Recommendations for the reporting of

malignant ovarian surface epithelial/stromal tumours*

Maria Rosaria RASPOLLINI; Lynn HIRSCHOWITZ; Harry HOLLEMA; Sigurd LAX; Glenn

MCCLUGGAGE; Francisco NOGALES; Jaime PRAT; and Michael WELLS

* These guidelines have been presented during the 24th European Congress of Pathology

held in Prague (Chech Republich) on September 2012 and endorsed by the

Gynaecopathology Working Group of European Society of Pathology

Introduction

Despite the relatively low incidence, malignant surface epithelial ovarian tumours
(carcinomas) present a high case-fatality ratio. Among the gynaecological malignancies,
ovarian cancer has the highest mortality rate in Europe. Ovarian cancer accounted for 4-
5% of all cancers in women in 2008 (Figures 1 and 2). More than two-thirds of women
have advanced disease at the time of diagnosis.[1-3]

The reporting of ovarian neoplasms is facilitated by the use of a synoptic reporting
protocol or checklist and should be carried out meticulously to avoid diagnostic errors,
provide clinicians with all of the important information necessary for staging and thereby
ensure appropriate and tailored treatment.

It is also important to note that although the biologic aggressiveness differs for the
different types of ovarian tumours,[4-6] staging and grading are the most important
determinants of the prognosis of these neoplasms.[7] In addition, the importance of the

tumour typing will likely become more important in the future with the introduction of targetted therapies and specific treatments for different tumour types.

Classification of ovarian tumours is complicated by the wide range of morphological types; moreover several tumours have overlapping histological features. Most ovarian tumours reflect one of the following types of differentiation according to the three major histogenetic compartments of the ovaries: the surface epithelium and the underlying stroma, the specialized ovarian stroma, and the germ cells. In addition, there is a range of secondary or metastatic tumours that not uncommonly involves the ovary; and finally, there is also a rare group of miscellaneous tumours and tumours of uncertain origin that arise in the ovary. The scope of these guidelines is to provide a straightforward but comprehensive method for the reporting of malignant ovarian surface epithelial/stromal tumours. Essential training in ovarian tumour pathology is desirable because of the complexity of these tumours and pathologists should not hesitate to seek a second opinion when necessary. We hope, nonetheless, that the use of these guidelines will help pathologists to provide consistent, high quality reports for this challenging group of neoplasms.

Features to be included in the final pathology report

General information

- Patient identification: last name and forename, age/date of birth, hospital identification number
- Details of surgical specimen: biopsy, partial oophorectomy, oophorectomy, salpingo-oophorectomy (including laterality), hysterectomy with salpingo-oophorectomy or other – (specify); accompanying specimens e.g. peritoneal biopsies, peritoneal washings, omentectomy, appendicectomy, lymph-nodes.

- Relevant clinical information (if provided): hormonal status, medical history, hormonal therapy, family history, results of previous biopsies or cytology samples, tumour markers, previous chemotherapy.[8-9]

Gross description

- Integrity of specimen: intact or fragmented tumour; ovarian capsule intact or ruptured/breached (if the tumour capsule is ruptured, find out if it was before surgery or at surgery).

- Tumour size in 3 dimensions (mm)

- Description of the colour and consistency of the tumour, the degree of heterogeneity in appearance, the presence of cysts, papillae or solid areas, and the presence of necrosis and/or haemorrhage.

- Relationship to adjacent or attached structures

Tumour sampling recommendations

- Ovarian mass: sampling of the tumour should be adequate to reflect its heterogeneity at macroscopic examination. Particular care should be taken to take tissue blocks at interfaces (i.e.to include apparently normal and abnormal areas or solid and cystic areas). In general, at least one block/cm of tumour is recommended. Sampling should include any capsular deposits and areas of suspected capsular breach/rupture.

- Fallopian tube: at least one block to include any abnormal areas for carcinomas other than serous carcinoma. In cases of serous carcinoma the entire tube should be processed to exclude the possibility of primary Fallopian tube carcinoma, and examined according to the SEE-FIM protocol (Sectioning and Extensively

Examining the FIMbriated end; the proximal fallopian tube is serially sectioned at ~3mm intervals, stopping approximately 10 mm before the distal end of the fallopian tube. The fimbria are then sectioned longitudinally to maximize exposure of the fimbrial plicae for histological examination). [10] Uterus: at least 4 blocks (2 cervix and 2 endomyometrium of which one should be full thickness); all areas of abnormal serosa.

- Omentum: if there is obvious macroscopic involvement the tumour deposits should be sampled selectively; usually one or two block will suffice. Sampling of 3-5 blocks is recommended in cases where there is not macroscopic involvement. [11]

- Lymph-nodes: the number of lymph-nodes recovered from each site should be recorded. If nodes contain metastatic tumour macroscopically they need only to be sampled, but the remainder should be submitted in their entirety for histological examination. [12]

- Appendix: it should be submitted in its entirety for histological examination in cases of mucinous ovarian tumours. [13] For other tumour subtypes, selective sampling is recommended.

- Other staging biopsies: these should be submitted in their entirety for histological examination for complete pathological staging; the anatomical location should be specified. [14] If larger specimens are submitted, e.g. a segment of bowel, selective sampling of abnormal areas is adequate.

Microscopic features

- presence of capsular involvement or breach.

- histological type: according to the World Health Organization (WHO) 2003 classification. [15]

- histological grade: report the tumour grade and specify the grading system. To ensure uniformity of the grading the ESP recommends the use of the binary histological grading system for ovarian serous carcinoma.[16-19] Clear cell carcinoma, undifferentiated carcinoma and carcinosarcoma are graded as high-grade tumours, and mucinous and endometrioid carcinomas are graded according to the combined FIGO grading system for endometrial carcinoma.[20-21]

- presence of borderline component.

- extent of local tumour spread (this is based on the T component of the TNM classification). [22]

- microscopic evidence of lymphovascular invasion

- microscopic evidence of tumour involvement of the staging biopsies

- microscopic evidence of tumour involvement of fallopian tube, uterus, omentum.[23]

- other features which may impact on diagnosis or prognosis) (putative precursor lesions such as endometriosis, histological features after chemotherapy, ancillary investigations (optional), e.g. immunohistochemistry, if performed)

- epithelial primary ovarian tumours are staged according to FIGO staging.[22] In some institutions AJCC/TNM staging is also applied.

Figure legends:

Figures 1 and 2 - Ovary: 2008 estimates. European Age-Standardised Incidence and Mortality Rates per 100,000 population, Females, EU27 Countries.

Prepared by Cancer Research UK.

Original data sources: European age-standardised rates were calculated by the Statistical Information Team at Cancer Research UK, 2011 using data from GLOBOCAN, IARC, version 1.3. http://globocan.iarc.fr/

References

1) Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer clin. 2008; 58: 71-96.

2) Goff BA, Mandel LS, Melancon CH, Muntz HG. Ovarian carcinoma diagnosis. Cancer. 2000; 89: 2068-2075.

3) Goff BA, Mandel LS, Melancon CH, Muntz HG. Frequency of symptoms of ovarian cancer in women presenting to primary care clinics. JAMA. 2004; 291: 2705-2712.

4) Mackay HJ, Brady MF, Oza AM, Reuss A, Pujade-Lauraine E, Swart AM, Siddiqui N, Colombo N, Bookman MA, Pfisterer J, du Bois A, Gynecologic Cancer InterGroup. Prognostic relevance of uncommon ovarian histology in women with stage III/IV epithelial ovarian cancer. Int J Gynecol Cancer. 2010; 20: 945-952.

5) Gershenson DM. The heterogeneity of epithelial ovarian cancer. Cancer. 2010; 116: 1400-1402.

6) Bamias A, Psaltopoulos T, Sotiropoulos M, et al. Mucinous but not clear cell histology is associated with inferior survival in patients with advanced stage ovarian carcinoma treated with platinum-paclitaxel chemotherapy. Cancer. 2010; 116: 1462-1468.

7) Chan JK, Tian C, nMonk BJ, Herzog T, Kapp DS, Bell J, Young RC. Prognostic factors for high-risk early-stage epithelial ovarian cancer. A Gynecology Oncology Group Study. Cancer. 2008; 112: 2202-2210.

8) McCluggage WG, Lyness RW, Atkinson RJ, et al. Morphological effect of chemotherapy on ovarian carcinoma. J Clin Pathol. 2002; 55: 27-31.

9) Miller K, Price JH, Dobbs SP, McClelland RH, Kennedy K, McCluggage WG. An immunohistochemical analysis of post-chemotherapy ovarian carcinoma. J Clin Pathol. 2008; 61: 652-657.

10) Medeiros F, Muto MG, Lee Y, Elvin JA, Callahan MJ, Feltmate C, Garber JE, Cramer DW, Crum CP. The tubal fimbria is a preferite site for early adenocarcinoma in women with familiar cancer syndrome. Am J Surg Pathol. 2006; 30: 230-236.

11) Usubutun A, Ozseker HS, Himmetoglu C, Balci S, Ayhan A. Omentectomy for Gynecologic Cancer. How much sampling is adequate for microscopic examination? Arch Pathol Lab Med. 2007; 131: 1578-1581.

12) Nomura H, Tsura H, Susumu N, Fujii T, Banno K, Kataoka F, Tominaga E, Suzuki A, Chivoda T, Aori D. Lymph node metastasis in grossly apparent stages I and II epithelial ovarian cancer. Int J Gynecol Cancer. 2010; 20: 341-345.

13) Leen SL, Singh N. Pathology of primary and metastatic mucinous ovarian neoplasms. J Clin Pathol. 2011 Nov 10. Epud ahead of print.

14) Scroff R, Brooks RA, Zighelboim I, Powell MA, Thaker PH, Mutch DG, Massad LS. The utility of peritoneal biopsy and omentectomy in the up staging of apparently early ovarian cancer. Int J Gynecol Cancer. 2011; 21: 1208-1212.

15) World Health Organization Classification of Tumours. Pathology & Genetics. Tumours of the breast and female genital organs. Tavassoli FA & Devilee P eds. IARC Press: Lyon 2003.

16) Malpica A, Deavers MT, Lu K, Bodurka DC, Atkinson EN, Gershenson DM, et al. Grading ovarian serous carcinoma using a two-tier system. Am J Surg Pathol. 2004; 28: 496-504.

17) McCluggage WG. Morphological subtypes of ovarian carcinoma: a review with emphasis on new developments and pathogenesis. Pathology. 2011; 43: 420-432.

18) Hannibal CG, Vang R, Junge J, Kjaerbye-Thgesen A, Kurman RJ, Kjaer SK. A binary histologic grading system for ovarian serous carcinoma is an independent prognostic factor: a population-based study of 4317 women diagnosed in Denmark 1978-2006. Gynecol Oncol. 2012; 125: 655-660.

19) Prat J. Ovarian carcinomas: five distinct disease with different origins, genetic alterations, and clinicopathological features. Virchows Arch. 2012; 460: 237-249.

20) Shimizu Y, Kamoi S, Amada S, Akiyama F, Silverberg SG. Toward the development of a universal grading system for ovarian epithelial carcinoma : testing of a proposed system in a series of 461 patients with uniform treatment and follow-up. Cancer. 1998; 82: 893-901.

21) Silverberg SG. Histopathologic grading of ovarian carcinoma: a review and proposal. Int J Gynecol Pathol. 2000; 19: 7-15.

22) AJCC Cancer Staging Manual, Seventh Edition. Springer-Verlag eds: New York 2010.

23) Winter III WE, Maxwell GL, Tian C, Sundborg MJ, Rose GS, Rose PG, Rubin SC, Muggia F, McGuire WP. tumour residual after surgical cytoreduction in prediction of clinical outcome in stage IV Epithelial ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2008; 26: 83-89.