ABSTRACT & COMMENTARY

Association Between Maternal Characteristics, Abnormal Serum Aneuploidy Analytes, and Placental Abruption

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

SYNOPSIS: A study using data from the California State Prenatal Screening Program has indicated a strong relationship between abnormal first and second trimester analyte values, as well as maternal characteristics, with placental abruption. This has stimulated a discussion of the possible benefit of retaining this type of biochemistry screening for prediction of other pregnancy complications.


The incidence of placental abruption is thought to be about 1 in 100 pregnancies, but this number has been derived mostly from hospital records. The true incidence is higher because many pregnancies complicated by small placental separations uneventfully continue on, leaving little incentive to document at the time of delivery that it ever happened. Recently, there has been a major focus on the prediction of preeclampsia. Almost as a byproduct of this investigation, a study by Blumenfeld et al has linked serum analytes, along with maternal characteristics, with the later emergence of placental abruption. The authors mined information from the California Prenatal Screening Program database between 2009 and 2010. After excluding pregnancies complicated by aneuploidy, neural tube defects, abdominal wall defects, and placenta previa, 137,915 pregnancies remained — 1017 of whom were diagnosed to have an abruption. Each patient in the database had pregnancy-associated plasma protein-A (PAPP-A) and human chorionic gonadotropin (hCG) drawn between 10/0 weeks and 13/6 weeks and a full quad screen (estriol, inhibin-A, hCG, and alpha-fetoprotein [AFP]) drawn in the second trimester.

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The maternal variables showing increased rates of abruption were: maternal age > 34 years (odds ratio [OR], 1.4; 95% confidence interval [CI], 1.2-1.6), hypertension (OR, 2.5; 95% CI, 1.6-3.8), preeclampsia (OR, 3.8; 95% CI, 3.1-4.8), pre-gestational diabetes (OR, 2.0; 95% CI, 1.2-3.3), previous preterm birth (OR, 2.6; 95% CI, 1.4-4.7) or inter-pregnancy interval < 6 months (OR, 1.8; 95% CI, 1.2-2.7). Curiously, obesity seemed to be a deterrent to abruption (OR, 0.6; 95% CI, 0.4-0.9).

Regarding the ability of analytes to predict abruption, the winners were low PAPP-A (< 5th percentile; OR, 1.6; 95% CI, 1.3-2.0), high AFP (> 95th percentile; OR 2.3, 95% CI, 1.4-3.8), and high inhibin-A (> 95th percentile; OR, 1.9; 95% CI, 1.4-2.4). The best performer among maternal characteristics was hypertension. However, if patients with this condition were excluded, then only patients of advanced maternal age, low PAPP-A, and high AFP remained significantly linked with abruption.

**COMMENTARY**

Some of the maternal characteristics results, especially hypertension and preeclampsia, are not surprising, but maternal age and short inter-pregnancy interval are worth a few words. These two factors point toward an unhealthy or no-longer-ready environment for proper placental implantation. Abruption occurs at the decidual/myometrial border where the early changes in spiral artery remodeling occur. If the placental building blocks are not laid down on solid bedrock or rich soil, then these placentas are prone to disruption later in pregnancy.

The analyte pattern in abruption is fascinating. PAPP-A is a placental growth hormone, low levels of which have been associated with later fetal growth restriction and other complications of pregnancy.1 AFP is produced by the fetus. The placenta’s job as a gatekeeper is to keep substances of higher molecular weight, like AFP, from entering the maternal circulation. One of the first clues for placental disruption waiting to happen may be the leaking across the placenta of small amounts of AFP. All it takes is a little bit since the concentration of AFP in the fetus is measured in mg/mL, in the amniotic fluid in ug/mL, but in the maternal circulation in ng/mL.

About one in 10-15 patients will have some bleeding or spotting in pregnancy, and the diagnosis of abruption is made often by exclusion. There are only three possible causes for vaginal bleeding: placenta previa, placental separation, or external cervical bleeding. The last condition is easy to exclude by a simple speculum exam and the first is diagnosed by a simple trans-abdominal or, better yet, a transvaginal sonogram. Abruption can be a slam dunk diagnosis if an extra membranous clot is seen, but about 50% of the time, the blood tracks extra-membranously to and through the cervix without leaving behind any traces. Under these circumstances, the diagnosis is made by the often-used “what else could it be” approach. In this scenario, an elevated AFP might point even more toward abruption.

We are frequently confronted with patients who have been diagnosed to have a “silent abruption,” meaning there is an echo spared area at the uterine/placental interface, or, more commonly, at the edge of the placenta, but with no bleeding. In the former scenario, the echo-spared area generally represents dilated maternal basal veins and can be documented by the use of power or color Doppler. The latter often represents a marginal lake into which intervillus blood flows at such a slow velocity that it is not to be appreciated with standard color flow settings. However, this slow swirling flow can be seen by super-magnifying the area with 2-D ultrasound alone. Clots do not do this. Again, in these clinical settings, serum analytes may be adjunctively useful.

In his companion commentary, Odibo pointed out that the sequential screen and/or quad screen may not be around for long, since the standard aneuploidy screening tests are now being replaced by the more accurate cell-free DNA testing. Even the concept of screening for neural tube defects with AFP alone has been challenged. Why? Because second trimester ultrasound imaging of the fetal posterior fossa (to demonstrate or exclude a Chiari malformation) is a far superior screening and diagnostic method for open neural tube defects. To counter, AFP proponents point to its superior public health benefit, since ultrasound expertise is inconsistent throughout the country and not all patients have easy access to second trimester ultrasound exams. Drawing blood
for AFP requires minimal resources and one gets the bonus of sometimes useful information about other conditions such as abruption, pre-eclampsia, and even placenta accreta (about 50% of patients with placenta accreta have elevated levels of AFP). To accentuate the latter point, the authors of another paper in the same issue of the journal, using pooled data, showed that ultrasound is less precise in detecting accreta than was earlier reported — now showing an 18% false negative rate. Any case of unanticipated placenta accreta could end in disaster, but if the AFP were elevated in the face of an equivocal or even a “negative” ultrasound diagnosis of accreta (with a 1 in 5 chance of being wrong), one might still wish to prepare for this at the time of delivery. Perhaps we should think twice before abandoning second trimester biochemistry screening altogether.

REFERENCES

ABSTRACT & COMMENTARY

The OPTIMAL Trial: SSLF and ULS for Apical Vaginal Prolapse

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

SYNOPSIS: Two years after vaginal surgery for prolapse and stress urinary incontinence, uterosacral ligament suspension and sacrospinous ligament fixation had similar outcomes. Perioperative pelvic floor muscle training did not improve urinary symptoms or prolapse symptoms.


The objective of this study was to evaluate two primary aims in women undergoing surgery for prolapse and stress urinary incontinence: 1) compare 24-month surgical outcomes of sacrospinous ligament fixation (SSLF) and uterosacral ligament suspension (ULS) for apical vaginal or uterine prolapse; and 2) evaluate the effect of perioperative behavioral therapy with pelvic floor muscle training (BPMT) on urinary symptoms at 6 months and on anatomic outcomes prolapse symptoms 24 months after surgery. This was a randomized trial comparing two operations for both apical vaginal prolapse and stress urinary incontinence that was conducted at nine sites between January 2008 and May 2013. Women were randomized to surgical procedure and then randomized to BPMT. The primary outcome for the prolapse surgical intervention was a composite outcome of surgical success. This was defined by three measures: 1) anatomic success: no apical descent greater than one-third into vaginal canalor anterior or posterior vaginal wall beyond the hymen; 2) no bothersome vaginal bulge symptoms; and 3) no re-treatment for prolapse at 2 years. The primary outcomes for the physical therapy intervention were as follows: 1) at 6 months, urinary symptom scores using the Urinary Distress Inventory; and 2) at 24 months, both prolapse symptom scores measured by the Pelvic Organ Prolapse Distress Inventory and anatomic success, as defined previously. Differences between the surgical groups in the primary outcome of surgical success at 24 months and other categorical outcomes were evaluated using generalized linear models. A priori power calculation was performed.

The study enrolled 418 eligible women, and 408 women underwent the behavioral therapy randomization preoperatively. Of these, 374 women were randomized to both the surgical intervention (188 for ULS, 186 for SSLF) and behavioral intervention (186 for BPMT, 188 for usual care) and were included in the analysis. Women in the surgical and the behavioral intervention groups had similar clinical characteristics, with the exception of a greater degree of posterior vaginal prolapse in the SSLF group and a higher median number of vaginal deliveries in the ULS group. There were no differences in surgical interventions between the BPMT and usual care groups. A TVT was performed in 99% of the study population.

At 2 years, there was no statistically significant difference
in surgical success between the surgical groups (ULS 59.2% [93/157] vs SSLF 60.5% [92/152]) and no clinically significant differences in any of the four primary outcome components. There was a low rate of adverse events that was not significantly different between groups. Overall, 18.0% of women (55/305) developed bothersome vaginal bulge symptoms, 17.5% (54/308) had anterior or posterior prolapse or both beyond the hymen, and 5.1% (16/316) underwent either conservative or surgical retreatment by 2 years. Recurrent prolapse was more likely to occur in the anterior compartment. The proportion of women with recurrent anterior (ULS 15.5% vs SSLF 13.7%) or posterior prolapse (ULS 4.5% vs SSLF 7.2%) beyond the hymen was not significantly different between treatment groups. Surgical groups were not significantly different for most secondary outcome measures. There were no significant differences between BPMT and usual perioperative care in the 6-month and 24-month primary and secondary outcomes.

■ COMMENTARY
Pelvic organ prolapse and urinary incontinence are prevalent conditions that often coexist. Pelvic organ prolapse occurs when the uterus and/or vagina descend and may protrude from the vaginal opening. Studies indicate women have an 11% risk of prolapse and incontinence surgery over their lifetime. In the United States, approximately 300,000 surgeries are performed annually for prolapse. The majority are performed vaginally. Two main vaginal procedures are widely used in the correction of apical prolapse — the sacrospinous ligament fixation and the uterosacral ligament vaginal vault suspension. The SSLF procedure attaches the vaginal apex to the sacrospinous ligament using an extraperitoneal approach. The ULS uses an intraperitoneal approach to bilaterally attach the vaginal apex to the proximal uterosacral ligaments. Comparative data regarding the relative efficacy and safety of these two procedures did not exist prior to this study.

BPMT has been shown to be an effective treatment for pelvic floor symptoms, with incontinence cure rates as high as 78% and improved prolapse stage in up to 17%. Its possible role as perioperative adjunct therapy had not been previously explored.

This randomized study provides robust evidence of the benefits, risks, and complications of two very commonly used vaginal surgeries for the repair of apical prolapse. By using standardized anatomic and functional outcomes, this study provides important information for both patients and providers and can help inform our preoperative counseling.

This study found that in women with apical vaginal prolapse and stress urinary incontinence, surgical outcomes for two common apical transvaginal prolapse repair procedures were not different. Surgical success was defined as a composite definition that included anatomic findings, patient-reported symptoms, as well as retreatment. This study found success rates of 60%, which were notably lower than the success rates reported in the literature for these procedures, which range from 70-90%. Are we truly surprised that USL and SSLF are not different? What is remarkable to me is that two commonly performed vaginal procedures for apical prolapse are only successful 60% of the time and that only a small portion of women chose retreatment. Compared to sacrospinous ligament fixation, the abdominal sacrocolpopexy appears to be associated with less recurrent prolapse and less dyspareunia. Most women I counsel about having surgery for prolapse want to have surgery once and cringe when I tell them known success rates for vaginal procedures. We are in great need for the development of safe, effective, and durable vaginal procedures for the repair of vaginal apical prolapse.

REFERENCES
In 2010, after considering evidence supporting a tubal etiology for ovarian epithelial cancer, the gynecologic tumor group in British Columbia (BC) initiated a province-wide ovarian cancer prevention initiative. An informational and instructional DVD was distributed to all obstetricians and gynecologic surgeons in BC. This DVD outlined the role of the fallopian tube in ovarian cancer and explained the association of high-grade serous cancer with inherited BRCA1/2 mutations. Three recommendations were made to clinicians: 1) consideration of bilateral salpingectomy (BS) at the time of hysterectomy, even with ovarian preservation; 2) consideration of excisional BS for permanent contraception; and 3) referral of all patients with high-grade serous cancer for hereditary cancer counselling and genetic testing for BRCA1/2 mutations. In combination, these recommendations were projected to reduce ovarian cancer rates in the province of BC by 40% over 20 years.

In this paper, the authors performed a population-based retrospective cohort study to assess the effects of the educational campaign on surgical outcomes (operating time, surgical approach, indication, length of hospital stay, and perioperative complications) of 43,931 women in British Columbia from 2008-2011 who underwent hysterectomy that was performed with and without BS or bilateral salpingo-oophorectomy (BSO) or who underwent permanent contraception by means of BS or tubal ligation. The cohorts were defined by surgical technique (± BS).

Over the time period studied, the proportion of surgeries at which BS was performed increased significantly for both hysterectomy (5% in 2008 to 35% in 2011, \( P < 0.001 \)) and permanent contraception (0.5-33%, \( P < 0.001 \)). The greatest increase was in women younger than age 50 years. BS required significantly more operative time for both procedures (hysterectomy mean increase 16 minutes; sterilization 10 minutes, \( P < 0.001 \) for both). No significant differences were observed in the risks of hospital stay, readmission or blood transfusions in women who underwent hysterectomy, or permanent contraception with BS.

The authors concluded that an educational campaign to increase risk-reduction salpingectomy at the time of benign gynecologic surgery was effective in increasing the number of procedures performed, and this change in practice did not result in an increased risk of operative or perioperative complications.

**COMMENTARY**

Ovarian cancer is an awful disease with a grim prognosis, as most tumors are diagnosed at an advanced stage. The recent interest in prophylactic salpingectomy as a risk-reduction strategy follows from clinical data that have demonstrated that prophylactic bilateral salpingooophorectomy reduces the risk of serous ovarian cancer associated with germline BRCA mutations. Detailed serial sectioning of the fallopian tubes removed from BRCA-positive women have revealed the presence of precursor lesions in the fimbria called “tubal intraepithelial carcinomas (TICs),” with no correlating precursor lesions within the ovary. More recent studies from women not tested for BRCA with serous ovarian cancers have documented similar lesions in the fimbriated end of the tube in at least 40-60% of cases. Taken together, these are compelling evidence to consider risk-reduction salpingectomy when the tubes are accessible during benign gynecologic surgery in low-risk women.

But should women considering permanent contraception be counseled to undergo BS? Arguments for this position are that the technique is simple and within the scope of most surgeons who perform surgical permanent contraception procedures by either laparoscopy or mini-laparotomy. A recent commentary published in Obstetrics & Gynecology cited the McAlpine paper as sufficient demonstration of safety to advocate routine BS for permanent contraception. However, my take on the results of McAlpine et al suggest a more conservative approach is warranted. While the paper documents that the number of BS procedures increased during the time period studied and that morbidity was low, this was not a randomized study or even a prospective cohort design. Imagine your last easy case and last very difficult case. Would you have made the same decision to proceed with an elective BS at the time of each of these surgeries? Given this, the fact that surgical morbidity was not increased in the BC study likely reflects case selection bias. If the decision was to proceed with BS even with difficult cases (as might be the case if you convince yourself and your patient that this is the goal of the operation), the results may have been different. In addition, the surgical time (already significantly longer with BS) may have been considerably longer. An additional 10 minutes may not seem like a long time, but operating room charges are by the minute, and additional surgical equipment is also needed to perform BS. Will insurers increase reimbursement if BS if performed for permanent contraception? Probably not.

Perhaps the most serious limitation of the Canadian study is the absence of data on the safety of BS in the postpartum setting. Visualization of the fallopian tube is limited during mini-laparotomy, and the veins within the broad ligament are greatly distended (more so if the uterus is exteriorized at the time of cesarean section). In my opinion, data from well-designed prospective studies are needed to gauge the safety of BS in the postpartum setting.
Most women will never develop ovarian cancer, and the number of BS procedures needed to prevent one case of serous ovarian cancer in low-risk women has not been established. Nor has the cost, overall safety, and long-term risks of the intervention. Remember that while the hypothesis of a tubal etiology for serous ovarian cancer is compelling, there are no clinical or epidemiologic data that support the benefit of risk reduction BS in low-risk women. While McAlpine and her coauthors hypothesize that routine BS will reduce ovarian cancer rates in BC by 40% over the next 20 years, this estimate does not excuse the lack of data. We do have robust epidemiologic data supporting a risk reduction with oral contraceptive use and traditional tubal ligation, so alternatives to BS exist and need to be factored into the conversation.

We recommend this approach in our Family Planning Clinic when women at low risk for ovarian cancer present for consultation on permanent contraception. First, consider a LARC method as these involve no surgery, provide a contraceptive benefit similar to permanent contraception, and some methods offer additional health benefits (e.g., LNG IUS treatment of heavy menstrual bleeding, endometrial protection). Next, decide if an abdominal or hysteroscopic approach is preferred. For pregnant women, a postpartum procedure is usually the best choice for overall efficacy, cost, and convenience. For interval procedures, many women elect to avoid abdominal surgery by undergoing hysteroscopic permanent contraception and are not candidates for BS. For women who wish to proceed with laparoscopy, we present a discussion of simple tubal interruption with Filshie clips or bilateral salpingectomy. We counsel that the latter procedure is offered for the additional health benefit of risk reduction for ovarian cancer, but that the evidence for this benefit is preliminary and based on results from high-risk women. They are told that BS will require more surgical time, involves an additional trocar site, and may increase risks of bleeding or injury to adjacent organs, in particular the ovary (although this risk is likely very small). We also mention that the feasibility and safety of BS may be affected by surgical findings. Given this discussion, about a quarter of our patients elect BS as a primary abdominal approach.

REFERENCES:

SPECIAL FEATURE

Tubal Sterilization: Has the Time Come for Routine Bilateral Salpingectomy?

By Rebecca H. Allen, MD, MPH

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Ovarian cancer causes approximately 14,000 deaths in the United States each year, making it the most common cause of gynecologic cancer death and the fifth leading cause of cancer death in women after lung, breast, colorectal, and pancreatic cancer. The lifetime risk of developing ovarian cancer for the average woman in the United States is 1.4%. Unfortunately, there are no effective screening tests for the disease, it is often diagnosed in the late stages, and the survival rates are poor. The recent discovery that epithelial ovarian serous carcinomas, the most common histologic subtype, actually originate in the distal fallopian tube has important implications for ovarian cancer prevention. The possibility that ovarian cancer could be prevented by removing the fallopian tubes at the time of other gynecologic surgeries (e.g., hysterectomy and tubal sterilization) is tantalizing. This approach, termed “opportunistic salpingectomy,” is defined as removing the fallopian tubes in low-risk women who have completed childbearing and are undergoing pelvic surgery for another indication. The practice is now becoming widespread in North America among gynecologists. Nevertheless, long-term studies on the effectiveness of this strategy for prevention of ovarian cancer are lacking. In addition, there are no data on the potential theoretical harms in terms of salpingectomy affecting ovarian blood supply and inducing premature menopause.

While the American Congress of Obstetricians and Gynecologists (ACOG) has yet to comment on the matter, the Society of Gynecologic Oncology (SGO) in the United States issued a statement in November 2013 that said, “For women at average risk of ovarian cancer, risk-reducing salpingectomy should also be discussed and considered with patients at the time of abdominal or pelvic surgery, hysterectomy, or in lieu of tubal ligation.”
They also recommend that pathologic evaluation include representative sections of the tube, any suspicious lesions, and entire sectioning of the fimbriae. Similarly, SGO’s counterpart in Canada stated that, “Due to its cancer prevention potential, it is recommended that physicians discuss the risks and benefits of bilateral salpingectomy with patients undergoing hysterectomy or requesting permanent, irreversible contraception.”

In 2010, gynecologic oncologists from the province of British Columbia in Canada began an educational initiative that informed general gynecologists about the role of opportunistic salpingectomy in ovarian cancer prevention. The investigators recommended that gynecologists 1) consider bilateral salpingectomy at the time of hysterectomy, 2) consider bilateral salpingectomy for permanent sterilization instead of tubal ligation, and 3) refer all women with high-grade serous cancer for genetic counseling and testing for BRCA 1/2 mutations. According to a recent report, from 2008 (before the initiative) to 2011 (after the initiative), hysterectomy with bilateral salpingectomy (BS) increased from 5% of all hysterectomies to 35%. Similarly, BS for sterilization increased from 0.5% to 33% of sterilization procedures. Among the 44,000 women included, a retrospective cohort analysis showed that the mean additional surgical time for BS with hysterectomy and BS for sterilization was 16 minutes and 10 minutes, respectively. While the authors reported that some of the sterilizations were postpartum, other than saying “most” were done at the time of cesarean, they did not mention more details. However, there were no differences between traditional hysterectomy and tubal ligation and hysterectomy with BS and sterilization with BS in terms of length of stay, blood transfusion, or hospital readmission even controlling for postpartum procedures. The authors plan to follow this cohort and population level rates of ovarian cancer in the province to determine whether these surgeries reduce the risk of future ovarian cancer, an analysis which may take 15-30 years.

While adding BS to hysterectomy or interval sterilization is feasible and does not seem to increase short-term complications, the effect of this routine practice on future ovarian function is unknown. Preliminary studies on this have been underpowered and too short in length (3-6 months postoperatively) to determine if any effect is apparent. It has been documented for some time that hysterectomy by itself can be associated with early menopause; therefore, adding bilateral salpingectomy may not have much of an additional impact. However, routine salpingectomy for sterilization is another story.

Tubal ligation, by itself, has been associated with reduced ovarian cancer incidence. Interestingly, recent studies have clarified that this protection seems to be limited to the endometriosis-related subtypes of ovarian cancer, clear cell and endometrioid. Removing the entire tube, therefore, may protect against all subtypes of epithelial ovarian cancer. In addition, some argue that bilateral salpingectomy is a superior sterilization technique compared to tubal ligation. Nevertheless, opting for bilateral salpingectomy rather than tubal ligation could have unforeseen consequences. In the short term, routine salpingectomy after delivery for sterilization may require larger incisions after vaginal delivery, and there may be more bleeding complications due to the engorged pelvic vessels. Even if limited to interval sterilization, bilateral salpingectomy may have an effect on future ovarian function. We just do not have any data on the long-term effects of routine BS for premenopausal women undergoing sterilization. For women at low risk of ovarian cancer, the risks of reduced ovarian function on cardiac health may outweigh the benefit of decreased ovarian cancer rates. Let’s not forget that cardiac disease is the number one cause of death among women.

Furthermore, where does this leave hysteroscopic sterilization? This is an innovation that moved sterilization into the office with its attendant convenience for women and decreased complications compared to laparoscopic sterilization. While some argue that given the required follow-up, the ultimate failure rate of hysteroscopic sterilization is higher than laparoscopic surgery, there is still a role for a sterilization procedure that does not require abdominal surgery. Ultimately, it will be up to the individual woman to decide which risks and benefits are most important to her based on her personal and family history when considering opportunistic salpingectomy. While it seems reasonable and safe to offer women BS who are undergoing hysterectomy or other pelvic procedures, women should be informed that there are no long-term data demonstrating that opportunistic salpingectomy reduces the risk of ovarian cancer or what the effects will be on ovarian function. While we anticipate that is the case and it seems logical, I wonder what the number needed to treat will be; in other words, how many women will have to undergo bilateral salpingectomy to prevent one case of ovarian cancer? This issue is evolving and more studies clearly need to be done before we have good answers for our patients. Nevertheless, it seems that everyone has already jumped on the bandwagon of opportunistic salpingectomy. Let’s hope that in 30 years, opportunistic salpingectomy is not revealed to be an unnecessary procedure.

REFERENCES
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CME QUESTIONS

1. Which of the following maternal characteristics is not associated with abruption?
   a. Advanced maternal age
   b. Preeclampsia
   c. Hypertension
   d. Obesity

2. Ultrasound will fail in detecting about one in five patients with placenta accreta.
   a. True
   b. False

3. When hypertension is eliminated from the analysis, only three variables remain statistically significantly associated with placental abruption. Which of the following is not a factor?
   a. Low PAPP-A
   b. High AFP
   c. Advanced maternal age
   d. High in inhibin-A

4. Which of the following is not true about procedures for prolapse and stress urinary incontinence?
   a. Uterosacral ligament suspension and sacrospinous ligament fixation have similar success rates.
   b. Uterosacral ligament suspension and sacrospinous ligament fixation have similar adverse events.
   c. The anterior vaginal wall is the most likely compartment to fail after uterosacral ligaments suspension or sacrospinous ligament fixation for apical prolapse.
   d. There is a clear role for perioperative pelvic floor physical therapy after surgery for prolapse and incontinence.

5. Limitations of the British Columbian study of the safety of prophylactic bilateral salpingectomy at the time of benign gynecologic surgery include:
   a. Case selection bias is likely, as the design was a retrospective cohort analysis.
   b. Information on costs associated with the surgical procedures was available only from Vancouver.
   c. Women who underwent bilateral salpingectomy at the time of cesarean section were included in the postpartum group.
   d. Obese women were not allowed to participate in the study.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:
• Explain the latest data regarding diagnosis and treatment of various diseases affecting women;
• Discuss new data concerning prenatal care, neonatal health, and complications arising in pregnancy and the perinatal period; and
• Discuss the advantages, disadvantages, and cost-effectiveness of new testing procedures in women’s health.