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Bariatric Surgery: Does It Affect Pregnancy Outcomes?

ABSTRACT & COMMENTARY

By *Rebecca H. Allen, MD, MPH*

Assistant Professor, Department of Obstetrics and Gynecology, Warren Alpert Medical School of Brown University, Women and Infants Hospital, Providence, RI

Dr. Allen reports no financial relationships relevant to this field of study.

Synopsis: *In this large, retrospective cohort study, women with a history of bariatric surgery were at a small increased risk of both spontaneous and medically indicated preterm birth and small for gestational age births. However, this was only true among women with an early pregnancy body mass index < 35 kg/m².*

Source: Roos N, et al. Perinatal outcomes after bariatric surgery: Nationwide population based matched cohort study. *BMJ* 2013;347:f6460 [Epub ahead of print].

THIS IS A POPULATION-BASED, RETROSPECTIVE COHORT STUDY FROM SWEDEN that evaluated the association between bariatric surgery and perinatal outcomes. The authors identified subjects through the national medical birth register (includes 98% of all births in Sweden) and the national patient register (includes information on hospital admissions and surgeries) by using each person's Swedish personal identity number. They were able to access data on weight at first prenatal visit,

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smoking, education level, age, parity, gestational diabetes, and pre-pregnancy hypertension. Bariatric surgeries were classified into gastric bypass, vertical banded gastroplasty, and gastric banding. Subjects were matched to controls with no history of bariatric surgery on age, parity, body mass index (BMI) in early pregnancy, smoking status, education level, and delivery year in a 5:1 ratio.

A total of 1,742,702 births were analyzed, of which 2562 occurred after bariatric surgery for the treatment of obesity. Type of surgery was divided approximately into one-third vertical banded gastroplasty, one-third gastric bypass, and one-third gastric banding. The surgery to delivery interval was < 1 year in 2.4%, 1-2 years in 16%, 2-5 years in 39%, and ≥ 5 years in 42% (median 4.2 years). Overall, 9.7% of births in the bariatric surgery group were preterm (< 37 weeks) compared to 6.1% in the matched controls (risk difference, 3.6%; 95% confidence interval [CI], 2.4-4.9%; *P* < 0.001). Of these, 4.5% in the bariatric group compared to 2.5% in the matched control group were medically indicated (*P* < 0.001) and 5.2% compared to 3.6% were spontaneous preterm births (*P* < 0.001). The risk of delivering a small for gestational age infant was higher in the bariatric group (5.2% vs 3.0%; risk difference, 2.2%; 95% CI, 1.3-3.2%; *P* < 0.001). Effect modification was seen with BMI level where the highest risk of preterm birth was in women who had bariatric surgery and a BMI < 35 kg/m², but no increased risk was seen in women with a BMI of ≥ 35 kg/m². Neither the type of bariatric surgery nor the interval between the bariatric surgery and the delivery affected the results. When the

Farewell and Welcome

It is with great sadness that I announce Frank Ling, an original member of the editorial board of *OB/GYN Clinical Alert*, has decided to step down. His sense of humor, honest and insightful commentary, and willingness to address complex issues such as gynecologic pain will be missed. Frank's wide interests in the specialty represent the very best traditions of generalist practice. Please join me in wishing him well with his future activities.

One area that Frank has consistently reported on during his tenure has been benign gynecologic surgery and urogynecology. To ensure that these topics remain well-covered in these pages, I am very pleased to announce that Dr. Chiara Ghetti has agreed to join the editorial board as a regular contributor. You should have noticed her first contribution in last month's issue. After completing her residency and fellowship in urogynecology at Oregon Health & Science University, Chiara joined the faculty at the University of Pittsburgh. She is presently an Associate Professor of Obstetrics & Gynecology in the Division of Female Pelvic Medicine and Reconstructive Surgery at the Washington University School of Medicine. In addition to being board certified in urogynecology, Chiara is also an active member of the North American Society for Psychosocial Obstetrics and Gynecology. We are indeed fortunate that this shared interest in gynecologic surgery and the psychosocial aspects of gynecologic care follow in Frank's tradition. Please join me in welcoming her to the editorial board of *OB/GYN Clinical Alert*.

bariatric group was compared to a group of controls who would have been eligible for bariatric surgery based on their weight, the excess risk of preterm birth was attenuated but still increased (9.5% vs 7.2%; risk difference, 2.4%; 95% CI, 1.1-3.6%; *P* < 0.001).

■ COMMENTARY

Obesity in pregnancy is a major problem in the United States with more than one-half of pregnant women being overweight or obese.¹ We know that overweight and obese pregnant women are at higher risk of pregnancy complications including miscarriage, stillbirth, gestational diabetes, hypertensive disorders including preeclampsia, and cesarean delivery.² One of the most effective treatments for obesity is bariatric surgery, which is presently recommended for a BMI of ≥ 40 kg/m² or a BMI of ≥ 35 kg/m² with significant medical comorbidities. The number of reproductive-aged women who are choosing bariatric surgery to treat their obesity is increasing.¹ Whether women who undergo bariatric surgery to lose weight and then get pregnant are still at increased risk of pregnancy complications is unclear. Before this study, one meta-analysis of three cohort studies suggested that after bariatric surgery, women were at no higher risk of preterm birth or fetal

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Questions & Comments

Contact **Leslie Coplin**, Executive Editor,
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growth restriction compared to the general population or obese controls.³ However, other smaller studies indicated a concern regarding nutritional levels after bariatric surgery influencing fetal growth.

Some experts recommend delaying conception for 12-24 months after bypass surgery. This is to allow the period of rapid weight loss to occur without any risk of compromising fetal growth from poor nutrition in the mother.⁴ Because fertility often increases after bariatric surgery, women who want to delay pregnancy need to be placed on a reliable contraceptive method. All contraceptive methods are options for women after bariatric surgery except for oral contraceptives in women who have had a mal-absorptive procedure (Roux-en Y gastric bypass or bilio-pancreatic diversion). Depending on the type of bariatric surgery performed, women should be evaluated antenatally for vitamin and mineral deficiencies such as iron, vitamin B12, folate, vitamin D, and calcium.⁴ Consultation with a nutritionist and surveillance of fetal growth with ultrasound may also be indicated depending on their pre-pregnancy weight.

This Swedish study is a well-done, matched, population cohort study that took advantage of national databases to ensure a representative sample. However, this study also falls victim to the inherent limitations of observational epidemiology.⁵ One, the absolute risk differences are small but carry statistical significance because of the large sample size. Two, there was no relationship between the time interval of surgery to delivery and pregnancy outcomes, which does not seem to make clinical sense. One would expect worse outcomes in women who get pregnant within 1-2 years of bariatric surgery during the period of rapid weight loss. Three, the BMI level in early pregnancy influenced the results but not in the direction one would anticipate. Women with a BMI of < 35 kg/m² had the highest risk of preterm birth, not women with a BMI ≥ 35 kg/m². The authors don't have any explanations for these findings. Even though this study used matched controls, there can still be unmeasured confounders present that could influence the results. In addition, the authors did not have access to pre-surgery weight and degree of weight loss between surgery and pregnancy. Although this study received press attention, I don't think it definitively answers the question about the risks of pregnancy after bariatric surgery. Certainly, as clinicians we want to encourage women to have a healthy weight prior to pregnancy. Given all the factors that influence pregnancy outcomes, it will be difficult to isolate the effect of bariatric surgery itself. In the meantime, women who become pregnant after bariatric surgery should be carefully monitored for fetal growth. If the patient is still obese, it may be necessary to use ultrasound rather than fundal heights as the measurement tool. ■

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Surgical Excision of Endometriomas and Effect on Ovarian Reserve

ABSTRACT & COMMENTARY

By Michael A. Thomas, MD

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Dr. Thomas reports no financial relationships relevant to this field of study.

Synopsis: In a prospective cohort study, women with endometriomas (> 2 cm) were found to have a decrease in ovarian reserve parameters compared to healthy controls 1 and 6 months after the endometriomas were removed.

Source: Uncu G, et al. Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve. *Hum Reprod* 2013;28:2140-2145.

THESE AUTHORS SOUGHT TO DETERMINE WHETHER SURGICAL excision of endometriomas is associated with short- or long-term effects on ovarian reserve. A cohort of 30 women who underwent surgical removal of endometriomas (> 2 cm) because of pain or subfertility was compared to an age- and gravid-matched control group of 30 otherwise healthy women who did not have a diagnosis of endometriosis. All endometriomas were removed laparoscopically by two experienced surgeons. At the time of surgery, the endometriomas were incised and the cyst wall was stripped away from the ovarian stroma by blunt dissection. Hemostasis was achieved with cautery. The pre-operative use of GnRH agonist was not utilized. Of the 30 women with endometriomas, 15 had unilateral cysts and 15 had bilateral cysts. Eighteen women had multiple endometriomas. Ovarian reserve was measured by antim-

ullerian hormone (AMH) and antral follicle count (AFC) at baseline in both groups, and at 1 month and 6 months after surgery in the endometrioma group only.

Mean baseline AMH was 2.81 ng/mL for endometrioma patients and 4.20 ng/mL for controls ($P = 0.02$). Mean baseline AFC was 9.73 in endometrioma subjects and 14.7 in controls ($P > 0.01$). Postoperatively, AMH declined to 2.07 ng/mL at 1 month and 1.82 ng/mL at 6 months and AFC did not change (11.0 at 1 month and 10.4 at 6 months). Only the decrease in AMH from baseline to 6 months was statistically significant ($P = 0.02$). This decline in AMH was not significantly correlated with laterality of endometriomas (unilateral or bilateral), patient age, baseline AFC, diameter of the largest endometrioma, or the number of follicles removed from the ovary at the time of surgeries.

■ COMMENTARY

Approximately 0.8-5% of women in the reproductive age range are affected by endometriosis. It is well understood that their fecundity (0.02-0.10) is much lower than that found in women without endometriosis (0.15-0.20).¹ Early investigators have noted that 25-50% of infertile women have endometriosis and that 30-50% of women with a diagnosis of endometriosis have infertility issues.² Women with infertility undergoing laparoscopy have a 48% incidence of endometriosis compared to 5% found in fertile patients undergoing tubal ligation.³

Endometriomas are found in 20-40% of these women who have been diagnosed with endometriosis and can be found inadvertently during an infertility work up.⁴⁻⁶ However, indications for routine surgical removal of endometriomas prior to the start of any treatment for infertility are not clear.⁷⁻⁹

This study demonstrates two things that all practicing gynecologists should consider when treating patients who have endometriomas. The first is that endometriomas are associated with a decrease in ovarian reserve as measured by both AMH and AFC. Clinically, this makes sense because when you see endometriomas on ultrasound, there is usually only a small rim of normal ovarian stroma remaining. It is almost as if the endometrioma is “eating away” at what was once a normal ovary.

The second important finding from this article is that the surgical excision of an endometrioma will cause a decrease in AMH, but no significant change in AFC at 6 months after removal. This decrease in AMH occurred despite the fact that surgical intervention was performed to “save” ovarian integrity. However, the technique of “stripping” the endometrioma cyst wall may decrease recurrence of a future endometrioma, but may adversely affect the number of residual follicles remaining in the ovary.

Though the control group was not assessed after 6

months, AMH and AFC typically remain stable in otherwise healthy women in the late 20s to early 30s. The mean age of the endometrioma group was 29.0 years and the mean age of the control group was 30.1 years. However, a 6-month blood test and ultrasound would have made the study more complete.

In a recent study that also looked at the effects of endometrioma removal on ovarian reserve without a control group, 65 women underwent laparoscopic excision.¹⁰ The mean age was 28.4 years. AMH and AFC were obtained at 6 weeks and 6 months after surgery. These investigators noted a significant decrease in AMH from baseline (1.78 ng/mL) to 6 months (0.72 ng/mL) ($P < 0.001$) and the AFC increased from 4.9 at baseline to 6.4 at 6 months ($P = 0.008$). This study showed a potential rebound effect on the number of ovarian follicles counted, but this may demonstrate that AFC is probably not the best marker for ovarian reserve in this patient population because its determination is very subjective and likely to vary from sonographer to sonographer.

Because most patients with endometriomas also have concurrent moderate-to-severe adhesive disease, surgical intervention is usually helpful in relieving pelvic pain, constipation, and dyspareunia by decompressing the bulging ovary, lysing adhesions, and subsequently restoring pelvic anatomy. However, routine endometrioma removal should probably not be performed in the asymptomatic patient who wants to preserve her fertility because of the potential to have a detrimental long-term effect on ovarian reserve.

More studies for a longer period of observation should be undertaken on endometrioma excision with age-matched controls that are compared to either an endometrioma group that undergoes surgical excision and a second group that is observed without surgical intervention. ■

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Emergency Contraception: A Copper IUD May Be the Best Choice

ABSTRACT & COMMENTARY

By Jeffrey T. Jensen, MD, MPH, Editor

Synopsis: Women presenting for emergency contraception were offered a copper IUD or Plan B. Those who chose an IUD had a lower cumulative risk of unintended pregnancy at 1 year.

Source: Turok DK, et al. Emergency contraception with a copper IUD or oral levonorgestrel: An observational study of 1-year pregnancy rates. *Contraception* doi: 10.1016/j.contraception.2013.11.010.

THE AUTHORS PERFORMED A PROSPECTIVE OBSERVATIONAL study to investigate 1-year pregnancy rates among women who present for emergency contraception. Women presenting to two family planning clinics in Utah requesting emergency contraception received scripted counseling information about use of the copper T380 IUD and single-dose oral levonorgestrel (LNG) 1.5 mg. Eligible subjects with no contraindications to either method who consented to participate were allowed to choose either method. The primary outcome was the unintended pregnancy rate for the 1 year after enrollment, and the sample size was selected to detect a 6% difference between the methods. A total of 542 women met all inclusion criteria and consented to participation; 215 (40%) chose the copper IUD and 327 (60%) chose oral LNG. More than half of all subjects were nulligravid, and planned IUD insertion failed in 42 women (19%) who requested the method. The 1-year follow-up was more than 80% and most (64%) IUD users contacted at 1 year had continued with the method. The primary outcome was analyzed according to “intent-to-treat” and with actual use that took into account that not all of the subjects who desired an IUD were able to obtain one at the initial visit. Among women who chose an IUD,

the 1-year cumulative pregnancy rate was 6.5% vs 12.2% in those choosing oral LNG (hazard ratio [HR], 0.53; 95% confidence interval [CI], 0.29-0.97). The actual difference in cumulative pregnancy was even more impressive when the IUD group was restricted to only those women who received a device: 5.2% for copper IUD users vs 12.3% for oral LNG users (HR, 0.42; 95% CI, 0.20-0.85). Since this was not a randomized study, the authors also conducted a multivariable logistic regression model controlling for demographic variables and this confirmed that women who chose the IUD for emergency contraception had fewer pregnancies over the next year than those who chose oral LNG (HR, 0.50; 95% CI, 0.26-0.96). Overall, these results provide strong evidence for the use of a copper IUD as a strategy for reducing unintended pregnancy in women who present for emergency contraception.

■ COMMENTARY

This interesting real-world study evaluates emergency contraception in a novel way by assessing the risk of unintended pregnancy over the subsequent year. The visit for emergency contraception is a teachable moment, just like the visit for a urine pregnancy test. Both of these encounters result from the non-use, improper use, or failure of a contraceptive method. The emergency contraception consult is an event upstream from the pregnancy test, and the existing data suggest that prompt use of emergency contraception after an episode of unprotected intercourse can reduce the risk of pregnancy.¹ Levonorgestrel EC is now available over-the-counter, while the slightly more effective ulipristal acetate (Ella[®]) is prescription only. Unfortunately, the clinical trial results with emergency contraception have not shown substantial population-wise benefits in reducing unintended pregnancy rates.² Part of this is due to the fact that women don't access emergency contraception in time, and over-the-counter status may help this, but another likely explanation is that women experience repeated episodes of unprotected intercourse. For this reason, it is not surprising that providing ongoing regular contraception is the most important intervention for women presenting for emergency contraception or a pregnancy test evaluation.

The study by Turok et al was not powered to address the question of comparative efficacy of the copper IUD and LNG EC as emergency contraceptive agents, but it is interesting to note that there were four pregnancies resulting from emergency contraception failures in the oral LNG group (1%) and none in the IUD group. These data are consistent with larger studies that support high efficacy with post-coital placement of a copper IUD; no pregnancies were observed in a cohort of more than 1600 Chinese women.³ The data from the Utah group is the first comparator study to support these large descriptive series.

There were two big surprises in this paper. The first

is that so many women were willing to accept a copper IUD during the encounter for emergency contraception. It is important to note that none of the subjects came to the clinic requesting an IUD. After receiving information about both methods, about equal numbers of women picked the LNG and the IUD. This suggests that adequate counseling makes a difference in this decision. The disappointing surprise was the very high number of failed IUD placements (19%). The typical rate of failed placement in clinical trials is around 2% so this was very high, and not explained by nulliparity. Better provider training should address this issue. The positive spin is that even with this very high rate of failed placement, the overall chance of pregnancy is lower in women who pick an IUD even if they do not receive the device at the initial consult. These results were robust and not changed after authors adjusted the results for key confounders.

So maybe an office visit for an emergency contraception consult is a good idea after all. The caveat is that this should not delay the initiation of emergency contraception, so family planning clinics and interested office practices need to have same-day availability. Counseling should include the option for placement of a copper IUD. ■

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Special Feature

Pelvic Radiation in Endometrial Cancer: Are We Cutting Off Our Nose to Spite Our Face?

By Robert L. Coleman, MD

Professor, University of Texas; M.D. Anderson Cancer Center, Houston

Dr. Coleman reports no financial relationships relevant to this field of study.

Synopsis: Long-term complications, particularly secondary cancers, were significantly more common in patients receiving whole pelvic radiation (vs brachytherapy alone) for early-stage endometrial cancer. No

difference in overall survival was found in women receiving additional radiation therapy.

Source: Onsrud M, et al. Long-term outcomes after pelvic radiation for early-stage endometrial cancer. *J Clin Oncol* 2013;31:3951-3956.

BETWEEN 1968 AND 1974, 568 PATIENTS WITH STAGE 1 ENDOmetrial cancer were treated adjuvantly with vaginal brachytherapy and then randomized to either external beam whole pelvic radiation (n = 288) or no further therapy (n = 280). A trial reported in 1980 demonstrated no improvement in overall survival for the addition of pelvic radiation.¹ This current trial was conducted to examine the long-term effects of external beam radiation therapy (EBRT) in this population. Stratification was made for age given the high degree of noncancer mortality. After median 20.5 years (range, 0-43.4 years) of follow-up, no statistically significant difference was revealed in overall survival ($P = 0.19$) between treatment groups. However, women younger than age 60 years had significantly higher mortality rates after EBRT (hazard ratio [HR], 1.36; 95% confidence interval [CI], 1.06-1.76) than the control group. The risk of secondary cancer increased after EBRT, especially in women younger than age 60 years (HR, 2.02; 95% CI, 1.30-3.15). The HR for secondary cancer in women older than age 60 years was 0.81 (95% CI, 0.45-1.43). The median time to a secondary cancer was 15 years. The authors conclude no survival benefit of external pelvic radiation in early-stage endometrial carcinoma. In women younger than age 60 years, pelvic radiation decreased survival and increased the risk of secondary cancer. Adjuvant EBRT should be used with caution, especially in women with a long life expectancy.

■ COMMENTARY

It's actually quite remarkable that in the 33 years since this landmark paper was published, the role of adjuvant radiation is still not defined in women with early-stage endometrial cancer.¹ While, in some regard, the good overall prognosis of this cohort does not lend itself to be "modality evaluable," the topic of external beam pelvic radiation therapy is hotly debated, and routinely used as standard of care in many parts of the world. However, in locations where surgical staging (pelvic and para-aortic lymphadenectomy) is universally applied or patient-individualized, adjuvant treatment plans are primarily based on findings in uterine and extrauterine tissue samples. In this context, patients without metastatic disease but deemed at high risk for recurrence are increasingly being treated with systemic chemotherapy. This pattern of care has largely eliminated pelvic radiotherapy from many treatment algorithms. Thus, three principle issues can frame the debate of which adjuvant therapy is most appropriate in early-stage endometrial cancer: assessment of risk, role of lym-

phatic dissection (surgical staging), and the ultimate impact of therapy (survival).

Endometrial cancer is largely considered among the most “survivable” of the gynecological tumors given its predominately early stage at diagnosis and curative impact of simple organ removal. Overall, the 5-year survival for women with early stage endometrial cancer exceeds 85%. However, a small proportion of these patients will experience recurrence, despite a negative evaluation of extra-uterine disease. Patterns of recurrence are roughly one-third local, one-third distant, and one-third both local and distant in nature. Recognizing these issues and the difficulty in curing all but the most focal of recurrences, researchers have devised a series of clinical trials to evaluate adjuvant therapy in the hopes of mitigating this risk. As mentioned, the first randomized trial to do so was that of Aalders and colleagues. In this trial, women with stage I endometrial cancer were given adjuvant vaginal brachytherapy to address recurrence at the vaginal cuff and then were randomized to either whole pelvic radiation or no further therapy. The trial’s accrual window was opened 45 years ago, used clinical staging (based on preoperative findings), and delivered radiation with fairly low-energy cobalt machines in a two-field (AP-PA) exposure. The results demonstrated a decrease in local recurrence with pelvic radiation therapy, but no difference in overall survival (see Table). Despite this remarkable trial’s conclusions, each of the variables mentioned (old staging criteria, lack of lymphadenectomy, and radiation technique) were criticisms to widespread adoption of the practice. Also, since

vaginal brachytherapy was given to all patients, its contribution to the findings was questioned.

In 1987, the Gynecologic Oncology Group (GOG) launched a trial to evaluate pelvic radiation vs no further therapy in women undergoing formal surgical staging with stage IB, grade 2-3, or IC grade 1-2 uterine cancer. Like the previous trial, local recurrence was increased in the no further therapy arm but overall survival was similar.² Also similar to the previous trial, long-term toxicity was increased in women receiving adjuvant pelvic radiotherapy. Review of the risk stratification from the GOG trial identified a cohort of women in which additional therapy appeared to improve long-term outcomes over no further therapy. In light of these findings, subsequent trials conceded that there were a group of low-risk patients for whom adjuvant therapy was of no benefit and could be safely eliminated. However, the argument as to whether surgical staging was necessary to identify these patients continued, and unfortunately, is still unresolved.

Since the risk of nodal metastases is not much different than the risk of recurrence (about 10%), the merit of unselected adjuvant therapy is still questioned. This contention was bolstered by the PORTEC trial, which randomized 714 women with “intermediate risk” for recurrence to the same treatment arms outlined in GOG 99, but in this case, did not require lymphatic evaluation.³ As can be seen in the Table, the recurrence risk, survival, and toxicity observations are nearly matched to GOG 99. Subsequently, several trials have been conducted to try to clarify the first two tenets of the debate: risk assessment and the

Trial	No of Patients and Eligibility	Surgery	Randomization	Age (Mean)	Local recurrence	Survival	Complications
Aalders ¹	540 Stage I	TAH-BSO	VBT vs VBT + Pelvic XRT	60	7% vs 2% at 5 years <i>P</i> < 0.01	89% vs 91% at 5 years <i>P</i> = NS	No initially reported; increased risk of secondary malignancy in Pelvic XRT at 20-year follow-up
GOG 99 ²	392 Stage IB, I, II (occult)	TAH-BSO, Pelvic LN	NAT vs Pelvic XRT	61	12% vs 3% at 2 years <i>P</i> < 0.01	86% vs 92% at 4 years <i>P</i> = NS	8% GI at 2 years for Pelvic XRT
PORTEC ³	714 Stage IB grade 2-3 IC grade 1-2	TAH-BSO	NAT vs Pelvic XRT	66	14% v 4% at 5 years <i>P</i> < 0.001	85% vs 81% at 5 years <i>P</i> = NS	3% GI at 5 years Trend for increased secondary malignancy at 15-year follow-up
PORTEC-2 ⁴	427 age > 60, IB grade 3 Stage IC or IIA, grade 1-2, stage	TAH-BSO LN was optional	VBT vs Pelvic XRT	62	< 2% vs < 2% <i>P</i> = NS	85% vs 80% at 5 years <i>P</i> = NS	GI < 1% and 2% grade 3 at 5 years
ASTEEN/EN.5 ⁵	905 Stage IA/B grade 3, Stage IC, Stage IIA, IIB	TAH-BSO part of study was lymphadenectomy randomization	NAT vs Pelvic XRT Half of patients also received VBT optional	66	15% vs 12% <i>P</i> = NS	85% vs 85% at 5 years <i>P</i> = NS	GI 3% vs 7% at 5 years

need for lymphadenectomy, using variously defined factors.^{4,5} These generally consider age, grade of the tumor, myometrial invasion, involvement of the lymph-vascular spaces, and tumor size/location. The bottom line is that while routine lymphadenectomy as a staging procedure accurately identifies those patients with metastatic disease, the impact on long-term outcome is limited. One response to the lack of this evaluation is increased use of pelvic radiation to “cover” the regional lymphatics for potential early metastatic (but undiagnosed) disease. As has been well covered in several meta-analyses, the practice leads to equivalent outcomes, but as was identified in the Aalders and PORTEC-1 trials, comes with a cost — the risk for secondary malignancy.^{6,7}

Long-term risk from therapy is an uncommon topic in most gynecological malignancies. This is because outside of non-epithelial ovarian and early-stage cervix and endometrial cancer, expected survival is far shorter than the time frame for a second cancer to develop. However, the current trial emphasizes the importance of evaluating the cost of therapy both short- and long-term. Since many of the patients apparently cured of their primary disease received DNA damaging therapy unnecessarily (i.e., not risk stratified), the issue is of great relevance. One effort to mitigate both recurrence and toxicity risk is the use of short-term adjuvant chemotherapy added to vaginal brachytherapy. Since nearly two-thirds of recurrences will include an element of distant disease, it is hypothesized that systemic chemotherapy may be better situated to address this risk. Since vaginal brachytherapy appears to be as good as pelvic radiation in patients undergoing accurate staging, the combination of two would appear an ideal combination. However, the proof of chemotherapy efficacy is lacking despite one randomized trial that suggests its equivalence to pelvic radiation.⁸ It is hoped that the strategy, currently being evaluated in a Phase 3 trial, can provide long-term benefit while lowering long-term adverse events. These will be welcomed additions if proven, because more than ever, patients are experiencing long post-diagnosis survivorships. ■

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CME Questions

1. In the study by Roos et al, women with a history of bariatric surgery and morbid obesity (BMI \geq 40 kg/m²) in their subsequent pregnancy were at higher risk of preterm birth.
 - a. True
 - b. False
2. What is the incidence of endometriomas in women who have been diagnosed with endometriosis?
 - a. 10-20%
 - b. 20-40%
 - c. 40-60%
 - d. None of the above
3. The most likely explanation for the observed decrease in cumulative pregnancy risk at 1 year among women accepting a copper IUD for emergency contraception was:
 - a. the provision of highly effective long acting contraception at the same visit.
 - b. lower side effects than levonogestrel.
 - c. lower cost to patient than over-the-counter pills.
 - d. low expulsion rates for IUDs are seen with insertion at mid cycle.
4. Which of the following statements accurately represents the findings in the trial of pelvic radiation for early-stage endometrial cancer?
 - a. Overall survival was statistically improved in women receiving pelvic radiation after surgery for early-stage endometrial cancer.
 - b. In women younger than age 60 years, mortality was increased with pelvic radiation therapy.
 - c. Locoregional recurrence risk was improved with vaginal brachytherapy.
 - d. Secondary malignancy was statistically increased among women age 60 and older.

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