



FIGO's staging classification for cancer of the ovary, fallopian tube, and peritoneum: abridged republication

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Over the past quarter of a century, several scientific developments have challenged traditional concepts in ovarian cancer. First, it was recognized that ovarian cancer is not a homogeneous disease, but rather a group of diseases—each with different morphology and biological behavior. Approximately 90% of ovarian cancers are carcinomas (malignant epithelial tumors) and, based on histopathology, immunohistochemistry, and molecular genetic analysis, at least five main types are currently distinguished: high-grade serous carcinoma (HGSC, 70%); endometrioid carcinoma (EC, 10%); clear-cell carcinoma (CCC, 10%); mucinous carcinoma (MC, 3%); and low-grade serous carcinoma (LGSC, <5%) [1,2]. These tumor types (which account for 98% of ovarian carcinomas) can be reproducibly diagnosed by light microscopy and are inherently different diseases, as indicated by differences in epidemiologic and genetic risk factors; precursor lesions; patterns of spread; and molecular events during oncogenesis, response to chemotherapy, and prognosis [2,3]. Much less common are malignant germ cell tumors and potentially malignant sex cord-stromal tumors. The biomarker expression profile within a given histotype is consistent across stages. Ovarian cancers differ primarily based on histologic type.

In the era of personalized cancer medicine, reproducible

histopathologic diagnosis of tumor cell type is a *sine qua non* for successful treatment. Different tumor histotypes respond differently to chemotherapy. The International Federation of Gynecology and Obstetrics (FIGO) Committee on Gynecologic Oncology unanimously agreed that histologic type should be designated at staging.

The finding of high-grade serous tubal intraepithelial carcinoma (STIC), in patients with *BRCA* mutation undergoing risk-reducing salpingo-oophorectomy (RRSO) [4] also influenced the new FIGO staging. Although STIC is capable of metastasizing and, therefore, cannot be considered a true carcinoma *in situ*, compelling evidence for a tubal origin of *BRCA*-positive HGSC has accumulated over the past decade [5,6]. The relative proportion of HGSCs of ovarian and tubal derivation is unknown, mainly because tumor growth in advanced-stage cancers conceals the primary site. Even in cases involving *BRCA* mutation, evidence of a tubal origin of HGSCs is incomplete and a multicentric origin of these tumors cannot be excluded.

The process of the proposed changes to the staging of ovarian, fallopian tube, and primary peritoneal cancer started three years ago under the leadership of the Chair of the FIGO Committee on Gynecologic Oncology, Professor Lynette Denny. The proposal was sent to all relevant gynecologic oncology organizations and societies worldwide. The new staging was reached by consensus of those participating in the FIGO meeting held in Rome, Italy, on October 7, 2012 and approved two weeks later.

The following is the consensus agreement that resulted from these efforts and represents new criteria for staging of these gynecologic cancer (Table 1).

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Table 1. 2014 FIGO ovarian, fallopian tube, and peritoneal cancer staging system and corresponding TNM

Stage I. Tumor confined to ovaries or fallopian tube(s)

T1-N0-M0

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

T1a-N0-M0

IB: tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings

T1b-N0-M0

IC: tumor limited to one or both ovaries or fallopian tubes, with any of the following:

IC1: surgical spill

T1c1-N0-M0

IC2: capsule ruptured before surgery or tumor on ovarian or fallopian tube surface

T1c2-N0-M0

IC3: malignant cells in the ascites or peritoneal washings

T1c3-N0-M0

Stage II. Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer

T2-N0-M0

IIA: extension and/or implants on uterus and/or fallopian tubes and/or ovaries

T2a-N0-M0

IIB: extension to other pelvic intraperitoneal tissues

T2b-N0-M0

Stage III. Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes

T1/T2-N1-M0

IIIA1: positive retroperitoneal lymph nodes only (cytologically or histologically proven):

IIIA1(i) Metastasis up to 10 mm in greatest dimension

IIIA1(ii) Metastasis more than 10 mm in greatest dimension

IIIA2: microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes

T3a2-N0/N1-M0

IIB: macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes

T3b-N0/N1-M0

IIIC: macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)

T3c-N0/N1-M0

Stage IV. Distant metastasis excluding peritoneal metastases

Stage IVA: pleural effusion with positive cytology

Stage IVB: parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

Any T, any N, M1

MAIN CHANGES

The primary site (i.e., ovary, fallopian tube, or peritoneum) should be designated where possible. In some cases, it might not be possible to delineate the primary site clearly; such cases should be listed as “undesignated”. The histologic type should be recorded.

Stage I ovarian or fallopian tube cancer is confined to the ovaries or the fallopian tubes and peritoneal fluid/washings.

Tumor rupture, surface involvement by tumor cells or presence of malignant cells in the ascites or peritoneal washings warrants a stage of IC. It is not possible to have stage I peritoneal cancer.

Stage II ovarian cancer comprises a small and heterogeneous group making up less than 10% of ovarian cancers. It is defined as extension or metastasis to extraovarian/ extratubal pelvic organs and may include curable tumors that have directly extended to adjacent organs but have

not yet metastasized, as well as tumors that have seeded the pelvic peritoneum by metastasis and, therefore, have a poor prognosis. The Committee felt that subdividing this small category further into IIB1 and IIB2 (i.e., microscopic and macroscopic pelvic peritoneal metastases) was not based on evidence/biology. All stage II disease is treated with adjuvant chemotherapy, so subclassification is not essential. Also, the old substage IIC (i.e., IIA or IIB but with tumor on surface, capsule ruptured, or ascites or positive peritoneal washing) was considered redundant and eliminated.

Most ovarian cancers are HGSCs that usually present in stage III, with the vast majority (84%) stage IIIC [7]. These tumors characteristically spread along peritoneal surfaces involving both pelvic and abdominal peritoneum. Less than 10% of ovarian carcinomas extend beyond the pelvis with exclusively retroperitoneal lymph node involvement. Evidence in the literature indicates that these cases have a better prognosis than that of tumors with abdominal peritoneal involvement [8-14]. The new staging includes a revision of stage III patients and assignment to stage IIIA1 based on spread to the retroperitoneal lymph nodes without intraperitoneal dissemination. Stage IIIA1 is further subdivided into IIIA1(i) (metastasis ≤ 10 mm in greatest dimension) and IIIA1(ii) (metastasis > 10 mm in greatest dimension), even if there are no retrospective data supporting quantification of the size of metastasis in IIIA1. Involvement of retroperitoneal lymph nodes must be proven cytologically or histologically.

Stage IV is defined as distant metastasis and includes patients with parenchymal liver/splenic metastases and extra-abdominal metastases; 12% to 21% of patients present with stage IV disease [7]. Extension of tumor from omentum to spleen or liver (stage IIIC) should be differentiated from isolated parenchymal metastases (stage IVB).

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