Ovarian conservation for grade 2–3 endometrial cancer in premenopausal patients: should they stay or should they go?

Koji Matsuo, Jason D Wright

Historically, the surgical treatment of endometrial cancer included hysterectomy along with oophorectomy. Interest in ovarian conservation for endometrial cancer has increased after the publication in 2009 of a study that suggested that ovarian conservation was safe for young patients with endometrial cancer. Since the publication of this study, mounting evidence has emerged suggesting that ovarian conservation in premenopausal patients is not associated with either increased all-cause or endometrial cancer mortality and may decrease cardiovascular mortality. Ten years following the 2009 analysis, the National Comprehensive Cancer Network clinical practice guidelines endorsed this concept in 2018 and suggested that ovarian conservation could be considered in selected premenopausal patients. To date, the majority of prior studies have predominately focused on patients with grade 1 endometrioid tumors, and there is a paucity of data on the oncologic safety of patients with grade 2–3 endometrioid tumors. In this issue, Nasioudis and colleagues examined the safety of ovarian conservation in patients with stage I, grade 2–3 endometrioid tumors. Their evaluation of surgical practice across the Commission on Cancer-accredited facilities from 2004 to 2015, only 7% of 29,141 patients aged ≤45 years had ovarian conservation. Further, there was a fourfold decrease in ovarian conservation from 2005 to 2015. The ovarian conservation group was less likely to undergo nodal evaluation compared with the oophorectomy group. The 5-year overall survival rates were comparable between the ovarian conservation and oophorectomy groups for both grade 2 and 3 tumors; these results externally validate prior analyses.

The study team additionally provided information for risk factors for adnexal metastasis among stage I, grade 2–3 endometrioid tumors. Lymph node metastasis, large tumor size (>4 cm), lympho-vascular space invasion, and malignant peritoneal cytology were associated with adnexal metastasis. Information on gross versus microscopic adnexal metastasis, organ type (fallopian tube or ovary) as well as depth of myometrial invasion were, however, not available. Premenopausal patients were associated with increased risk of adnexal metastasis. Given that synchronous ovarian cancer is a common secondary primary malignancy in premenopausal patients, second primary ovarian cancer may have been classified as an adnexal metastasis by pathology evaluation in some cases.

The authors appropriately recognize a number of limitations of the current analysis. Preoperative tumor characteristics undoubtedly played a role in surgical planning, however the data collection mechanism of the National Cancer Database does not record preoperative tumor grade. A prior study demonstrated that approximately 25% of patients with a preoperative grade 1 endometrioid lesion are found to have grade 2 or 3 tumors after hysterectomy. Similarly, data on follow-up surgery are unavailable. Interval oophorectomy after the primary surgery may have been performed in a subset of patients who had unexpected high-grade tumors identified.

While data on survival are encouraging, information on recurrences, particularly in the adnexa, would be of great utility. Lastly, while analysis of higher grade tumors is an important contribution, the study cohort contains patients with highly variable prognoses and the sample size for some subsets of patients was small. For example, only 20 patients with stage IB, grade 2–3 tumors were included, significantly limiting the power of sub-group analyses.

The study raises a number of important questions. First, why did the rate of ovarian conservation decline so dramatically over the course of a decade? One could reasonably argue that data in this setting are limited, yet over the time period of the study, numerous cohort studies emerged suggesting that ovarian conservation was safe. More updated data to discern if these trends have continued would be of great interest. Together with other studies, the analysis of real-world practice clearly suggests that despite the oncology safety, surgeons and patients are not comfortable retaining the ovaries in grade 2–3 endometrioid tumors.

Second, should ovarian conservation be routinely offered to premenopausal patients with higher grade endometrioid endometrial cancer? This question will...
be of even greater clinical importance as the incidence of endo-
metrial cancer in young women continues to increase. The long-
term health effects of surgical menopause for patients <40 years
of age can be profound. Despite the limitations of observational
data, a randomized controlled trial to address this topic is extremely
unlikely. As such, shared decision-making of the risks, benefits, and
gaps in knowledge as to whether the ovaries should stay or go is
warranted.

Author affiliations
1 Division of Gynecologic Oncology, Department of Obstetrics and Gynecology,
University of Southern California, Los Angeles, California, USA
2 Norris Comprehensive Cancer Center, University of Southern California, Los
Angles, California, USA
3 Division of Gynecologic Oncology, Department of Obstetrics and Gynecology,
Columbia University College of Physicians and Surgeons, New York, New York, USA

Contributors Concept: KM and JDW. Manuscript draft: KM. Manuscript editing:
JDW. Project supervision: JDW.

Funding This study was funded Ensign Endowment for Gynecologic Cancer
Research.

Competing interests Research grant, Merck, royalties, UpToDate (JDW).

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Commissioned; internally peer reviewed.

ORCID iDs
Koji Matsuo http://orcid.org/0000-0002-6232-8701
Jason D Wright http://orcid.org/0000-0001-6390-825X

REFERENCES