Gastric Cancer

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Incidence

- **9th commonest cancer in males and 8th in females in the Jordan.**
- 145 **new cases each year.**
- **Male to female ratio 5:3.**
- **Occurs mainly in elderly. Less than 8% of cases below age 55.**
- **Steadily increases with age and peaks 7th decade.**
- **Major geographical difference: Incidence high in Japan and some parts of Asia.**

Risk factors

- Wide international variations in incidence and the dramatic falls seen across the developed world suggest that environmental factors are very important in gastric carcinogenesis.

H. pylori infection, gastric atrophy, and gastritis

- ***H. pylori is the most important risk factor***

- **Most cases of gastric cancer are associated with the presence of *H. pylori in the stomach.***

- ***H. pylori infection is a common bacterial infection with a high prevalence in the developing* world**.
  Poor hygiene
  crowded living conditions
  low socio-economic status

- ***H. pylori infection doubles the risk of non-cardiac gastric cancer and the risk is even higher in* those with the cagA-positive strain.**

- **The precancerous lesion severe chronic atrophic gastritis can be induced by *H. pylori* infection. This is a premalignant condition that increases the risk of gastric cardia cancer by 11-fold and gastric non-cardia by 3-fold**.

- **Risk increases with the severity of gastric atrophy such that those with multifocal gastric atrophy have more than 90 times increased risk of gastric cancer**

Nutritional

- **Low fat/protein diet**

- **High salt intake**
  Risk is three times higher in those with a daily salt intake of 16g/day or higher.

- **Heavily salted foods are high in N-nitroso compounds, which increase the risk of non-cardia**
  stomach cancer in those with *H. pylori infection*

- **Vegetables are a major source of nitrates and together with fruit have a protective effect**
  against stomach cancer. The antioxidants of fruit and vegetables inhibit the formation of Nnitroso compounds.

- **Processed meat (especially bacon, ham, and sausages)**

- **Frying and grilling food**
  heterolytic amines

Smoking and alcohol

- **Smokers have double the risk of gastric cancer and the risk remains higher for 10–20 years after giving up**.
- **Nitrosamines**
- **A causal factor for gastric cancer.**
- **Heavy alcohol consumption**

Medical conditions

- ***Obesity***

  2-fold increased risk

- ***Pernicious anaemia***

  2–3 times increased risk

- **Previous gastric surgery**

Pathology

- **WHO classification 1990**

  Morphology
- **Five types**

  Adenocarcinoma

  Adenosquamous cell carcinoma

  Squamous cell carcinoma

  Undifferentiated carcinoma

  Unclassified carcinoma.
- **Adenocarcinoma**

  growth pattern papillary

  tubular

  mucinous

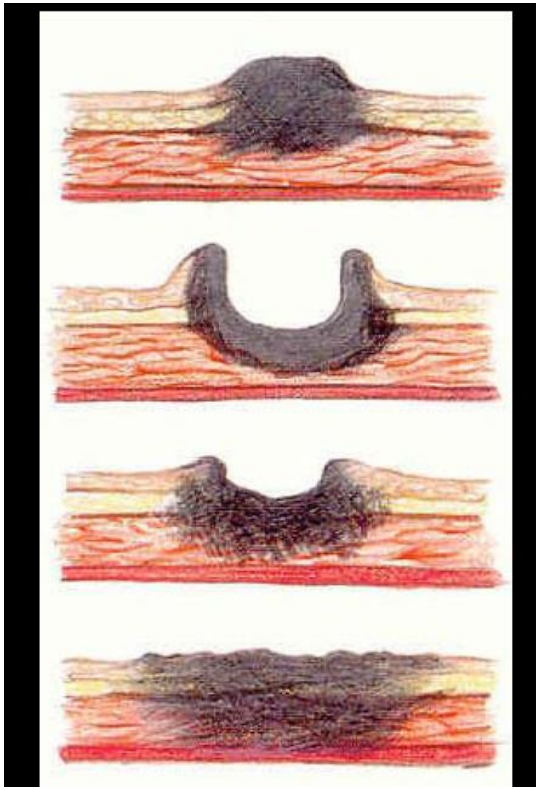
  signet ring.

  Each type further subdivided by degree of differentiation.

- **Widely used system, but offers little in terms of patient management.**

Borrmann's classification

- Developed in 1926.
- **Divides gastric cancer into five types based on macroscopic appearance of the lesion:**
  - **Type 1: polypoid or fungating lesion;**
  - **Type 2: ulcerated lesion surrounded by raised borders**
  - **Type 3: ulcerated lesion with infiltration to the gastric wall;**
  - **Type 4: diffusely infiltrating lesion (Linitis *plastica when it involves whole stomach);***
  - **Type 5: lesions that do not fit to any of the above.**



Borders' classification

- Developed in 1942 and is the original classification.
- Classifies gastric carcinoma on the degree of cellular differentiation independent of morphology.
- Ranges from type 1 (well differentiated) to type 4 (anaplastic).

Lauren classification

- **1965**
- ***The intestinal type:***
  typically arises in the presence of a precancerous condition
  gastric atrophy or intestinal metaplasia,
  more common in men
  incidence increases with age
  dominant type in areas in which gastric cancer is epidemic
  well differentiated
  spread haematogenously to distant organs.
- ***The diffuse type:***
  poorly differentiated
  lacks gland formation
  composed of signet ring cells.
  Clusters of small uniform cells, tends to spread submucosally and metastasizes early by transmural extension and via lymphatics.
  Poor prognosis
  More common in women and younger age groups
  Associated with blood type A and familial cases suggesting genetic aetiology.

Symptoms

- **Gastric adenocarcinoma lacks specific symptoms early in its course.**
- **Vague symptoms of epigastric discomfort and indigestion – often ignored by patients mistaking it for gastritis.**
- **Pain tends to be constant and unrelieved by food or antacid therapy.**
- **More advanced cancer presents with weight loss, dysphagia, loss of appetite, early satiety, or vomiting.**

Physical signs

- **Develop late.**
- **Most commonly associated with locally advanced or metastatic disease.**
- **Findings may include:**

  palpable abdominal mass

  palpable supraclavicular (Virchow's)

  periumbicular(sister Mary Joseph's) nodule

  jaundice

  ascites

  cachexia.

Clinical evaluation and staging

- Flexible upper endoscopy
- Blood test
- Double-contrast barium swallow
- Endoscopic ultrasound scan (EUS)
- CT (computed tomography)
- Diagnostic laparoscopy

Flexible upper endoscopy

- **Modality of choice once gastric cancer is suspected.**
- **Multiple biopsies (seven or more required) from ulcer edges.**
- **Avoid biopsying ulcer crater (may reveal necrotic debris only).**
- **Note the size, location, and morphology of the tumour.**

Blood test

- ***Full blood count:***

  anaemia

- ***Liver function test:***

  abnormal in advanced disease and sign of liver metastasis

- ***Coagulation:***

  abnormal in advanced disease

Double-contrast barium swallow

- **Cost effective and 90% diagnostic accuracy**
- **However, unable to distinguish benign from malignant lesions**
- **Endoscopy preferable**

Endoscopic ultrasound scan (EUS)

- Can assess the extent of gastric wall invasion and nodal status.
- Better accuracy for T1 and T3 lesions, but poor for T2 (cannot assess invasion of the muscularis propria).
- Superior to CT for T1 and T3 tumours.
- Cannot reliably distinguish tumour from fibrosis, thus not suitable for evaluating response to therapy.
- Good for evaluating lymph nodes and have added advantage of fine-needle aspiration.
- Overall staging accuracy is about 80%.
- Complimentary to CT and not a replacement.

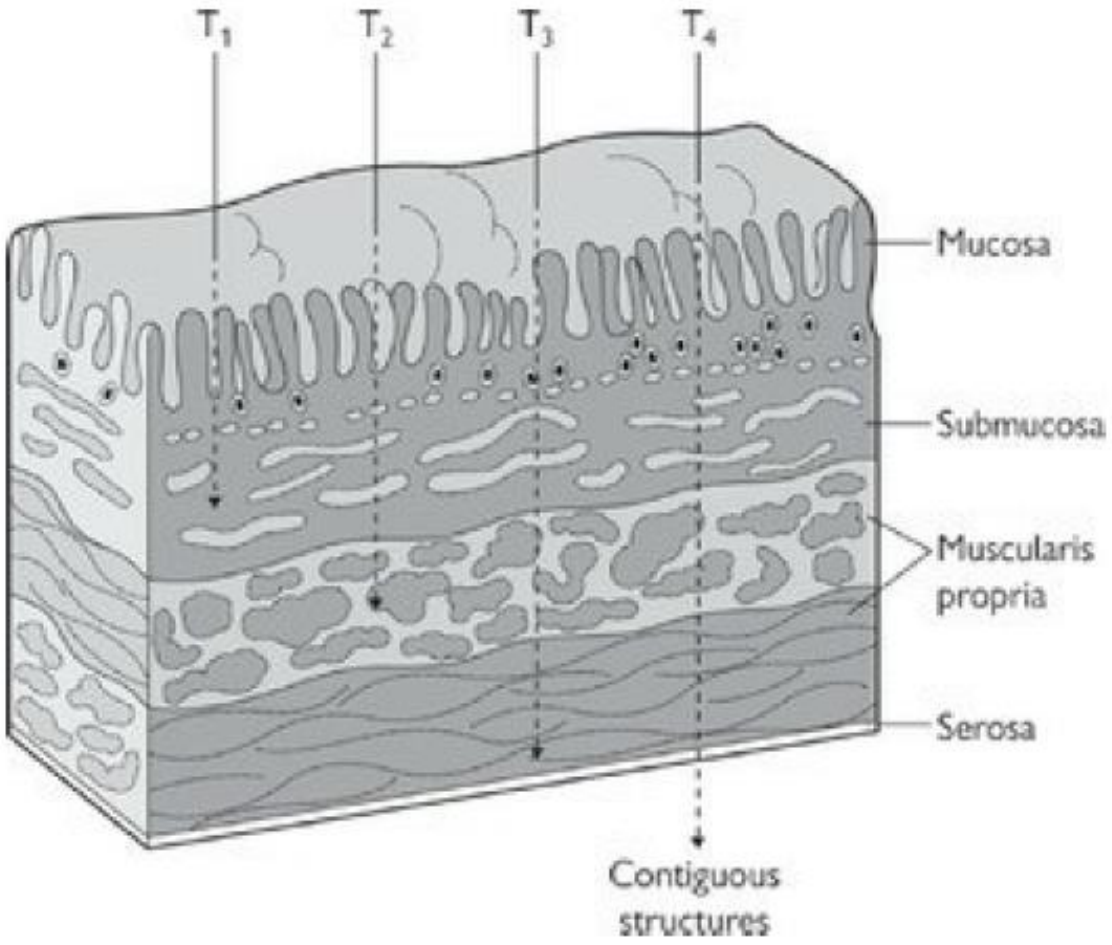
CT (computed tomography)

- **Chest, abdomen, and pelvis**
- **Cannot distinguish T1 and T2 tumour (i.e. early gastric cancers)**
- **Cannot detect small (<5mm) metastasis in the liver or on peritoneal disease.**
- **Nodal detection relies on size and is a poor predictor of involvement particularly in the chest.**
- ***PET-CT may improve the detection of distant metastasis. Not a routine exam Mainly* used in follow-up and where there is a suspicion of progression.**
- **Overall accuracy of 80–85%.**

Diagnostic laparoscopy

- **Due to the inherent inaccuracies of CT and EUS, laparoscopy is indicated for evaluation of patients with locoregional disease**
- **Can detect metastatic disease in 30% of patients who are judged to be resectable on CT and EUS.**
- **Addition of laparoscopic ultrasound may improve detection of liver and peritoneal metastasis**
- ***Cytology of peritoneal fluid obtained at laparoscopy may reveal the presence of free* intraperitoneal gastric cells**

Staging systems



- ***Regional lymph nodes (N)***

  NX: nodes cannot be assessed

  N0: no lymph node metastasis.

  N1: 1–6 positive nodes.

  N2: 7–15 positive nodes.

  N3: more than 15 positive nodes.

- ***Distant metastasis (M)***

Stage 0	Tis, N0, M0
Stage 1A	T1, N0, M0
Stage 1B	T1, N1, M0 T2a/b, N0, M0
Stage II	T1, N2, M0 T2a/b, N1, M0 T3, N0, M0
Stage IIIA	T2a/b, N2, M0 T3, N1, M0 T4, N0, M0
Stage IIIB	T3, N2, M0
Stage IV	T4, N1–3, M0 T1–3, N3, M0 Any T, any N, M1

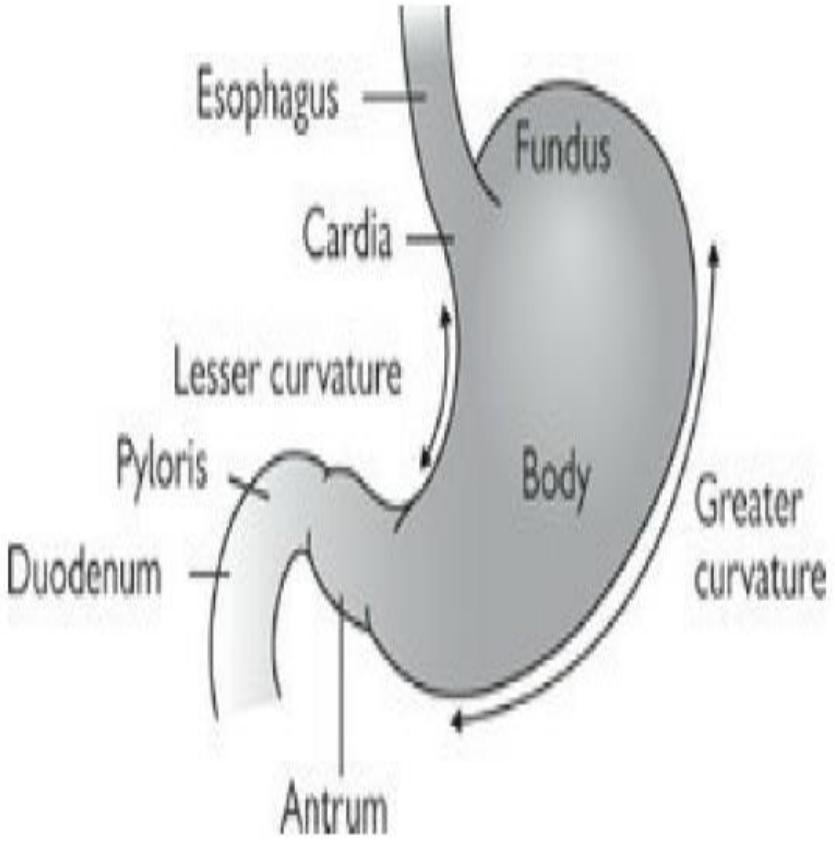
- ***Stage IV disease (M1):*** palliation therapy.
- All other stages if medically fit consider for diagnostic laparoscopy for further staging.

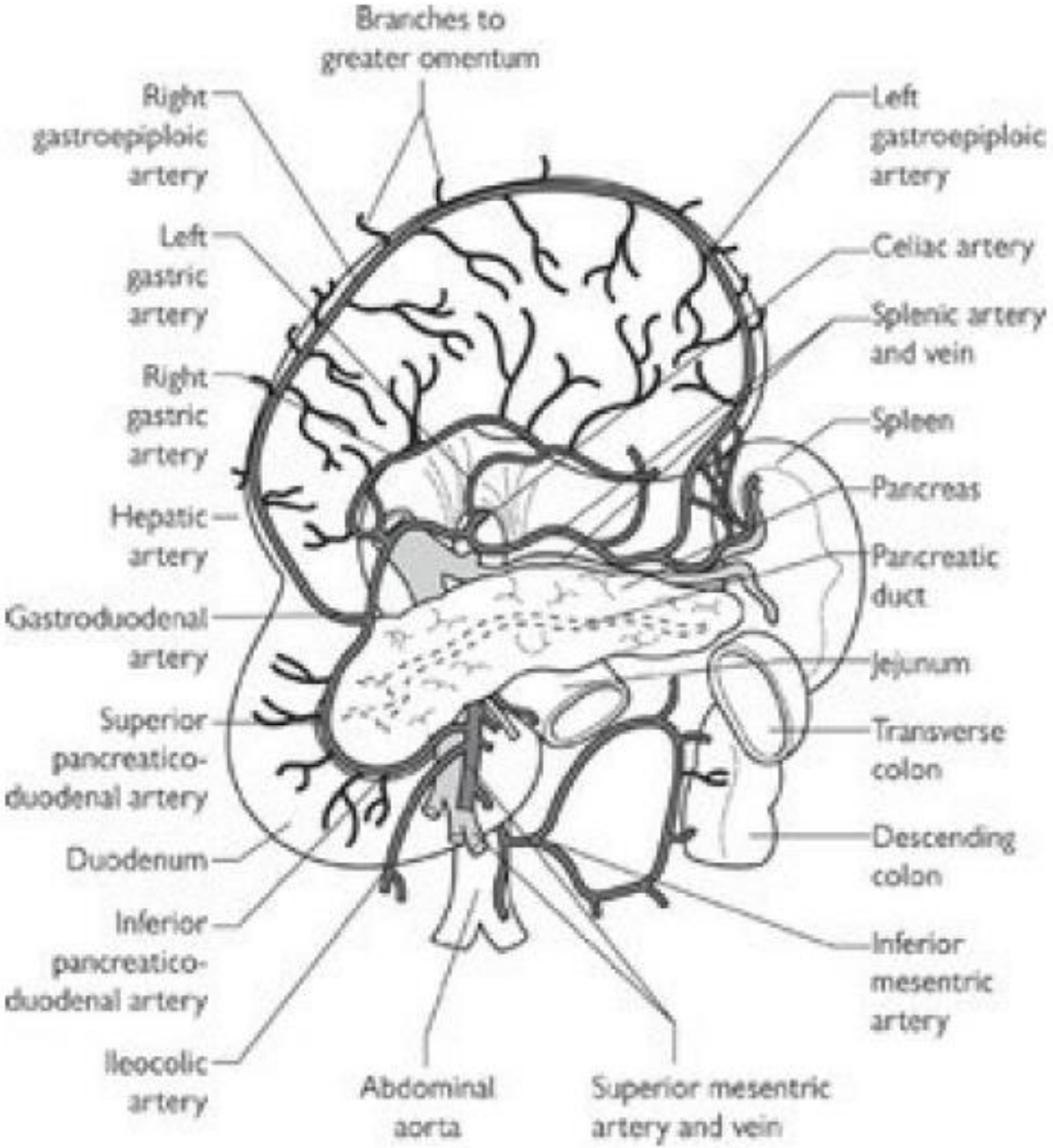
After laparoscopy

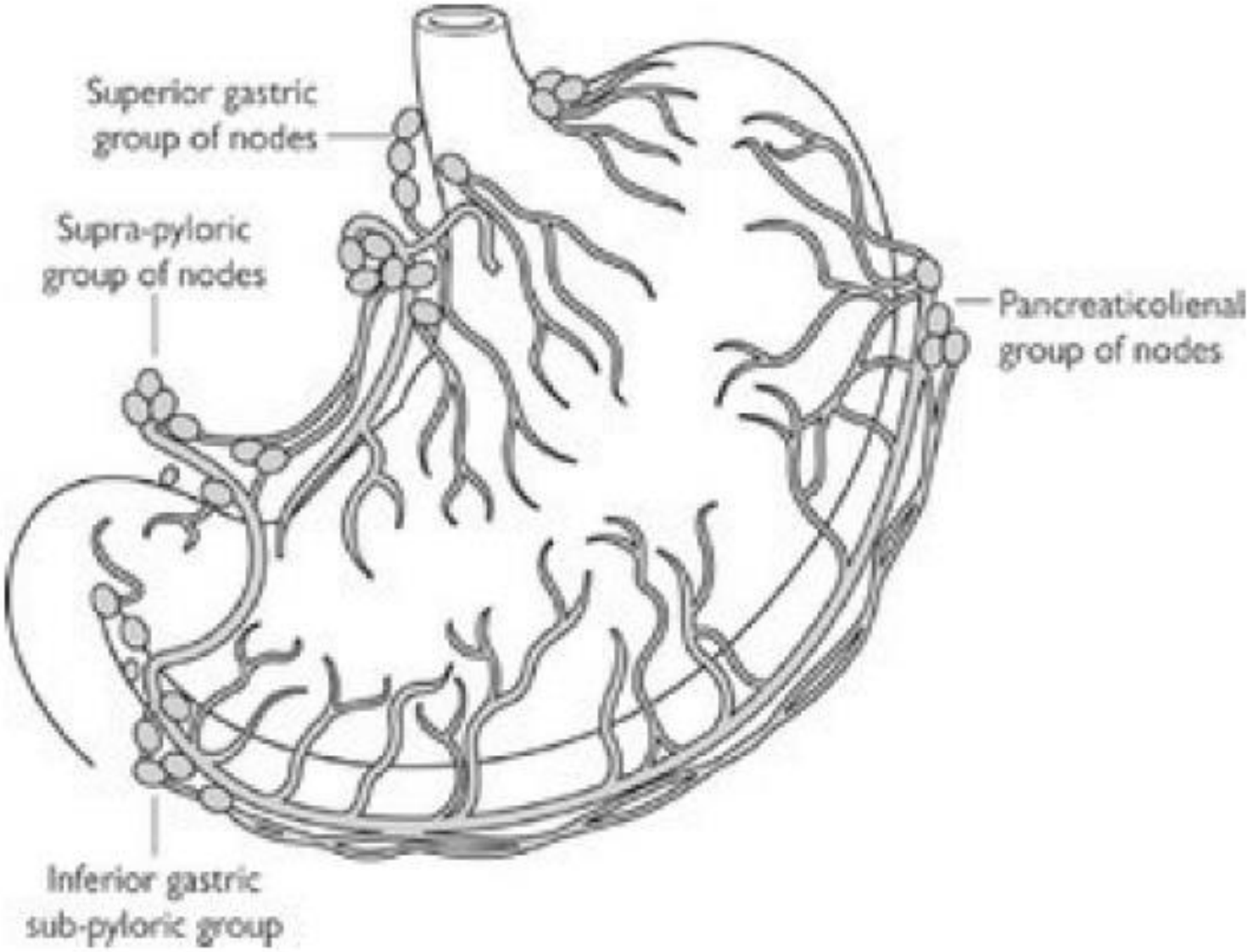
- Stage M1 palliation only.
- Stage M0, but medically unfit either palliation only or radiotherapy and 5-FU radiosensitization.
- Stage M0 and medically fit, T1 or less. For surgery.
- Stage M0 and medically fit, T2 or higher. Neoadjuvant chemotherapy with ECF (MAGIC trial protocol) followed by surgery.

Gross anatomy

- **Relations of the stomach:**
- **anteriorly – left lobe of the liver;**
- **superiorly – the diaphragm;**
- **medially – the liver;**
- **laterally – spleen;**
- **inferiorly – transverse mesocolon, caudate lobe of liver, crura of the diaphragm, and retroperitoneal nerves and vessels.**




Branches to greater omentum
Right gastroepiploic artery
Left gastric artery
Right gastric artery
Hepatic artery
Gastroduodenal artery
Superior pancreatico-duodenal artery
Duodenum
Inferior pancreatico-duodenal artery
Ileocolic artery
Abdominal aorta
Superior mesentric artery and vein
Left gastroepiploic artery
Celiac artery
Splenic artery and vein
Spleen
Pancreas
Pancreatic duct
Jejunum
Transverse colon
Descending colon
Inferior mesentric artery


Superior gastric
group of nodes
Supra-pyloric
group of nodes
Pancreaticolienal
group of nodes
Inferior gastric
sub-pyloric group

Surgical management

- **Primary treatment for gastric carcinoma.**
- **Less than 50% of patients at presentation currently are resectable.**
- **Extent of gastric resection is determined by the need to obtain R0 margin.**
- **6cm clearance from edge tumour is required in order to decrease risk of local recurrence.**

- **Proximal tumours**

  total gastrectomy

- **Distal tumours**

  subtotal gastrectomy

Lymph node dissection

- **controversial.**
- **The Japanese classification system is used to define extent lymphatic dissection performed**

  Group 1 nodes (N1): perigastric lymph nodes *lesser curvature*
  greater curvature

  Group 2 (N2): nodes *left gastric artery*
  common hepatic artery
  coeliac artery
  splenic artery

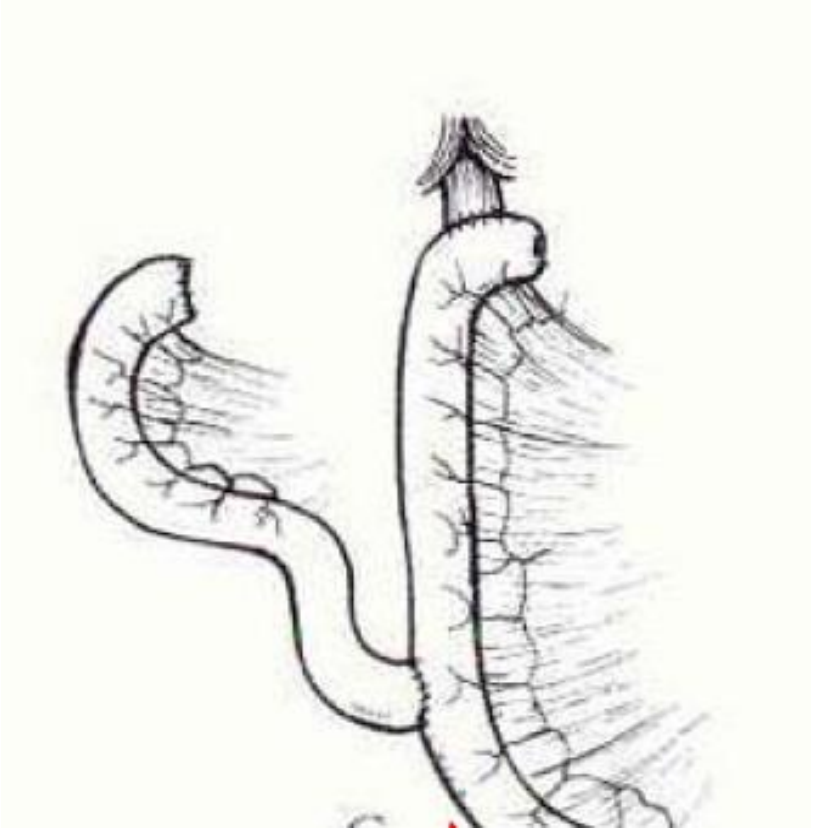
  Group 3 (N3): more distant nodes
  para-aortic nodes

- **D1 D2 D3**

- **D1 vs. D2**

  Higher morbidity and mortality for D2 compared to D1 gastrectomy.
  No difference in overall survival between D1 and D2.

Roux-en-Y reconstruction



Complications of gastric surgery

- **Early complications**

  Bleeding

  Infection

  Anastomotic leak

- **General complications**

  Cardio-respiratory complications

  Deep vein thrombosis

  pulmonary embolism

Late complications

- ***Early dumping***
- 20–30min after ingestion of a meal
- Autonomic response
- serotonin, bradykinin-like ,substances, neurotensin, and enteroglucagon
- **GI symptoms:** nausea and vomiting, sense of fullness, belching, abdominal cramps, and explosive diarrhoea.
- **Cardiac symptoms:** palpitations, tachycardia, sweating, fainting, dizziness, flushing, and visual disturbance
- Symptoms usually subside with time

Late complications

- Late dumping
- 2–3h after ingestion of a meal
- **large amount of carbohydrates to the proximal small intestine**

  quickly absorbed
  sudden hyperglycaemia
  large amount of insulin
  profound hypoglycaemia
  catecholamines from the adrenal gland

  tachycardia, sweating, confusion, and dizziness
- **Symptoms similar to hypoglycaemic shock**

Endoscopic mucosal resection (EMR)

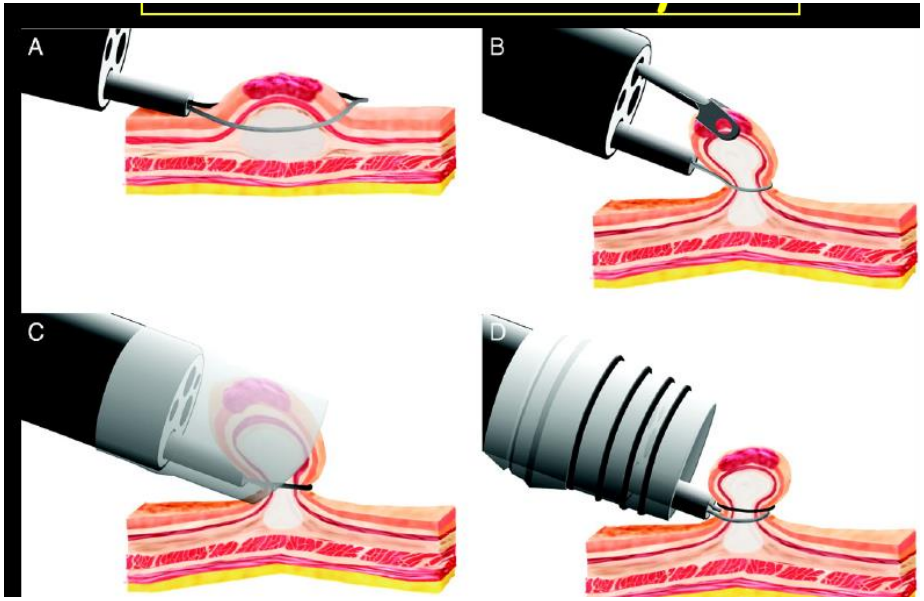
- Most experience with EMR is in Japan where there is higher incidence of early gastric cancer and an active screening programm.
- **Indications for EMR**

  well or moderately differentiated

  tumour size less than 30mm

  absence of ulceration

  no evidence of invasive findings



Adjuvant chemoradiotherapy

M1	**Palliative therapy**
R0 resection and T1, NO	Observe
R0 and T2 and higher	ECF chemotherapy
R1 resection	Radiotherapy plus concurrent 5-FU sensitization followed up by ECF chemotherapy if T2 and higher
R2 resection	5-FU based radiosensitization or ECF chemotherapy or best supportive care if unfit
Primary palliative chemotherapy	Reassess and if good response consider surgery

Surveillance

- First 3 years follow-up should be intensive, since recurrence is most common at this stage
- Follow-up should be 4–6 months for first 3 years, thereafter annually
- History, physical examination, and routine blood profile should be conducted at each followup visit
- CT scan should be performed yearly for first 3 years or sooner if suspicious
- Yearly gastroscopy on patients who have undergone subtotal gastrectomy