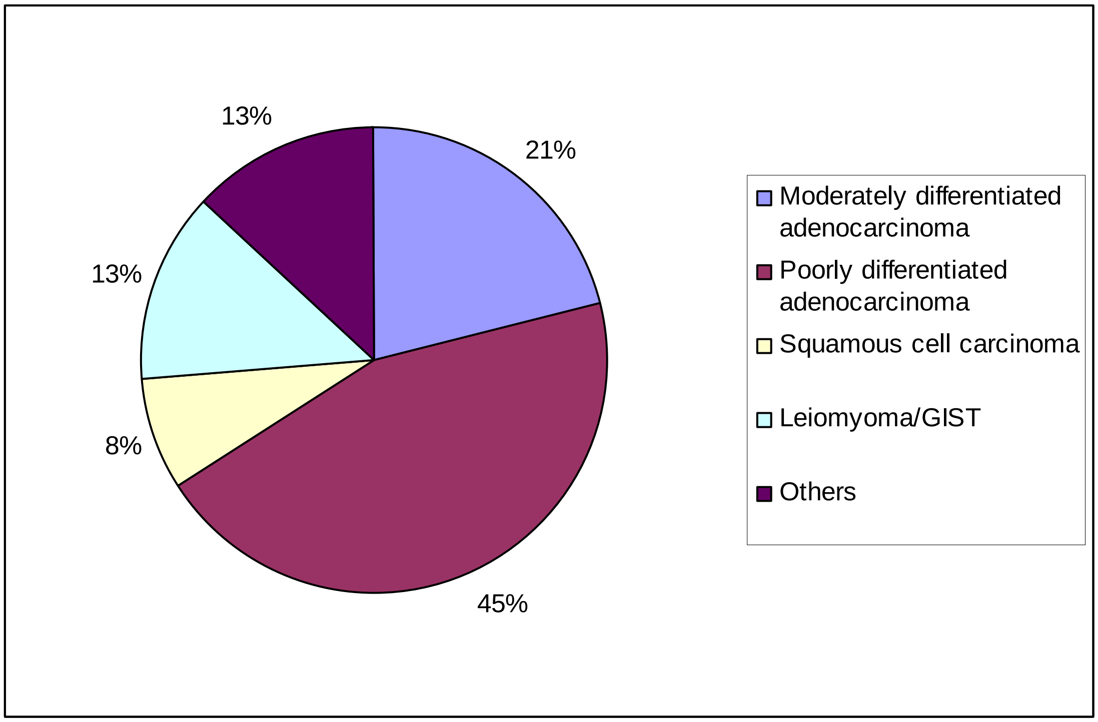

Figure 6.4: Profile of final biopsy report of patients

Since majority of the cases were carcinoma stomach, the most common biopsy reports were moderately or poorly differentiated adenocarcinoma. Squamous cell carcinoma was reported in esophageal lesions. Other rare lesions like schwannoma, leiomyoma, GIST, lymphoma or corrosive strictures were also included.

6.2.3 Intraoperative data

Duration of surgery was clearly seen to be dependant upon the type of operation done. Mean duration of esophagectomy was 7 hours while that for total gastrectomy was 4 ½ hours.

Stapled anastomosis was done in 13 out of the 38 cases (34.2%) while the rest were handsewn. Of the 13 stapled anastomosis, one patient developed leak while of the remaining 25 cases who underwent a hand sewn anastomosis, 5 had anastomotic leaks as according to barium contrast studies. However, a chi square test did not show any significance for association.

Intraoperative hypoxia was recorded in only one case (McKeown's esophagectomy). Intraoperative hypotension occurred in 5 cases. Mean blood loss recorded during surgery was 492 ml. 19 of the 38 cases did not require blood transfusion.

6.2.4 Postoperative data

The number of ventilator days postoperatively ranged from 0 to 11 days. 29 cases did not require postoperative ventilation while 5 patients required 2 or more days of postoperative ventilation. Similarly, 26 cases required did not require postoperative monitoring in Surgical ICU while remaining cases required 1 to 15 days in ICU. 4 out of 38 cases developed postoperative ARDS. Margins were free only in 20 of the 38 cases (52%).7 out of the 38 cases did not develop post-operative fever. The number of episodes of spikes of fever ranged from 1 to 10 with a mean value of 2.26 spikes(SD- 1.76),for the first ten days post-operatively.

6.3 COMPARISON OF TECHNETIUM AND BARIUM IMAGING IN DETECTING SUBCLINICAL ANASTOMOTIC LEAKS

6.3.1 Leak in Technetium sulphocolloid scan

Technetium sulphocolloid scans detected 10 leaks out of the 38 study cases. Of these, 9 leaks were reported as blind fistulous tracks from the anastomotic site with pooling of radioactive contrast. One scan was reported as consistent pooling of radioactive contrast at the anastomotic site depicting a contained leak. Of the 10 cases that were shown to be leak positive by technetium, 5 were also picked up by barium while the remaining 5 were missed by barium.

6.3.2 Leak in Barium contrast studies

Barium contrast studies detected 6 leaks out of the 38 cases studied. Of the 6 cases, one leak was detected exclusively by barium contrast studies while all other 5 leaks were detected by both the studies.

6.3.3 Technetium sulphocolloid esophageal scintigram – normal

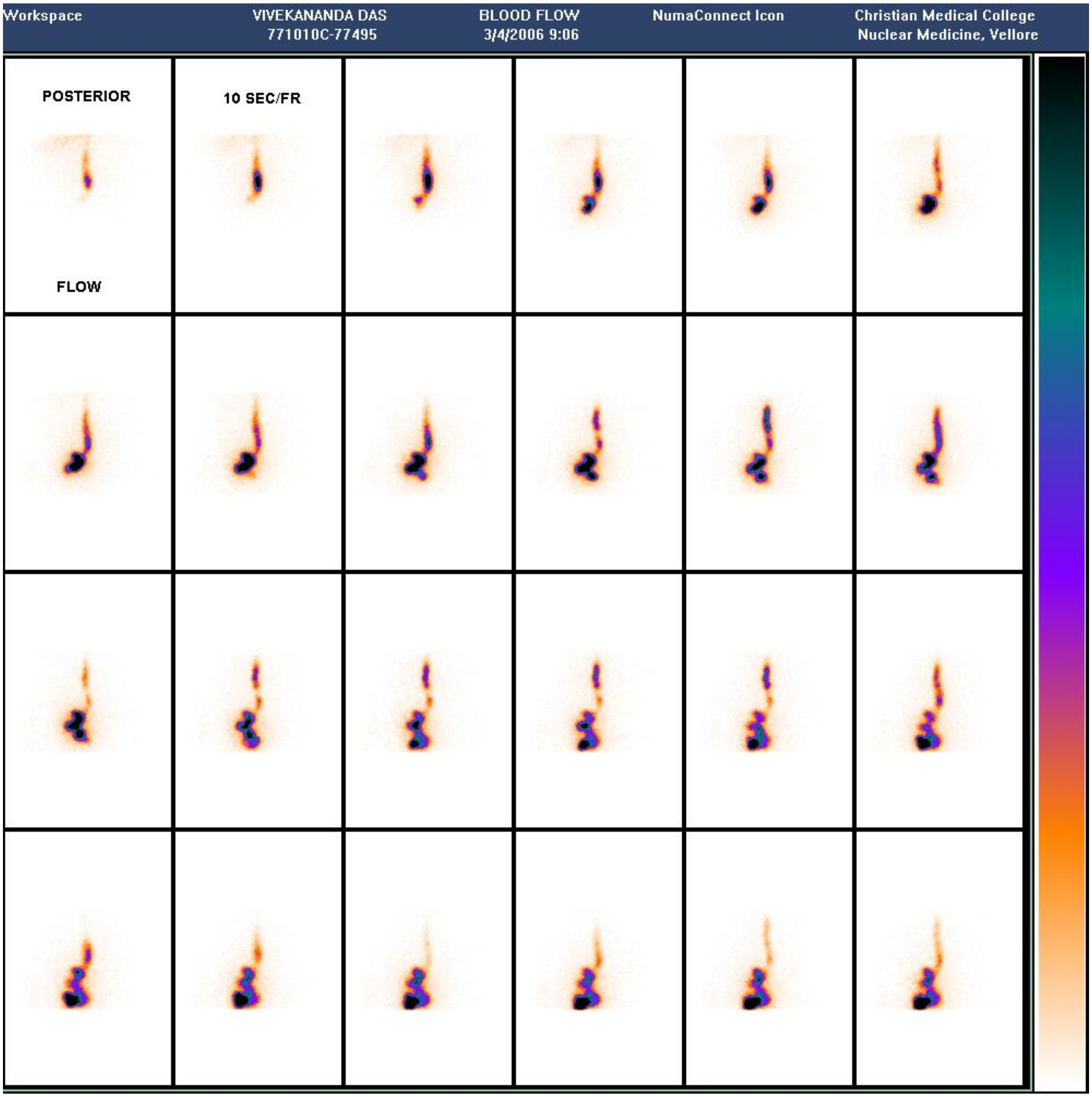

Figure 6.5 Normal technetium sulphocolloid scintigram (dynamic images)

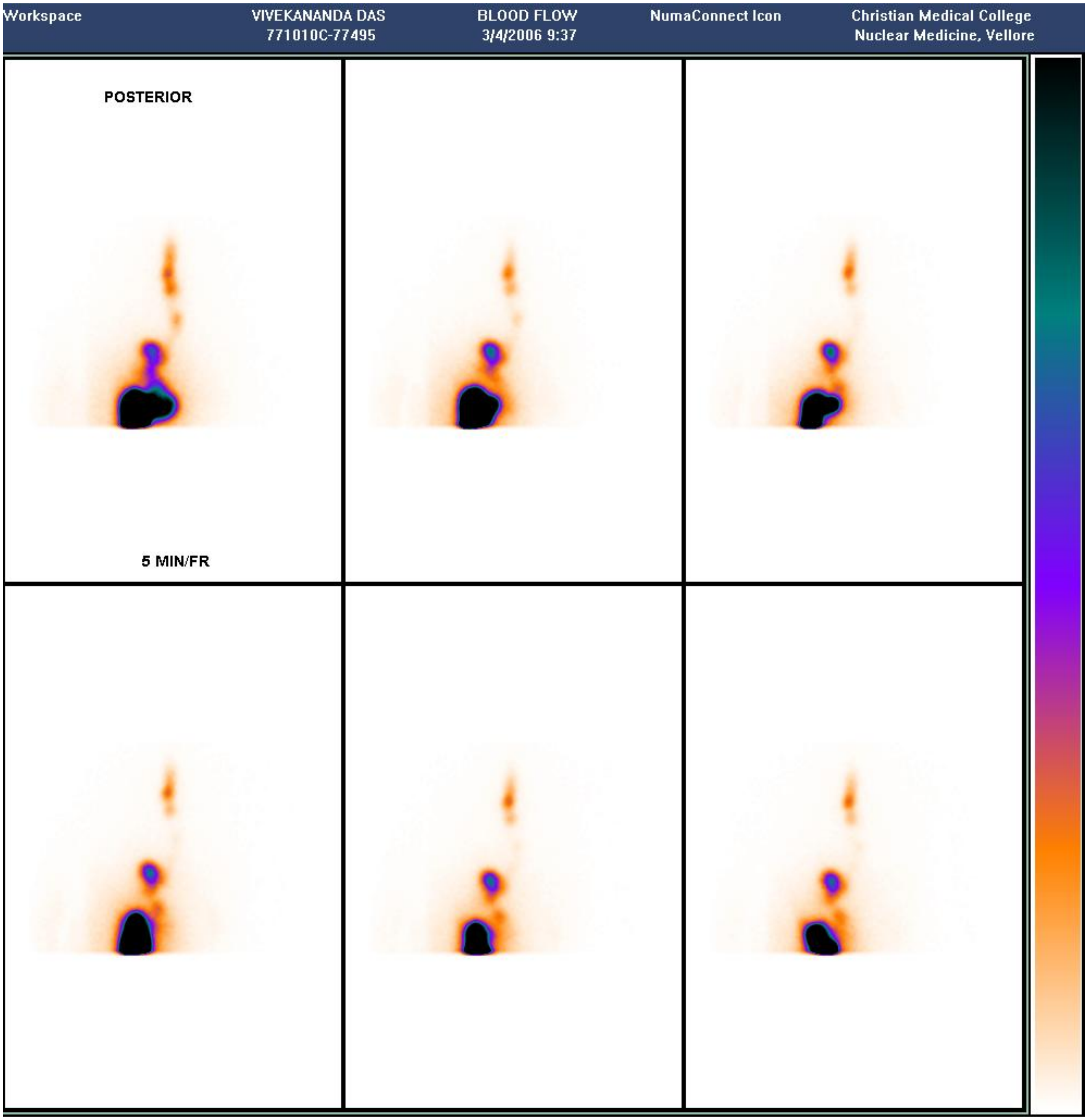

Figure 6.6 Normal technetium sulphocolloid scintigram (static images)

6.3.4 <u>Technetium sulphocolloid esophageal scintigraphy – anastomotic leak</u>

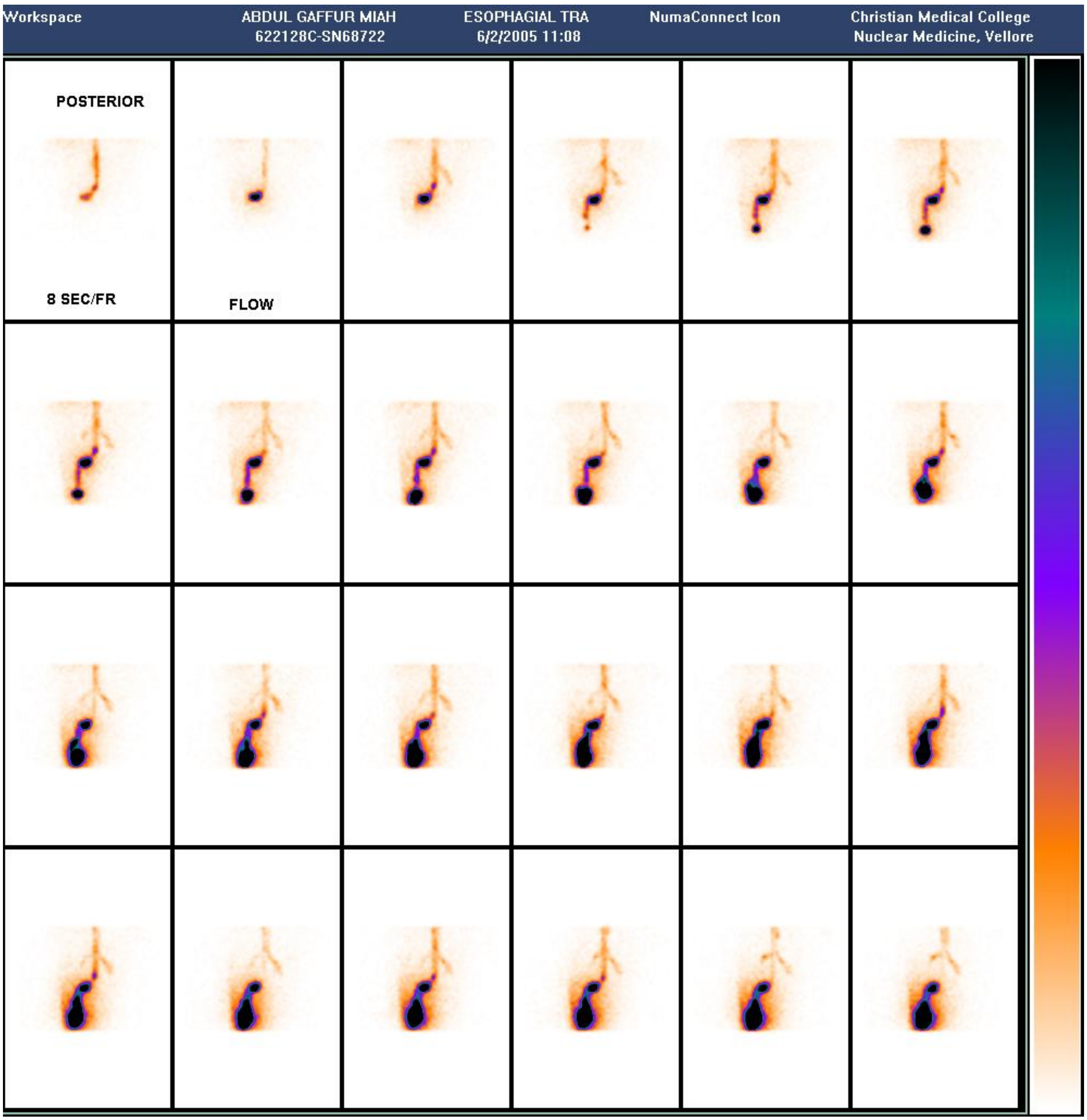

Figure 6.7 Technetium sulphocolloid esophageal scintigraphy-anastomotic leak (dynamic images)

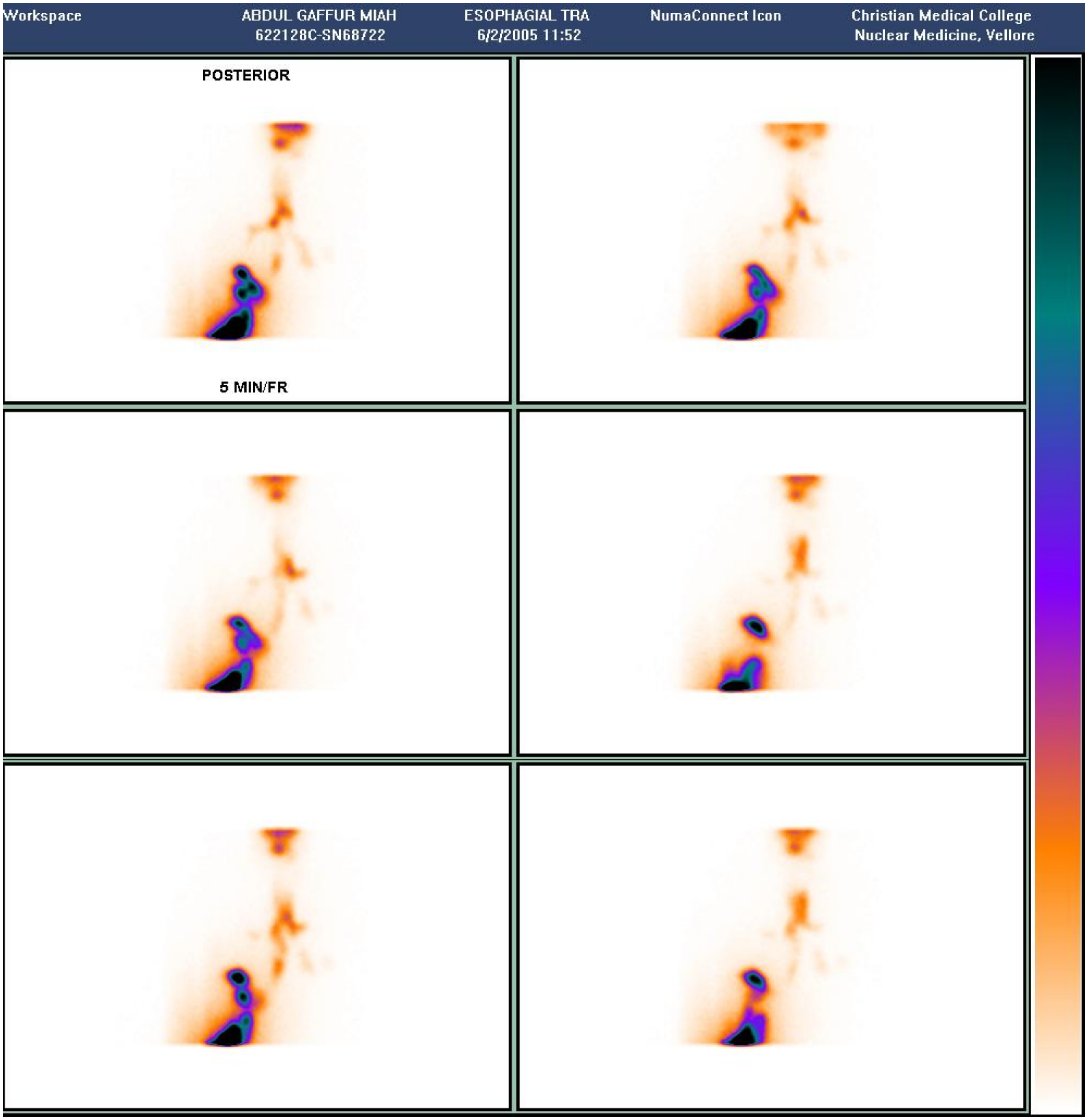

Figure 6.8 Technetium sulphocolloid esophageal scintigraphy-anastomotic leak (static images)

6.3.5 **Results**

		Barium study		Total
		Leak present	No leak	
Technetium	Leak present	5	5	10
Scintigraphy	No leak	1	27	28
Total		6	32	38

Table 6.3 Barium contrast studies Vs Technetium scinitigraphy

Data analysis of the results of the above imaging studies was done with the kappa statistic. Kappa expresses the extent to which the observed agreement exceeds that which should be expected by chance alone. Landis and Koch suggested that a kappa greater than 0.75 represent excellent agreement beyond chance, a kappa of 0.4 to 0.7 represents intermediate to good agreement and below 0.4 represents poor agreement[51].

Kappa value was calculated to be 0.533 with a standard error of 0.162. This value according to Landis and Koch is of good agreement between the two studies.

6.4 COMPARISON OF DISCOMFORT ANALOGUE SCORES

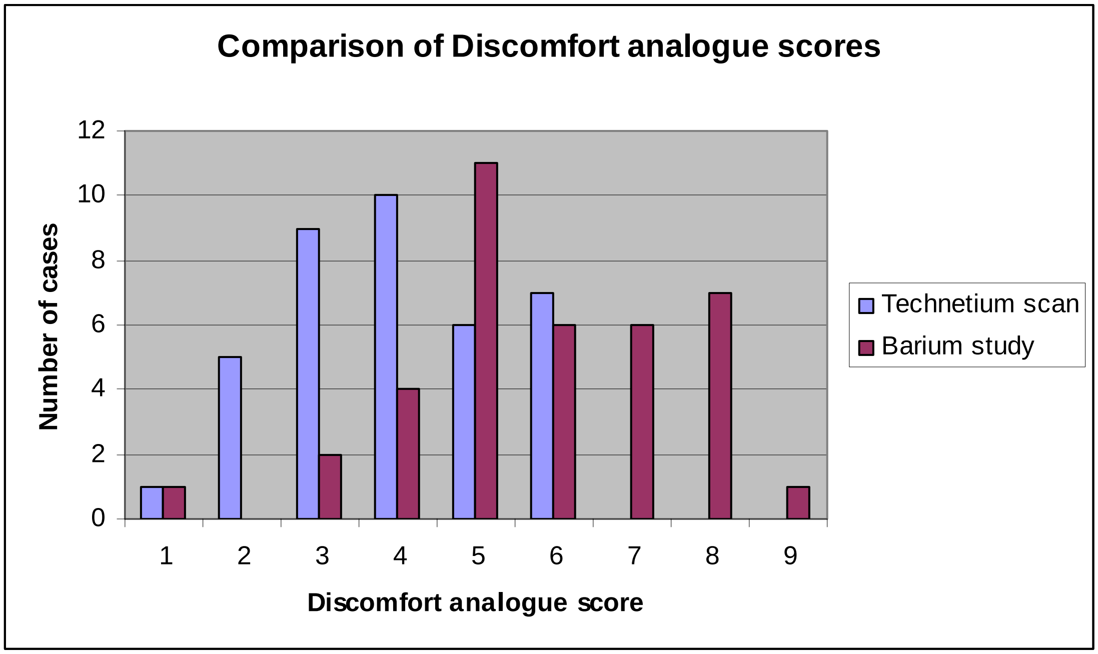

Figure 6.9

The above graph shows a clear separation of scores towards 0 to 5 for Technetium scans and towards 5 to 10 for barium scans. The mean value for discomfort during administration of the technetium study was 3.95 and the mean value for discomfort during administration of the contrast study was 5.84 .The significance of this difference was tested using a paired samples test, for which a ‘t’ value of -5.029 ($p<0.001$) was obtained and the result was taken as significant.

7. Discussion

Anastomotic leaks are one of the commonest complications after esophageal operations. The most effective way of managing anastomotic leaks is to detect it at a sub clinical level. This allows the treating surgeon to alter his management plans so as to hasten closure of the leak and prevent progression into a clinical leak. Studies have already demonstrated that barium contrast studies, which is the current investigation of choice, is not the ideal one.

There is as yet no gold standard for the detection of sub clinical anastomotic leaks. Some studies have used clinical leaks as the gold standard while some have used esophagoscopy. It is assumed that all subclinical leaks need not progress into a clinical leak and therefore progression into a clinical leak is not a suitable gold standard for evaluation of a test to diagnose subclinical leaks. No studies are available in literature about the sensitivity of esophagoscopy but scopy in a postoperative setting may do more harm than good to the anastomosis. Therefore, one of the limitation of the study was the lack of a proper gold standard to calculate the validity criterion.

Barium studies, even though far from being ideal, is the best investigation currently available. Since there was no proper gold standard, it was decided to assess the agreement in the reporting of the Technetium nuclear images and the barium contrast images. In this study, this agreement was assessed with a Kappa statistical analysis. A kappa value of 0.533 with a standard error of 0.162 shows a good agreement between the two studies in terms of detecting sub clinical anastomotic leaks. The analysis also shows that technetium scans detected 5 anastomotic leaks that were not detected by barium scans while barium scans detected only one case over technetium scans. This observation though statistically not significant, can be explained either as a higher sensitivity rate of technetium scans over barium scans or as a higher false positivity rate of technetium over barium scans. Further studies aiming at estimating sensitivity and specificity of this diagnostic test need to be done.

Advantages of Technetium scans

This study shows a good agreement between the two investigations. Technetium scans can be considered superior to barium if there are clear advantages of technetium over the same variables in barium.

The advantages of technetium as seen during this study were as follows:

1. Technetium sulphocolloid scans used plain water as its vehicle when compared to the more viscous barium. Plain water was more physiological in the GI tract and thereby had the least effect on the anastomotic site.
2. The radiation hazard posed by technetium is very minimal when compared with contrast imaging. This fact is elaborated in the literature review.
3. The cost of a technetium scan in our institution was only Rs. 700 when compared to Rs. 1600 for a barium scan.
4. Technetium has a half life of 6 hours after which it is excreted from the body through the kidney. Barium, on the other hand is a suspension and is excreted in stools because of which it is dependant on proper bowel function. For the same reason, previously

administered barium can interfere with repeat barium scans especially if there was a leak.

5. Technetium that leaks into the abdomen or thorax is not known to cause complications like peritonitis unlike barium.
6. The discomfort analogue score is significantly higher following barium studies as confirmed by relevant statistical tests (p value < 0.001). Moreover, one of the cases who were excluded from the study did not tolerate barium.

Disadvantages of Technetium scan

1. Routine use of technetium scan can only be considered in a setting where infrastructure for nuclear scan imaging exists.
2. Technetium scans have poor delineation of the GI tract in terms of luminal defects as compared to barium which has excellent visualization of the bowel lumen.
3. Skeletal visualization is not possible with technetium scans because of which exact level of lesion may not be identified.

Association of patient related factors to anastomotic leak

Various studies have described the association of patient related factors in the development of anastomotic leaks. Some of the patient related associations that have been already established are presence of comorbidities, previous history of radiotherapy and chemotherapy and nutritional status as according to the preoperative albumin level. The occurrence of intraoperative hypoxia and hypotension, duration of anaesthesia, total blood loss, postoperative ventilator days and development of ARDS and sepsis have also been known to have an association with development of anastomotic leaks.

In this study, an attempt was made to determine the association of these factors on the development of anastomotic leaks. Leaks detected by barium studies were used for these associations. Of all the associations studied, only the number of postoperative ventilator days showed some association with development of anastomotic leak but it was not statistically significant.

The fact that sub clinical anastomotic leak and not anastomotic leak was the end point of the study would probably be one of the reasons for the lack of association of these factors. Moreover, the number of leaks as according to barium studies was only 6 which is a very small number to make any conclusions from. The sample size was also too less for determining associations.

8. Conclusion

1. Technetium sulphocolloid esophageal scintigraphy have a good agreement with barium contrast studies in detecting sub clinical anastomotic leaks.
2. The sensitivity of technetium scans could not be assessed due to lack of a proper gold standard.
3. Technetium scintigraphy was found to have detected more sub clinical anastomotic leaks than barium.
4. Technetium sulphocolloid scans are more economical than barium contrast studies.
5. Technetium sulphocolloid imaging does not cause any of the complications of barium such as barium peritonitis or barium inspissation.
6. The amount of radiation exposure to the patient as well as his/her attendants is negligible.
7. Technetium is excreted from the body rapidly and so repeat scans are not confounded by the old technetium.

8. Technetium sulphocolloid scans use sterile water as its vehicle because of which it is more physiological and is easier for the patients.
9. Swallowing of technetium sulphocolloid produced statistically significant lesser discomfort to the patient as compared to barium as was proved by the comparison of the discomfort analogue score.
10. Further studies with larger sample sizes are needed for evaluating the validity criterion of Technetium sulphocolloid esophageal scintigraphy.

Limitations

Like any other study, this had certain limitations. The sample size was small. This was mainly due to the short duration of the study and due to limitation in the number of cases that were available for the study. A larger sample size would have probably helped in conclusively proving the validity of the study.

Literature shows a higher rate of leaks associated with esophagectomy than is seen in this study. In this study, there were only a small number of esophagectomies that could be studied due to a good proportion that became excluded from the study.

The lack of a proper gold standard was one of the major limitations of this study. Barium, being the routine imaging was considered the gold standard but the sensitivity and specificity of barium is highly debatable. A larger sample size or a more ideal gold standard would have helped in analyzing the sensitivity and specificity of Technetium sulphocolloid scans

10.Bibliography

1. Sabiston Textbook of Surgery, Volume I, 17th edition
2. Gray's anatomy, 39th edition
3. McGregor's Synopsis of Surgical Anatomy, 12th edition
4. Orringer MB, Forastiere AA, et al: Chemotherapy and radiotherapy before transhiatal esophagectomy for esophageal carcinoma. Ann Thorac Surg 49: 348-355, 1990.
5. Ajani JA: Current status of new drugs and multidisciplinary approaches in patients with carcinoma esophagus. Chest 113: 112S-119S, 1998.
6. Naunheim KS, Hanosh J, et al: Esophagectomy in the septuagenarian. Ann Thorac Surg 56: 880-884, 1993.
7. Hulscher JB, Tijssen JG et al: Transthoracic versus transhiatal resection for carcinoma of the esophagus: a meta-analysis. Ann Thorac Surg 72: 306-313, 2001.
8. Goldfaden D, Orringer MB et al: Adenocarcinoma of distal esophagus and gastric cardia: Comparison of results of transhiatal esophagectomy and thoracoabdominal esophagogastrectomy. J Thorac Cardiovasc Surg 91: 242-247, 1986
9. Hankins JR et al: Carcinoma of the esophagus: a comparison of the results of transhiatal versus transthoracic resection. Ann Thorac Surg 47: 700-705, 1989.
10. Orringer MB, Marshall B: Transhiatal esophagectomy: Clinical experience and refinements. Ann Surg 230: 392-400, 1999.
11. Orringer MB, Marshall B: Eliminating the cervical esophagogastric anastomotic leak with a side-to-side stapled anastomosis. J Thorac Cardiovasc Surg 119:277-288, 2000.
12. Shackleford's Gastrointestinal surgery- Esophagus volume
13. Pac M, Basoglu A: Transhiatal versus transthoracic esophagectomy for esophageal cancer. J Thoracic Cardiovasc Surg 106: 205-209, 1993
14. Savage C et al: Post-thoracotomy pain management. Chest Surg Clin North Am 12:251-263, 2002.
15. Hulscher JB et al: Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. N Eng J Med 347: 1662-1669, 2002.
16. Altorki N et al:Should en bloc dissection be the standard of care for esophageal carcinoma. Ann Surgery 234: 581-587, 2001
17. Lang H, Piso P: Management and results of proximal anastomotic leaks in a series of 1114 total gastrectomies for gastric carcinoma. Eur J Surg Oncol 2000 Mar; 26(2): 168-71
18. Czendes A, Diaz JC et al: Hepatogastroenterology, 1990 Dec;37 Suppl 2:174-7
19. Briel JW, Tamhankar AP, Hagen JA, DeMeester SR, Johansson J, Choustoulakis E, Peters JH, Bremner CG, DeMeester TR: Prevalence and risk factors for ischemia, leak, and stricture of esophageal anastomosis: gastric pull-up versus colon interposition. J Am Coll Surg. 2004 Oct;199(4):667-8
20. De Giacomo T, Francioni F, Venuta F, Trentino P, Moretti M, Rendina EA, Coloni GF: Complete mechanical cervical anastomosis using a narrow gastric tube after esophagectomy for cancer. Eur J Cardiothorac Surg. 2004 Nov; 26(5):881-4.

21. Michelet P, D'Journo XB, Roch A, Papazian L, Ragni J, Thomas P, Auffray JP: Preoperative risk factors for anastomotic leakage after esophagectomy: influence of thoracic epidural anaesthesia. Chest, 2005 Nov; 128(5): 3461-6

22. Lee Y, Fugita, Yamana H, Kakigawa T: Factors affecting leakage following esophageal anastomosis. Surg Today 1994; 24(1): 24-9

23. Wormuth JK, Heitmiller RF et al: Esophageal conduit necrosis. Thoracic Surg Clin 2006 Feb; 16(1): 11-22

24. Page RD, Shackcloth MJ, Russel GN, Pennefather SH: Surgical treatment of anastomotic leaks after oesophagectomy. Eur J Cardiothorac Surg. 2005 Feb;27(2):337-43.

25. Alanezi K, Urschel JD: Mortality secondary to esophageal anastomotic leak. Ann Thorac Cardiovasc Surg. 2004 Apr;10(2):71-5.

26. Muller JM, Erasmi H et al: Surgical therapy of esophageal carcinoma. Br.J. Surg.,77:845, 1990.

27. Fok M, Ah-Chong et al: Comparison of a single layer continuous hand sewn method and circular stapling in 580 esophageal anastomosis. Br.J.Surg., 78:34, 1991.

28. Katariya K, Harvey JC et al: Complications of transhiatal esophagectomy. Br.J.Surg., 78:342, 1991.

29. Dewar L., Gelford G et al: Factors affecting cervical anastomotic leak and stricture formation following esophagogastrectomy and gastric tube interposition. Am.J.Surg., 163:484, 1992.

30. Vigneswaran WT et al: Transhiatal esophagectomy for carcinoma esophagus. Ann Thorac. Surg., 56: 836, 1993.

31. Gandhi SK, Naunheim K at al: Complications of transhiatal esophagectomy. Chest Surg.Clin. North. Am., 7: 601, 1997.

32. Radiographic contrast agents – Miller

33. Roza et al,1971. The pathophysiology of barium; hypokalemic and cardiovascular effects. J.Pharmacol.Exp.Ther.177:433-39

34. Cochrane et al,1963. An experimental study of the effects of barium and intestinal contents on the peritoneal cavity. Am.J.Roentgenol.89:883-87

35. Rockert et al,1963. Tissue reaction to barium sulphate contrast medium. Acta Pathol. Microbiol.Scand.58:445-50.

36. Gardiner et al, 1973. Barium peritonitis.Am.J.Surg.125:350-52

37. Mahdoubi et al,1974. Barium embolisation following upper GI examination. Radiology 111:301-02

38. Harris et al, 1964. The osmotic effect of water soluble contrast medium oncircul;ating p;asma volume. Am.J. Roentgenol.91:694-98

39. G.Jacobson et al, 1961. Examination of patients with suspected perforated ulcer using a water soluble contrast medium. Am.J. Roentgenol. 86:37-49

40. Meyer et al, 1964. The use of water soluble contrast medium in suspected perforated ulcer. Radiol. Clin.North.Am 2:55-69

41. P.A.Mori et al, 1962. A sign of intestinal perforation. Radiology 79:401-07

42. Reich, S.B. et al, 1969. Production of pulmonary edema by aspiration of water soluble contrast media. Radiology 92: 362-67.

43. Tirnaksiz MB, Deschamps C, Allen MS, Johnson DC, Pairolero PC: Effectiveness of screening aqueous contrast swallow in detecting clinically significant anastomotic leaks after esophagectomy. Eur Surg Res , 2003 Mar-Apr; 37(2): 123-8

44. Diagnostic nuclear medicine- Powsner & Raeside

45. Merrill's Atlas of radiographic position and radiologic procedures, Volume 1 and 3, 10th edition.
46. Damilakis J, Stratakis J et al: Normalised dose data for upper gastrointestinal contrast studies performed to infants. Med Phys, 2006 Apr; 33(4): 1033-40
47. Delichas MG, Hatzioannou et al: Radiation doses to patients undergoing barium meal and barium enema examinations. Radiat Prot Dosimetry 2004; 109(3):243-7
48. Livingstone RS, Augustine P et al: Dose audit and evaluation of work practices during barium procedures using digital radiographic techniques. Health Phys, 2004 Oct; 87(4): 358-65
49. Crawley MT, Savage T, Oakley F: Patient and operator dose during fluoroscopy examination of swallow mechanism. Br J Radiol 2004 Aug; 77(920): 654-6
50. Strattman ML, McCarty TM, Kuhn JA: Radiation safety with breast sentinel node biopsy. Am J Surg 1999 Dec; 178(6): 454-7
51. Landis JR, Koch GG: The measurement of observer agreement for categorical data. Biometrics 33: 159, 1977

11.1 PROFORMA

Name of patient: Age: Sex: Hospital No.:

Clinical details

Symptoms with duration:

Treatment history:

Radiotherapy

Chemotherapy

Previous surgery

History of Smoking:

Comorbidities: Diabetes: Others:

Wt: Ht: BMI:

I**nvestigations**

Hb S. albumin: Level of lesion:

Biopsy:

Diagnosis:

Intraoperative period

Surgery done:

Duration of surgery: Duration of anaesthesia:

Components of anastomosis: Esophago-esophageal/ Esophagogastric/ Esophagojejunal/ Esophagocolic.

Use of staples for anastomosis:

Level of anastomosis: Upper/ Middle/ Lower third of esophagus

Prolonged hypoxia: Prolonged hypotension:

Total blood loss:

Transfusion requirement:

Postoperative period

No. of days on ventilator: No. of days in SICU:

Occurrence of ARDS:

Number of fever spikes in first 10 postoperative period:

Margin positivity in pathology specimen(in cases of malignancy):

Radioscintigraphy study

Discomfort analogue score: Presence of anastomotic leak:

Radiological contrast studies

Discomfort analogue score: Presence of anastomotic leak:

Clinical follow up

11.2 INFORMED CONSENT

I have been informed about a study being conductedin CMC hospital on patients who have undergone surgeries involving esophageal anastomosis. I have been informed about the components of the study and the pros and cons of it . I understand that my participation is completely voluntary and that I may choose to withdraw from this study at any time. I also understand that my refusal to take part in the study will not affect my treatment in any manner.

Having read and understood the consent form, I hereby agree to participate in the study.

Date:

Signature of patient

Name of patient

Signature if principal investigator:

(Dr. Sujith Varghese Thomas)

11.4 MASTER DATA – VARIABLE DESCRIPTION

Age :
1 - 20 to 29 years
2 - 30 to 39 years
3 - 40 to 49 years
4 - 50 to 59 years
5 - > 60 years

Sex: 1 - Male
2 - Female

Symptoms : Symptoms a to e represents a list of symptoms that patient presented with. There is no relationship to the timing or importance of symptoms.
Durat : Duration of the first significant symptom in months
RT : History of previous radiotherapy 0 – No 1 – Yes
Chem : History of previous chemotherapy 0 – No 1 – Yes
PrevSx : History of previous surgery
1 - Esophagogastric surgery
2 - Other GI surgery
3 - Thoracic surgery
4 - Others
Smok : Known cigarette smoker 0 - No 1 - Yes
DM : Known diabetic 0 - No 1 - Yes
HT : Known hypertensive 0 - No 1 - Yes
Others : Other comorbidities
1 - Tuberculosis
2 - Thyroid disorders
3 - Dyslipidemia
4 - Situs inversus
5 - CRF
Wt : Weight of patient in kg
Height : Height of patient in cm
BMI : Body mass index as weight / height^2
Hb : Hemoglobin in gm%
Seralb : Serum albumin in mg/dl
Levles : Level of lesion
1 - Middle third of esophagus
2 - Lower third of esophagus
3 - GE junction
4 - Proximal stomach
Biopsy : Final biopsy report
1 - Well differentiated adenocarcinoma
2 - Moderately differentiated adenocarcinoma
3 - Poorly differentiated adenocarcinoma
4 - Squamopus cell carcinoma
5 - Lymphoma
6 - Schwannoma
7 - Leiomyoma/ GIST
8 - Not applicable

Surge: Type of Operation done

1 - Ivor Lewis esophagectomy
2 - McKeown's esophagectomy
3 - Transhiatal esophagectomy
4 - Total gastrectomy
5 - Substernal colon bypass
6 - Distal esophagectomy + proximal gastrectomy

DurSx / Dur Ax : Duration of surgery and anaesthesia in minutes

Components of anastomosis :

1 - Esophagoesophageal
2 - Esophagogastric
3 - Esophagojejunal
4 - Esophago colic

Level of anastomosis :

1 - Upper third of esophagus
2 - Middle third of esophagus
3 - Lower third of esophagus

Staple : Use of stapled anastomosis

0 - Handsewn anastomosis
1 - Stapled anastomosis

Hypox : Presence of intraoperative hypoxia for more than 1 minute
0 - No 1 - Yes

Hypot : Presence of intraoperative hypotension requiring inotropes
0 - No 1 - Yes

Blood loss : Total intraoperative blood loss as evaluated by anaesthetist(ml)

Transfuse : Number of units of blood transfused intraoperatively

Ventd : Number of days on ventilator

SICU : Number of postoperative days in SICU

ARD : Occurrence of ARDS in the postoperative period 0 - No 1 - Yes

Fevers : Number of spikes of fever in the first 10 postoperative days

Margp : Margin positivity according to final biopsy report

1 - All margins free of tumor
2 - Proximal margin with tumor
3 - Distal margin with tumor
4 - Circumferential margin with tumor
5 - More than one margin with tumor

DAStech : Discomfort analogue score after Technetium imaging (0-10)

Techleak : Leak detected by Technetium scans 0 - No 1 - Yes

DASBa : Discomfort analogue score after barium study (0-10)

Barileak : Leak detected by barium study 0 - No 1 - Yes

Clinleak : Clinical diagnosis of leak 0 - No 1 - Yes