Cancers of The Bowel and Digestive System

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The digestive tract is a complex series of organs and several cancers can arise from it. This lecture considers the commonest and most important ones in the UK. These are notes rather than a full transcript of the lecture.

The key part of the digestive system which give rise to the most important cancers are worth a quick refresher. The oesophagus gets food from the mouth to the stomach. In the stomach acid and enzymes break down food. The pancreas produces powerful digestive enzymes and hormones including insulin. The colon absorbs water and the sigmoid and rectum regulate defecation. Important tumours arise in each of these organs. Although the small bowel is longer than any of these organs it is a much less common site for important tumours. Liver tumours have been covered in an earlier lecture on infections and cancer.

Bowel cancer.

When it comes to number of cases bowel cancer arising from the colon and sigmoid is the third commonest cancer in both men and women. Cancers of the oesophagus and pancreas are much less common. The outlook for bowel cancer is however significantly better than that for oesophageal and pancreatic cancer so in terms of mortality all three are among the top causes of cancer mortality in men and women in the UK.

Bowel cancer is rare before the age of 50 and is more common in men. Most bowel cancer is at the last bit of the large bowel, or the beginning of the large bowel. As with all solid tumours it is important that we consider the stage, the grade and the type of cancer, but stage is the most important for bowel cancer. The stage is how far it has spread and the size of the tumour; grade is how abnormal cells are; the type is which cell type the cancer comes from. For bowel cancer most are adenocarcinoma from mucus cells. As with most cancers, survival is much better in early stages. There is a five-year survival of over 90% in Stage 1 disease, over 80% in Stage 2, over 60% in Stage 3 but only 10% in Stage 4. This highlights the importance of early diagnosis. Treatment is both more successful and less invasive the earlier the stage.

Survival for bowel cancer has been improving steadily over time and has doubled in the last 40 years. Most people with bowel cancer now survive more than 10 years with minimal impact on the quality of life once treatment is complete. Since the key is early diagnosis screening is an important part of the approach to improving outcomes. Current screening is by FIT (faecal immunochemical test) and is offered to those aged 60-74 every two years. It uses antibodies that specifically recognise haemoglobin in the stool. Uptake is around 67% in England. Trials of screening in bowel cancer demonstrate it reduces cancer-related mortality.

The reason this is possible is that bowel cancers arise slowly and probably over years. They start off as small polyps which grow and then some of them become malignant.

Whilst ideally cancers are identified in screening many people still get identified by symptoms. These include blood in the stool, prolonged change in bowel habit, losing weight and new breathlessness

due to anaemia. Whilst most people who have these symptoms do not have cancer typical symptoms should lead to investigation usually by colonoscopy (a flexible camera passed up the bowel) or by CT scanning (colonography). In some cases, the first presentation is an emergency bowel obstruction or major symptoms and this often has less good outcomes.

Treatment for early-stage bowel cancer is usually based on surgery to remove it. The majority of Stage 1 and Stage 2 disease is surgery alone without chemotherapy. Stage 3 disease is more likely to have chemotherapy added. In Stage 4 disease surgery is much less likely as often the tumour has spread. In the earliest stages, cancer may be removed from within the lining using an endoscope. Alternatively, a section of the bowel may be removed and then re-joined. Exactly what surgery is performed depends on the site as well as the stage. It may be necessary to have a stoma bag either temporarily or in the case of lower cancers sometimes permanently. Surgery is continually advancing and whilst open surgery is still widely used, the oldest form including cutting open the abdomen, endoscopic surgery from the inside of the gut, laparoscopic (keyhole) surgery and robot assisted surgery are continually advancing.

Where patients need to have chemotherapy, which is usually in more advanced disease, it works on the usual basic mechanism of conventional chemotherapy which is to kill cells that are dividing. Cancer cells are more sensitive and slower to recover. A variety of drugs are used for chemotherapy, including platinum-based ones. Common side effects include fatigue, feeling and being sick, diarrhoea and tingling or numbness. Most of these go away after the chemotherapy is finished.

Targeted therapies which work on a different basis to chemotherapy are being used although they are currently experimental. They include antibodies which target the cancer cells or reduce blood vessel growth.

Radiotherapy is much less widely used in bowel cancer than some other cancers. It is generally in colon cancer that has spread, and rectal cancer even if it is not spread. It can either be external radiotherapy or internal radiotherapy. There are a variety of specialised forms of radiotherapy for metastases particularly in the liver.

As always prevention is better than cure. Over half of bowel cancer is thought to be potentially preventable. Modifiable risk factors include too little fibre in the diet, large amounts of processed meat, obesity, tobacco and alcohol. Exercise is protective. There are also genetic and familial risks.
Oesophageal cancer.

Oesophageal cancer is rarer than bowel cancer, more common in men than women and very rare before the age of 50. In contrast to bowel cancer, it is usually picked up due to symptoms which unfortunately only present late in disease. These include difficulty swallowing, indigestion and heartburn that will not go away, weight loss and pain in the throat behind the breastbone. These are normally investigated by endoscopy, but people will have CT or other imaging if a cancer is found.

Staging oesophageal cancer is relatively complex but as with other solid tumours lower stages have a better prognosis and more limited treatment. The type of cancer can be squamous cell carcinoma from the lining (most common), or adenocarcinoma from the glands. Prognosis is reasonable for stage I disease but unfortunately it is relatively rarely picked up at this point. There have been improvements in survival over the decades, but the outlook remains poor mainly due to late stage at diagnosis. This is in stark contrast to many other cancers where most survive for 10 years or more.

Surgery is the mainstay of treatment for Stage 1 removing all or some of the oesophagus. If patients have squamous cell carcinoma, they may also have chemoradiotherapy. For Stage 2 and 3 combination of chemotherapy, radiotherapy and surgery depends on whether it is a squamous or adenocarcinoma. Later the stage the more likely chemotherapy and radiotherapy will be used. As the long-term prognosis is not good for late disease much treatment is to improve symptoms. There may be a need for a stent to keep the oesophagus open and allow food to go down.

There is a strong socioeconomic and gender disparity for oesophageal cancer and is also more common in white than black or Asian British males and females. About 35% of cases are linked to smoking and obesity also increases risk. Alcohol increases the risk of squamous cell carcinoma. Gastro-oesophageal reflux and Barrett's increase the risk of adenocarcinoma.

Since late presentation is a major risk for oesophageal carcinoma there are currently studies to see whether screening for early disease is possible for example by way of a cryosponge but this is still at the experimental stage.

Pancreatic Cancer

The pancreas has several functions which includes digestive enzymes. Most cancers arise from the cells producing these and the majority are adenocarcinoma making up around 85% of all pancreatic cancers. It also produces insulin and glucagon which are essential for the regulation of glucose and occasionally tumours can arise from this; these are rare, and the outlook is much better.

Symptoms of pancreatic cancer are late in the disease and often vague. They depend on the site of the tumour in the pancreas. If the head of the pancreas near where the bile duct and pancreas open into the gut they are more likely to include weight loss, jaundice, bloating, pain after eating and changed stool. Other sites are more likely to have epigastric or back pain.

Initial diagnosis is radiographic with CT scan, CT angiography or MRI scan. They may subsequently be followed by endoscopic ultrasound to detect nodes or get a biopsy. There are blood markers such as CA19-9 which can help track the effect of treatment but not yet ideal for screening tests. Getting a screening test would be a huge step forward in pancreatic cancer since late diagnosis is a major problem.

Survival is low due to late diagnosis and has not improved massively over the last decades. When cancer of the pancreas is picked up early (less than 20%) is removed surgically in a major operation. This will usually be followed by chemotherapy which improves outlook, but the majority of people still die within two years. If surgery is not appropriate, then chemotherapy remains the mainstay of treatment currently. Targeted therapy and immunotherapy are being investigated but they are still experimental and there is only incremental progress. Symptom control is very important. People may need a stent if the pancreatic duct is blocked. Pain and depression are common and need active management.

Risk factors for pancreatic cancer include smoking, obesity, type II diabetes and chronic pancreatitis. 5 to 10% are due to inheritable factors including BRCA 1 and 2. People at high genetic risk may need screening before we get better screening tools.

Stomach Cancer

Stomach cancer is now relatively rare in the UK although still important worldwide. Gastric cancers decreased substantially, and this is probably mainly due to treatment of *H. pylori*, a bacterium. It considerably increases the risk for non-cardiac gastric cancer. *H. pylori* is treated most commonly due to peptic ulcer disease. Stomach cancer incidence has decreased 62% in the UK since the 1970s and is likely to continue to fall. Smoking and diet are also important. Stomach cancers particular common in Asia and parts of Latin America and historically (pre-1930s) were probably the most common fatal cancer. Our remarkable ability to treat or prevent infections has improved stomach cancer outlooks. This is also true for rectal cancer which is mainly caused by the HPV 16 virus for which girls, and increasingly boys, are vaccinated.

This lecture has considered major cancers of the digestive tract. Bowel cancer, the most common important one, has a good prognosis if detected early, and this has steadily improved over time. Pancreatic and oesophageal cancer, although less common, are important because they are often detected late and therefore have a high mortality rate. Cancers driven by infections or improving including stomach cancer and rectal cancer. For the major bowel, pancreatic and oesophageal cancers there are several common modifiable risk factors especially smoking and obesity and these need to be addressed.