Cancer Association of South Africa (CANSA)

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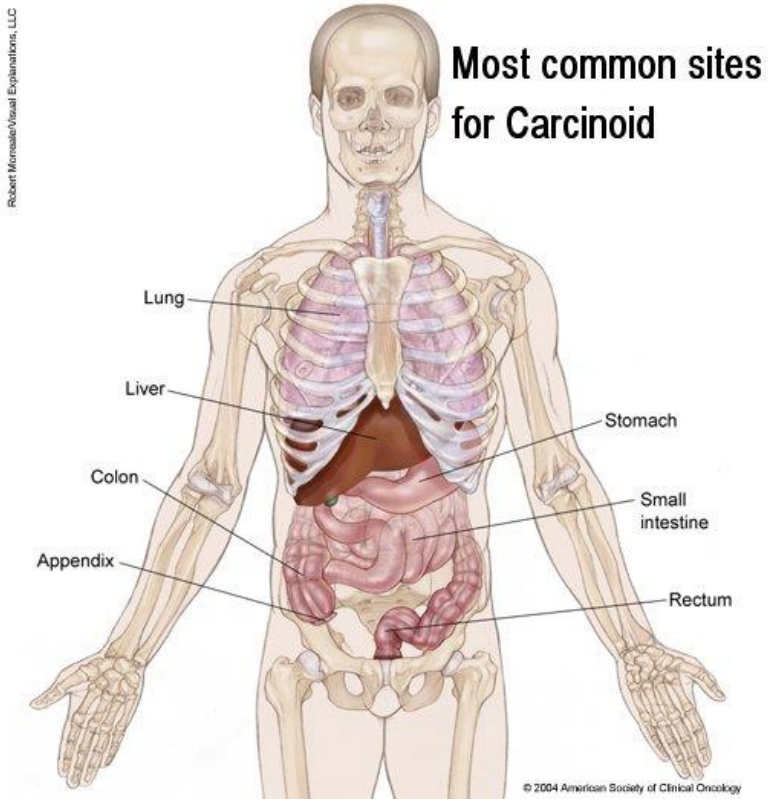
Fact Sheet on Carcinoid Tumours

Introduction

Carcinoid cancer and related neuroendocrine tumours (NETs) are small, slow growing tumours found mostly in the gastrointestinal system, but can be in other parts of the body such as the pancreas and the lung. Since most of these grow very slowly, compared to other cancers, it usually takes many years before they become sizable or cause symptoms.



[Picture Credit: Carcinoid Tumours]

Carcinoid tumours and other NETs usually originate in hormone-producing cells that line the small intestine or other cells of the digestive tract. They can also occur in the pancreas, testes, ovaries, or lungs. Carcinoid tumours can produce an excess of hormone-like substances, such as serotonin, bradykinin, histamine, and prostaglandins. Excess levels of these substances can sometimes result in a diverse set of symptoms called carcinoid syndrome. Other NETs can produce other hormonal substances causing a variety of other syndromes.

When carcinoid tumours occur in the digestive tract or pancreas, the substances they produce are released into a blood vessel that flows directly to the liver (portal vein), where enzymes destroy them. Therefore, carcinoid tumours that originate in the digestive tract generally do not produce symptoms

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unless the tumours have spread to the liver. The hormones secreted by other NETs, particularly those in the pancreas, do not necessarily require spread to the liver to cause symptoms.

When carcinoid tumours have spread to the liver, the liver is unable to process the substances before they begin circulating throughout the body. Depending on which substances are being released by the tumours, the person will have the various symptoms of carcinoid syndrome, insulinoma syndrome (it originates in the beta cells of the pancreas, which releases an unregulated amount of insulin - the patient may feel symptoms that include sweating, increased heat rate, shaking, paleness and a decreasing state of consciousness), Zollinger Ellison syndrome (a condition in which there is increased production of the hormone gastrin), and VIPoma syndrome (also known as Verner Morrison syndrome of watery diarrhoea, hypokalaemia, and achlorhydria).

Carcinoid tumours of the lungs, testes, and ovaries also cause symptoms without having spread, because the substances they produce bypass the liver and can sometimes circulate widely in the bloodstream.

Cingam, S.R., Kashyap, S. & Karanchi, H. 2020.
"Carcinoid tumors are slow-growing tumors arising from neuroendocrine cells and capable of secreting a variety of peptides and neuroamines. The common primary sites are the gastrointestinal (GI) tract (60%) followed by the tracheobronchial tree (25%), but other primaries may occur in the ovaries or kidneys. The most common location of carcinoids is the small intestine. The term carcinoid is usually used for well-differentiated and low to intermediate grade neuroendocrine tumors, and the term neuroendocrine carcinoma is used for the less frequent, poorly differentiated and high-grade neuroendocrine tumors."

Hilal, L., Jammal, M., Khalifeh, I., Tfayli, A. & Youssef, B. 2019.
"Head and neck neuroendocrine tumors (NET) are a rare type of cancer. NET can be classified according to the histopathological features. The typical carcinoid tumor is a well-differentiated tumor that is the least common among other types. Owing to its indolent behavior and variable radiological and pathological features, treatment of carcinoid tumors remains a challenge. "

Carcinoid Tumours
A carcinoid tumour starts in the hormone-producing cells of various organs, primarily the gastrointestinal tract (such as the stomach and intestines) and lungs, but also the pancreas, testicles (in males) or ovaries (in females). A carcinoid tumour is classified as a neuroendocrine tumour, which means it starts in cells of the neuroendocrine system that produce hormones.

Origin of carcinoid tumours
- 39% occur in the small intestine
- 15% occur in the rectum
- 10% occur in the bronchial system of the lungs
- 7% occur in the appendix
- 5% to 7% occur in the colon (large bowel)
- 2% to 4% occur in the stomach
- 2% to 3% occur in the pancreas
- About 1% occur in the liver

Howe, J.R. 2020.
"Carcinoid tumors are being seen with increasing frequency by surgeons and have become the most common type of tumors of the small bowel. These tumors produce a variety of hormones, which leads to many unique characteristics in terms of symptoms and presentation. Our knowledge of the natural history and treatment of these tumors continues to evolve, and this article will summarize these advances."

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.

What are the cancer stages?
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.

TNM staging
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 Carcinoid Tumours in South Africa

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

Carcinoid Syndrome

Many patients with metastatic carcinoid tumour will manifest the signs and symptoms of abnormal hormone production - the malignant carcinoid syndrome. Serotonin (5-hydroxytryptamine [5-HT]), synthesised by the tumour from tryptophan and metabolised to 5-HIAA, which appears in the urine, is particularly important because urinary 5-HIAA levels are used to monitor the course of carcinoid syndrome. However, the relationship of serotonin levels to symptoms of the clinical carcinoid syndrome is uncertain.

Carcinoid tumours also release the enzyme kallikrein, which acts on alpha$_2$-globulin to produce bradykinin and its precursor, lysyl-bradykinin, both of which can induce flushing.

Serotonin may be responsible for intestinal hypermotility and hypersecretion, but it probably does not cause the characteristic flushing that occurs with the carcinoid syndrome.

Vasodilation, which causes flushing, can be due to one or more substances released by the tumour cells, including bradykinin, tachykinins, and prostaglandins.

The symptoms of the carcinoid syndrome vary in frequency. Flushing is most frequent, followed by diarrhoea, heart disease, and bronchoconstriction.

[Picture Credit: Carcinoid Syndrome]

Pandit, S., Annamaraju, P. & Bhusal, K. 2020.
"Carcinoid syndrome refers to a group of symptoms caused by the systemic release of different kinds of humoral factors like polypeptides, biogenic amines, and prostaglandins mostly from well-differentiated neuroendocrine tumors. Previously well-differentiated neuroendocrine tumors were known as carcinoid tumors. Neuroendocrine tumors are derived from enterochromaffin cells that are ubiquitous in our body. It is reported that only about 10% of neuroendocrine tumors result into carcinoid syndrome."

Gade, A.K., Olariu, E. & Douthit, N.T. 2020.
"Carcinoid syndrome (CS) is a paraneoplastic syndrome caused by the release of serotonin and other substances from well-differentiated neuroendocrine tumors (NETs). The hallmark symptoms of carcinoid syndrome are flushing and diarrhea; atypical signs and symptoms can include wheezing, abdominal pain, valvular heart disease, telangiectasias, pellagra, and the complications of mesenteric fibrosis, including ureteral obstruction, bowel obstruction, and bowel ischemia. These symptoms are mediated by the release of serotonin (5-HT), histamine, kallikrein, prostaglandins, and tachykinins. The diagnosis of CS requires these symptoms and corresponding elevations in lab tests. Treatment options include surgery and medical management with somatostatin analogs."

Risk Factors for Carcinoid Tumours
Researchers are still learning about carcinoid tumours and what causes them. There are a few known risk factors for carcinoid tumours, and most are not factors you can control or change.

- Genetic syndromes - people with a rare genetic syndrome called Multiple Endocrine Neoplasia, type 1 (MEN1) have a higher risk of certain tumours, including carcinoid tumours. Those with a disease called neurofibromatosis type 1 are also at higher risk for developing carcinoid tumours

- Gender - women may be at slightly higher risk of developing carcinoid tumours. Researchers are not sure why

- Race - gastrointestinal carcinoid tumours are said to be more common in African-American men and women than in Caucasians whereas lung carcinoid tumours are more common in

Caucasians than in people of other races. It is not certain whether this applies to the South African population

- Stomach conditions - those individuals who have a stomach condition that reduces the amount of acid in the stomach and damages the stomach have a higher risk of carcinoid tumours in the stomach

- Smoking - smokers may be more likely to have certain types of lung carcinoid tumours. A recent study in Europe also found that smoking may double the risk of having a carcinoid tumour in the small intestine. But more research is needed to confirm these results.

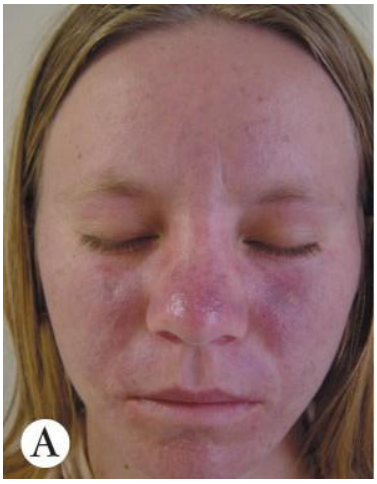
Signs and Symptoms of Carcinoid Tumours

The signs and symptoms of carcinoid syndrome depend on which chemicals the carcinoid tumour secretes into the bloodstream. The most common signs and symptoms of carcinoid syndrome include:

Skin flushing - the skin on the face and upper chest feels hot and changes colour — ranging from pink to red to purple. Flushing episodes may last from a few minutes to a few hours or longer. Flushing may happen for no obvious reason, though sometimes it can be triggered by stress, exercise or drinking alcohol

Facial skin lesions - purplish areas of spider-like veins may appear on the nose and upper lip

[Picture Credit: Carcinoid Skin Lesion]



Diarrhoea - frequent, watery stools sometimes accompanied by abdominal cramps may occur in people who have carcinoid syndrome

Difficulty breathing - asthma-like signs and symptoms, such as wheezing and shortness of breath, may occur at the same time you experience skin flushing

Rapid heartbeat - periods of fast heart rate could be a sign of carcinoid syndrome

Classification of Carcinoid Tumours

Carcinoid tumours generally are classified based on the location in the primitive gut that gives rise to the tumour, as follows:

- Foregut carcinoid tumours: divided into sporadic primary tumours (lung, bronchus, stomach, proximal duodenum, pancreas) and tumours secondary to achlorhydria

- Midgut carcinoid tumours: derived from the second portion of the duodenum, the jejunum, the ileum, and the ascending colon

- Hindgut carcinoid tumours: includes the transverse colon, descending colon, and rectum

Diagnosing Carcinoid Tumours

Because carcinoid tumours grow slowly, many are caught early, before they have had a chance to metastasize or cause symptoms. In many cases, they are found during routine tests or exams when looking for other problems.

These tumours are often found by accident. They are often found during a screening colonoscopy or endoscopy or because of abnormal results on a liver function test.

Sometimes the tumours are found because they are causing symptoms. If your doctor suspects a carcinoid tumour, there are a few different types of diagnostic tests to use.

The aetiology of carcinoid tumours is not known, but genetic abnormalities are suspected. Reported chromosomal abnormalities include changes in chromosomes, such as loss of heterogeneity, and numerical imbalances. The diagnosis is sometimes made because of unrelated findings, such as anaemia, endocrine disease, or autoimmune disease.

- Laboratory diagnosis of carcinoid tumours depends on the identification of the characteristic biomarkers of the disease. Measurement of biogenic amine levels (e.g., serotonin, 5-hydroxyindoleacetic acid [5-HIAA], catecholamines, histamine) and its metabolites in the platelets, plasma, and urine of patients can be helpful in making the diagnosis.

- Depending on the location of the tumour and metastasis, a combination of the following imaging modalities may be used to evaluate suspected carcinoid tumours:
  - Plain radiography
  - Upper and lower GI radiography with oral contrast agents
  - Computed tomography scanning
  - Magnetic resonance imaging
  - Angiography
  - Positron emission tomography scanning
  - Scintigraphy with metaiodobenzylguanidine (MIBG) and octreotide
  - Radionuclide imaging with somatostatin analogs attached to the radioactive tracer
  - Technetium-99m bone scanning

Guenter, R.E., Aweda, T., Carmona Matos, D.M., Whitt, J., Chang, A.W., Cheng, E.Y., Liu, X.M., Chen, H., Lapi, S.E. & Jaskula-Sztul, R. 2019

"Pulmonary carcinoids are a type of neuroendocrine tumor (NET) accounting for 1-2% of lung cancer cases. Currently, Positron Emission Tomography (PET)/CT based on the radiolabeled sugar analogue [^{18}F]-FDG is used to diagnose and stage pulmonary carcinoids, but is suboptimal due to low metabolic activity in these tumors. A new technique for pulmonary carcinoid imaging, using PET/CT with radiolabeled somatostatin analogs that specifically target somatostatin receptor subtype 2 (SSTR2), is becoming more standard, as many tumors overexpress SSTR2. However, pulmonary carcinoid patients with diminished SSTR2 expression are not eligible for this imaging or any type of SSTR2-specific treatment. We have found that histone deacetylase (HDAC) inhibitors can upregulate the expression of SSTR2 in pulmonary carcinoid cell lines. In this study, we used a non-cytotoxic dose of HDAC inhibitors to induce pulmonary carcinoid SSTR2 expression in which we

confirmed in vitro and in vivo. A non-cytotoxic dose of the HDAC inhibitors: thailandepsin A (TDP-A), romidepsin (FK228), suberoylanilide hydroxamic acid (SAHA), AB3, and valproic acid (VPA) were administered to promote SSTR2 expression in pulmonary carcinoid cell lines and xenografts. This SSTR2 upregulation technique using HDAC inhibitors could enhance radiolabeled somatostatin analog-based imaging and the development of potential targeted treatments for pulmonary carcinoid patients with marginal or diminished SSTR2 expression."

- Endoscopic procedures, such as the following, may be used for biopsy and diagnosis:
  - Bronchoscopy
  - Oesophagogastroscopy
  - Gastroscopy
  - Colonoscopy

- Blood and urine tests - these simple tests are often a first step in diagnosing carcinoid syndrome. Doctors use these tests to look for the excess hormones and other substances that carcinoid tumours produce.

- Biopsy - once the tumour has been found, the doctor may take a small piece of tissue from the tumour to look at it under a microscope. A biopsy is essential in diagnosing carcinoid tumour. Until one examines the cells under a microscope one will not know for certain what type of tumour one is dealing with. It also helps in determining what type of treatments the tumour will best respond to.

Prognosis or Outcome

Typical carcinoids are slow growers. Data on survival of patients with small tumours not causing Carcinoid Syndrome and without spread, treated by surgical removal alone, indicates that a complete cure is usually possible in these cases.

In those tumours that are somewhat larger and have spread to local tissues and local lymph nodes but which, along with these locally invaded tissues, are still totally removable surgically, the average survival has been 8 years with a range up to 23 years.

Even when the tumour from the small intestine has spread in a manner that has made complete surgical removal impossible, the older statistics show that approximately one half of the patients survive an average of 5 years. Since various types of treatment have been introduced in the past decade patients appear to have an even longer survival and improved quality of life.

Atypical carcinoids, which are a group whose microscopic appearance looks different and more aggressively malignant than the typical carcinoid, follow a more rapid course with a more uncertain outlook. An even worse forecast can be made for the very more malignant rare group called 'neuroendocrine carcinoma'. Atypical carcinoids can cause the Carcinoid Syndrome, but neuroendocrine carcinomas rarely do so.

The tempo of the course of the illness in patients with Carcinoid Syndrome is different than that of carcinoid patients without the functioning syndrome. However, this has been remarkably improved and the outlook is much more hopeful with the advent of octreotide and similar somatostatin

analogues and other new modes of treatment. In the early decades before effective treatment was available the average survival from the onset of flushing for a Carcinoid Syndrome patient was 3 years, and from the time of diagnosis was 2 years, though the range extended to over 10 years.

Seventy five percent of the patients would die as a consequence of the harmful effects on the body from the excessive amounts of potent hormones released into their circulation by the tumours. Tumour growth and spread itself was fatal in only 25% of cases. In the last 10 years, since we have used effective combinations of treatment with octreotide (and similar somatostatin analogues), various types of surgery, chemotherapy, hepatic artery injections and biological response mediators, the average survival time from the start of treatment (which unfortunately is often quite delayed after the diagnosis is made) has increased to almost 12 years - with a wide range often being observed.

Montminy, E.M., Zhou, M., Maniscalco, L., Abualkhair, W., Kim, M.K., Siegel, R.L., Wu, X.C., Itzkowitz, S.H. & Karlitz, J.J. 2020.
Background: Early-onset colorectal cancer (EOCRC) incidence rates (IRs) are rising, according to previous cancer registry analyses. However, analysis of histologic subtypes, including adenocarcinoma (the focus of CRC screening and diagnostic testing) and carcinoid tumors (which are classified as "colorectal cancer" in SEER [Surveillance, Epidemiology, and End Results] databases but have a distinct pathogenesis and are managed differently from adenocarcinoma), has not been reported.
Objective: To assess EOCRC IRs and changes in IRs over time, stratified by histology.
Design: Retrospective analysis.
Setting: Yearly IRs according to SEER 18 data from 2000 to 2016 on age-specific colon-only, rectal-only, and combined-site CRC cases, stratified by histology ("overall" CRC [all histologic subtypes], adenocarcinoma, and carcinoid tumors) and age.
Patients: 119 624 patients with CRC.
Measurements: IRs per 100 000 population, changes in 3-year average annual IRs (pooled IRs from 2000 to 2002 vs. those from 2014 to 2016), and annual percentage change (APC) in persons aged 20 to 29, 30 to 39, 40 to 49, and 50 to 54 years.
Results: The steepest changes in adenocarcinoma 3-year average annual IRs were for rectal-only cases in persons aged 20 to 29 years (+39% [0.33 to 0.46 per 100 000]; $P < 0.050$) and 30 to 39 years (+39% [1.92 to 2.66 per 100 000]; $P < 0.050$) and colon-only cases in those aged 30 to 39 years (+20% [3.30 to 3.97 per 100 000]; $P < 0.050$). Corresponding APCs were 1.6% ($P < 0.050$), 2.2% ($P < 0.050$), and 1.2% ($P < 0.050$), respectively. In persons aged 40 to 49 years, 3-year average annual IRs increased in both colon-only (+13% [12.21 to 13.85 per 100 000]; $P < 0.050$) and rectal-only (+16% [7.50 to 8.72 per 100 000]; $P < 0.050$) subsites. Carcinoid tumors were common, representing approximately 4% to 20% of all colorectal and 8% to 34% of all rectal cancer cases, depending on age group and calendar year. Colon-only carcinoid tumors were rare. Colorectal carcinoid tumor IRs increased more steeply than adenocarcinoma in all age groups, thus affecting the contribution of carcinoid tumors to overall cancer cases over time. These changes were driven by rectal subsites and were most pronounced in persons aged 50 to 54 years, in whom rectal carcinoid tumors increased by 159% (2.36 to 6.10 per 100 000) between 2000 to 2002 and 2014 to 2016, compared with 10% for adenocarcinoma (18.07 to 19.84 per 100 000), ultimately accounting for 22.6% of all rectal cancer cases.
Limitation: Population-based data.
Conclusion: These findings underscore the importance of assessing histologic CRC subtypes independently. Doing so may lead to a better understanding of the drivers of temporal changes in overall CRC incidence and a more accurate measurement of outcomes from efforts to reduce adenocarcinoma risk, and can guide future research.

Treatment of Carcinoid Tumours
Treatment of carcinoid tumours include:

- Surgery – it is the most common procedure to treat carcinoid tumours. It may be used to treat the primary tumour and nearby lymph nodes where the cancer has spread. Surgery also may be done if the cancer has spread to the liver. Surgical removal of the tumour may help carcinoid syndrome symptoms. The doctor may suggest one of the following types of surgery to treat a carcinoid tumour:

Rahouma, M., Kamel, M., Narula, N., Nasar, A., Harrison, S., Lee, B., Stiles, B.M., Lau, C., Altorki, N.K. & Port, J.L. 2019.
BACKGROUND: There is a paucity of data regarding the role of wedge resection (WR) in the management of bronchial carcinoid (BC) tumors. In this study, we queried the Surveillance, Epidemiology, and End Results (SEER) database to compare the oncologic outcomes of patients with BC tumors treated with WR or anatomic resection.
METHODS: The SEER database was retrospectively reviewed for patients with BC treated with surgical resection between 1973-2013. Patients who underwent WR were compared to those who underwent lobectomy or segmentectomy (Lob/Seg). Patients with multiple primaries and those who underwent pneumonectomy or have an unspecified surgical procedure were excluded. Differences in demographics and clinicopathological data were compared using Chi (χ^2) test or Mann Whitney U test. Overall and cancer specific survival (OS, CSS) were estimated using Kaplan-Meier method and differences were compared using log-rank test. Cox-regression multivariable analysis (MVA) was performed to explore factors associated with worse CSS. Propensity-score matching analysis was done to compare survival differences between WR and Lob/Seg.
RESULTS: A total of 22,350 patients with BC were identified, of them 4,450 met our inclusion criteria (3,511 Lob/Seg, *vs.* 939 WR). The median age was 59.0 years [interquartile range (IQR) =49.0-68.0], 67.6% were females and the median tumor size was 2 cm (1.5-3 cm). 4,119 patients had typical carcinoid (TC) and 331 had atypical carcinoid (AC). WR was performed more frequently in elderly patients, females, lower lobe tumors, TC's and in earlier stage disease. For patients with TC, there was no difference in CSS between WR and Lob/Seg in both the entire cohort (P=0.654) and in the propensity matched groups (P=0.900). However, for patients with AC, Lob/Seg was associated with better CSS compared to WR both in the entire cohort (P<0.001) and in the propensity matched groups (P=0.001). On MVA of the entire cohort, elderly patients, males, blacks, AC and advanced stages had worse CSS. While, the type of the procedure (WR *vs.*Lob/Seg) was not associated with CSS (HR =1.16, 95% CI: 0.85-1.60).
CONCLUSIONS: A WR may offer equivalent CSS in well-selected patients with early-stage TC. An anatomic resection appears warranted in AC.

- Bowel and colorectal resection: removal of the intestine and lymph nodes near the primary carcinoid tumour(s). Lymph nodes along the vessels that supply the affected intestine (called the mesentery) are removed. Removal of the mesentery is at least as important as removing the primary tumour. This requires advanced imaging and surgical techniques to assure complete removal of cancer and preservation of good intestinal function

- Liver resection: significant experience is needed to determine if liver surgery can and should be performed for carcinoid tumours, since most are in both sides of the liver. Advanced

planning and surgical techniques are important to ensure surgery is done only if the patient will benefit from it.

- Appendectomy: removal of the appendix, a common site for carcinoid tumours

- Radiofrequency ablation and cryoablation: these methods to destroy carcinoid tumours in the liver do not require surgical removal of the tumour (resection). They often are not as successful as surgery, but they may be helpful for some patients. Radiofrequency uses radio waves to heat tumours; cryoablation used cold to freeze the tumours. Each has advantages and disadvantages, and the doctor will involve the patient in deciding if there can be benefit from these treatments.

- Radiation therapy: usually is not used to treat carcinoid tumours. It may help individuals who cannot have surgery and it may help relieve pain if the cancer has spread.

- Chemotherapy: is not an effective treatment for carcinoid tumours in the bowel. It may be used, however, for neuroendocrine tumours starting in the pancreas or aggressive fast-growing neuroendocrine tumours.

- Targeted therapies: these innovative new drugs stop the growth of cancer cells by interfering with certain proteins and receptors or blood vessels that supply the tumour with what it needs to grow

- Octreotide: this drug, which is given by injection, contains a substance similar to the hormone somatostatin. A long-acting version can be given once a month. Lanreotide is a similar drug. Although octreotide usually does not shrink carcinoid tumours, it may slow their growth and help relieve symptoms. Side effects may include insulin resistance

- Interferon: these natural substances activate the body's immune system and sometimes slow the growth of carcinoid tumour cells.

Supportive Treatment

Besides the various anti-tumour treatments reviewed above, there are many benefits resulting from a nutritious high protein diet, vitamin supplements - particularly niacin, mineral supplements (such as potassium, magnesium, calcium, iron and even salt) when these are deficient due to diarrhoea.

In addition to the use of octreotide or lanreotide to control diarrhoea, conventional anti-diarrheal medications such as Lomotil and Imodium may be helpful. Cyproheptadine (Periactin) may also help the diarrhoea as well as flushing. Large portions of freshly grated nutmeg (1 teaspoon eaten 3 times a day) will sometimes control the diarrhoea remarkably well.

Antihistamines and alpha adrenergic blocking drugs such as Dibenzyline are sometimes used to prevent Carcinoid Syndrome attacks.

All carcinoid patients should avoid alcoholic beverages and physical and emotional stress since these can precipitate carcinoid crisis attacks.

Similarly, adrenaline like drugs should be avoided. These include various asthma inhalers, nasal decongestants and adrenaline itself.
Certain very severe and prolonged carcinoid crises associated with bronchial (lung) carcinoids or some carcinoids of the stomach are responsive to treatment with corticosteroids (prednisone, Decadron) and Thorazine or Compazine. There is recent emphasis for carcinoid inhibiting properties of black raspberry extract.

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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Carcinoid Skin Lesion
https://www.google.co.za/search?q=carcinoid+syndrome&biw=1517&bih=714&source=lnms&tbm=isch&sa=X&ei=EecfVKSfJ4be7Aa8pIHwCg&sqi=2&ved=0CAYQ_AUoAQ&dpr=0.9#facrc=_&imgdii=_&imgrc=qr6CPpa4BCC7GM%253A%3Bg6aZNnqpgv7jxM%3Bhttp%253A%252F%252Fwww.scielo.br%252Fimg%252Frevistas%252Fabd%252Fv83n6%252Fa09fig1out.jpg%3Bhttp%253A%252F%252Fwww.scielo.br%252Fscielo.php%253Fscript%253Dsci_arttext%2526pid%253DS0365-05962008000600009%3B729%3B418

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