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Ovarian Cancer: A Short, Brief Review

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ABSTRACT
Studies have shown that "OC is the leading cause of death among women diagnosed with gynecological malignancies". Studies have concluded that this ranks as the sixth most common cause of death among women. Studies have concluded that since the majority of cases of the disease are diagnosed at a more advanced stage, the outlook is not good for those who have it. Several studies have shown that a full gynecological exam, a transvaginal ultrasound, and lab tests like the CA-125 test are the most important parts of early detection strategies. Henceforth, in our study, we reviewed OC on the basis of etiology, statistics, pathology, staging, complications, histologically and differential diagnosis.
Key words: *OC, etiology, statistics, pathology, staging, complications, histologically, differential diagnosis.*

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INTRODUCTION

Studies have concluded that "ovarian cancer (OC) accounts for an estimated 239,000 new cases and 152,000 deaths worldwide annually".[1] Additionally, studies have concluded that "Eastern and Central Europe have seen the greatest rates (11.4 and 6.0 per 100,000, respectively)". Various studies have also shown that the "enormous population of China translates to an estimated 52,100 new cases and 22,500 associated deaths in 2015, despite the country's comparatively low incidence rate (4.1 per 100,000)".[2] Additionally, studies have concluded that it is "estimated that in the United States, in the same year, there would be 21,290 new cases and 14,180 deaths".[3] Studies have concluded that "anti-angiogenic bevacizumab and poly(ADP-ribose) polymerase (PARP) inhibitors have gained pace in the management of this gynecological malignancy in the last decade. According to studies, surgery and platinum-based chemotherapy are the usual treatments for this gynecological cancer". [4] Furthermore, studies have concluded that there is a 1 in 75 probability that a woman will acquire OC in her lifetime, and there is a 1 in 1004 chance that she will pass away from the disease. In addition to this, studies have also proved that the "disease typically shows its symptoms at a late stage, when the relative 5-year survival rate is only 29%. Only fifteen percent of cases are detected with a circumscribed tumor (stage 1), even though the five-year survival rate is ninety-two percent".[5] Surprisingly, studies have also concluded that the "overall 5-year relative survival rate normally fluctuates between 30% and 40% throughout the world, and it has seen only very minor improvements (2%–4%) since 1995".[6] In addition to this, studies have also concluded that since 1995, the survival rate has seen only very modest increases (2%–4%).[7] Thus, in our review we have discussed OC.

ETIOLOGY

Studies have concluded that "OC is associated with a wide range of risk factors".[8] Studies have also found that postmenopausal women are the ones who are most likely to contract this disease, and that increased disease incidence, advanced disease stage, and poorer reported disease survival rates are all associated with increased disease incidence.[8] According to a few case-control studies, having more children lowers one's risk of developing ovarian cancer, and having a greater age at first delivery is associated with an even lower risk.[8] Various other studies have concluded that a "positive family history of breast or OC is the single most important risk factor for OC".[9] Other than this, studies have concluded that a personal history of breast cancer also increases the likelihood of developing OC. [9] Numerous studies have shown that there is an "increased risk associated with smoking, particularly the risk of developing mucinous epithelial malignancies". [8]

STATISTICS

Studies have concluded that a "total of 21,750 new cases of OC will be diagnosed in the year 2020, accounting for 1.2% of all cancer cases worldwide".[10] Studies have also concluded that the number of deaths attributed to it is estimated to be 13,940.[10] Additionally, it was estimated, according to studies, that the relative survival rate during the next 5 years will be 48.6%.[10] In addition to this, studies also concluded that, if found at an "early stage of local spread, ovarian cancer has a 92.6% chance of survival for five years".[10] In addition to this, studies also revealed that, however, about "15.7% of cases of OC are diagnosed at the local stage, while around 58% are diagnosed at the stage when it has spread to other parts of the body (metastasized stage)".[10] In the years 2012–2016, the United States had an incidence rate that was, on average, 11.1 cases per 100,000 people when adjusted for age to the standard population in the year 2000.[11] Since ancient times, research has shown that the rate is "highest among non-Hispanic whites (11.6 per 100,000), then American Indians and Alaska Natives (10.3 per 100,000), Hispanics (10.1 per 100,000), non-Hispanic blacks, and Asian and Pacific Islanders".[11] In addition to this, studies also concluded that the "epithelial form of ovarian cancer accounts for ninety percent of all cases, with the serous subtype being the most common".[11] According to statistical models of investigation, the age-adjusted rates of newly diagnosed cases of ovarian cancer are on the decline. [11]

PATHOLOGY

Studies have concluded that most "OT, whether benign or malignant, develop from three main types of cells: epithelial cells, stromal cells, and germ cells. Studies show that most cancerous OT in developed countries come from epithelial cells". Studies have also concluded that there are also a "few sex cord-stromal tumors and germ cell tumors". [12] Chen et al. provide a comprehensive description of the "pathology and classification of OT". [13] Studies have concluded that the majority of epidemiologic research, including the current review, "centers around epithelial OC". Additionally, studies have concluded that epithelial ovarian cancer is a complex disease with various histologic subtypes that arise from different cell types. In addition to this, studies have shown that these subtypes differ in their development, molecular changes, gene expression, and prognosis.[14,15,16,17] Various studies have shown that "cancerous OT, also referred to as carcinomas, consist of five primary histotypes: high-grade serous (HGSOC; 70%), endometrioid (ENOC; 10%), clear cell (CCOC; 10%), mucinous (MOC; 3%), and low-grade serous (LGSOC; <5%)". [14,15]. Other than this, various other studies have shown that among the different categories, particularly serous and mucinous, there are tumors called borderline or low malignant potential (LMP) tumors. Other than this, studies have also shown that these tumors exhibit microscopic features of malignancy but do not invade the surrounding stroma.[18]

DIFFERENTIAL DIAGNOSIS[10]

1. "Colon cancer
2. Embryologic remnants
3. Gastric adenocarcinoma
4. Metastatic gastrointestinal carcinoma
5. Ovarian torsion
6. Peritoneal cyst
7. Retroperitoneal mass
8. Uterine fibroids
9. Endometriosis
10. Papillary adenocarcinoma
11. Serous adenocarcinomas
12. Undifferentiated adenocarcinomas
13. Small-cell adenocarcinomas
14. Brenner tumors"

STAGING

"Studies have shown that ovarian cancer is staged using the 8th edition of the American Joint Committee on Cancer (AJCC) staging system, as well as the International Federation of Gynecology and Obstetrics (FIGO) staging system and the accompanying Tumor, Node, and Metastasis (TNM) classification".[10]

"Stage I - Tumor limited to ovaries (one or both) or fallopian tube [10]

IA -Tumor limited to one ovary (capsule intact) or fallopian tube, no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings

IB -Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings
IC - Tumor limited to one or both ovaries or fallopian tubes, with any of the following:
IC1 -Surgical spill
IC2 -Capsule rupture before surgery or tumor on the ovarian or fallopian tube surface.
IC3 -Malignant cells in ascites or peritoneal washings".

"Stage II cancer has begun to spread. This stage is divided into two substages, A and B [10]
IIA: cancer has spread from the ovary or ovaries to the fallopian tubes and/or the uterus, or it has spread from the fallopian tubes to the ovaries and/or uterus.
IIB: cancer has spread in the peritoneal cavity to your bladder, colon, or rectum".
"Stage III - Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with microscopically confirmed peritoneal metastasis outside the pelvis and/or metastasis to the retroperitoneal (pelvic and/or para-aortic) lymph nodes.[10]
IIIA1 - Positive retroperitoneal lymph nodes only (histologically confirmed).
IIIA1i - Metastasis up to and including 10 mm in greatest dimension.
IIIA1ii - Metastasis more than 10 mm in greatest dimension.
IIIA2 - Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes.
IIIB - Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension with or without metastasis to the retroperitoneal lymph nodes.
IIIC - Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension with or without metastasis to the retroperitoneal lymph nodes (includes an extension of tumor to the capsule of liver and spleen without parenchymal involvement of either organ)".

"Stage IV - Distant metastasis, including pleural effusion with positive cytology; liver or splenic parenchymal metastasis; metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity), and transmural involvement of intestine[10]
IVA - Pleural effusion with positive cytology
IVB - Liver or splenic parenchymal metastases; metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); transmural involvement of intestine".

COMPLICATIONS [10,19]
1. "Fatigue or weakness (75%)
2. Nausea or vomiting (71%)
3. Constipation (49%)
4. Pedal edema (44%)
5. Anemia (34%)
6. Ascites
7. Bowel Obstruction
8. Pleural Effusion
9. Bladder Obstruction"

HISTOLOGICALLY
Studies have found that there are four distinct histological subtypes of epithelial ovarian cancer, which are referred to as endometrioid, clear cell, serous, and mucinous tumors. Studies have also concluded that they are then further classified into subtypes based on the particular biological traits and treatment responses of each person. Brenner and seromucinous are two examples of subtypes that occur much less often. Studies have further concluded that the terms "Type I tumors" and "Type II tumors" are used to refer to the two distinct subtypes of ovarian cancer. In addition, studies have shown that continuous ovarian cycles, which cause inflammation and endometriosis, are thought to be the main cause of this type of illness. This is why type II tumors are more likely to kill the patient. Various other studies have also concluded that, low-grade serous, endometrioid, clear-cell, and mucinous carcinomas are all included in the classification of type I tumors.[19] On the other hand, studies have shown that seromucinous and Brenner-type tumors are less common types of type I tumors. The vast majority of type I tumors develop from atypical proliferative tumors, which are often referred to as borderline tumors. Most type II tumors, like high-grade serous carcinoma, carcinosarcoma, and undifferentiated carcinoma, are caused by serous tubal intraepithelial carcinoma. The incidence of type II tumors is much lower than that of type I tumors. The exception to this rule is clear cell tumors, which are often of high grade. Type I side tumors, on the

other hand, generally develop at an early stage and are of a low grade.[19] Their usual proliferative activity level is rather low. They are diagnosed at an early stage, which results in a positive prognosis. Type II tumors, on the other hand, are high-grade cancers that almost always manifest at more advanced stages. These tumors are almost always found to be malignant. They have high proliferative activity with rapid and aggressive development as well as a high degree of chromosomal instability in comparison to type I, with the presence of p53 mutations in the majority of the cases. Additionally, studies have shown that they have a high degree of chromosomal instability in comparison to type II. In addition to this, they have a very high level of chromosomal instability.[19]

Studies have found that the most common subtype of ovarian cancer is known as ovarian serous carcinoma. It may manifest as low-grade serous carcinoma, which accounts for 10% of all serous subtype tumors, or as high-grade serous carcinoma, which accounts for 90% of all serous subtype tumors. There are also studies that say the low-grade subtype (LGSC) has less severe molecular abnormalities, less frequent mitosis, and less nuclear atypia. Studies have further concluded that the high-grade subtype (HGSC) shows significant nuclear atypia and mitosis (>12 per 10 high-power fields), in addition to higher copies of molecular abnormalities, as shown by cytogenetic studies.[20] In addition to this, studies have also concluded that HGSCs are usually discovered at a younger age and have a poorer prognosis than LGSCs, which typically manifest at a later age and have a mortality rate of 70% during a ten-year period.[20] In further research, it was found that grade-low serous carcinoma has a high frequency of KRAS and BRAF mutations, but grade-high serous carcinoma has a high frequency of p53 and BRCA 1 and 2 gene mutations but no KRAS/BRAF mutations. This is because grade-high serous carcinoma lacks the KRAS/BRAF mutation.[20] Studies have found that endometriosis is believed to be the root cause of ovarian endometrioid carcinomas. The cut sections reveal cystic areas that exhibit soft masses and red fluid, with less common solid parts showing significant bleeding and necrosis. In terms of their morphology, studies have also concluded that the cystic regions have a distinctive appearance. It has been shown that a mutation in the beta-catenin gene is one of the most common molecular abnormalities; nevertheless, it has not been possible to identify any significant molecular markers that are associated with this subtype. In addition to this, studies have also concluded that endometrioid carcinomas that originate from the ovaries and the uterus may be distinguished from one another based on the results of molecular research, despite the fact that they seem to be very similar morphologically. It is more likely for endometrioid tumors that come from the uterus to have microsatellite instability and PTEN changes than for endometrioid tumors that come from the ovary. However, endometrioid tumors caused by tissue from the ovary are less likely to exhibit these changes.[21] Studies have further investigated that single ovarian carcinomas have been found to have a reduced frequency of beta-catenin mutations when compared to synchronous tumors. [22] In addition to this, studies have also concluded that women who have this particular histological subtype of ovarian cancer are more likely to have early detection of the disease, which results in a better prognosis.

Studies have found that mucinous carcinoma of the ovary, or MOC for short, is often heterogeneous. This indicates that a single specimen of the illness may have a range of components, including benign and malignant tumors. In these tumors, KRAS mutations are rather common. The intestinal subtype will demonstrate the presence of glands that exhibit architectural and cytology clinical indicators of adenocarcinoma; nevertheless, it may lack stromal invasion due to the fact that it is commonly associated with metastases from the gastrointestinal tract (GI).[20] It may be challenging to identify between initial ovarian mucinous carcinomas and metastatic mucinous appendix carcinomas because of the close association between the two types of cancer. As a direct consequence of this, many gynecologic oncologists carry out routine appendectomies on every single patient who has MOC as a result.[23] Evidence of micro intrusions is much less common in intestinal subtype B order line tumors. The prognosis is considered favorable compared to the more common subtype of mucinous carcinoma, despite the fact that this invasive type of carcinoma is uncommon. This is due to the fact that the majority of cases, around 80%, are discovered at stage I itself.[20] To this day, it is not known which molecular shifts are to blame for the transition of a benign mucinous tumor into a malignant one.

Studies have found that the incidence of ovarian clear cell carcinomas is much lower compared to that of other kinds of ovarian cancer and accounts for less than 5% of cases overall. Histopathologically speaking, they show cellular clearance, a growth pattern characterized by cysts, and the usual development pattern of hobnails. Some research has also shown that immunohistochemically, an overexpression of BAX is the most common finding in stage I and stage II tumors. On the other hand, the production of the anti-apoptotic protein BCL-2 is higher in metastasized lesions than in primary lesions. Studies have also shown that clear cell ovarian carcinoma tumors in their early stages tend to have a lower BCL-2/BAX ratio than metastasized lesions, which have a higher ratio. This is in contrast to the higher relative ratio found in metastatic lesions. [8] Additionally, studies have shown that they are often found in their early

stages. This means that they have a good prognosis, the same as endometrioid cancers, which are similar to endometrioid malignancies.[10] Studies have further also concluded that cytokeratin-7 (CK7) shows strong and diffuse staining in all serous ovarian tumors.[10] Studies have also found that it is positive in eighty percent to one hundred percent of mucinous ovarian tumors.[10] Studies have also concluded that other ovarian epithelial tumors are also positive for CK7.[10] Additionally studies concluded that the percentage of mucinous ovarian tumors that are positive varies. Comparatively, metastatic colorectal carcinoma shows a positivity of around 25%, but over 96% of ovarian adenocarcinomas were positive for CK7.[10]

CONCLUSION

Studies have shown that even with the most advanced current clinical trials and the development of new treatment lines over the last several decades, OC continues to be one of the most fatal malignancies in women. The lack of successful early detection strategies for OC is a key contributor to the poor clinical outcome. There is a need to discover additional factors that contribute to OC. With a view to improved preventive and early detection strategies, further study is required to better understand the varied genesis of this devastating disease.

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