Cancer Association of South Africa (CANSA)

Fact Sheet on
Germ Cell Tumour of the Ovary

Introduction
Germ cell tumours begin in the reproductive cells (egg or sperm) of the body. Ovarian germ cell tumours usually occur in teenage girls or young women and most often affect just one ovary. The ovaries are a pair of organs in the female reproductive system. They are situated in the pelvis, on each side of the uterus (the hollow, pear-shaped organ where a foetus grows). Each ovary is about the size and shape of an almond. The ovaries make ova (eggs) and female hormones. Ovarian germ cell tumour is a general name that is used to describe several different types of cancer. The most common ovarian germ cell tumour is called dysgerminoma.

[Picture Credit: Ovarian Cancer]

“Ovarian germ cell tumors are a histologically diverse group of neoplasms with a common origin in the primitive germ cell. The vast majority are represented by mature cystic teratoma. In the minority are malignant germ cell tumors including immature teratoma, dysgerminoma, yolk sac tumor, embryonal cell carcinoma, and choriocarcinoma. This article reviews the histologic and immunohistochemical features of the most common ovarian germ cell tumors. The differential diagnoses for each are discussed.”
**Germ Cell Tumour of the Ovary**

Ovarian malignant germ cell tumours (OMGCTs) are heterogeneous tumours that are derived from the primitive germ cells of the embryonic gonad. OMGCTs are rare, accounting for about 2.6% of all ovarian malignancies, and typically manifest in adolescence, usually with abdominal pain, a palpable mass, and elevated serum tumour marker levels, which may serve as an adjunct in the initial diagnosis, monitoring during therapy, and posttreatment surveillance. Dysgerminoma, the most common malignant germ cell tumour, usually manifests as a solid mass. Immature teratomas manifest as a solid mass with scattered foci of fat and calcifications.

Ovarian Germ Cell Tumours (OGCT) are Subdivided into the following Clinicopathological Entities:

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Frequency of OGCT</th>
<th>Benign / Malignant</th>
<th>Uni- or Bilateral</th>
<th>Tumour Markers Expressed</th>
<th>Metastasis Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysgerminoma</td>
<td>35 – 50%</td>
<td>Malignant</td>
<td>10-15% are bilateral</td>
<td>Serum lactic dehydrogenase</td>
<td>Via Lymphatic System</td>
</tr>
<tr>
<td>Endodermal sinus Tumour (EST)</td>
<td>20%</td>
<td>Malignant</td>
<td>Usually Unilateral</td>
<td>AFP and hCG</td>
<td>Intraperitoneally</td>
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<tr>
<td>Embryonal Carcinoma</td>
<td>Rare</td>
<td>Malignant</td>
<td>Usually Unilaterally</td>
<td>AFP and hCG</td>
<td>Intraperitoneally</td>
</tr>
<tr>
<td>Polyembryoma</td>
<td>Rare</td>
<td>Malignant</td>
<td>Usually Unilaterally</td>
<td>AFP and hCG</td>
<td></td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>Very Rare</td>
<td>Malignant</td>
<td>Usually Unilaterally</td>
<td>hCG</td>
<td></td>
</tr>
<tr>
<td>Teratoma</td>
<td>Immature Account for 20% of Of malignant GCT</td>
<td>Benign or Malignant</td>
<td>12-15% are bilateral</td>
<td>Immature teratomas sometimes secrete AFP, serum LDH and CA-125</td>
<td></td>
</tr>
<tr>
<td>Mixed GCT</td>
<td>10-15%</td>
<td>Dependent upon the cell types present</td>
<td></td>
<td>Dependent upon the cell types present</td>
<td></td>
</tr>
</tbody>
</table>

**Incidence of Germ Cell Tumour of the Ovary in South Africa**

The South African National Cancer Registry (2014) does not provide any information regarding the incidence of Germ Cell Tumour of the Ovary.

**Risk Factors for Germ Cell Tumour of the Ovary**

The cause of ovarian teratomas is unknown.

**Signs and Symptoms of Germ Cell Tumour of the Ovary**

Germ cell tumours of the ovary are rare. They usually affect younger women and most can be cured. Many germ cell tumours are not cancer (benign), but some are cancer (malignant).
The symptoms include:
• pain or a feeling of pressure in the pelvis or tummy
• a feeling of fullness or gradual swelling of the tummy
• irregular periods or signs of pregnancy
• high temperatures (fevers), chills, feeling or being sick and pain in the abdomen.

Diagnosis of Germ Cell Tumour of the Ovary
Diagnosis relies on clinical findings, serum tumour markers and imaging.

Imaging includes pelvic ultrasonography and computed tomography of abdomen and pelvis (if extra ovarian metastasis is suspected) and chest X-ray (to detect metastasis to lung and mediastinum).

Dosage of human chorionic gonadotropin (hCG), lactate dehydrogenase (LDH) and alpha fetoprotein (alpha-FP) also contribute to the diagnosis, the prognosis and follow-up of the disease. 12 p isochromosome (i(12p)) and chromosome 12 over-representation are observed, in non teratomatous ovarian germ cell tumours while pure teratomas lack i(12p).

Diagnosis is only confirmed histologically after laparotomy or laparoscopy.

Treatment of Germ Cell Tumour of the Ovary
Most types and stages of germ cell cancers of the ovary are treated the same way, with surgery and chemotherapy.

Surgery: In general, all women with malignant germ cell tumours will have the same staging surgery that is done for epithelial ovarian cancer. For women who still want to be able to have children, the cancerous ovary and the fallopian tube on the same side are removed, but the uterus, the ovary, and the fallopian tube on the opposite side are left behind. This isn’t an option when the cancer is in both ovaries. If preserving fertility is not a concern, complete staging including removing both ovaries, both fallopian tubes, and the uterus is generally recommended.

Sometimes, the doctor might consider removing only a part of one ovary to allow a woman to keep her ovarian function. Even when both ovaries need to be removed, a woman may wish to keep her uterus to allow future pregnancy through the use of in-vitro fertilization.

If cancer has spread beyond the ovaries, debulking surgery may be done as a part of the initial surgery. This removes as much cancer as possible without damaging or removing essential organs.

Chemotherapy: Most women with germ cell cancer will need to be treated with combination chemotherapy for at least 3 cycles. The combination used most often is PEB (or BEP), and may include the chemotherapy drugs cisplatin, etoposide, and bleomycin. Dysgerminomas are usually very sensitive to chemotherapy, and can sometimes be treated with the less toxic combination of carboplatin and etoposide. Other drug combinations may be used to treat cancer that has recurred (come back) or has not responded to treatment. Germ cell cancers can raise blood levels of the tumour markers human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), and/or lactate dehydrogenase (LDH). If the blood levels of these are high before treatment
starts, they are rechecked during chemotherapy (usually before each cycle). If the chemotherapy is working, the levels will go down. If the levels stay up, it might be a sign that a different treatment is needed.

INTRODUCTION: To evaluate the survival effect of cytoreductive surgery in advanced stage malignant ovarian germ cell tumors (MOGCT).
MATERIAL AND METHODS: Clinicopathological data of patients with MOGCT that were treated between 1991 and 2014. Maximal debulking was defined as no gross residual tumor after primary or recurrence surgery; optimal and suboptimal debulking were used for patients with residual tumors of ≤1cm and >1cm, respectively.
RESULTS: In total, 31 patients with advanced stage MOGCT were analyzed. The median age at diagnosis was 21 (14-57) years. The median follow-up duration was 64.1 months. Of these 31 patients; 7 patients underwent sub-optimal debulking, 5 patients had optimal surgery and 18 had maximal debulking. Five-year DFS according to surgical resection rates were 29% in suboptimal debulking group, 75% in optimal debulking group and 93% in maximal cytoreduction group (p<0.001). Three of seven patients who underwent sub-optimal debulking were died of disease, however no deaths were seen in patients with optimal and maximal debulking. Five-year OS was 32% in suboptimal debulking group, and 100% in optimal and maximal debulking groups (p=0.001).
DISCUSSION: The benefit of cytoreductive surgery is less well-established in MOGCT of ovary compared to ovarian tumors of epithelial origin due to rareness of this histological subtype. Patients with MOGCT are usually younger and preservation of fertility is an important issue which may lead to suboptimal procedures, sometimes in exchange for diminished survival. Our data demonstrated that maximal cytoreduction should be aimed in patients with advanced stage MOGCT, as it is significantly associated with improved overall survival.

BACKGROUND/AIM: The aim of the study was to assess the clinical outcome of patients with malignant transformation of an ovarian mature teratoma.
PATIENTS AND METHODS: This study was conducted on 23 patients who underwent primary surgery at three Italian Gynecological Centers. Histologically, nine (39.1%) patients had squamous cell carcinoma, five (21.7%) had a thyroid carcinoma, six (26.1%) had a carcinoid, one (4.3%) patient had papillary renal carcinoma, one (4.3%) had medulloblastoma and one (4.3%) had intestinal-type mucinous adenocarcinoma.
RESULTS: All six patients with stage I squamous cell carcinoma had no evidence of disease (NED) after a median time of 141 months. Of the three patients with stage IIb-IIIC squamous cell carcinoma, two had NED after 119 and 154 months, and one died of the disease 9 months after diagnosis. All five women with stage I thyroid carcinoma had NED after a median of 60 months. Of the six patients with stage I carcinoid, five had NED after a median of 168 months, whereas one died due to carcinoid heart disease. The three patients with stage I renal carcinoma, medulloblastoma and mucinous adenocarcinoma had NED after 24, 141 and 149 months, respectively.
CONCLUSION: The clinical outcome of early-stage malignancies associated with mature ovarian teratomas is excellent following treatment.

BACKGROUND: Lymphadenectomy has been widely used in the treatment of malignant germ cell tumor of the ovary (OGCT), which is a kind of ovarian cancers occurred mostly in young women and adolescent girls. But the clinical decision mainly depends on the doctor’s experience without a well-defined guideline. This population-based study aimed to evaluate the prognostic impact of lymphadenectomy in different stages of malignant germ cell tumors of the ovary.
METHODS: Patients with known status of lymphadenectomy in different stages of OGCT were explored from the Surveillance, Epidemiology, and End Results (SEER) program database from 1973 to 2013. We used

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propensity score matching algorithm to reduce the selection bias between the two study groups. Survival curves, univariate and multivariate Cox proportional hazards model were applied to evaluate the prognostic impact of lymphadenectomy in different stages of OGCT.

RESULTS: We included 1,996 OGCT patients in the study, and 818 (41%) of them had lymph node resection. Compared to the LND- group, patients with lymph node resection tended to be at stage II and III, had larger tumor sizes and diagnosed as dysgerminoma. The influence of diagnosis ages, marital status and tumor grades were significantly decreased by applying the propensity score matching. Lymphadenectomy-positive (LND+) group demonstrated significantly worse survival than the lymphadenectomy-negative (LND-) group in later stages (stage III, overall, \(P=0.027\), cancerspecific, \(P=0.006\); stage IV, overall, \(P=0.034\), cancer-specific, \(P=0.037\)). While, both the overall and cancer-specific survival showed no significant differences between LND+ and LND- in stage I (overall, \(P=0.411\), cancer-specific, \(P=0.876\)) and stage II (overall, \(P=12\), cancer-specific, \(P=0.061\)). Univariate (overall, \(HR=1.497, CI=1.010-2.217, P=0.044\); cancer-specific, \(HR=1.524, CI=1.067-2.404, P=0.050\)) and multivariate (overall, \(HR=1.580, CI=1.046-2.387, P=0.030\); cancer-specific, \(HR=1.661, CI=1.027-2.686, P=0.039\)) Cox proportional model both verified the association between the lymph node resection and better survival in the whole cohort.

CONCLUSION: Lymphadenectomy significantly increased the survival probability of OGCT patients in stage III and IV, but had no significant influence on early-stage patients (stage I and II), indicating lymphadenectomy should be performed in a stage-dependent manner in clinical utility.

### 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](https://www.sanctr.gov.za/) 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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Ovarian Cancer

Ovarian Germ Cell Tumour
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