Cancer Association of South Africa (CANSA)

Fact Sheet
on
Adrenal Gland Cancer

Introduction
A cancerous tumour of the adrenal gland is called an adrenal cortical carcinoma and is a condition where there is abnormal multiplication of cells. A noncancerous tumour of the adrenal gland is called a benign adenoma.

A tumour begins when normal cells change and grow uncontrollably, forming a mass. A tumour can be benign (noncancerous) or malignant (cancerous, meaning it can spread to other parts of the body).

Each person has two adrenal glands - one located on top of each of the body’s two kidneys. These glands are important to the body’s endocrine (hormonal) system. Each adrenal gland has two main parts that function separately:

“Malignancy must be considered in the management of adrenal lesions, including those incidentally identified on imaging studies. Adrenocortical carcinomas (ACCs) are rare tumors with an estimated annual incidence of 0.7-2 cases per year and a worldwide prevalence of 4-12 cases per million/year. However, a much higher incidence of these tumors (>15 times) has been demonstrated in south and southeastern Brazil. Most ACCs cause hypersecretion of steroids including glucocorticoids and androgens. ACC patients have a very poor prognosis with a 5-year overall survival (OS) below 30% in most series. Pheochromocytoma or paraganglioma (PPGL) is a metabolically active tumor originating from the chromaffin cells of the adrenal medulla. The incidence of PPGL is 0.2 to 0.9 cases per 100,000 individuals per year. Pheochromocytomas are present in approximately 4-7% of patients with adrenal incidentalomas. Classically, PPGL manifests as paroxysmal attacks of the following 4 symptoms: headaches, diaphoresis, palpitations, and severe hypertensive episodes. The diagnosis of malignant PPGL relies on the presence of local invasion or metastasis. In this review, we present the...
clinical and biochemical characteristics and pathogenesis of malignant primary lesions that affect the cortex and medulla of human adrenal glands.”

Incidence of Adrenal Gland Cancer in South Africa
The National Cancer Register of 2014 does not provide any statistics regarding the incidence of adrenal gland cancer in South Africa.

Signs and Symptoms of Adrenal Gland Cancer
Some other symptoms of adrenal cancer that produce excess cortisol and aldosterone in adults can include:
- high blood pressure
- high blood sugar
- low potassium levels
- weight gain
- irregular periods
- changes in genitalia
- easy bruising
- nervousness
- feeling of anxiety
- depression
- headache
- excessive perspiration
- frequent urination
- muscle cramps
- excessive hair growth
- changes in libido

Diagnosis of Adrenal Gland Cancer
One or more of the following may be employed in the diagnosis of adrenal gland cancer:

Laparoscopy - this procedure uses a laparoscope, a thin, flexible tube with a tiny video camera on the end. It is inserted through a small surgical opening in the patient's side to allow the surgeon to see where the cancer is growing.

Biopsy - imaging tests may find tumours, but often the only way to know for sure that a tumour is cancerous is to remove a sample of tumour tissue to look at under the microscope. This is called a biopsy.

Tests for adrenal hormones - blood and urine tests to measure levels of adrenal hormones are important in deciding whether a patient with signs and symptoms of adrenal cancer has the disease.
Tests for high cortisol levels - the tests used in this case include measuring levels of cortisol in the blood and in the urine.

Tests for high aldosterone levels - the level of aldosterone will be measured and will be high if the tumour is making aldosterone.

Tests for high androgen or oestrogen

Chest X-ray - this can show if the cancer has spread to the lungs. It may also be useful to determine if there are any serious lung or heart diseases.

Ultrasound - ultrasound tests use sound waves to take pictures of parts of the body.

Molecular markers - studies analysing the role of genes and proteins in a person’s tumour are underway. The focus of these studies is to help fine-tune the diagnosis of adrenal gland tumours and predict treatment results.

Computed tomography (CT) - the CT scan is an x-ray procedure that produces detailed cross-sectional images of your body.

Positron emission tomography (PET) - in this test, radioactive glucose (sugar) is injected into the patient’s vein.

Magnetic resonance imaging (MRI) - MRI scans use radio waves and strong magnets instead of x-rays.

Byeon, K.H., Ha, Y.S., Choi, S.H., Kim, B.S., Kim, H.T., Yoo, E.S., Kwon, T.G., Lee, J.N. & Kim, T.H. 2018. BACKGROUND AND OBJECTIVES:
The adrenal gland is a frequent site for metastasis, and a solitary adrenal mass is often observed during staging workup or imaging follow-up in patients with extra-adrenal malignancy. To create an appropriate management plan, it is essential to distinguish between benign adrenal lesions and metastasis in patients with extra-adrenal cancer having solitary adrenal masses. Therefore, here we evaluated the predictive factors for adrenal metastasis in patients with extra-adrenal malignancy having solitary adrenal mass.

MATERIALS AND METHODS:
From September 2003 to June 2016, we retrospectively reviewed patients with extra-adrenal malignancy having solitary adrenal mass on a cancer staging workup or follow-up study who subsequently underwent adrenalectomy at our institution. All patients underwent preoperative functional studies; those with positive results were excluded from this study. Characteristics of oncology patients with adrenal mass including age, sex, body mass index, smoking, mass location, mass size, hypertension, diabetes mellitus, precontrast Hounsfield unit (HU), and synchronous or metachronous adrenal mass based on the time of the extra-adrenal cancer diagnosis were analyzed.

RESULTS:
Of the total 68 patients with extra-adrenal cancer having solitary adrenal mass, 22 had pathologically confirmed adrenal metastasis. Primary cancers consisted of hepatocellular cell carcinoma (n = 7), renal cell carcinoma (n = 7), lung cancer (n = 4), colon cancer (n = 3), and breast cancer (n = 1). On multivariate analysis, a higher precontrast HU (P = 0.001, odds ratio [OR] = 1.105, 95% confidence interval [CI] = 1.042-1.172), male sex (P = 0.019, OR = 9.782, 95% CI = 1.462-65.461), and metachronous adrenal mass ( P = 0.007, OR = 11.090, 95% CI = 1.937-63.490) were observed as...
predictive factors for adrenal metastasis in patients with extra-adrenal cancer having solitary adrenal mass. The cut-off value of precontrast HU to distinguish between metastasis and benign lesions was 36.2 (sensitivity = 81.8%; specificity = 91.3%).

CONCLUSION:
High precontrast HU (> 36), male sex, and metachronous adrenal mass are predictive factors for adrenal metastasis in patients with extra-adrenal malignancy having solitary adrenal mass.

Staging of Adrenal Gland Cancer
Staging is a way of describing where the tumour is located, if or where it has spread and whether it is affecting the functions of other organs in the body. Doctors use diagnostic tests to determine the tumour’s stage.

One tool that doctors use to describe the stage is the TNM system. TNM is an abbreviation for tumour (T), node (N), and metastasis (M). Doctors look at these three factors to determine the stage of cancer. The TNM system tells the doctor:

- How large the primary tumour is and where is it located (Tumour, T)
- Whether the tumour has spread to the lymph nodes (Node, N)
- Whether the cancer has metastasised to other parts of the body (Metastasis, M)

Treatment of Adrenal Gland Cancer
Different types of treatments are available for patients with adrenocortical carcinoma. Some treatments are standard (the currently used treatment), while some are being tested in clinical trials.

Treatment may include:
- Surgery - surgery to remove the adrenal gland (adrenalectomy) is often used to treat adrenocortical carcinoma.
- 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.
- Chemotherapy - 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.
- Biologic therapy - biologic therapy is a treatment that uses the patient's immune system to fight cancer.
- Targeted therapy - is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells.


OBJECTIVE: To update French oncology guidelines concerning adrenal cancer.

METHODS: Comprehensive Medline search between 2016 and 2018 upon diagnosis, treatment and follow-up of adrenal cancer to update 2013 guidelines. Level of evidence was evaluated according to AGREE-II.

RESULTS: Adrenal cancers are mainly represented by adrenocortical carcinomas (AC), malignant pheochromocytomas (MPC) and adrenal metastases (AM). Medical background of these tumors is
either the exploration of hormonal or tumor symptoms, or an adrenal incidentaloma. Etiological explorations are based on hormonal biochemical assessment, morphological and functional imaging and histological analysis. AC and MPC are mostly sporadic but hereditary origin is still possible. The suspicion of AC is driven mainly by radiological signs of malignancy, signs of local invasion or distant metastasis, and type of hormonal secretion but the accurate diagnosis is histological. The diagnosis of MPC is clinical, biological and radiological. The diagnosis of MS involves a percutaneous biopsy. Medical files should be discussed within the COMETE - Adrenal Cancer Network (Appendix 1). Oncological adjuvant treatments are specific for the histological type. In the AC, their indication depends on the risk of recurrence and is based on mitotane, external radiotherapy or chemotherapy. In the MPC, it is based on internal radiotherapy and chemotherapy. Metastatic forms treatment is exceptionally surgical. Debulking is uncommon. For metastatic unresectable AC, treatment is based on mitotane monotherapy or triple chemotherapy. For metastatic unresectable MPC, treatment is based on exclusive metabolic radiotherapy or triple chemotherapy. Recurrences are frequent and sometimes delayed, which justifies a close and long follow-up.

**CONCLUSION:** The curative treatment of Adrenal cancers is surgical provided. This treatment is rarely sufficient alone, the prognosis is then pejorative.


**PURPOSE:** This study aimed to report on our institutional experience in the use of stereotactic body radiation therapy (SBRT) for the treatment of adrenal gland metastases. Specifically, we examined the outcomes and toxicity from this treatment modality on adjacent organs at risk.

**METHODS AND MATERIALS:** Data were retrieved from patients with adrenal metastases who were treated with SBRT between 2008 and 2017. Patients with primary adrenal malignancies were excluded. Toxicities were graded in accordance with the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. Time-to-event rates were calculated from the date of SBRT delivery.

**RESULTS:** In total, 35 patients with adrenal metastases were identified. Four patients were treated for bilateral disease. The median dose was 40 Gy (range, 20-54 Gy) in 5 fractions (range, 1-6 fractions). The median follow-up time was 37 months (range, 14-451 months) from disease diagnosis and 7 months (range, 1-54 months) from the SBRT start date. With death treated as a competing risk event, the cumulative incidence of local failure was 7.6% at 1 year after SBRT and 19.2% at 3 years. The median overall survival (OS) time was 19 months (95% confidence interval, 8-54 months) and tumor size correlated with survival ($P = .0006$). Patients with metastases <2.9 cm had a median OS of 54 months compared with 11 months for those with adrenal metastases ≥2.9 cm ($P = .01$). Incidence of grade 2 toxicity was 17% with no case of grade ≥3 toxicity. SBRT did not impact renal function with a mean estimated decline in glomerular filtration rate of only 2.6 ± 8 mL/min/1.73 m² compared with baseline. Combined kidneys V5 and combined renal cortex V17.5 did not correlate with a change in estimated glomerular filtration rate ($P = .7$ and $P = .9$, respectively).

**CONCLUSIONS:** SBRT offers excellent local control for the treatment of adrenal gland metastases with very low toxicity rates and no significant short-term impact on renal function.

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.sancr.gov.za/

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Sources and References Consulted or Utilised

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https://www.google.co.za/search?q=adrenal+glands&source=Inms&tbs=isch&sa=X&ei=DUGLUuvbCKKv77AcwiGADw&sqi=2&ved=0CAcQ_AUoAQ&biw=1366&bih=642#facrc= _&imgdii= &imgrc=xh_48MG2Z4C2ZM%3A%3B1asyyv4rxATcTM%3Bhttps%253A%252F%252Fwww.adrenalcharge.com%252Fbenefits%252Fassets%252Fimages%252Fadrenal-gland.jpg%3Bhttps%253A%252F%252Fwww.adrenalcharge.com%252Fbenefits%252F%3B400%3B389


American Cancer Society

Research 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]
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Cancer.Net
http://www.cancer.net/cancer-types/adrenal-gland-tumor/staging
http://www.cancer.net/cancer-types/adrenal-gland-tumor/latest-research

Emedicinehealth

EndocrineWeb

KidsHealth
http://kidshealth.org/parent/general/body_basics/endocrine.html

Laparoscope
https://www.google.co.za/search?q=flexible+laparoscope&source=lms&tbm=isch&sa=X&ei=Pk6LUvKBBMW47AbO7oEQ&ved=0CAcQ_AUoAQ&biw=1366&bih=642#facrc=&imgdii=_&imgarc=3A3XQtYkCCwMMPM%3A%3BydsItqWCrD62BtM%3Bhttp%253A%252F%252Fwww.crossmsistore.com%252Fmedia%252Fcatalog%252Fproduct%252Fcache%252Ff1%252Fimage%252F9df78eab33525d08d6e5fb8d27136e95%252Ff%252Ffscn1262.jpg%3Bhttp%253A%252F%252Fwww.crossmsistore.com%252Fidx%252Findex.php%252Folympus-ltf-laparoscope-semi-rigid.html%3B4000%3B3000

MacMillan Cancer Support
http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Endocrine/Adrenalglands.aspx

Major Endocrine Organs
https://www.google.co.za/search?q=endocrine+system&source=lms&tbm=isch&sa=X&ei=q9c2UtvmJtSrhex21CQCw&sqi=2&ved=0CAcQ_AUoAQ&biw=1366&bih=614&dpr=1#facrc=_&imgdii=_&imgarc=5C7Bq5ssKeYhrM%3B%3BF7Zp8xaozEytXM%3Bhttp%253A%252F%252Fbuzzle.com%252Fimage%252Fdiagram%252Fhuman-body%252Fendocrine-glands.jpg%3Bhttp%253A%252F%252Fbuzzle.com%252Farticles%252Fendocrine-system-facts.html%3B5%3B50%3B550


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National Cancer Institute

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]
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Wikipedia
http://en.wikipedia.org/wiki/Endocrine_system