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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

Induction of Labor at 39 Weeks

By John C. Hobbins, MD

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

SYNOPSIS: The authors of an abstract presented at the annual meeting of the Society for Maternal-Fetal Medicine suggested that inducing low-risk obstetrical patients at 39 weeks is associated with significantly diminished rates of cesarean delivery and the need for neonatal respiratory support.

SOURCE: Grobman W. A randomized trial of elective induction of labor at 39 weeks compared with expectant management of low risk nulliparous women. Abstract from the Society for Maternal-Fetal Medicine. *Am J Obstet Gynecol* 2018;218(Suppl):S601.

Usually, clinical alerts in obstetrics and gynecology are generated from published reports that have been vetted through rigorous peer review, but this month I wanted to be out ahead of a media airing of an abstract that was published in the proceedings of the 2018 annual meeting of the Society for Maternal-Fetal Medicine in Dallas. The research was presented during the opening plenary session as a late-breaking paper that could affect the way obstetrics is practiced. William Grobman relayed the results of a randomized, clinical trial (RCT), supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, to determine if benefit could be accrued from empiric elective inductions at 39 weeks of gestation, rather than awaiting spontaneous delivery.

Low-risk nulliparous women with ultrasound-documented gestational ages were randomized at 38 weeks to have either an induction of labor (IOL) at 39/0 to 39/4 weeks or to forgo elective delivery until 40/5 weeks, but not past 42/2 weeks. The primary outcome studied was the incidence of adverse outcomes, and the secondary outcome variable was the cesarean delivery rate (CR). All patients had cervical Bishop scores at the time of enrollment.

Forty-one hospitals participated in the study. After exclusions were applied, 3,062 patients were allocated to the IOL group and 3,044 to the electively managed (EM) control group. Not surprisingly, the IOL group, on average, delivered earlier than the EM group, but by only four days (39/3 vs. 40/0 weeks; $P < 0.001$). There was a trend toward a lower rate of composite adverse neonatal outcomes in the IOL group (4.4% vs. 5.4%; 95% confidence interval [CI], 0.64-1.01). Although there was a significantly lower need for neonatal respiratory support

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in the IOL group (3.0% vs. 4.2%; 95% CI, 0.55-0.93), all other neonatal variables were similar between groups. On the maternal side, the CR was significantly lower in the IOL group (18.6% vs. 22.2%; 95% CI, 0.76-0.93), as well as the risk of preeclampsia and/or hypertension alone (9.1% vs. 14.1%; 95% CI, 0.56-0.74), with no difference in postpartum hemorrhage (4.6% vs. 4.5%).

■ COMMENTARY

This study could stand traditional obstetrical management on its head. The IOL had steadily crept up to 23.7% in 2011, but it leveled off to 23.3% the next year,[1] likely because of awareness of the unfortunate fallout of increased neonatal morbidity associated with unexpected prematurity in early-term deliveries. In 2009 and again in 2013, the American College of Obstetrics and Gynecology (ACOG) suggested that elective delivery by any route be delayed until 39 weeks.[2] Most published randomized studies comparing IOL with EM have dealt with patients who were post-term, but there were two non-randomized studies that alerted clinicians to a possible benefit of induction in low-risk patients at term.[3,4] In 2016, during a debate at the annual ACOG meeting regarding the efficacy of IOL vs. EM in term patients (39 to 40 weeks), both debaters, including the one assigned to be pro-EM (Dr. Charles Lockwood), concluded that the existing data pointed toward induction.[5] They and other authors have called for evidence via an RCT at 39 weeks. Well, here it is, and it deals with low-risk women, 63% of whom had unfavorable cervices by Bishop score — just the ones with whom we have been least likely to meddle. And, lo and behold, induction seems to improve outcomes, rather than creating morbidity.

You may have noticed from previous alerts that on occasion I have taken a nihilistic approach to various obstetrical management options, simply because, at times, Mother Nature appears to be smarter than we are. However, that same Mother Nature, who was responsible for the remarkable human brain, heart, and placenta, also brought us cancer. So maybe her timing of spontaneous labor in uncomplicated pregnancies is a bit off — certainly if the goal is to avoid perinatal complications. Another possibility is that our basic calculation for an estimated date of confinement (EDC) is flawed.

The EDC story started in 1744, with the Dutch professor Herman Boerhaave, who determined in 100 pregnant women that the average time of delivery occurred at 40 menstrual weeks. Later, this was highlighted by a German professor, Carl Naegele, in 1812, but it was never clear whether the starting point was the first day of the last menstrual period (LMP) or the last day. Naegele's rule later was adjusted so that clinicians would always use the first day of LMP, with 280 days being assigned as term.

The obvious problem with using LMP as a starting point are the errors in calculation caused by early or late ovulation. To weed out these confounders, ultrasound has been used to determine more precisely when the first day of the LMP "should have been."

Below is current information on pregnancy length based on either ultrasound documentation in the first trimester or precisely documented ovulations.

1. The average time of delivery in uncomplicated first-time pregnancy was 40/5 weeks (285 days) and in multiparous patients it was 40/3 weeks (283 days).[6,7]
2. By applying ultrasound dating, the rate of post-term pregnancies (≥ 42 weeks) was diminished from 10.3% in those with clinically "certain" LMP to 2.7%.[8] If the ultrasound was done between 11 and 14 weeks, 68% of patients delivered within 11 days of their EDCs.[9]
3. The fewest neonatal complications occurred between 39/0 weeks and 41/6 weeks.[10]

So, the age-old "wheel of fortune" carried in the coat pockets of providers is only a couple of days off in predicting EDC, and this information should not affect the meaning of the above featured study, done by some of the most respected investigators in the field.

A strong word of caution. Before we automatically endorse the concept of inducing every pregnant patient at 39 weeks, this information needs to be peer-reviewed formally, digested, and debated. Another RCT with similar results also would help. Although now the data certainly appear very compelling, individual circumstances vary and a preference for non-intervention from an informed patient always should be respected. ■

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ABSTRACT & COMMENTARY

Obesity and Prolapse: Are They Related?

By Chiara Ghetti, MD

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

SYNOPSIS: Women with a body mass index in the overweight and obese range are more likely to experience pelvic organ prolapse compared to women in the normal range.

SOURCE: Giri A, Hartmann KE, Hellwege JN, et al. Obesity and pelvic organ prolapse: A systematic review and meta-analysis of observational studies. *Am J Obstet Gynecol* 2017;217:11-26.e3.

The objective of this study was to systematically review existing evidence to summarize the association between pelvic organ prolapse (POP) and obesity as measured by body mass index (BMI), as well as to identify characteristics that can explain the variations in findings across studies. Eligible studies in this meta-analysis were in the English language, had a minimum of 40 subjects of any age, and were required to report effect estimates on the relationship between BMI categories and POP in women. Studies that included postsurgical trial outcomes were not included. The primary outcome for the meta-analysis was the presence of POP in any compartment as a dichotomous variable (yes, no). The authors identified 70 original research articles, of which 22 studies were eligible for the meta-analysis. Eligible articles were unique studies that reported risk ratios between categories of BMI and POP or provided data that allowed for calculation of risk ratios.

The 22 studies in the meta-analysis included more than 95,000 subjects and more than 17,000 cases of prolapse, of which 3,043 cases constituted clinically significant POP. Results demonstrated that compared to subjects in the normal weight BMI category, subjects in the overweight and obese categories had meta-analysis risk ratios of at least 1.54 (95% confidence interval [CI], 1.29-1.83) and at least 1.71 (95% CI, 1.42-2.06), respectively, if objectively measured, clinically significant POP was assessed. Subgroup analyses suggested that the associations between obesity and prolapse were stronger for objectively measured, clinically significant prolapse than for self-reported POP. The association between prolapse and obesity increases as BMI increases.

■ COMMENTARY

POP is a common condition with prevalence rates varying from 10-50% depending on the age group.[1-4] Risk factors for prolapse long have included genetic predisposition, vaginal delivery, parity, aging, and BMI. In a recent systematic review investigating the risk factors for prolapse, Vergeldt et al concluded that obesity was the only truly modifiable risk factor for prolapse.[5] In women who desire childbearing, obesity likely remains one of the only truly modifiable risk factors.

The authors of this systematic review and meta-analysis looked more deeply into the relationship between obesity and the risk of prolapse. Briefly, as defined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, a systematic review:

> … is a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyze and summarize the results of the included studies. Meta-analysis refers to the use of statistical techniques in a systematic review to integrate the results of included studies.[6]

Systematic reviews and meta-analyses are only as robust as the existing literature allows. The current study was limited by the dearth of prospective studies investigating the relationship between prolapse and BMI and the limited studies that met the authors' stringent criteria. In addition, the ways in which we have defined and documented

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prolapse have changed over the years, leading to variability throughout the studies. There are many unanswered questions about the effect of obesity on the development of prolapse, but despite limitations the authors found a positive significant relationship between obesity and prolapse.

BMI is calculated by the formula: weight (kg)/[height (m)]^2. Many of us have electronic medical records that automatically calculate BMI. As a reminder, BMI categories are defined as normal/healthy weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), class 1 obesity (30-34.9 kg/m^2), class 2 obesity (35-39.9 kg/m^2), and class 3 obesity or severe obesity (previously morbid obesity; > 40 kg/m^2). More than one-third of U.S. adults suffer from obesity.[7] Some estimates predict that 85% of adults will be overweight or obese by 2030 in the United States alone.[8]

By personal experience, certainly 50% of my patients are overweight or obese. This is an aspect of care we must face head-on and cannot ignore. Studies show that many obese patients receive mistreatment or are subjects of bias, discrimination, or shaming, even within physicians' offices. When I ask patients and family members about weight, they often relate they have been told to lose weight, but that is about it. Patients truly are eager to receive guidance. However, obesity counseling is one more aspect of care I do not feel trained to address. I recently set out to find resources to help me better discuss this chronic, multifactorial disease with patients.

I discovered that in 2015, Dr. Mark S. DeFrancesco, then ACOG president, developed the Wellness Work Group on Obesity; this work led to the development of an Obesity toolkit.[9] This wonderful online resource is available on ACOG.org and includes additional links to other resources such as the Why Weight? provider discussion tool kit developed by the STOP Obesity Alliance.[10] Resources such as these speak to the barriers and challenges providers face when addressing obesity, but also provide tools to start these difficult conversations, such as assessing patient readiness, developing communication strategies, setting realistic goals, and more. An obesity algorithm also is available through the Obesity Medicine Association.[11]

With so many diets on the market, patients frequently ask which diet is best. Just as I have been preparing this commentary, Garnder et al published the results of a randomized, controlled trial comparing low-fat to low-carbohydrate diets in the *Journal of the American Medical Association*.[12] They found that no one dietary strategy was superior, but concluded that dietary modification remains a key to successful weight loss. We don't have to get caught up in the small details of weight management recommendations. What I have distilled from some of the resources above is that taking a few minutes to open a discussion about weight in a warm, empathic way may allow us to return to the issue with more ease at each subsequent visit. Discussing obesity as a chronic disease can help frame our conversation and make it less threatening. By listening to patients' experiences, we may be able to better assess their awareness and readiness, and take small steps to help patients identify personal goals. You don't have to go at it alone. I have been fortunate to partner with the weight management program at our institution to provide patients with dietary and nutrition education, as well as formalized weight loss programs that span diet, medication, and surgery. Your hospital or institution likely has similar resources.

We all know about the morbidity and mortality associated with obesity and the increased risk of hypertension, coronary artery disease, diabetes, cancer, sleep apnea, just to name a few.[13] Based on this study, we now can add POP to the many risks associated with obesity. As women's healthcare providers, we are uniquely poised to help women make strides in grappling with this chronic, debilitating disease throughout many critical life stages. ■

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ABSTRACT & COMMENTARY

Breast MRI Exams Increase the Biopsy Rate Without Improving Cancer Detection

By Jeffrey T. Jensen, MD, MPH

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Dr. Jensen reports he is a consultant for and receives grant/research support from Bayer, Merck, ContraMed, and FHI360; receives grant/research support from Abbvie, HRA Pharma, Medicines 360, and CONRAD; and is a consultant for the Population Council.

SYNOPSIS: Compared to women who undergo breast cancer screening with mammography alone, those receiving MRI exams experience a two- to fivefold increased rate of core and surgical biopsy. However, the biopsies have a lower cancer yield rate than mammography alone.

SOURCE: Buist DM, Abraham L, Lee CI, et al. Breast biopsy intensity and findings following breast cancer screening in women with and without a personal history of breast cancer. *JAMA Intern Med* 2018; Feb. 12. doi: 10.1001/jamainternmed.2017.8549. [Epub ahead of print].

Women's health providers must help patients make decisions on preventive health care, including cancer screening. An improved understanding of the biology of cervical cancer has allowed us to better focus our screening efforts on molecular testing, and women have benefited from the improved precision and reduction in screening interval. However, no such progress has occurred with respect to breast cancer screening. Since 2015, many states have passed laws requiring notifying women with dense breasts of limitations of mammography. This has greatly increased the use of supplemental testing, such as ultrasound and magnetic resonance imaging (MRI). However, few studies have evaluated the population benefits and risks of additional screening.

To better inform this debate, Buist and colleagues performed an observational cohort study of six Breast Cancer Surveillance Consortium registries (Carolina Mammography Registry [North Carolina], Kaiser Permanente Washington Registry [Washington State], Metro Chicago Breast Cancer Registry, New Hampshire Mammography Network, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System) that included a population-based sample of 812,164 women undergoing screening between 2003 through 2013. The primary objective of the study was to compare mammography screening alone to MRI (with or without mammography) and evaluate biopsy rates and yield in the 90 days following screening. The authors evaluated biopsy intensity (fine needle aspiration) and biopsy result within biopsy intensity (benign, high-risk benign, ductal carcinoma in situ [DCIS], or invasive), adjusting for demographic and facility characteristics, and stratified results by screening episode type and personal history of breast cancer (PHBC).

Women in the population sample underwent a total of 2,048,994 breast screening episodes during the study period: 101,103 and 1,939,455 in women with and without PHBC, respectively. This sample included 8,436 women who received an MRI (3,763 with PHBC, 4,673 without PHBC).

Compared to mammography alone (23.6; 95% confidence interval [CI], 22.4-24.8), age-adjusted core and surgical biopsy rates (per 1,000 episodes) doubled following MRI exams among women with PHBC (57.1; 95% CI, 50.3-65.1) and increased more than fivefold in women without PHBC (from 14.9 [95% CI, 14.7-15.0] to 84.7 [95% CI, 75.9-94.9]). However, the increased intensity of screening did not increase the biopsy yield in high- or average-risk women. The DCIS and invasive biopsy yield actually was significantly higher following mammography (404.6; 95% CI, 381.2-428.8) compared with MRI (267.6; 95% CI, 208.0-337.8) in women with a PHBC, and nonsignificantly higher, but in the same direction, in women without PHBC (mammography, 279.3 [95% CI, 274.2-284.4]; MRI, 214.6, [95% CI, 158.7-280.8]). MRI did increase the detection of high-risk benign lesions regardless of PHBC. The higher biopsy rates and lower cancer yield following MRI were not explained by increasing age or higher five-year breast cancer risk.

Overall, these results add to a growing literature on the potential harms of breast cancer screening. Based on the absence of benefit, the authors suggested that clinicians counsel women that, when compared to mammography alone, undergoing a screening MRI increases their risk of undergoing an unnecessary core or surgical breast biopsy.

■ COMMENTARY

I am bothered by the trend in medicine to use additional imaging as the solution to diagnostic uncertainty. When I teach students, I remind them that imaging is not treatment. Prior to ordering any test, the clinician must consider the expected results and actions. Great clinicians understand the risks and limitations of testing, and communicate pros and cons to patients in understandable language. The highly emotional subject of breast cancer screening requires clear discussion of potential harms as well as benefits.

Last year, the U.S. Preventive Services Task Force published updated guidelines for breast cancer screening,[1] recommending biennial screening mammography for all women aged 50 to 74 years. For women younger than 50 years of age, the recommendation for screening mammography received a "C" grade (moderate certainty that the net benefit of screening, while positive, is small). As we have discussed previously in *OB/GYN Clinical Alert*, the decision to undergo screening more frequently than every other year or before age 50 requires an evaluation of potential benefits and harms.[2] Harms include the risk of undergoing an invasive procedure that does not result in an improved outcome following a supplemental screening tests. In a recent review, Nelson et al considered potential harms to include both false-positive and false-negative imaging results, "overdiagnosis," anxiety and other psychological responses, pain during procedures, and radiation exposure.[3] They defined overdiagnosis as a diagnosis of DCIS or invasive breast cancer considered unlikely to become clinically important in the women during their lifetime in the absence of screening. Keep in mind that there is no consensus definition of overdiagnosis, and it is difficult to determine the significance of a breast cancer diagnosis to an individual woman. Our goal is not to increase the detection of breast cancer, but to reduce breast cancer mortality, so all screening tests must be evaluated by this metric.

The current study by Buist et al adds to our understanding of the effect of supplemental MRI screening for breast cancer detection. Women who underwent an MRI were more likely to undergo an invasive biopsy, but these biopsies were less likely to yield a diagnosis of DCIS or invasive cancer. Low-risk women without a PHBC had the lowest biopsy yields. We would term these "false-positive" screening tests. Women receiving negative results generally feel relieved, but do they benefit from additional screening? Researchers have estimated that with current breast cancer treatment protocols, 3,448 women need to be screened to prevent one breast cancer death.[4] For each breast cancer death prevented, three women receive an overdiagnosis of a nonfatal cancer and undergo surgery (including mastectomy) and/or medical treatments.[5] In other words, as we increase breast cancer screening, we tend to increase overdiagnosis, magnifying screening costs without affecting the risk of breast cancer death.

Every medical school, including my own, wants to market itself as a "Cancer Center." Battling cancer should be a major goal for medical science. Unfortunately, I see much of the effort centered on new diagnostic modalities that are not treatment. We seduce the public with the prospect of advanced imaging, robotics, and personalized medicine. Not surprisingly, they expect miracles. As clinicians, we need to help our patients negotiate the false (or premature) claims. Cautioning women with dense breasts that additional screening with MRI will increase their risk of undergoing an invasive biopsy procedure, but not significantly decrease their risk of breast cancer mortality, requires time and effort, but is our responsibility. ■

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ABSTRACT & COMMENTARY

The Latest in Genetic Screening for Gynecologic Malignancies

By Molly A. Brewer, DVM, MD, MS

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

SYNOPSIS: Genetic testing is changing rapidly. With the advent of more sophisticated genetic mutation panels, it is important that providers of women's healthcare consider appropriate referral and testing for those women at increased risk of malignancy.

SOURCE: Ring KL, Garcia C, Thomas MH, Modesitt SC. Current and future role of genetic screening in gynecologic malignancies. *Am J Obstet Gynecol* 2017;217:512-521.

With the advent of new panels screening for genetic oncologic mutations and as first-line clinicians for women, gynecologists need to be aware of the changes that have occurred over the last two years in genetic testing. As outlined by Ring et al, the current recommendation is panel testing for women with a strong family history of gynecologic cancers, such as ovarian or endometrial cancer, and a personal history of breast, ovarian, or endometrial cancer. Since Myriad Genetics lost its patent on the BRCA genes,[1] many companies now offer genetic panels that test for a number of genes that only recently have been associated with gynecologic and breast cancers. Even five years ago, ovarian cancer was thought to be associated only with a deleterious germline mutation 5-10% of the time. As these authors note, approximately 24% of ovarian cancers are associated with a germline mutation.[2] Unfortunately, there still is not consistent identification of women at risk for germline mutations nor consistent referral for testing for these mutations.[3]

Although BRCA1 and BRCA2 are the more commonly recognized gene mutations, multiple other pathways may carry germline mutations leading to gynecologic cancers. One pathway leads to acquisition of Lynch syndrome (also known as hereditary nonpolyposis colorectal cancer). Lynch syndrome is responsible for approximately 15% of hereditary ovarian cancers, which often histologically are endometrioid or clear cell cancers. These women are at increased risk of colorectal, endometrial, gastric, small bowel, genitourinary, pancreatic, and glioblastoma cancers. Approximately 8% of all endometrial cancers are associated with Lynch syndrome.

In addition to BRCA1 and BRCA2 mutations, other mutations of DNA repair pathways affect RAD51C, RAD51D, and BRIP1, which may carry a 10% lifetime risk of ovarian cancer.[4] PALB2 and BARD1 are associated with an increased risk of breast cancer, but have not been associated with ovarian cancer.

Another identifiable oncologic gene mutation is the one associated with PTEN (Cowden syndrome). Women with these mutations have up to a 28% risk of endometrial cancer as well as hamartomas, which usually are benign lesions. POLD1, which works with the Lynch syndrome genes, has an increased risk of both endometrial and colon cancer.[5] Women with a BRCA1 mutation have an increased risk of serous endometrial cancer.[6] Women with adenoma malignum of the cervix may have Peutz-Jeghers syndrome, and young women with rhabdomyosarcoma may carry a DICER1 mutation. These women should be considered for genetic testing. These are all examples of gynecologic cancers associated with identifiable gene mutations.

■ COMMENTARY

So how can women's health providers keep these new germline mutations straight? The most important aspect of patient care in a suspected patient is to take a careful family history and make appropriate referrals to one of several practitioners, depending on the individual's needs.[7] If you have access to a cancer genetic counselor, it is more appropriate to refer patients for genetic counseling and appropriate testing, because genetic counselors are more up-to-date on what to test for as well as how to counsel patients.

Barriers to genetic testing are mainly due to the lack of consistent information on the importance of genetic testing.[8] If you do not have access to genetic counselors, panel testing is a reasonable alternative. However, prior to making treatment recommendations, it would be prudent to seek help about how to counsel patients on interpretation of the test results. A surgical oncologist can better counsel on appropriate breast cancer strategies and a gynecologic oncologist can better counsel on appropriate gynecologic strategies. Removing a woman's ovaries and tubes before she has children probably is not in the patient's best interest, even if her gene panel is positive. This requires delicate counseling and screening recommendations. However, increased screening may be appropriate for both breast and ovarian cancer, depending on the mutation discovered.

One of the errors I see routinely is the referral of a patient with a mutation that is considered a variant of uncertain significance for prophylactic surgery. It is not appropriate to recommend prophylactic surgery unless the variant is reclassified as a deleterious mutation. Again, this is better managed with the help of genetic counselors who routinely communicate with the companies that follow these mutations and reclassify those mutations as deleterious if they track with clusterings of cancer. If they are reclassified as benign polymorphisms, then the patient not only does not need prophylactic surgery, she does not need increased surveillance.

The world of cancer-associated mutations has changed dramatically in the last 10 years and we expect it to continue to do so. To keep up with new findings, it is important to have a relationship with a genetic counselor and a gynecologic oncologist who can help sort through these new changes. ■

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CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. The rate of which of the following was unchanged in patients electively induced at 39 weeks?
a. Postpartum hemorrhage
b. Cesarean delivery
c. Need for neonatal respiratory support
d. Hypertension/preeclampsia

2. Based on the study by Giri et al, which of the following statements is true?
a. Obesity is not associated with the development of pelvic organ prolapse.
b. Obesity is a not a modifiable risk factor for pelvic organ prolapse.
c. Obesity should not be of concern to obstetrician gynecologists.
d. Obesity is strongly associated with pelvic organ prolapse and this association increases as BMI increases.

3. Compared to women undergoing breast cancer screening with mammography alone, results for women who undergo MRI screening include which of the following?
a. A reduction in false-positive exams that lead unnecessary biopsies in high-risk women
b. A decrease in breast cancer mortality in women with dense breasts
c. A higher rate of invasive biopsy procedures, but lower detection rate of DCIS and/or invasive cancer
d. A lower rate of invasive biopsy procedures, but higher detection rate of DCIS and/or invasive cancer

4. Ovarian cancer is associated with a deleterious mutation:
a. 100% of the time.
b. 10% of the time.
c. 24% of the time.

CME/CE 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.

[IN FUTURE ISSUES]

Special Feature: Update on Managing Early Pregnancy Loss