oversimplified in light of the molecular classification of endometrial cancer. Future studies should aim to validate a molecular classification system and determine associated modifiable risk factors to decrease the rising incidence and mortality associated with endometrial cancer.

Courtney M. Eakin, MD
Department of Obstetrics and Gynecology
University of California, Los Angeles
Los Angeles, CA

Daniel S. Kapp, MD, PhD
Department of Radiation Oncology
Stanford University
Stanford, CA

John K. Chan, MD
Division of Gynecologic Oncology
California Pacific Medical Center
Palo Alto, CA

The authors report no conflict of interest.

This research was supported by the National Institutes of Health (grant number T32CA251072).

REFERENCES

The risk of pelvic organ prolapse in total hysterectomy and subtotal hysterectomy

TO THE EDITORS: Husby et al investigated the risk of pelvic organ prolapse (POP) in women who underwent hysterectomy using the Danish National Patient Registry. The authors demonstrated that the risk of POP surgery was higher in women who had undergone hysterectomy than in those who still had their uterus. To eliminate bias in their analysis, the researchers used a 1:5 matching method based on age and calendar year. Despite these attempts, there are several issues with the study.

First, there is a problem with the composition of the subgroups. The authors argued that hysterectomy, excluding vaginal hysterectomy, was associated with POP (adjusted hazard ratio [aHR], 1.5; 95% confidence interval [CI], 1.0–2.4). However, excluding laparoscopic-assisted vaginal hysterectomy (LAVH) and vaginal hysterectomy from the subgroup analysis seems more reasonable. Furthermore, the authors explained that vaginal hysterectomy is difficult to perform when the vagina is narrow, and there is no descent of the uterus. This is a feature shared, in part, not only with vaginal hysterectomy but also with LAVH. In addition, the authors reported that total hysterectomy (aHR, 1.5; 95% CI, 0.9–2.4) and subtotal hysterectomy (aHR, 1.5; 95% CI, 0.6–3.5) were not associated with POP. Total hysterectomy and subtotal hysterectomy account for 95% of all hysterectomy cases. Therefore, it is overstated to claim that all hysterectomies are POP related. Moderately, it seems logical to claim that total hysterectomy and subtotal hysterectomy are unrelated to POP.

Second, there is a problem with target group selection. If POP was present in a patient before study selection, they should have been excluded from the target group or adjusted in the analysis. Patients with POP who had not undergone surgery were not excluded from the study group. For example, if a woman with mild uterine prolapse underwent a hysterectomy without colpopexy, this woman was assigned to the hysterectomy group. Therefore, among the finally selected women, women with POP before selection should have been excluded, regardless of whether they had undergone POP surgery.

Third, another bias that is present in the study was omitting pessary use from the primary outcome. Pessaries are so widely used that they are found in 19% of all POP treatments. In contrast, short vaginal length and previous pelvic surgery are risk factors for pessary failure. Because women who have undergone hysterectomy are more likely to experience pessary failure, they are more likely to need POP surgery. It is the same concept that a tubal pregnancy with a fetal heartbeat has a higher surgical risk than a tubal pregnancy without a fetal heartbeat. The reason is that a woman with a tubal pregnancy with a fetal heartbeat is more likely to experience methotrexate failure. Therefore, pessary use should be included in the primary outcome.

We respect the exciting work of the authors. Nonetheless, the conclusion of this study suggested that the POP risk associated with total and subtotal hysterectomy might be
overestimated. Therefore, we believe that adjusting their findings or rephrasing their conclusions is necessary to improve the study.

Myounghwan Kim, MD, PhD
Jin-Sung Yuk, MD, PhD
Department of Obstetrics and Gynecology
Sanggye Paik Hospital
School of Medicine
Inje University
Seoul, Republic of Korea
cnnsbs@naver.com
The authors report no conflict of interest.

REFERENCES

Reply: The risk of pelvic organ prolapse after hysterectomy

We thank Drs Kim and Yuk for their interest in our study. They drew attention to the composition of subgroups and the inclusion of women who underwent laparoscopic-assisted vaginal hysterectomy (LAVH) in our subgroup analysis. The reasons for this were as follows:

1. LAVH has not been well defined during 1977 to 2018 and includes a variety of surgical techniques, especially in earlier years.
2. In Denmark, LAVH was often performed when anatomic conditions did not allow vaginal hysterectomy; therefore, the anatomic predisposition for pelvic organ prolapse (POP) may not occur for women undergoing LAVH.

We reiterated the subgroup analysis, excluding women undergoing LAVH, and found virtually the same result as the article (hazard ratio: 1.6 [95% confidence interval (CI), 1.0-2.5] vs 1.5 [95% CI, 1.0-2.4]).

Drs Kim and Yuk claimed that a logical conclusion of our study would be that total hysterectomy and subtotal hysterectomy are unrelated to POP. However, even though statistical significance is not reached for the subgroups of hysterectomy, we see a clear tendency of association between the respective hysterectomies and subsequent POP. We believe it is highly probable that a type 2 error causes the insignificance. To date, we are working on a study that includes nulliparous and parous women, and this larger cohort will enable firmer conclusions on surgical routes separately.

Drs Kim and Yuk stated that if POP was present in a patient before study selection, they should have been excluded from the target group or adjusted in the analysis. We agree that this is an important issue, which we have considered carefully. Mild uterine prolapse is common; thus, we expect high numbers in both the hysterectomy and the reference group. However, the problem is that women are only diagnosed if they are seen by a gynecologist at a hospital. Therefore, the women in the hysterectomy group are more likely to be diagnosed with POP, which would skew the adjustment. Similarly, excluding all women with previous POP would create a falsely healthy population of women undergoing hysterectomy.

Lastly, Drs Kim and Yuk led our attention to pessary use. Unfortunately, we do not have valid information about pessary use. Thus, we cannot preclude that this would slightly affect the results. We appreciate this addition to the limitation of our study.

Karen R. Husby, MD
Department of Obstetrics and Gynecology
Herlev and Gentofte University Hospital
Borgmester Ib Juuls Vej 1, 2730 Herlev
Copenhagen, Denmark
Faculty of Health and Medical Sciences
University of Copenhagen
Copenhagen, Denmark
karen.ruben.husby.02@regionh.dk

Kim O. Gradel, DVM, PhD
Center for Clinical Epidemiology
Odense University Hospital
Odense, Denmark
Research Unit of Clinical Epidemiology
Department of Clinical Research
University of Southern Denmark
Odense, Denmark
Niels Klarskov, MD, DMSc
Department of Obstetrics and Gynecology
Herlev and Gentofte University Hospital
Copenhagen, Denmark