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HISTOLOGIC AND MOLECULAR STAGING OF ENDOMETRIAL CANCER

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Context:
The most important advance in the knowledge of endometrial carcinoma was made in 1983; i.e., separation of endometrioid (type I) from nonendometrioid (type II) which are two different diseases clinically, pathologically and regarding molecular genetics.
Objective:
The current FIGO staging system is almost 40 years behind. Indeed, the 2009 FIGO staging considers only one disease instead of “at least” two (endometrioid/low-grade and nonendometrioid/high-grade) which merit separate staging classification, particularly at stage I.
Methods:
The validity of this classification has been confirmed and expanded by 2013 The Cancer Genome Atlas (TCGA) (POLE/ultramutated, MI/hypermutated, low copy number and high-copy number; the latter group including serous carcinomas and serous-like G3 endometrioid carcinomas which behave like serous tumors; and POLE-mutated G3 endometrioid which behave very well even without chemotherapy).
Main Outcome:
Histotype should be reported; i.e., endometrioid or nonendometrioid (serous, clear cell, carcinosarcoma, mixed, undifferentiated, and dedifferentiated carcinomas); however, all nonendometrioid carcinomas are G3 and grading nonendometrioid tumors is useless. On the other hand, all G1-2 tumors are endometrioid carcinomas. Obviously, designing a specific staging system for each histotype would not be practical, but separating low-grade (G1 and G2) from high-grade (G3) for the purpose of staging -not for treatment but prognosis- is quite reasonable.
Results:
Distinguishing G1 from G2 endometrioid carcinoma may be difficult. There is not a clear cut division between G1 and G2 and overlapping is common.
Regarding fertility sparing surgery in young patients, it wouldn’t matter whether the carcinoma is G1 or G2; it is G3 that really matters.
G3 includes a gray zone pointed out by TCGA (serous and serous-like endometrioid) which can be reduced by immunohistochemistry (p53, MMR); also POLE mutation is worth investigating as positive cases may not need chemotherapy and have very good prognosis. Thus, p53, MMR (IHC) and POLE

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mutation analysis should be done in all G3 carcinomas. Noteworthy, G3 endometrioid carcinomas represent a small fraction of endometrial carcinomas compared with low-grade carcinomas, which are far more common.

Conclusions:

Low-grade (G1 and G2) and high-grade (G3) endometrial carcinomas represent two different diseases and a separate stage I classification is recommended.