Cancer Association of South Africa (CANSA)

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Fact Sheet
on
Primary Peritoneal Cancer

Introduction

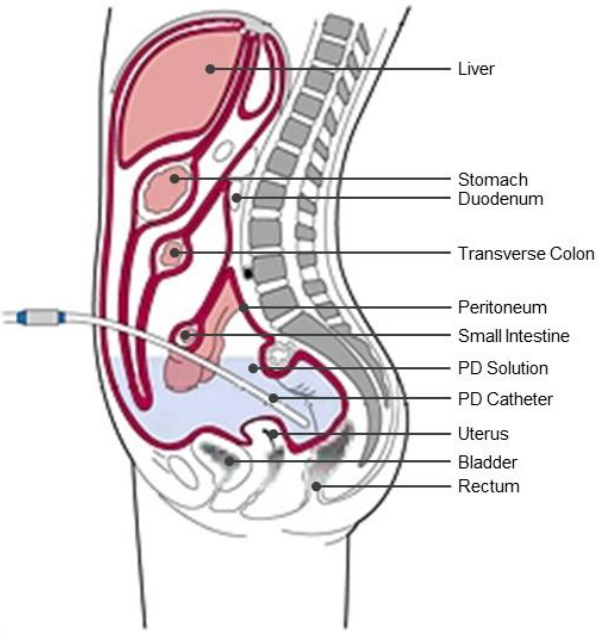
The peritoneum consists of the parietal peritoneum – a heterogeneous, serous, semi-permeable membrane that lines the abdominal wall – and the visceral peritoneum, which covers the abdominal organs (Figure 1). Its surface area is approximately 1-2 m^2.

In males, the peritoneum is a closed-sac system, whereas in females it is an open-sac system with the fallopian tubes and ovaries connecting to the peritoneal cavity.

[Picture Credit: Peritoneum]

The peritoneal cavity, located between the parietal and visceral peritoneum, contains approximately 100 mL of serous fluid and becomes the dialysate compartment during peritoneal dialysis (PD) from which exchange of solutes with the blood can occur.

Figure 1. Anatomy of the Peritoneum



Primary Peritoneal Cancer (PPC)

Primary peritoneal cancer (PPC) is a relatively rare cancer that develops most commonly in women. PPC is a close relative of epithelial ovarian cancer, which is the most common type of malignancy that affects the ovaries. The cause of primary peritoneal cancer is unknown.
It is important for women to know that it is possible to have primary peritoneal cancer even if their ovaries have been removed.

Primary peritoneal cancer (PPC) is a rare cancer of the peritoneum. It is very similar to the most common type of ovarian cancer called epithelial cancer. This is because the lining of the abdomen and the surface of the ovary come from the same tissue when humans develop from embryos in the

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womb. Doctors now think that most high grade serous cancers actually start in the far end of the fallopian tube rather than the surface of the ovary or peritoneum.

PPC is a cancer that mainly affects women. There are no exact numbers of how many people get it. Research suggests that between 7 and 15 out of 100 women (7 to 15%) who have advanced ovarian cancer will actually have PPC. It is very rare in men. Most people are over the age of 60 when they are diagnosed.

Anwar, A. & Kasi, A. 2020.
"The invasion of the serous membrane lining the abdominal cavity, viscera, and coelom in amniotes by malignant cells is called peritoneal surface malignancy or peritoneal cancer (PC). It is divided into primary and secondary types. The de novo origin of cancer in the mesothelium of the abdomen causes primary mesothelioma. In contrast, the dissemination of tumor cells in the peritoneal cavity from other sites results in secondary peritoneal cancer. Primary cancer has been classified based on its histology by investigators. Extraovarian primary peritoneal carcinoma (EOPPC), serous surface papillary carcinoma, papillary serous carcinoma of the peritoneum, extra ovarian Mullerian adenocarcinoma, and normal-sized ovarian carcinoma syndrome all are different terms used for the first type.
Other types include malignant mesothelioma (MPM), multicystic mesothelioma, leiomyosarcomas, leiomyomatosis peritonealis disseminata, and desmoplastic small round cells tumor (DSRCT). Swerdlow first reported EOPPC as 'Mesothelioma of pelvic peritoneum' in a case report published in 1959. It behaves similarly to serous ovarian cancer with little or no involvement of ovaries. All the types have variable histological features but are alike in their presentation, diagnostic evaluation, and treatment methods. Secondary or metastatic peritoneal carcinomatosis arises commonly from primitive malignancies involving gastrointestinal and gynecological structures. The metastasis occurs via transcoelomic, vascular, or lymphatic routes. It was first described in 1931 as a local spread from ovarian cancer.
Primary cancer is classed as stage III or IV and metastasis as stage IV. The vague clinical presentation is responsible for late diagnosis and an overall decrease in survival. The surgical resection and intraperitoneal chemotherapy form hallmarks for disease eradication. However, a better understanding of peritoneum physiology and tumor seeding pathways combined with advancement in technologies has led to the development of effective treatment therapies. In the absence of extensive systemic disease, locoregional control of the disease can provide a promising role in the management of this late-stage cancer."

Incidence of Primary Peritoneal Cancer (PPC) in South Africa
The South African National Cancer Registry (2017) does not provide any information regarding the incidence of Primary Peritoneal Cancer.

Link between Ovarian Cancer and Primary Peritoneal Cancer
Peritoneal cancer acts and looks like ovarian cancer. This is mainly because the surface of the ovaries is made of epithelial cells, as is the peritoneum. Therefore, peritoneal cancer and a type of ovarian cancer cause similar symptoms. Doctors also treat them in much the same way.

Women at risk for ovarian cancer are also at increased risk for peritoneal cancer. This is even more likely if one has the BRCA1 and BRCA2 genetic mutations. Older age is another risk factor for peritoneal cancer.

Signs and Symptoms of Primary Peritoneal Cancer (PPC)
Unfortunately, because of the vague nature of its symptoms, PPC is usually diagnosed in advanced stages of disease, when achieving a cure is difficult.

The symptoms of PPC are more commonly gastrointestinal rather than gynaecologic in nature, and include abdominal bloating, changes in bowel habits and an early feeling of fullness after eating.

When bloating is severe, nausea and vomiting may result. Occasionally, patients with PPC present with a blockage of the intestines related to tumour on or next to the bowels. Normal vaginal bleeding is infrequently seen in patients with PPC.

Diagnosis of Primary Peritoneal Cancer (PPC)
In addition to asking about symptoms, one's doctor may review one's medical history and conduct a physical examination, which may involve examining for abnormalities in these areas:

- Uterus
- Vagina
- Ovaries
- Fallopian tubes
- Stomach
- Bladder
- Colon and rectum

Tests may include:
Ultrasound - high-frequency sound waves produce a picture called a sonogram

CA-125 blood test - this test measures levels of a chemical in the blood called CA-125. If levels are high, peritoneal or ovarian cancer may be present. But CA-125 can be high for other reasons. So, this test cannot confirm a diagnosis of these cancers

CT scan - a computer linked to an X-ray machine produces detailed pictures of the inside the body

Lower GI Series or Barium Enema - with this test, the patient first receives an enema containing a white, chalky solution called barium. This outlines the colon and rectum on an X-ray. It makes it possible to spot some tumours as well as other problems

Upper GI Series - with this test, barium is swallowed and the oesophagus, stomach, and duodenum (the first part of the small intestine) are outlined on an X-ray

Biopsy - a surgeon removes tissue by opening the abdomen during a laparotomy or by inserting tools through small holes in the abdomen (laparoscopy). A pathologist studies the tissue sample under a microscope to confirm a diagnosis of cancer

Paracentesis - in cases where surgery is not possible or ascites (presence of fluid in the peritoneal cavity) could be due to other causes, the doctor may instead remove fluid for examination under a microscope. This is called paracentesis

Ovarian and peritoneal cancers look the same under a microscope. So, the pattern and location of any tumours helps indicate which type of cancer is present.

Uehara, T., Yoshida, H., Fukuhara, M., Yoshida, M., Motoi, N., Sugawara, S., Sone, M., Arai, Y., Tamura, K., Uno, M., Ishikawa, M. & Kato, T. 2020.
Objective: To compare the efficacy of ascitic fluid cell block (ACB) with that of core needle biopsy (CNB) or the CA125/CEA ratio in diagnosing primary tubo-ovarian cancer in female patients with peritoneal carcinomatosis (PC) with ascites.
Methods: This retrospective study examined female patients with PC with ascites who had available results for ACB, peritoneal tumor CNB, and the CA125/CEA ratio. Several measures of the accuracy of ACB and the CA125/CEA ratio were calculated and compared, with CNB as the reference standard.
Results: Of 81 patients with available results, 57 were clinically diagnosed with primary tubo-ovarian cancer. Overall, 52, 47, and 64 patients were diagnosed via CNB, ACB, and CA125/CEA ratio > 25, respectively. CNB and ACB identified the cancer origin in 91.4% and 82.7% cases, respectively. The concordance ratio of the immunohistochemical findings between ACB and CNB was 93.6%. Two patients with inconclusive CNB results were diagnosed with primary tubo-ovarian cancer via ACB. The sensitivity, specificity, positive predictive value, negative predictive value, and positive likelihood ratio were 86.5%, 93.1%, 95.7%, 79.4%, and 12.5, respectively, for ACB and 94.2%, 48.3%, 76.6%, 82.4%, and 1.82, respectively, for CA125/CEA ratio > 25.
Conclusions: ACB is not inferior to CNB in diagnosing primary tubo-ovarian cancer; the two methods complement each other. ACB can substitute CNB in diagnosing primary tubo-ovarian cancer in selected PC patients. ACB is superior to a CA125/CEA ratio of >25 in diagnosing primary tubo-ovarian cancer. ACB is effective, reliable, and convenient for diagnosing primary tubo-ovarian cancer in PC patients with ascites.

Staging of Primary Peritoneal Cancer (PPC)
Staging is important as it assists in knowing how far the disease has spread. It also assists the oncologist to decide on relevant treatment.

Treatment of Primary Peritoneal Cancer (PPC)
The treatment a patient may receive depends on a number of things including:

- The size of the cancer
- Where the cancer is in the abdomen
- The patient's general health

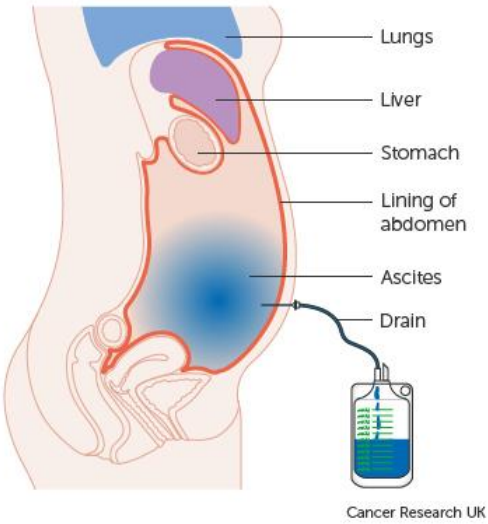
The treatment for PPC is the same as for advanced epithelial ovarian cancer. Because PPC is usually at an advanced stage when it is diagnosed it can be difficult to treat. The aim of treatment for advanced cancer is usually to shrink the cancer and control it for as long as possible.
The main treatments may include:

Surgery - the aim of surgery is to remove as much of the cancer from the abdomen as possible before chemotherapy. This is called debulking surgery. Chemotherapy tends to work better when there are only small tumours inside the abdomen. The surgery usually includes removing your womb, ovaries, fallopian tubes, and the layer of fatty tissue called the omentum. The surgeon may also remove any other cancer that he/she can see at the time of surgery.

Chemotherapy - chemotherapy uses anti-cancer (cytotoxic) drugs to destroy cancer cells. These drugs work by disrupting the growth of cancer cells. One may have chemotherapy:

- Before surgery to reduce the size of the cancer
- After surgery when you have recovered
- On its own if you are unable to have surgery

Radiotherapy - radiotherapy uses high energy waves to kill cancer cells. Radiotherapy is not often used for PPCs. But doctors may use it to shrink tumours and reduce symptoms.



Cancer Research UK

Mikkelsen, M.S., Christiansen, T., Petersen, L.K., Blaakaer, J. & Iversen, L.H. 2019.
Background and objectives: Hypertherm intraperitoneal chemotherapy (HIPEC) is increasingly used in the treatment of ovarian, tubal, and primary peritoneal cancer (OC). The aim was to evaluate short-term morbidity of cytoreductive surgery (CRS) and carboplatin HIPEC.
Methods: Prospective feasibility study performed from January 2016 to December 2017. Twenty-five patients with primary OC (FIGO III-IV) received upfront or interval CRS combined with carboplatin HIPEC at dose 800 mg/m^2. Primary outcome measurements: grade 3 to 5 adverse events within 30 days according to Common Terminology Criteria for Adverse Events. Secondary outcome measurements: reoperation rate, length of hospital stay, readmission rate, and time from surgery to systemic chemotherapy administration.
Results: No deaths (grade 5) or grade 4 adverse events were observed. Eleven patients (44.0%) experienced at least one grade 3 adverse event, the most common being an infection (28.0%) and neutropenia (12.0%). The reoperation rate was 8.0%. The median hospital stay was 14 days (range 9-25 days), and five patients (25.0%) were readmitted within 30 days after surgery. Median time from surgery to the administration of the first dose of systemic chemotherapy was 41 days (range 24-81 days).
Conclusion: Our small-scale prospective study supports that CRS and carboplatin HIPEC used for primary advanced-stage OC is feasible with acceptable morbidity.

Other treatments - if the patient is unable to have chemotherapy, he/she can still have treatment to control any symptoms, such as pain, weight loss, and fluid in the abdominal cavity. Fluid can build up between the two layers of the peritoneum. This fluid build-up is called ascites. It can be very uncomfortable and heavy. The doctor can drain the fluid off using a procedure called abdominal paracentesis or an ascitic tap. The diagram demonstrates this.

Lavoue, V., Huchon, C., Adkladios, C., Alfonsi, P., Bakrin, N., Ballester, M., Bendifallah, S., Bolze, P.A., Bonnet, F., Bourgin, C., Chabbert-Buffet, N., Collinet, P., Courbiere, B., Rouge, T De la M., Devouassoux_Shisheboran, M., Falandry, C., Ferron, G., Fournier, L., Gladieff, L., Golfier, F., Gouy, S., Guyon, F., Lambaudie, E., Leary, A., Lecuru, F. Lefrere-Belda, MA., Leblanc, E., Lemoine, A., Narducci, F., Ouldamer, L., Pautier, P., Planchamp, F., Pouget, N., Ray-Coquard, I., Rousset-Jablonski, C., Senechal=Davin, C., Touboul, C., Thomassin-Naggara, I., Uzan, C., You, V. & Daraï, E. 2019.
"An MRI is recommended for an ovarian mass that is indeterminate on ultrasound. The ROMA score (combining CA125 and HE4) can also be calculated (Grade A). In presumed early-stage ovarian or tubal cancers, the following procedures should be performed: an omentectomy (at a minimum, infracolic), an appendectomy, multiple peritoneal biopsies, peritoneal cytology (grade C), and pelvic and para-aortic lymphadenectomies (Grade B) for all histologic types, except the expansile mucinous subtypes, for which lymphadenectomies can be omitted (grade C). Minimally invasive surgery is recommended for early-stage ovarian cancer, when there is no risk of tumor rupture (grade B). Adjuvant chemotherapy by carboplatin and paclitaxel is recommended for all high-grade ovarian and tubal cancers (FIGO stages I-IIA) (grade A). For FIGO stage III or IV ovarian, tubal, and primary peritoneal cancers, a contrast-enhanced computed tomography (CT) scan of the thorax/abdomen/pelvis is recommended (Grade B), as well as laparoscopic exploration to take multiple biopsies (grade A) and a carcinomatosis score (Fagotti score at a minimum) (grade C) to assess the possibility of complete surgery (i.e., leaving no macroscopic tumor residue). Complete surgery by a midline laparotomy is recommended for advanced ovarian, tubal, or primary peritoneal cancers (grade B). For advanced cancers, para-aortic and pelvic lymphadenectomies are recommended when metastatic adenopathy is clinically or radiologically suspected (grade B). When adenopathy is not suspected and when complete peritoneal surgery is performed as the initial surgery for advanced cancer, the lymphadenectomies can be omitted because they do not modify either the medical treatment or overall survival (grade B). Primary surgery (before other treatment) is recommended whenever it appears possible to leave no tumor residue (grade B). After primary surgery is complete, 6 cycles of intravenous chemotherapy (grade A) are recommended, or a discussion with the patient about intraperitoneal chemotherapy, according to her risk-benefit ratio. After complete interval surgery for FIGO stage III disease, hyperthermic intraperitoneal chemotherapy (HIPEC) can be proposed, in accordance with the modalities of the OV-HIPEC trial (grade B). In cases of postoperative tumor residue or in FIGO stage IV tumors, chemotherapy associated with bevacizumab is recommended (grade A)."

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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