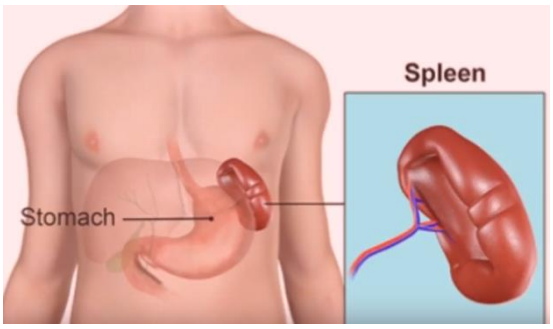
Cancer Association of South Africa (CANSA)

Fact Sheet
on
Cancer of the Spleen

Introduction

The **spleen** is an organ found in virtually all vertebrates. Similar in structure to a large lymph node, it acts primarily as a blood filter.



[Picture Credit: Spleen]

The spleen plays important roles in regard to red blood cells (also referred to as erythrocytes) and the immune system. It removes old red blood cells and holds a reserve of blood, which can be valuable in case of haemorrhagic shock, and also recycles iron. As a part of the mononuclear phagocyte system, it metabolises haemoglobin removed from senescent erythrocytes. The globin portion of haemoglobin is degraded to its constitutive amino acids, and the haeme portion is metabolised to bilirubin, which is removed in the liver.

The spleen also synthesises antibodies in its white pulp and removes antibody-coated bacteria and antibody-coated blood cells by way of blood and lymph node circulation. A study published in 2009 using mice found that the spleen contains, in its reserve, half of the body's monocytes within the red pulp. These monocytes, upon moving to injured tissue (such as the heart), turn into dendritic cells and macrophages while promoting tissue healing. The spleen is a centre of activity of the mononuclear phagocyte system and can be considered analogous to a large lymph node, as its absence causes a predisposition to certain infections.

In humans, the spleen is brownish in colour and is located in the left upper quadrant of the abdomen.

Cancer of the Spleen

Cancer of the spleen is a malignancy of white blood cells involving tumour deposits in the spleen. There are a number of different types of spleen cancers including lymphoma, non-Hodgkin's lymphoma and some types of T-cell lymphomas.

Most splenic cancer do not start in the spleen, and those that do, are almost always lymphomas. Lymphoma is a type of blood cancer that develops in the lymphatic system. It is more common for a

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lymphoma to start in another part of the lymphatic system and invade the spleen than it is for lymphoma to start in the spleen itself.

Lymphoma is probably the most common splenic malignancy and is usually a manifestation of generalised lymphoma. Primary splenic lymphoma is rare. Most of the primary splenic lymphomas are non-Hodgkin lymphomas (marginal zone cell lymphoma). The most common finding is splenomegaly, but it may be absent in up to 30% of lymphoma patients.

Ultrasound may depict a solitary lesion or slightly ill-defined inhomogeneous hypoechoic lesions. Another pattern is a general diffuse inhomogeneity with minute hypoechoic lesions less than 1 cm in size.

Staging of lymphomas on CT can be limited as only 45%–70% of lymphomas show diffuse splenic infiltration or tumour foci less than 1 cm in diameter so that the diagnosis of lymphoma can sometimes only be made microscopically. The focal lesions with diameter from 1 to 10 cm are typically of low attenuation and rarely enhance so may be better demonstrated on post-contrast scans.

MRI findings are non-specific and similar to those of metastases from other primary tumours. Typically, lymphomas are hypointense or nearly isointense on T1-weighted images and hyperintense on T2-weighted images. Injection of contrast medium may improve detection of splenic lymphoma.

Although the spleen is the most vascular organ in the body, it is an infrequent site for metastatic disease (3.4% of metastatic carcinoma). Explanations proposed for the relative paucity of splenic metastases have included:

- the sharp angle made by the splenic artery which makes it difficult for tumour emboli to enter the spleen
- the rhythmic contractile nature of the spleen which squeezes out the tumour emboli
- the absence of afferent lymphatics to carry metastatic tumour to the spleen; and
- anti-tumour activity due to a high concentration of lymphoid tissue in the spleen.

Apart from these factors, the frequency of splenic metastases may have been underestimated as they are often asymptomatic and occur late in the disease. Splenic metastases are most commonly found in malignant melanoma, lung, breast or ovarian carcinomas.

On ultrasound, they can show various degrees of echogenicity, but are usually hypoechoic.

On CT, splenic metastases typically appear as hypodense lesions which may be solid or cystic and with inhomogeneous contrast enhancement indicating a mixture of vascularisation or necrosis.

On MRI, metastases are predominantly hypointense on T1-weighted images and hyperintense on T2-weighted images, with occasionally inhomogeneous contrast enhancement. MRI is more accurate for the detection of splenic metastases which are necrotic or haemorrhagic.

Shimono, J., Miyoshi, H., Arakawa, F., Yamada, K., Sugio, T., Miyawaki, K., Eto, T., Miyagishima, T., Kato, K., Nagafuji, K., Akashi, K., Teshima, T. & Ohshima, K. 2019.
"The hepatitis C virus (HCV) is a single-stranded RNA virus which is thought to be involved in the onset of B cell lymphoma. HCV-positive diffuse large B cell lymphoma (DLBCL) has been reported to clinically manifest in extranodal lesions (e.g., in the liver, spleen, and stomach). Here, we investigated HCV-

positive and -negative primary splenic DLBCL (p-spDLBCL) and non-primary splenic DLBCL (ordinary DLBCL). Furthermore, to examine HCV lymphomagenesis, RNA in situ hybridization (ISH), RT-PCR (reverse-transcription polymerase chain reaction), and NS3 immunostaining of HCV viral nonstructural proteins were performed. HCV-positive p-spDLBCL patients presented fewer B symptoms (asymptomatic) and better performance status, with elevated presence of splenic macronodular lesions and more germinal center B cell (GCB) sub-group cases than HCV-negative p-spDLBCL patients. However, HCV-positive ordinary DLBCL patients were found to have more non-GCB sub-group cases than HCV-negative ordinary DLBCL patients. HCV-positive DLBCL patients showed 20.6% (7/34) NS3 positivity, 16.7% (1/6) HCV-RNA in situ positivity, and 22.2% (2/9) detection of HCV-RNA in tumor tissue by RT-PCR. Splenic samples were found to have a higher frequency of HCV detection than lymph node samples, thus suggesting that HCV may be closely related to lymphomagenesis, especially in splenic lymphoma."

Tumour Grade and Tumour Stage

Tumour grade and stage are terms used to describe the severity of a tumour, while tumour grade describes the appearance of cancerous cells in the tissue by examining them under a microscope.

Tumour stage encompasses:

- The location of the tumour.
- The size and/or extent of the original tumour.
- Whether cancer cells have spread to lymph nodes or anywhere else in the body.
- The number of tumours present.

Doctors use tumour grade, cancer stage, and a patient's age and general health to decide the course of treatment for the patient and determine prognosis. Prognosis describes all factors including the disease course, cure rate, chances of survival, and risk of recurrence of cancer.

<u>What are the cancer stages?</u>

Different systems of cancer staging are used to describe the types of cancer. Below is a common method in which stages are ranged from 0 to IV.

- Stage 0: The tumour is confined to its place of origin (in situ) and has not spread to nearby tissue.
- Stage I: The tumour is located only in the original organ, is small, and has not spread.
- Stage II: The size of the tumour is large but has not spread.
- Stage III: The tumour has become larger and may have spread to surrounding tissues and/or lymph nodes.
- Stage IV: The tumour has spread to other distant organs of the body, which is known as the metastasis stage.

<u>TNM staging</u>

Another common staging method used for cancer is the TNM system, which stands for tumour, node (which means spread of the tumour to lymph nodes), and metastasis. When a patient's cancer is staged using the TNM system, a number will be present along with the letter. This number signifies the extent of the disease in each category - tumour, node, and metastases.

Another system of cancer staging divides cancer into five stages, which include:

- In situ: Abnormal cells are present but have not spread to nearby tissue.
- Localized: Cancer is located only in the original organ and shows no sign of its spread.
- Regional: Cancer has spread to nearby lymph nodes, tissues, or organs.
- Distant: Cancer has spread to distant parts of the body.
- Unknown: The stage cannot be figured out due to a lack of enough information.

What are the cancer grades?

Cancer grades are based on examination of the suspected tissue sample under a microscope. This involves surgically removing a piece of the suspected cancerous tissue and sending it to the lab for analysis. The entire procedure is known as a biopsy.

A doctor who specializes in diagnostic tests (pathologist) examines the cells of the tissue and determines whether they are harmless (benign or noncancerous) or harmful (malignant or cancerous). They describe the microscopic appearance of the cells and assign a numerical "grade" to most cancers. Generally, a lower grade indicates slow-growing cancer and a higher grade indicates fast-growing cancer.

The most commonly used grading system is as follows:

- Grade I: Cancer cells that look like normal cells but are not growing rapidly.
- Grade II: Cancer cells that don't look like normal cells with their growth being faster than normal cells.
- Grade III: Cancer cells that look abnormal and have the potential to grow rapidly or spread more aggressively.

Sometimes, the following system can be used:

- GX: Grade cannot be assessed (undetermined grade)
- G1: Well-differentiated (low grade)
- G2: Moderately differentiated (intermediate grade)
- G3: Poorly differentiated (high grade)
- G4: Undifferentiated (high grade)

Incidence of Cancer of the Spleen in South Africa

The National Cancer Registry (2017) does not provide any information regarding the incidence of cancer of the spleen.

Padilla, O., Tam, W. & Geyer, J.T. 2020.

"Hematopoietic neoplasms involving the spleen are uncommon, but T cell neoplasms involving the spleen are extremely rare. The rarity of splenic involvement by T cell neoplasms has resulted in a limited body of literature describing their splenic characteristics. As a result, our purpose in this review article is to provide and summarize some of the characteristics seen by different T cell neoplasms that may involve the spleen."

Signs and Symptoms of Cancer of the Spleen

The following are common signs and symptoms of cancer of the spleen:

- Abdominal pain or fullness, especially in the upper abdomen
- Bone and joint pain
- Easy bleeding or bruising
- Fatigue
- Fever and chills
- Frequent infections
- Night sweats
- Swollen lymph nodes
- Unexplained weight loss (when not trying to lose weight)

Serious Symptoms that Might Indicate a Life-threatening Condition in Cancer of the Spleen

In some cases of cancer of the spleen, complications can arise that are life threatening. Immediate expert medical assistance should be sought:

- Bluish colouration of the lips or fingernails
- Change in level of consciousness or alertness, such as passing out or unresponsiveness
- Change in mental status or sudden behaviour change, such as confusion, delirium, lethargy, hallucinations and delusions
- Chest pain
- Chest tightness
- Chest pressure
- Heart palpitations
- High fever (higher than 38^{o}C)
- Rapid heart rate (tachycardia)
- Respiratory or breathing problems, such as shortness of breath, difficulty breathing, laboured breathing, wheezing
- Severe abdominal pain.

Causes of Cancer of the Spleen

A number of factors increase the risk of developing leukaemia and lymphoma, cancers that may involve in the spleen. Not all individuals with risk factors will develop cancer of the spleen. Risk factors include:

- Advanced age (although cancer of the spleen can occur at all ages)
- A compromised immune system due to such conditions as HIV/Aids
- A history of having used corticosteroids
- A history of having used medication during organ transplant
- History of previous cancer of cancer treatment, e.g. lymphoma or leukaemia
- Exposure to heavy metals
- Exposure to radiation

Treatment of Cancer of the Spleen
Treatment for cancer of the spleen cancer will depend on the type of cancer and how much it has spread. The removal of the spleen is a possible treatment.

Spleen removal surgery is called a splenectomy. A splenectomy is a procedure usually done in cases such as: trauma, blood disorders (idiopathic thrombocytopenia purpura (ITP), thalassaemia, haemolytic anaemia, sickle cell anaemia), cancer (lymphoma, Hodgkin disease, leukaemia), and hypersplenism to name a few.

Spleen removal is typically a minimally invasive laparoscopic surgery, meaning that surgeons make several small incisions and use special surgical tools and a small camera to conduct the surgery. In certain cases, a surgeon may opt for one large incision, instead.

One can live without a spleen because other organs, such as the liver and lymph nodes, can take over the duties of the spleen. Nevertheless, removing the spleen can have serious consequences. One will be more at risk to develop infections. Often, doctors recommend getting vaccines, including a pneumococcus vaccine, Haemophilus B vaccine, Meningococcal vaccine, and yearly flu vaccine after a splenectomy. It is important to see a doctor at the first sign of infection if one does not have a spleen.

Fallah, J. & Olszewski, A.J. 2019.
OBJECTIVES: To examine the use of splenectomy, chemotherapy, and subsequent overall survival (OS) in contemporary patients with splenic lymphomas.
METHODS: We analyzed records of 6450 patients with various splenic lymphomas recorded in the National Cancer Data Base (2004-2013). Survival was compared using Mantel-Byer test to account for guarantee-time bias, stratified by age, sex, comorbidities, and lymphoma stage.
RESULTS: Splenectomy rate was overall 58%, and varied from 49% in splenic marginal zone (SMZL) to 77% in follicular lymphoma (FL). It significantly decreased across all histologies over time (overall from 69% in 2004, to 44% in 2013). Thirty-day mortality after splenectomy was 4%. Chemotherapy use varied from 40% in FL to 76% in diffuse large B-cell lymphoma (DLBCL), but increased significantly only for SMZL and T-cell lymphomas over time. Overall, 57% of splenectomies were performed as diagnostic procedures, which was significantly less common in academic hospitals ($p < 0.0001$). Following a diagnostic splenectomy, chemotherapy was not administered to 29% of patients with DLBCL, 49% with mantle cell, and 42% with T-cell lymphomas. Median OS ranged from 12.4 years for FL to 1.0 year for T-cell lymphomas. We found no association between performance of splenectomy and OS across all histologies. Patients with DLBCL who did not receive chemotherapy after a diagnostic splenectomy had significantly worse OS ($p = 0.001$). The association between post-splenectomy chemotherapy and OS was not observed in FL or SMZL.
CONCLUSION: many splenic lymphomas may be treated without surgery, but a high proportion of diagnostic splenectomies indicates an ongoing need for less invasive diagnostic modalities.

Yoshizawa, J., Kubo, N., Ishizone, S., Karasawa, F. & Nakayama, A. 2017.
BACKGROUND: Solitary metastasis of a malignancy to the spleen is rare, particularly for gastric cancer. Only a few case reports have documented isolated splenic metastasis from early gastric cancer. We describe a case of splenic metastasis from early gastric cancer.
CASE PRESENTATION: A 60-year-old man underwent a distal gastrectomy for early gastric cancer. It infiltrated the submucosa with pathological nodal involvement (pT1bN2M0, stage IIB). One year after the gastrectomy, an abdominal computed tomography scan showed a low-density lesion, 17 mm in diameter, at the upper pole of the spleen. Positron emission tomography/computed tomography

showed focal accumulation of fluorine-18 fluorodeoxyglucose in the spleen without extrasplenic tumor dissemination or metastasis. We diagnosed splenicmetastasis of gastric cancer, and performed a splenectomy. Histological examination confirmed moderately differentiated tubular adenocarcinoma and poorly differentiated adenocarcinoma (solid type) that was consistent with the features of the primary gastric cancer. The splenic tumor was pathologically and immunohistochemically diagnosed as a metastasis from the gastric carcinoma. More than 18 months after the splenectomy, the patient has had no evidence of recurrent gastric cancer.
CONCLUSION: When solitary metastasis to the spleen is suspected during the postoperative follow-up of a patient with gastric cancer, a splenectomy is a potentially effective treatment.

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.

For additional information, please visit: www.sanctr.gov.za/
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Health Grades
http://www.healthgrades.com/conditions/spleen-cancer

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http://www.cancer.gov/clinicaltrials/learningabout/what-are-clinical-trials

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Right Diagnosis
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Live Science
http://www.livescience.com/44725-spleen.html

Spleen
http://medmum.com/spleen-pain/

Tumour Grade and Tumour Stage
https://www.medicinenet.com/cancer_101_pictures_slideshow/article.htm

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