Lower Digestive System - Stomach Cancer

The breaking down of food molecules for use by body cells is called digestion, and the **organs that collectively perform this function comprise the digestive system.**

The organs of digestion are traditionally divided into two groups:

1. the gastrointestinal (GI) tract or alimentary canal and

2. the accessory structures.

Epidemiology and Aetiology

Gastric cancer was once the second most common cancer in the world. In most developed countries, however, rates of stomach cancer have declined dramatically over the past half century.

In Japan, gastric adenocarcinoma is the most common cancer in both males (75 cases per 100,000 population) and females (35 cases per 100,000 population). In Australia, the incidence of gastric adenocarcinoma is much less, affecting 9.2 males and 4.5 females per 100,000 population.

Decreases in gastric cancer have been attributed in part to widespread use of refrigeration, which has had several beneficial effects: increased consumption of fresh fruits and vegetables; decreased intake of salt, which had been used as a food preservative; and decreased contamination of food, by carcinogenic compounds arising from the decay of unrefrigerated meat products.

Salt and salted foods may damage the gastric mucosa, leading to inflammation and an associated increase in DNA synthesis and cell proliferation. Other factors likely contributing to the decline in stomach cancer rates include lower rates of chronic Helicobacter pylori infection, thanks to improved sanitation and the use of antibiotics. The increased use of screening programmes in some countries may also have played a part in reducing the incidence of gastric cancer.

Epidemiology and Aetiology (cont)

Nevertheless, gastric cancer is still the second most common cause of cancer-related death in the world, and it remains difficult to cure in Western countries, primarily because most patients present with advanced disease. Even patients who present in the most favourable condition and who undergo curative surgical resection often die of recurrent disease.

Tremendous geographic variation exists in the incidence of this disease around the world. Rates of the disease are highest in Asia and parts of South America and lowest in North America. The highest death rates are recorded in Chile, Japan, South America, and the former Soviet Union.

There are multiple risk factors for the development of gastric adenocarcinoma, including precursor conditions, genetic and environmental conditions, and age. Helicobacter pylori infection is associated with risk of stomach cancer.

Helicobacter pylorus is a bacterium that commonly infects the mucosa of the stomach. Infection with helicobacter pylori can cause stomach inflammation and peptic ulcers. It also increases the risk of stomach cancer, but only a small number of infected people develop stomach cancer.

Other known risk factors for stomach cancer include:

Long-term inflammation of the stomach: People who have conditions associated with long-term stomach inflammation (such as the blood disease pernicious anemia) are at increased risk of stomach cancer. Also, people who have had part of their stomach removed may have long-term stomach inflammation and increased risk of stomach cancer many years after their surgery.

Smoking: Smokers are more likely than non-smokers to develop stomach cancer. Heavy smokers are most at risk.

Epidemiology and Aetiology (cont)

Family history: Close relatives (parents, brothers, sisters, or children) of a person with a history of stomach cancer are somewhat more likely to develop the disease themselves. If many close relatives have a history of stomach cancer, the risk is even greater.

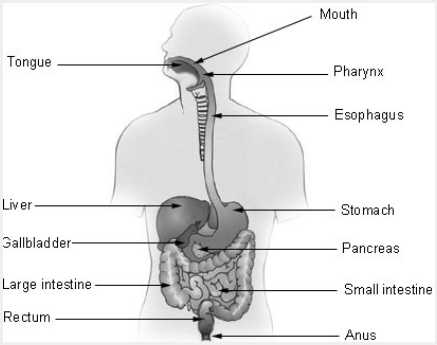
Poor diet, lack of physical activity, or obesity: Studies suggest that people who eat a diet high in foods that are smoked, salted, or pickled have an increased risk for stomach cancer. While people who eat a diet high in fresh fruits and vegetables may have a lower risk of this disease.

A lack of physical activity may increase the risk of stomach cancer. People who are obese may have an increased risk of cancer developing in the upper part of the stomach. The most common symptoms of stomach cancer are loss of appetite, abdominal discomfort, weight loss, weakness (from anemia), nausea and vomiting, and tar like stools.

Approximately 95% of all malignant gastric neoplasms are adenocarcinomas, and **in general, the term gastric cancer refers to adenocarcinoma of the stomach**.

Other malignant tumors are very rare and include squamous cell carcinoma, adenoacanthoma, carcinoid tumours, and leiomyosarcoma. Although no normal lymphoid tissue is found in the gastric mucosa, the stomach is the most common site for lymphomas of the gastrointestinal tract. The differentiation between adenocarcinoma and lymphoma can sometimes be difficult but is essential because staging, treatment, and prognosis are different for each disease.

Digestive system



Anatomy and disease process

The **stomach is a hollow J shaped organ** which begins at the gastro-esophageal (GE) junction and ends at the pylorus; it is usually divided into three sections.

The uppermost part is the cardia; the middle and largest part is the body, or fundus; and the distal portion, the pylorus, which connects to the duodenum.

Understanding the vascular supply of the stomach allows understanding of the routes of haematogenous spread.

The vascular supply of the stomach is derived from the celiac artery. The left gastric artery, a branch of the celiac artery, supplies the upper right portion of the stomach. The common hepatic artery branches into the right gastric artery, which supplies the lower portion of the stomach, and the right gastro-epiploic branch, which supplies the lower portion of the greater curvature.

Understanding the lymphatic drainage can clarify the areas at risk for nodal involvement by cancer.

The lymphatic drainage of the stomach is complex. Lymphatic drainage follows the arterial supply. Most lymphatic's drain ultimately to the celiac nodal area, lymphatic drainage sites include the splenic helium, supra-pancreatic nodal groups, porta hepatis and gastro-duodenal areas.

Anatomy and disease process (cont)

The wall of the stomach has five layers. From the lumen out, the layers include the mucosa, the sub-mucosa, the muscularis layer, the sub-serosal layer, and the serosal layer.

The peritoneum of the greater sac covers the anterior surface of the stomach. A portion of the lesser sac drapes posteriorly over the stomach.

The gastro-oesophageal junction has limited or no serosal covering. The right portion of the anterior gastric surface is adjacent to the left lobe of the liver and the anterior abdominal wall.

The left portion of the stomach is adjacent to the spleen, the left adrenal gland, the superior portion of the left kidney, the ventral portion of the pancreas, and the transverse colon.

Diagnosis

The best test to diagnose gastric cancer is **gastroscopy**. Gastroscopy is a day procedure that involves the passage of a flexible tube down the oesophagus and into the stomach which allows the surgeon to visualise the cancer and also take biopsies to confirm the diagnosis. The procedure is done with sedation and takes approximately ten minutes.

Disease process

The site of stomach cancer is classified on the basis of its relationship to the long axis of the stomach. Approximately 40% of cancers develop in the lower part, 40% in the middle part, and 15% in the upper part; 10% involve more than one part of the organ. Cancer of the stomach may extend directly into the pancreas, diaphragm, transverse colon, and duodenum. The liver and lungs are common sites of distant metastases.

Staging

The minimum staging procedures once the diagnosis of gastric cancer has been confirmed with gastroscopy include:

Anatomy and disease process (cont)

1. **Blood tests** – indicates metastatic spread to the liver.

2. **Chest x-ray** - looking for metastatic spread to the lung.

3. **CT scan of the abdomen and chest** - to ascertain spread to the lungs and liver.

4. **Endoscopic Ultrasound** - procedure similar to a gastroscope, and is the best test to determine the depth and local invasion of the tumour. It also allows biopsies to be taken of surrounding lymph nodes to determine if they are involved, which determines the treatment management plan.

5. **Staging laparoscopy** - to determine presence of small cancer nodules and lymph node involvement within the abdominal cavity that CT scan can miss. Laparoscopy is a minor procedure that is done when all other staging procedures are clear. It is done to prevent major surgery being performed in patients whose cancer is not curable.

Other tests that may be used to look for metastatic spread are PET scans and MRI scans.

Staging of gastric cancer is usually performed using the TNM classification system. In the TNM staging system, a score is given for each of the three areas of interest:

Degree of tumour invasion (T staging)
Lymph node involvement (N staging)
Presence of distant metastases (M staging)

TNM Staging: Gastric Cancer

Table II. TNM classification (4th edition) for gastric cancer

Tis	*In situ*
T1	Limited to mucosa or submucosa
T2	Muscularis propria involved
T3	Serosal involvement
T4	Invasion outside the stomach
N0	No lymph node involvement
N1	Lymph node involvement 3 cm away from primary tumor
N2	Regional lymph node involvement (left gastric, common hepatic, celiac, splenic)
N3	Intra-abdominal distant lymph node involvement (duodenal, mesenteric, para-aortic, retropancreatic)
M0	No distant metastasis.
M1	Distant metastasis
Stage II	T1N1M0; T2N0M0
Stage II	T1N2M0; T2N1M0; T3N0M0
Stage III	T2N2M0; T3N1-2M0; T4N0-1M0
Stage IV	T4N2M0; T1-4N3

Treatment Management Options

Treatment for stomach cancer may involve surgery, chemotherapy, or radiation therapy.

Radical surgery is highly successful in the treatment management of stomach cancer if disease is limited to the mucosa, but the incidence of such early lesions at diagnosis is rare.

The majority of patients with operable stage II, IIIA, or IIIB disease have at least a 60% chance of tumour recurrence and death within 5 years of diagnosis. This group therefore might benefit from adjuvant therapy.

Surgery: The type of surgery for stomach cancer depends mainly on the anatomical position of the tumour. The surgeon may remove the whole stomach or only the part that has the cancer.

Partial (subtotal) Gastrectomy for tumours at the lower part of the stomach: The surgeon removes the lower part of the stomach containing the tumour. The surgeon attaches the remaining part of the stomach to the intestine. Nearby lymph nodes and other tissues may also be removed.

Total Gastrectomy for tumours at the upper part of the stomach: The surgeon removes the entire stomach, nearby lymph nodes, parts of the oesophagus and small intestine, and other tissues near the tumour. Rarely, the spleen also may be removed. The surgeon then connects the oesophagus directly to the small intestine.

The propensity for gastric carcinoma to spread by means of sub-mucosal lymphatics suggests that a 5cm margin of normal tissue proximally and distally may be optimal. The 5-year survival rate for a curative surgical resection ranges from 60-90% for patients with stage I, 30-50% for patients with stage II disease, and 10-25% for patients with stage III disease. Due to the high likelihood of local and systemic relapse, some physicians offer adjuvant therapy.

Treatment Management Options (cont)

Chemotherapy has been shown to increase survival and the time it takes the disease to progress, compared to best supportive care alone. An improved quality of life with chemotherapy compared to best supportive care has also been demonstrated.

Several chemotherapeutic agents have shown activity against gastric adenocarcinoma, including fluorouracil, mitomycin, cisplatin, doxorubicin and methotrexate. A standard regime includes the combined use of fluoropyrimidine and cisplatin.

Patients with gastric tumours may also be tested for their human epidermal growth factor receptor 2 (HER2) status. Those with HER2 positive tumours can be treated with trastuzumab in addition to the standard fluoropyrimidine/cisplatin regimen.

Radiation Therapy

Gastric adenocarcinoma is relatively resistant to radiotherapy, with the doses required exceeding the tolerance of surrounding structures including the bowel, kidney and spinal cord. As a result, **the use of radiotherapy is limited to symptom control of the palliative patient.** The role of irradiation as adjuvant therapy in completely resected but high-risk patients is being evaluated.

Radiation therapy, usually administered with concomitant 5-fluorouracil (5-FU)-based chemotherapy, is indicated in locally confined gastric cancer that is either not technically resectable or occurs in medically inoperable patients.

Patients who undergo gastric resection and have either incomplete tumour resection or truly positive margins of resection are appropriately managed by combined-modality therapy.

Radiation Therapy Planning and Treatment

The irradiation field should include unresected or residual tumour or the tumour bed plus major nodal regions.

Dose-limiting organs and structures in the upper abdomen are numerous (stomach, small intestine, liver, kidneys, and spinal cord).

With properly shaped fields, doses of **45 to 50.4 Gy in 1.8- to 2.0-Gy fractions** can be delivered to stomach and small intestine with a 5% or less risk of severe toxicity.

Radiation therapy treatment volumes

Target volumes for stomach cancer irradiation based on the sites of loco-regional failure should include for all patients;

-the gastric tumour bed
-anastomosis and stump
-regional lymphatics.

Major nodal chains at risk include lesser and greater curvature, celiac axis, pancreatic duodenal, splenic, suprapancreatic, and porta hepatis.

Beam Arrangements

Parallel-opposed anteroposterior-posteroanterior (AP/PA) fields are the most practical arrangement for the major portion of tumour nodal irradiation.

In most patients a portion of both kidneys will be within the AP-PA treatment field, but at least two thirds to three quarters of one kidney should be excluded (can include entirety of both kidneys to the level of 20 Gy if necessary).

For patients with gastro oesophageal junction or proximal to mid-gastric cancers, one half to two thirds of the left kidney can often be spared as a result of accurate field definition, which is aided by pre- and postoperative imaging studies and clip placement.

The pancreatic duodenal nodes can be included, if indicated, while sparing 75% to 90% of the right kidney.

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Not published yet.
Last updated 26th October, 2016.

Radiation Therapy Planning and Treatment (cont)

However, for distal gastric lesions with narrow or positive duodenal resection margins, the duodenal circumference may need to be included as target volume. In such instances 50% or more of the right kidney is within the field, and two thirds to three fourths of the left kidney should be spared. Chronic renal problems are infrequent when these techniques are utilised.

Dose fractionation regimes

With single daily fractions, the usual dose is**45 to 52 Gy delivered in 1.8- to 2.0-Gy fractions over 5.0 to 5.5 weeks,** with a field reduction after 45 Gy. Reduced boost fields to small areas of residual disease can sometimes be cautiously carried to doses of **55 to 60 Gy.**

Palliative Radiation Therapy

Evidence evaluating the use of radiation therapy in patients with locally recurrent or metastatic carcinoma of the stomach is limited due to small patient numbers. The role of radiation therapy in patients with advanced stomach cancers is likely to be limited to palliation of symptoms—such as bleeding or controlling pain secondary to local tumour infiltration and biliary obstruction. Although minimal data is available, radiation therapy seems to be fairly effective (from anecdotal experience) in controlling bleeding, as is true in other sites. This can often be accomplished at relatively low radiation doses. Pain from local tumour invasion can also be palliated, although the doses required are higher (45 Gy).

Treatment sequelae and patient ca

Toxicity is often the limiting factor in radiation therapy involving both the lower and upper digestive system.

The acute effects of radiation include mucosal denudation.

Treatment sequelae and patient ca (cont)

Late effects consist of fibrotic changes leading to reduced mobility and ischemia.

Multi-field and conformal radiation therapy, as well as accurate and reproducible patient positioning techniques, reduce the volume of normal tissue exposed to radiation and can decrease the potential toxicity.

However, the treatment management approaches for radiation toxicity are mainly supportive care. The increased use of concurrent chemotherapy and radiation therapy, has required enhanced awareness of potential effects and better methods to decrease toxicity, as this combination of treatments is associated with a higher rate of gastro-intestinal toxicity.

Radiation to the upper abdomen can produce anorexia and nausea, which may exacerbate the patient's already poor nutritional status.

Transient mal-absorption may occur as a result of diffuse damage to the bowel mucosa in the irradiated field.

Symptoms such as inflammation, endarteritis, and fibrosis, with possible stricture formation or ulceration, may further compromise absorption function.

Common complaints during gastric irradiation include: Anorexia, Nausea, and Fatigue