Cancer Association of South Africa (CANSA)

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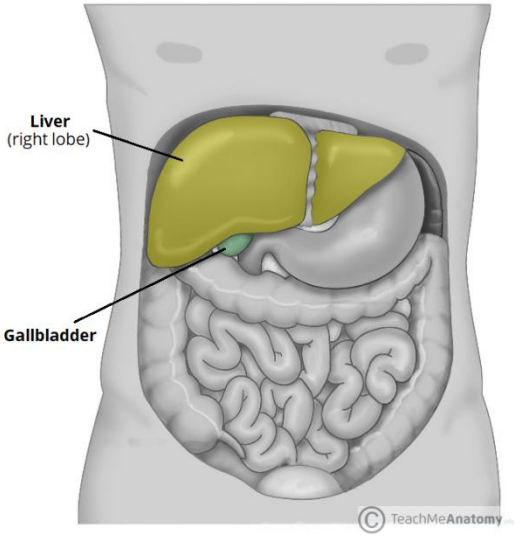
Fact Sheet
on
Cancer of the Gallbladder

Introduction

The gallbladder is part of the biliary system, which is part of the gastrointestinal tract. It lies in the right upper portion of the abdomen and affixed to the undersurface of the liver. It is approximately the size of a small pear. Its primary function is to concentrate and store vile which is produced by the liver. The stored bile is released via the common bile duct and joins the pancreatic duct where it forms the Ampulla of Vater. The release of bile from the gallbladder is stimulated by the presence of food in the stomach and duodenum.



Cancer of the Gallbladder

Key points of Gallbladder Cancer:

Gallbladder Cancer is rare and nearly all of them are adenocarcinomas. An adenocarcinoma is a cancer that starts in gland-like cells that line many surfaces of the body, including the inside the digestive system.

Gallbladder cancer is a disease in which malignant (cancer) cells form in the tissues of the gallbladder.

- Being female can increase the risk of developing gallbladder cancer.
- Signs and symptoms of gallbladder cancer include jaundice, fever, and pain.
- Gallbladder cancer is difficult to detect (find) and diagnose early.

Incidence of Cancer of the Gallbladder

The outdated National Cancer Registry (2014), known for under reporting, does not provide any information about Cancer of the Gallbladder. It combines Cancer of the Gallbladder with that of Cancer of the Liver.

According to **Bruni, *et al*.,** (2019), the burden of Cancer of the Gallbladder for South Africa for 2018 is estimated as (based on Globocan estimates):

- Annual number of Cancer of the Gallbladder cases 574

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- Annual number of Cancer of the Gallbladder deaths 287

Risk Factors for Cancer of the Gallbladder

Doctors do not know exactly what causes gallbladder cancer. They do know that, like all cancer, an error, known as a mutation, in a person's DNA causes uncontrolled rapid growth of cells.

Chronic inflammation of the gallbladder is the biggest risk factor for gallbladder cancer.

Some studies have shown that if one has a first degree relative with gallbladder cancer one is five times more likely to develop gallbladder cancer.

People who smoke or work in the metal or rubber industries are more likely to develop gallbladder cancer.

Several other risk factors for gallbladder cancer are being researched, for example, diet, being overweight and taking hormone replacement therapy (HRT).

Signs and Symptoms of Cancer of the Gallbladder

Signs and symptoms of Cancer of the Gallbladder may be caused by gallbladder cancer or by other conditions. Check with a medical doctor if any of the following signs and symptoms are present:

- Jaundice (yellow discolouration of the skin and whites of the eyes)
- Pain and/or discomfort above the stomach
- Loss of appetite
- Fever
- Nausea and vomiting
- Abdominal bloating
- Passing dark yellow urine
- Passing pale-coloured faeces
- Presence of a lump or lumps in the abdomen
- Itchy skin

Diagnosis of Cancer of the Gallbladder

Gallbladder cancer is uncommon. When gallbladder cancer is discovered at its earliest stages, the chance for a cure is very good.

In addition to a physical examination, the following tests may be used to diagnose gallbladder cancer:

Biopsy - the removal of a small amount of tissue for examination under a microscope. The sample of tissue can be taken 1 of several ways:

- During a surgery
- With a minimally invasive surgical technique known as laparoscopy
- With a fine needle or thick needle aspiration (a core biopsy), using a computed tomography (CT or CAT) scan or ultrasound to guide the needle placement

- In some cases, a biopsy is done by passing an endoscope through the mouth, past the stomach, and into the first part of the intestine

Endoscopic retrograde cholangiopancreatography (ERCP) – while the patient is lightly sedated, the doctor inserts an endoscope through the mouth, down the oesophagus, and into the stomach and small bowel. A smaller tube or catheter is passed through the endoscope and into the bile ducts.

Percutaneous cholangiography - a thin needle is inserted through the skin and into the gallbladder area. A dye is injected through the needle so that a clear image will show up on x-rays. By looking at the x-rays, the doctor may be able to see whether there is a tumour in the gallbladder

Laparoscopy – use is made of an endoscope to look at the gallbladder and other internal organs. The tube is inserted through a small incision in the abdomen

Computed tomography (CT or CAT) scan

Magnetic resonance imaging (MRI

Ultrasound

Endoscopic ultrasonography - a special endoscope, which is a long flexible scope, is inserted through the mouth after sedation. It can reach the stomach and some of the intestine. It has an ultrasound probe at the end that can be used to look for tumours and guide biopsy with a small needle

Positron emission tomography (PET) or PET-CT scan

Various blood tests – Liver function test; CA 19-9 tumour marker test; Carcinoembryonic antigen (CEA) test

Shukla, S.K., Singh, G., Shahi, K.S., Bhuvan, & Pant, P. 2018.
Background: Gallbladder cancer is the most common malignant cancer of the bile ducts and third most common gastrointestinal malignant in the world for public health. Its relatively low incidence and confused symptoms result in advanced disease at the time of presentation, contributing to poor prognosis and reduced survival associated with this disease. The main function of the gallbladder is to store excreted bile acids from the liver in preparation for a meal. Its main risk factor is prolonged exposure to biliary calculations, although bacterial infections and other inflammatory conditions are associated. Chronic inflammatory bowel conditions are associated with gallbladder cancer. T stage translates to identifying residual disease at reoperation for incidental gallbladder cancer and residual disease negatively affects survival.
Conclusion: It is the most common cancer of gallbladder, gallbladder cancer remains a rare disease. Gallbladder cancer is a rare disease that can be accidentally diagnosed after cholecystectomy or accidentally, often with more advanced disease. The prognosis is generally extremely poor and improvements in surgical resection of this approach have to be re-evaluated, while the role of chemotherapy and radiotherapy remains controversial.

Treatment of Cancer of the Gallbladder

Surgery - is a common treatment for gallbladder cancer. It may be performed to completely remove the tumour if the cancer is still localized, or to relieve symptoms or pain if the cancer is more widespread. The procedure to remove the gallbladder is called a cholecystectomy.

Krell, R.W. & Wei, A.C. 2019.
"Gallbladder cancer is the most common biliary tract malignancy. Margin-clearing surgery is a cornerstone of gallbladder cancer management, but several aspects of surgical management are controversial."

Chemotherapy – is often prescribed in addition to surgery to help prevent recurrence of gallbladder cancer.

Javle, M., Zhao, H. & Abou-Alfa, C.K. 2019.
"Gallbladder cancer is an aggressive cancer that continues to be an important health care issue in certain regions of the world such as Southeast Asia and Latin America. Most patients are diagnosed at an advanced, unresectable stage and systemic therapy is their only option. Gallbladder cancer patients have traditionally been included in clinical trials for biliary tract cancer. Thus, systemic chemotherapy options for this cancer are similar to those for cholangiocarcinoma, including gemcitabine and cisplatin in the first line and FOLFOX in the second-line setting. Ongoing phase III clinical trials may change the systemic therapy paradigm for this cancer. Molecular profiling has indicated important genetic differences between gallbladder cancer and cholangio-carcinoma, which affects choice of targeted therapy. Her2/neu amplification, PIK3CA mutations and DNA repair genetic aberrations are relatively frequent and represent actionable targets for this cancer."

Radiation therapy - may be prescribed to shrink the size of a tumour or to help kill cancer cells that may be left after surgery.

Verma, V. & Crane, C.H. 2019.
"Locally advanced gallbladder cancer poor prognosis due to a high distant metastatic rate and poor overall disease control. The impact of standard therapeutic options is unfortunately modest. Due to the rarity of the disease, evidence-based management continues to evolve. The goal of this review is to highlight the contemporary landscape of radiation therapy for gallbladder cancer. First, the rationale for radiation therapy is described. This includes the risk of locoregional recurrence following resection based on patterns-of-failure data, along with the high locoregional disease burden being a frequent cause morbidity and mortality in unresected cases. Additionally, improvements in systemic therapy over the next decade could shift contemporary patterns of failure more towards proportionally higher locoregional recurrence rates. Second, clinical data of radiation therapy for gallbladder cancer are discussed. These include consideration of postoperative chemoradiotherapy for margin- and/or node-positive cases. Patients with localized unresectable disease could benefit from ablative radiation therapy, based on promising data in non-gallbladder cancer pancreaticobiliary neoplasms. The use of advanced radiation therapy technologies such as proton beam therapy, as a means to deliver ablative radiation therapy in a potentially safer manner, is also mentioned. Lastly, the emerging concept of neoadjuvant therapy for gallbladder cancer is also described, in efforts to allow more patients to receive curative resection."

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers

- Tests to find new ways of screening for cancer

The **South African National Clinical Trials Register** provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

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Sources and References Consulted and/or Utilised

Bruni, L., Albero, G., Serrano, B., Mena, M., Gómez, D., Muñoz, J., Bosch, F.X.& de Sanjosé, S. 2019. ICO/IARC Information Centre on HPV and Cancer (*HPV Information Centre*). Human Papillomavirus and Related Diseases in South Africa. Summary Report 17 June 2019. [Date Accessed]

Gallbladder
https://teachmeanatomy.info/abdomen/viscera/gallbladder/
https://www.ncbi.nlm.nih.gov/books/NBK482488/

Gallbladder Cancer
https://www.cancer.gov/types/gallbladder/patient/gallbladder-treatment-pdq#_1
https://www.mayoclinic.org/diseases-conditions/gallbladder-cancer/symptoms-causes/syc-20353370
https://www.cancer.org/cancer/gallbladder-cancer/about/what-is-gallbladder-cancer.html
https://www.cancer.net/cancer-types/gallbladder-cancer/symptoms-and-signs
https://www.nhs.uk/conditions/gallbladder-cancer/
https://www.healthline.com/health/gallbladder-cancer
https://emedicine.medscape.com/article/278641-overview
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3104187/
https://www.msdmanuals.com/home/liver-and-gallbladder-disorders/gallbladder-and-bile-duct-disorders/tumors-of-the-bile-ducts-and-gallbladder
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4649107/
https://www.cancervic.org.au/cancer-information/types-of-cancer/gall_bladder_cancer/gall-bladder-cancer-overview.html
https://medlineplus.gov/gallbladdercancer.html
https://www.health.harvard.edu/a_to_z/gallbladder-and-bile-duct-cancer-a-to-z
https://www.wcrf.org/dietandcancer/gallbladder-cancer
https://www.cancercenter.com/cancer-types/gallbladder-cancer/symptoms

Gallbladder Picture
https://teachmeanatomy.info/abdomen/viscera/gallbladder/

Javle, M., Zhao, H. & Abou-Alfa, C.K. 2019. Systemic therapy for gallbladder cancer. *Chin Clin Oncol* 8(4):44, Aug, 2019.

Krell, R.W. & Wei, A.C. 2019. Gallbladder cancer: surgical management. *Chin Clin Oncol*, 8(4):36. Aug 2019.

Shukla, S.K., Singh, G., Shahi, K.S., Bhuvan, & Pant, P. 2018. Staging, treatment, and future approaches of gallbladder carcinoma. *J Gastrointest Cancer*, 49(1):9-15, Mar 2018.

Verma, V. & Crane, C.H. 2019. Contemporary Perspectives on the use of radiation therapy for locally advanced gallbladder cancer. *Chin Clin Oncol*, 8(4):41, Aug 2019.