# Treatment

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When Barrett’s oesophagus is discovered, the treatment is that of the underlying GORD. Pharmacological therapy generally is the same as treatment of symptomatic GORD patients. Antireflux surgery is indicated if it is associated with GORD symptoms. A randomised trial suggested that aspirin, as a chemoprevention agent, in combination with a high-dose PPI, may improve outcomes in patients with Barrett’s oesophagus measured by progression to cancer and mortality . In patients with dysplastic Barrett’s oesophagus without suspicion of invasive cancer, the epithelium can be ablated or resected. Indication for such procedures in non-dysplastic Barr ett’s oesophagus is controversial. Ablative therapy aims to completely eradicate all intestinal metaplasia. When the mucosa regenerates after ablation in a non-acidic environ - ment (when a high-dose PPI is prescribed), a ‘neosquamous’ lining is formed. Ablative approaches that are supported by evidence include photodynamic therapy , RFA and cryother - ap y . Among these methods, RFA is most popular because there is evidence of its e ff ectiveness, cost and side-e ff ect pro - file. EMR by the cap method or multiband technique can be done to remove the whole segment of the mucosa. When this is applied to cir cumferential Barrett’s oesophagus, the stric - ture rate is high when healing occurs . The procedure can be performed in stages, allowing mucosal healing to occur first in one half of the oesophagus before a second stage to remove - the other half, thus lessening the chance of stenosis. In con - trast, the incidence of stricture formation is low following - RFA, because the depth of ablation extends to the muscularis mucosae only . Endoscopic ablation should only be applied to flat lesions without nodularity , ulceration or irregular contour. Suc h features are suggestive of invasive neoplasm that should be inv estigated and treated by EMR or endoscopic submucosal dissection (ESD). ESD, though more technically demanding, provides en bloc resection of the index lesion with better mar - gins for histological diagnosis. EMR is easier and large areas can be resected in a piecemeal manner. If histological exam - ination of the resected tissue demonstrates the absence of inva - sive cancer, or T1a tumour, only the ‘biopsies’ can be reg arded as curative. When T1b lesions are found on histology , or when the resection margins (lateral or deep) are in volved, additional therapy including oesophagectomy should be considered. Regardless of treatment performed, the patient should enter a surveillance programme to detect recurrent or persistent Bar - rett’s oesophagus or neoplasia.

# mucosa Systematic cold biopsy Con /f_i rmed dysplasia by two

# independent pathologists Inde /f_i nite for HGD or LGD dysplasia T1a OAC MDT Repeat OGD with OGD every 6 discussion maximal acid months until: suppression 2 consecutive Therapeutic evidence of non- intervention dysplastic BO De /f_i nite dysplasia Follow non- Follow LGD Endoscopic dysplasia or HGD eradication /f_l owchart /f_l owchart therapy

Barrett’s oesophagus /uni25CF /uni25CF /uni25CF /uni25CF

Endoscopic examination and biopsies are crucial in the diagnosis of Barrett’s oesophagus Dysplasia should be con /f_i rmed by at least two experienced pathologists Surveillance or ablation are options for low-grade dysplasia In patients with high-grade dysplastic Barrett’s oesophagus, ablative, endoscopic resection and oesophagectomy should be considered

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Stage-directed therapy Treatment principles depend on the disease stage and phys - iological reserve of patients. Patients should be discussed in a multidisciplinary team to decide on the best course of management. When distant metastatic disease is identified palliation is the aim. Endoscopic treatment The chance of nodal metastasis depends on the depth of infiltration of the primary tumour. Cancers that are confined - to the mucosa (T1a) rarely metastasise, but squamous

tumours that have infiltrated the submucosa (T1b) have a substantial risk of nodal spread. In adenocarcinoma, the corresponding risk is less. Such early cancers may be amenable to curative - endoscopic treatment ( Figure 66.51 ). EMR involves the injection of saline (or other solutions such as glycerol or hyaluronic acid) into the submucosal plane to raise the mucosal - lesion; it is then sucked into a cap fitted onto the tip of the endoscope, looped by a snare wire and cut by electrocautery . The limitation of this method is the size of the cap, so it is . generally recommended for smaller lesions. For larger lesions, if resected by EMR, piecemeal resection is required; therefore, it is associated with higher incomplete resection and recurrence rates. ESD is more complex. It involves first marking the margins of the lesion, then submucosal injection, cutting the mucosal edges along the line of marking, submucosal dissection of the tumour from its bed (superfi cial to the muscle layer) and lastly haemostasis. There are various ‘knives’ that can be inserted via the biopsy channel of the endoscope to carry out these procedures. Technically ESD is more demanding than EMR but is not limited by the size of the lesion for en bloc resection. There is an increased risk of postresection stricture formation if too much of the circumference of the mucosa (such as over two-thirds) is removed. This chance is somewhat reduced by steroid treatment (often endoscopic injection at the time of EMR/ESD, combined with oral medication for some time). For early Barrett’s cancer, EMR and ESD are options, and additional circumferential resection or ablation of the whole length of Barrett’s mucosa can be done. For ablative therap y , RFA is most commonly used. RFA energy is delivered by the bipolar electrode and the energy causes frictional heating of cellular water molecules. After ablation, in the presence of a non-acid milieu (suppressed by a high-dose PPI), the epi - thelium would regenerate to be squamous cell mucosa. The advantage of RFA is that it is technically easy to operate but the drawback is that no surgical specimen for detailed histopatho - logical examination is available. Other examples of ablative technique include cryotherapy or photodynamic therapy .

(b) Figure 66.50 Positron emission tomography/computed tomography (CT) scan for staging of oesophageal cancer and assessment of response to neoadjuvant therapy. The patient underwent neoadjuvant chemoradiotherapy. The tumour had high /f_l uorodeoxyglucose uptake (SUV before treatment (b) . After chemoradiotherapy the SUV dropped to 4.1 with a corresponding reduction in size of the cancer seen on CT max scan (a) . 23.5) max

Because the pretreatment distinction of T1a and T1b dis ease may not be accurate, it may be prudent to perform endo scopic resection first in case of uncertain diagnosis. Should the resected specimen be found to be T1a with clear margins and without lymphovascular permeation in the pathological examination, the endoscopic treatment is deemed curative. If the tumour is found to be deeper than e xpected or if resection margins are not clear, further therapy can be planned. Surgery The primary indication for surgical resection is for potential cure, which can be achieved in patients whose tumours are confined to its wall and only limited local/regional disease is found. One should aim to maximise the chance of an R0 resection (macroscopic and microscopic clearance of proximal, distal and lateral margins), a parameter that has consistently been shown to result in the best long-term survival. Surgical resection alone is generally indicated for more advanced cancers when endoscopic treatment is unlikely to be curative (T1b, T2, N0). For patients with more advanced disease ( ≥ T3, N+), multimodality treatment is usually preferred. Patient selection and preparation Oesophagectomy is a major procedure; patients should be assessed carefully for operative risk and their physiological status optimised. Cardiorespiratory assessments are essential. Patients must stop smoking and alcohol intake. Chest physio therapy is instituted,

and incentive spirometry is a good preop erative exercise. Patients with high-grade oesophageal tumour stenosis may have lost a substantial amount of weight. A fine-bore nasogastric tube can be placed for nutritional support while work-up is performed. Feeding jejunostomy is an alter native. Enhanced recovery after surgery (ERAS) programmes entail preoperative ‘pre-habilitation’ as well ( Table 66.5 measures are aimed to optimise patients for surgery . Immedia preoperative preparations include prophylactic antibiotics and Ivor Lewis , 1895–1982, surgeon, North Middlesex Hospital, London, later Rhyl, UK. Norman Cecil Tanner , 1906–1982, surgeon, Charing Cross Hospital, London, UK. - deep vein thrombosis prophylaxis. Bowel preparation is not - necessary unless a colonic interposition is intended. Surgical techniques Choice of surgical approach The choice of the appropriate technique depends mainly on: (i) the location of the tumour, (ii) the intended extent of lymphadenectomy , and (iii) the reconstructive technique. The surgeon should be well versed in the methods adopted to di ff er - ent clinical situations. For ease of description, the following sections discuss the surgical approach by tumour location. Cervical oesophageal cancer Surgery involves removing the pharynx, larynx and oesoph - agus (pharyngo-laryngo-oesophagectomy); a gastric pull-up is used to anastomose with the neo-pharynx. In cases where involvement of the cervical oesophagus is limited, pharyngo-laryngo-cervical oesophagectomy can be carried out without the need for total oesophageal resection. The resultant gap can be bridged using either a free jejunal graft, or various musculocutaneous flaps. Definitive chemoradiotherapy has become the preferred alternative treatment to preserve the larynx. Surgery is therefore mostly reserved for salvage, when there is an incomplete response or for recurrent disease. Intrathoracic oesophageal cancer - The surgical procedures usually performed are: - /uni25CF Left thoracoabdominal incision. Via a large incision tra - versing the chest and upper abdomen, the whole left upper quadrant of the abdomen and left thoracic cavity are accessed at the same time for oesophagectomy , gastro - - plasty and anastomosis ( Figure 66.52a ). /uni25CF Lewis–Tanner (or Ivor Lewis) procedure. This is a two- ). All phase oesophagectomy consisting of laparotomy for gas - te tric mobilisation and tubularisation, followed by a right

(a) (b) Figure 66.51 Schematic diagrams showing technique of (a) endoscopic mucosal resection – cap with submucosal injection and snare excision; (b) endoscopic submucosal dissection.

thoracotomy for oesophageal resection. The gastroplasty is delivered into the right thoracic cavity for an oesophago gastrostomy near the apex of the chest ( Figure 66.52b /uni25CF McKeown or three-stage oesophagectomy . This con sists of the mobilisation of the thoracic oesophagus and lymphadenectomy via a thoracotomy (usually right side), followed by abdominal and neck incisions for preparation of the oesophageal substitute (usually the stomach) and its delivery to the neck for a cervical anastomosis. /uni25CF Left thoracic resection (Sweet oesophagectomy). Via a single posterolateral incision on the left chest wall (usually fifth to sixth intercostal space), the oesophagus is mobilised. The diaphragm is opened and the gastroplasty prepared from this opening. The stomach is delivered to the left tho racic cavity for anastomosis. Kenneth Charles McKeown , 1912–1995, surgeon, Darlington Memorial Hospital, Durham, UK. Richard H Sweet , 1901–1962, surgeon, Massachusetts General Hospital, Boston, MA, USA. /uni25CF Transhiatal oesophagectomy . Through a cervical and ab - - dominal approach, the oesophagus is mobilised via both ). directions, being stripped out bluntly from its mediastinal - bed. The gastric conduit is delivered to the neck for cervi - cal anastomosis ( Figure 66.53 ). /uni25CF Minimally invasive surgical approaches. Traditional open procedures (described above) are increasingly replaced by minimally invasive methods, by a combination of video- assisted thoracoscopy (V ATS) and

laparoscopy or robotic techniques ( Figure 66.54 ). Both thoracic and abdominal phases can be performed via minimally invasive tech - niques, or one phase can be minimally invasive and the other by open surgery (hybrid procedures). The anastomo - - sis can be constructed in the chest or the neck.

Preoperative Preoperative counselling Nutritional assessment Nasogastric tube feeding for those with signi /f_i cant stenosis of the oesophagus, and oral supplement in those at risk of malnutrition Preoperative exercise General and incentive spirometry + pre-habilitation programme Stop smoking and alcohol intake Chest physiotherapy Carbohydrate loading on day of surgery No solid food 6 hours before and /f_l uid 2 hours before surgery. Carbohydrate loading night before and /f_i nishes 2 hours before surgery No need for bowel preparation unless colonic interposition is planned Intraoperative Prophylactic antibiotics DVT prophylaxis Mechanical +/– pharmacological Judicious use of intraoperative /f_l uids Avoid hypothermia Minimally invasive surgery if possible Epidural analgesia Postoperative Nutrition POD1 carbohydrate drink, gradual advancement to soft diet by POD5 (if no vocal cord palsy and assessment by speech therapist shows no risk of aspiration) PPN/TPN/feeding via jejunostomy in those at nutritional risk and oral intake insuf /f_i cient Nasogastric tube Removal on POD1 (if no vocal cord palsy and assessment by speech therapist shows no risk of aspiration) Analgesia Epidural analgesia/patient-controlled analgesia/multimodal analgesia Chest drain Single closed small-calibre drain (19Fr Blake drain), removal POD3–4 when output <200–300 /uni00A0 mL/day Early mobilisation From POD1, supervised by physiotherapist Urinary catheter Early removal as soon as close monitoring of urine output is not essential Intravenous /f_l uid Balanced intravenous /f_l uid to avoid over- and underhydration DVT prophylaxis DVT, deep vein thrombosis; POD, postoperative day; PPN, peripheral parenteral nutrition; TPN, total parenteral nutrition.

(b) Oesophagogastric junction cancer The options detailed above for intrathoracic cancers also apply to cancers of the OGJ. Suitability depends in part on the extent of oesophageal and gastric involvement by cancer and the intended extent of resection and lymphadenectomy . In addition, an extended total radical gastrectomy can be performed. The whole stomach and the lower oesophagus (accessed via the oesophageal hiatus from the abdomen) are resected and intestinal continuity is restored with a jejunal Roux loop (Roux-en-y reconstruction). In selected patients with early disease, a proximal gastrectomy can be performed as nodal spread to the distal stomach is rare. César Roux , 1857–1934, Professor of Surgery and Gynaecology , Lausanne, Switzerland, described this method of forming a jejunal conduit in 1908.

Figure 66.52 The common open approaches for surgery of the oesophagus: (a) left thoracoabdominal; (b) two-stage Lewis–Tanner (Ivor Lewis) approach. In the McKeown approach a third incision in the neck is made to allow anastomosis to the cervical oesophagus. (a) 5 mm 4 5 cm 5 6 10 mm 7 10 mm Figure 66.54 Port sites for video-assisted thoracoscopic oesophagectomy in the left lateral position (b) . Port sites can vary depending on the surgeon’s preference. Figure 66.53 Transhiatal oesophagectomy whereby the oesophagus is mobilised blindly using /f_i ngers from the neck and hand inserted from the abdomen. (b) (a) and laparoscopic gastric mobilisation

Lymphadenectomy ensures adequate nodal sampling for staging, improves local disease control and increasingly there is evidence to show the prognostic impact of extended lymphadenectomy . The most appropriate extent of lymph adenectomy remains somewhat controversial. Transhiatal

oesophagectomy does not allow adequate mediastinal nodal dissection (for the mid- and upper thoracic part oesophageal mobilisation is mostly a ‘blind’ procedure) and thus is often chosen by surgeons who perform only a limited lower medi astinal dissection f or OGJ adenocarcinoma. Squamous cell cancers are mostly more proximally located and the transhiatal approach may be dangerous except in early cancers. T he extent of lymphadenectomy can be defined as ‘fields’. Two-field dissection refers to lymphadenectomy of the mediastinum and upper abdomen around the coeliac trifur cation. The mediastinal ‘field’ is further classified as (i) stan dard: lymphadenectomy below the tracheal bifurcation, (ii) e xtended: standard lymphadenectomy plus right paratracheal nodal dissection including those around the right recurrent laryngeal nerve, and (iii) total: extended lymphadenectom plus nodal dissection along the left recurrent laryngeal nerve chain ( Figure 66.55 ). The third field refers to bilateral cervical lymphadenectomy , including those in the paratracheal as well as supraclavicular fossae. The most appropriate extent of lymphadenectomy remains a contentious issue. For patients with squamous cell cancers, most surgeons would perform at least a total two-field showed significant nodal metastases, especially around the bilateral recurrent laryngeal nerves. In selected patients and in particular those with upper thoracic cancers, additional third - field nodal dissection is perfor med (three-field lymphadenec - - tomy). For oesophageal adenocarcinoma, most surgeons perform an infracarinal two-field lymphadenectomy . For OGJ tumours (in particular those with limited oesophageal extent and centre on the OGJ), surgeons are divided among those who prefer oesophagectomy and those who perform e xtended - total gastrectomy with limited lower oesophageal resection and lymphadenectomy . The issue is unsettled. The extent of resection (and lymphadenectomy) has to be balanced against associated morbidities and physiological reserve of the indi - vidual patient. - Reconstruction - Restoration of intestinal continuity after oesophageal extirpa - tion is mostly done using a gastric conduit. The right gastro - epiploic vessels are its main blood supply . A pyloric drainage y procedure is optional, with some surgeons advocating its use to facilitate gastric emptying, after the inevitable vagotomy . In the case of a previous gastr ectomy , or if concomitant pathology (such as gastric cancer) requires its removal, the colon (right ileocolon, left or transverse colon) can be used. The surgery is more extensive and three anastomoses are required. The conduit can be placed in the right thoracic cavity (as in after a Lewis–Tanner oesophagectomy) or the neck for cervical

(a) (b) Figure 66.55 The lymph node station nomenclature according to the Japanese classi /f_i cation. Extent of mediastinal lymphadenectomy. /uni00A0 (a) Standard mediastinal lymphadenectomy includes stations below the tracheal bifurcation. includes standard lymphadenectomy + right paratracheal nodal dissection including those around the right recurrent laryngeal nerve. mediastinal lymphadenectomy includes extended lymphadenectomy + left paratracheal area and nodes along the left recurrent laryngeal nerve. Two- /f_i eld lymphadenectomy includes mediastinal dissection plus nodal dissection around the coeliac axis and three- /f_i eld dissection includes cervical lymphadenectomy. (c) (b) Extended mediastinal lymphadenectomy (c) Total

choices of routes of reconstruction exist: posterior mediastinal, retrosternal or subcutaneous. Perioperative care For most patients, a standardised clinical pathway is helpful, along the lines of the ERAS protocol ( Table 66.5 ). ERAS is a global perioperative quality improvement initiative based on attenuation of the stress response to surgical injury . The gastrointestinal system is

central to many of the core ERAS elements, including carbohydrate loading, no prolonged fasting, avoidance of mechanical bowel preparation, avoid ance of nasogastric intubation, maintaining fluid balance and early feeding. Employing these ERAS care practices leads to improved clinical outcome. Management of complications Complications are common as patients are often elderly with pre-existing morbidities and surgery is extensive. Atelectasis and pneumonia are managed by chest physiotherapy , adequate pain relief, avoidance of fluid overload, appropriate antibiotics and, if needed, sputum suction by bronchoscopy . Atrial fibrilla tion occurs in around 15–20% of patients; it is benign in most and is treated by antiarrhythmic medication. In some patients, it is a reflection of underlying serious complication, such as bronchopneumonia, or more importantly surgical morbidities such as anastomotic leak or ischaemia of the conduit. Its occurrence should prompt appropriate investigations, such as endoscopy . Recurrent laryngeal nerve injury is not uncommon when superior mediastinal lymphadenectomy or neck nodal dissection is carried out. Postoperatively the patient will expe rience hoarseness of the voice, coughing becomes less e ff ective and aspiration may be a problem when the diet is introduced. Active chest therapy and delay of oral intake may be necessary . and coughing e ff ort and lower the chance of aspiration. More definitive therapy may be needed if vocal cord function does not return. Gross ischaemia of the conduit usually presents within the first 2–3 days after the operation and dictates taking down of the conduit, adequate drainage and staged reconstruction later once sepsis is under control ( Figure 66.56 ). In selected cases immediate reanastomosis is an option if the patient is haemo - dynamically stable and an adequate length of healthy stomach remains. Clinically apparent thoracic anastomotic leaks usually - occur within the first week. Signs of sepsis and excessive out - put from the chest drain, which may be turbid in colour, may lead to the diagnosis. The location and magnitude of the leak can be visualised by a water-soluble contrast study . A carefully performed flexible endoscopic examination is also helpful and will not worsen the leak. For small, contained leaks, CT-guided drainage or use of a luminal vacuum Endo-Sponge™ may suf - fice. In septic patients with a sizeable leak, exploration is war - ranted to establish drainage. Direct repair is seldom possible. For cervical anastomosis, leakage is suspected when there is inflammation and pain of the neck wound. Turbid infected - discharge is found when the skin stitches are removed. Leaks that are truly confined to the neck are simply trea ted by lay - ing the wound open with daily washing and frequent changes of dressing. Leaks that communicate with the mediastinum , may require for mal exploration and placement of mediastinal drains. In all leaks, treatment with broad-spectrum antibiotics is required, guided by microbial culture and sensitivity . Nutri - tional support is essential. With an intrathoracic stomach, care - - ful endoscopic placement of a fine-bore feeding tube into the duodenum for enteral feeding is useful. Injection of fibrin g lue, placement of intraluminal stents, use of a luminal vacuum

# (a) (b) Figure 66.56 (a) Cervical wound with erythema, swelling and discharge of purulent material,

# typical of a cervical anastomotic leak. (b) An ischaemic gas

tric conduit; 5 cm of the stomach appeared unhealthy and required resection.

increasingly used to treat leaks; sealing of the leak allows early control of sepsis and resumption of oral alimentation. The stent can be removed afterwards, depending on the severity of the leak in the first place. Usually , 4–6 weeks will su ffi ce for adequate healing. A chylous leak is suspected when there is excessive chest drainage. A milk challenge, looking at the colour of the e ffl uent before and after taking milk by mouth or via the nasogastric tube, will usually be obvious. This can be aided by biochemical testing of the drain fluid, measuring triglyceride level or chylo microns. In a low-output fistula of less than 0.5–1 litre per day , conservative management with total parenteral nutrition or a mid-chain triglyceride diet may su ffi ce. In case of persistence or if the output is more than 1 litre per day , prolonged conservative treatment is not recommended and early re-exploration is warranted. A lymphangiogram preoperatively will help locate the site of leakage, and intraoperative milk feed will also serve the same purpose. The site of the leak can then be clipped or sutured. Increasingly , however, the interventional radiological method of percutaneous embolisation has gained success and has reduced the need for surgical re-exploration.

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