Cancer Association of South Africa (CANSA)

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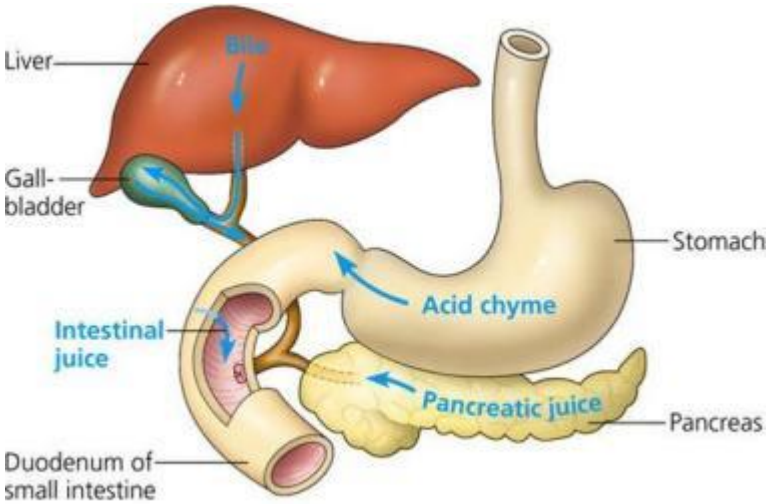
Fact Sheet
on
Duodenal Cancer

Introduction

The duodenum is the first part of the small intestine. The other parts are the jejunum and the ileum. Digestion of food, which commences in the stomach, continues in the duodenum once the chyme enters the duodenum from the stomach. The stomach acid is neutralised in the duodenum because of the alkaline environment inside the duodenum. The entry of chyme triggers the release of digestive pancreatic enzymes and bile which enter the duodenum via the pancreatic and common bile ducts, respectively. These 2 ducts join the duodenum at the ampulla of Vater**,** or the hepatopancreatic ampulla.



Picture Credit: Duodenum

The pancreatic juice contains enzymes and bicarbonate to neutralise the stomach acid. The pancreatic enzymes are lipase (breaks down fats), protease (breaks down protein) and amylase (breaks down carbohydrates). Bile is a dark green or brownish coloured fluid produced by the liver. Bile is passed to the gallbladder and then into the duodenum to help with the digestion of fat.

The chyme is gradually pushed down the duodenum by peristaltic waves which flow down the length of the digestive tract. Most of the digestion of the protein, fats and carbohydrate in the chyme is done by the enzymes in the duodenum, before the resultant mixture is passed further into the small intestine.

Duodenal Cancer

Duodenal cancer develops in the small intestine, which is part of the digestive system and connects the stomach to the colon.

Researched and Authored by Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

The small intestine, or small bowel, is a long, folded tube that sits in the lower abdomen. It consists of three parts: the duodenum, the jejunum, and the ileum.

Duodenal cancer starts in the duodenum, which is the uppermost portion of the small intestine.
There are four main types of small intestine cancer:

Adenocarcinoma initially develops in the glandular cells that line the inside of the small intestine. Adenocarcinomas are the most common type of small intestine cancer, accounting for approximately
Sarcoma begins in the muscle and other supporting tissues of the small intestine. Around 10% of small intestine cancers are sarcomas
Carcinoid tumours are slow-growing and develop in the neuroendocrine cells of the small intestine. Neuroendocrine cells produce hormone-like substances
Lymphomas form in cells called lymphocytes. These are part of the immune system and are present in most parts of the body, including the intestines
Gastrointestinal stromal tumour

Small intestine cancers are rare and is more common in older people, particularly in those aged over 60 years.

Incidence of Duodenal Cancer in South Africa
The National Cancer Registry (2017) does not provide any information regarding Duodenal Cancer. All Cancers of the Small Intestine are grouped together and listed under 'Small Intestine'.

According to the National Cancer Registry (2017) the following number of cases of cancer of the Small Intestine was histologically diagnosed during 2016. Histologically diagnosed means that a tissue sample was forwarded to a pathology laboratory where a specially trained pathologist confirmed a cancer diagnosis after viewing the tissue sample under a microscope.

Group - Males 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	81	1:2 206	0,20%
Asian males	6	1:839	0,62%
Black males	31	1:4 843	0,24%
Coloured males	11	1:1 335	0,23%
White males	33	1:1 013	0,15%

Group - Females 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	74	1:2 611	0,18%
Asian females	10	1:645	0,78%
Black females	31	1:4 673	0,16%
Coloured females	5	1:3 774	0,11%
White females	28	1:1 185	0,16%

The frequency of histologically diagnosed cases of cancer of the Small Intestine in South Africa for 2017 was as follows (National Cancer Registry, 2017):

Group - Males 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	1	0	7	14	29	16	11	3
Asian males	0	0	0	1	2	1	2	0
Black males	0	0	3	7	16	4	1	0
Coloured males	0	0	1	2	3	4	1	0
White males	1	0	3	4	8	7	7	3

Group - Females 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	0	1	4	8	12	23	21	5
Asian females	0	0	0	1	0	3	5	1
Black females	0	1	2	3	6	10	7	2
Coloured females	0	0	0	1	1	2	1	0
White females	0	0	2	3	5	8	8	2

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Risk Factors for Duodenal Cancer

Diet and health history can affect the risk of developing small intestine cancer.

Anything that increases one's risk of getting a disease is called a risk factor. Having a risk factor does not mean that one will get cancer; not having risk factors also does not mean that one will not get cancer.

Risk factors for small intestine cancer include the following:

- Tobacco use
- Alcohol consumption
- Eating a high-fat diet
- High consumption of red meat
- Consumption of smoked foods
- High intake of salt
- Having Crohn disease
- Having celiac disease
- **Inherited conditions**. These are health issues that a person inherits from a parent. Those that may increase the risk of developing small intestine cancer include:
    - familial adenomatous polyposis (FAP)
    - Lynch syndrome
    - Peutz-Jeghers syndrome
    - Cystic fibrosis

Signs and Symptoms of Duodenal Cancer

Duodenal cancer, can cause a variety of symptoms, such as:

- unexplained weight loss
- abdominal pain
- bloody stools
- diarrhoea
- a lump in the abdomen

- nausea
- vomiting
- weakness and fatigue
- anaemia, which is a low number of red blood cells
- jaundice, which causes the skin and the whites of the eyes to become yellow

However, having these symptoms does not mean that a person has cancer. A range of conditions can cause similar symptoms, including irritable bowel syndrome and inflammatory bowel disease. As these symptoms can suggest several different health conditions, a person should consult a doctor as soon as they appear.

Diagnosis of Duodenal Cancer
In addition to a physical examination, the following tests may be used to diagnose duodenal cancer:

Blood tests - a test of the number of red blood cells in the blood can indicate whether the cancer is causing any bleeding. Tests for your liver and kidney function may also be performed. The results will determine if either of those organs may be affected by the cancer and find out how healthy those organs are before having treatment for small bowel cancer.

X-ray - an X-ray is way to create a picture of the structures inside of the body using a small amount of radiation. It can help the doctor find a tumour.

Biopsy - a biopsy is the removal of a small amount of tissue for examination under a microscope. Other tests can suggest that cancer is present, but only a biopsy can make a definite diagnosis. A pathologist then analyses the sample(s). A pathologist is a doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease.

Endoscopy **-** a test called an endoscopy allows the doctor to see the inside the gastrointestinal system. The person may be sedated while the doctor inserts a thin, lighted, flexible tube called an endoscope through the mouth, down the oesophagus, and into the stomach and small bowel.

Computed tomography (CT or CAT) scan - a CT scan take pictures of the inside of the body using x-rays taken from different angles. A computer combines these images into a detailed, 3-dimensional or 3-D image that shows any abnormalities or tumours. A CT scan can be used to measure the tumour's size.

Positron emission tomography (PET) or PET-CT scan - *a* PET scan is usually combined with a CT scan (see above).

Laparotomy - in this procedure, a surgical incision is made in the abdomen to check for disease. Sometimes, tissue samples are taken and, often, surgery is performed at the same time to remove the tumour.

Yamasaki, Y., Takeuchi, Y., Kanesaka, T., Kanzaki, H., Kato, M., Ohmori, M., Tonai, Y., Hamada, K., Matsuura, N., Iwatsubo, T., Akasaka, T., Hanaoka, N., Higashino, K., Uedo, N., Ishihara, R., Okada, H. & Iishi, H. 2020.
Objectives: Endoscopic biopsies for nonampullary duodenal epithelial neoplasms (NADENs) can induce submucosal fibrosis, making endoscopic resection difficult. However, no biopsy-free method exists to distinguish between NADENs and non-neoplasms. We developed a diagnostic algorithm for duodenal neoplasms based on magnifying endoscopy findings and evaluated the model's diagnostic ability.

Methods: Magnified endoscopic images and duodenal lesion histology were collected consecutively between January 2015 and April 2016. Diagnosticians classified the surface patterns as pit, groove or absent. In cases of nonvisible surface patterns, the vascular pattern was evaluated to determine regularity or irregularity. The correlation between our algorithm (pit-type or absent with irregular vascular pattern) and the lesion histology were evaluated. Four evaluators, who were blinded to the histology, also classified the endoscopic findings and evaluated the diagnostic performance and interobserver agreement.
Results: Endoscopic images of 114 lesions were evaluated (70 NADENs and 44 non-neoplasms, 31 in the superior and 83 in the descending and horizontal duodenum). Of the NADEN surface patterns, 88% (62/70) were pit-type, while 79% (35/44) of the non-neoplasm surface patterns were groove-type. Our diagnostic algorithm for differentiating NADENs from non-neoplasms was high (sensitivity 96%, specificity 95%) in the descending and horizontal duodenum. The evaluators' diagnostic performances were also high, and interobserver agreement for the algorithm was good between each diagnostician and evaluator (κ = 0.60-0.76).
Conclusion: Diagnostic performance of our algorithm sufficiently enabled eliminating endoscopic biopsies for diagnosing the descending and horizontal duodenum.

Treatment of Duodenal Cancer
There are three types of standard treatment that may be used:

Kodera, Y. 2020.
Although the incidence of each rare cancer is low, the estimated annual incidence rate of all rare cancers added together reportedly corresponded to 22% of all cancer diagnoses in Europe. To cope with most rare cancers, each physician is burdened with literature search and consultation through private relationships to find how the patients should be diagnosed and treated. Treatment guidelines will be of huge assistance in such situations, and should preferably be compiled for selected rare cancers for which information is more often sought after. The author established a research team funded by the Ministry of Health, Labor and Welfare, Japan, under the title of "Improvement of quality in medical support system for rare cancer through compilation of guidelines". This research team is a joint force of several experts from various fields of oncology, and guidelines on rare cancer of various categories, such as brain tumors, retroperitoneal sarcomas, penile cancer and duodenal cancer are currently on the way to publication. This manuscript describes the footsteps of the members of this research team who concentrates on a project to compile guidelines for the diagnosis and treatment of duodenal cancer, which is expected to go to print by the end of 2020.

Akce, M., Jiang, R., Zakka, K., Wu, C., Alese, O.B., Shaib, W.L., Behera, M. & El-Rayes, B.F. 2019.
Background: Small bowel adenocarcinomas (SBAs) are rare tumors. Management of SBA is extrapolated from colorectal cancer treatments. Recent evidence suggests that the biology and molecular features of SBA differ from colorectal cancer. The aim of this study was to evaluate the management and outcome of SBA patients. PATIENTS AND METHODS: The National Cancer Data Base (NCDB) was queried for patients with SBA between 2004 and 2013 using ICD-O-3 histology code 8140/3 and topography codes C17.0, C17.1, C17.2, C17.8, and C17.9. Univariate and multivariate survival analyses were conducted to analyze the association between SBA location and overall survival (OS) stratified by stage. Treatment outcomes of surgery, radiation, and systemic therapy were compared.
Results: A total of 7954 SBA patients were identified; duodenum (D) 4607 (57.9%), jejunum (J) 1241 (15.6%), ileum (I) 857 (10.8%), and unspecified 1249 (15.7%). A total of 53.6% patients were male, and 76.6% white. Median age was 66 years. D mostly presented as stage IV disease (37.6%), J as stage II (34.5%) and IV disease (33.8%), and I as stage II (32.2%) and III (30.3%) disease (P < .001). Grade distribution was similar among D, J, and I; the majority were moderately differentiated (40.8%-55.0%), followed by poorly differentiated (30.9%-

35.8%) and well differentiated (6.0%-12.4%) (P < .001). D underwent surgery (50.2%) less often than J (90.8%) and I (94.5%) (P < .001). Adjuvant radiation was provided in 8.5% of D, 2.6% of J, and 2.1% of I (P < .001). Adjuvant chemotherapy was provided in 21.9% of D, 50.2% of J, and 42.0% of I (P < .001). The rate of adjuvant chemotherapy was the highest in patients with stage III SBA, and was as follows: D (43.4%), J (65.4%), and I (63.6%) (P < .001). In univariate and multivariate analyses of all patients, adjuvant chemotherapy was associated with improved OS in stage II-III SBA patients. J had the best 5-year OS rate (42.0%; 95% confidence interval, 38.8-45.1, P < .001), and D had the worst (23.0%; 95% confidence interval, 21.6-24.2, P < .001). In multivariate analysis stratified by stage, chemotherapy was associated with improved OS in patients with stage II-IV SBA.
Conclusion: Most SBA patients present with stage IV disease. D underwent surgery less often than J and I. Stage II and III D received adjuvant chemotherapy less often compared to stage II and III J and I. Adjuvant chemotherapy was associated with improved OS in patients with stage II-III disease. J had the best 5-year OS rate, and D had the worst.

Surgery - surgery is the most common treatment of small intestine cancer. One of the following types of surgery may be done:

- Resection: Surgery to remove part or all of an organ that contains cancer.
- Bypass: Surgery to allow food in the small intestine to go around (bypass) a tumour that is blocking the intestine but cannot be removed.

After the doctor removes all the cancer that can be seen at the time of the surgery, some patients may be given radiation therapy to kill any cancer cells that are left. Treatment given after the surgery, to lower the risk that the cancer will come back, is called adjuvant therapy.

López-Domínguez, J., Busquets, J., Secanella, L., Peláez, N., Serrano, T. & Fabregat, J. 2019.
Introduction: Duodenal adenocarcinoma is a rare malignancy. Given the rarity of the disease, there is limited data related to resection results. The objective is to analyze results at our hospital after the curative resection of duodenal adenocarcinoma (DA).
Methods: The variables were retrospectively collected from patients operated on between 1990 and 2017 at our hospital.
Results: A total of 27 patients were treated. Twenty-three patients (85%) underwent pancreaticoduodenectomy, and 4 patients (15%) with tumors located in the third and fourth portions of the duodenum underwent segmental duodenal resection. The overall postoperative morbidity was 67% (18 patients). Postoperative mortality was 7% (2 patients); however, postoperative mortality related to surgery was 4% (1 patient). All patients had negative resection margins. A median of 18 lymph nodes (range, 0-38) were retrieved and evaluated, with a median of 1 involved node (range, 0-8). Median follow up was 23 (9-69.7) months. Actuarial overall survival was 62.2 (25.2-99.1) months. Actuarial disease-free survival was 49 (0-133) months.
Conclusions: The surgical treatment of duodenal adenocarcinoma is associated with a high morbidity, although it achieves considerable survival. Depending on the tumor location and if there is no pancreatic infiltration, segmental duodenal resection with negative margins is an alternative to cephalic pancreaticoduodenectomy.
Keywords: Adenocarcinoma duodenal; Duodenal adenocarcinoma; Duodenectomía; Duodeno-pancreatectomía cefálica; Pancreaticoduodenectomy; Segmental duodenal resection.

Radiation therapy - radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. There are two types of radiation therapy:

- External radiation therapy uses a machine outside the body to send radiation toward the cancer.

- Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer.

The way the radiation therapy is given depends on the type of the cancer being treated. External radiation therapy is used to treat small intestine cancer.

Chemotherapy - is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy).

New types of treatment are being tested in clinical trials include:
Biologic therapy - is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer. This type of cancer treatment is also called biotherapy or immunotherapy.

Radiation therapy with radiosensitisers - radiosensitisers are drugs that make tumour cells more sensitive to radiation therapy. Combining radiation therapy with radiosensitisers may kill more tumour cells.

Oshima, K., Noguchi, K., Tomimaru, Y., Nagase, H., Ogino, T., Hirota, M., Oshima, K., Tanida, T., Noura, S., Imamura, H., Akagi, K., Iwazawa, T. & Dono, K. 2019.
"There have been few reports discussing treatments for primary duodenal cancer. In this study, 15 cases of primary duodenal cancer that were treated by curative resection in our hospital between April 2005 and December 2017 were analyzed to study appropriate operative procedures. Prognostic analysis revealed that the median of relapse-free survival and overall survival were 49 months and 74 months, respectively. The 5-year survival rate was 47%. On univariate analysis of relapse-free survival, lymph node metastasis($p<0.01$)and post-operative adjuvant therapy($p=0.02$)were significant independent prognostic factors. Analysis of the relationship between lymph node metastasis and the depth or location of tumors suggested that pancreaticoduodenectomy with lymph node dissection should be performed to achieve radical resection, since there were some cases that involved lymph node metastasis around the pancreatic head or hepatoduodenal ligament.""

Yanagimoto, Y., Omori, T., Jeong-Ho, M., Shinno, N., Yamamoto, K., Takeuchi, Y., Higashino, K., Uedo, N., Sugimura, K., Matsunaga, T., Miyata, H., Ushigome, H., Takahashi, Y., Nishimura, J., Yasui, M., Asukai, K., Yamada, D., Tomokuni, A., Wada, H., Takahashi, H., Ohue, M., Yano, M. & Sakon, M. 2019.
BACKGROUND: Pancreatoduodenectomy is considered to be a very invasive treatment for early superficial duodenaltumors (SDTs), which have a lower risk of lymph node metastasis. Partial resection of the duodenum with endoscopic submucosal dissection for SDT resection is an attractive technique but it is associated with a high risk of complications. We describe our technique for SDT resection.
METHOD: It includes the following elements: freeing the transverse mesocolon, exposing and mobilizing the second part of the duodenum and the head of the pancreas (Kocher maneuver), confirming the location of the ulcer bed for endoscopic submucosal dissection, and laparoscopic suturing by hand in the seromuscular layer of the duodenum. We performed this technique in 10 patients between March 2015 and March 2017.
RESULTS: The median tumor diameter and resected tissue diameter were 36 (20-54) and 41 (25-60) mm, respectively. Curative resection (R0) with negative margins was achieved for all patients. There were no conversions to open surgery in this series. No postoperative complications were above grade 2 in the Clavien-Dindo classification system. No recurrences were observed during the medium-term follow-up period.
CONCLUSION: This technique is safe and feasible and can be an option for surgical SDT 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.

For additional information, please visit: www.sanctr.gov.za/

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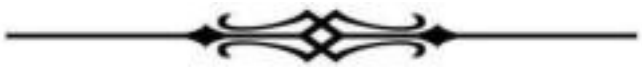

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