

“IS POPULATION-BASED SCREENING FOR ENDOMETRIAL CANCER FEASIBLE?”

ANDREW M. KAUNITZ, MD
(EXAMINING THE EVIDENCE; APRIL 2011)

In endometrial cancer, timely treatment is as vital as early detection

Dr. Kaunitz’s commentary reminded us how vital early detection of endometrial cancer is, especially recurrent cancer. We had a 54-year-old postmenopausal African-American patient (G2P2002) come to our medical school clinic complaining of severe abnormal bleeding, with clots, of 2 months’ duration. Pelvic ultrasonography (US) revealed an endometrial thickness of 1.1 cm, and a biopsy detected complex atypical hyperplasia with areas of invasive adenocarcinoma. We referred the patient to a gynecologic oncologist, who performed total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and peritoneal washings. The final pathology report revealed stage 1c grade II adenocarcinoma. Because of the deep myometrial invasion and grade II lesion, adjuvant radiation therapy was recommended, but the patient declined it and failed to follow up with regular examinations.

Five years later, the patient was back, saying, “Doctor, my cancer has recurred.” She said she could feel a mass in her vagina—a mass she had noticed 18 months earlier! Now that she was symptomatic, with rectal pressure, vaginal bleeding, and pain, she was seeking medical attention.

On examination, a crowning 8-cm mass distended the vagina. The mass was tender and hemorrhagic and obliterated the vagina. A biopsy revealed grade II endometrioid adenocarcinoma, consistent with the previous endometrial adenocarcinoma. Because the mass was not



APRIL 2011

resectable, the patient was referred for radiation therapy and chemotherapy.

Twenty percent of women who have endometrial cancer experience recurrent disease, usually within 24 to 36 months.^{1,2} Recurrence is the detection of disease more than 3 months after successful extirpative therapy.³ When disease is detected before 3 months, it is considered persistence of the original disease. Recurrence usually portends a poor prognosis if the disease is disseminated.³ The most common site of recurrence is the vaginal cuff.^{2,4} Postoperative radiotherapy can reduce this risk.⁴

In 1994, Rose and colleagues found an elevated CA 125 level in as many as 87% of women who had recurrent disease.⁵ In fact, CA 125 was elevated in women even before a recurrence could be identified, regardless of stage.⁵ Approximately 94% of women who had an elevated CA 125 level at recurrence had an initial preoperative CA 125 that was elevated.⁵ Therefore, CA 125 may be useful in predicting which patients are at risk of recurrence.⁵

In this case, the patient is still

alive and receiving chemotherapy.

With an early diagnosis and treatment and appropriate follow-up, endometrial cancer can be a curable disease.

Daniel M. Avery Jr, MD

Marion D. Reed, MD

J. Michael Straughn Jr, MD

University of Alabama School of Medicine
Tuscaloosa, Ala

References

1. Rotman M, Aziz H, Halpern J, Schwartz D, Sohn C, Choi K. Endometrial carcinoma. Influence of prognostic factors on radiation management. *Cancer*. 1993;71(4 suppl):1471-1479.
2. Sugimura K, Okizuka H. Postsurgical pelvis: treatment follow-up. *Radiol Clin N Am*. 2002;40(3):659-680.
3. Chi DS, Barakat RR. Surgical management of advanced or recurrent endometrial cancer. *Surg Clin North Am*. 2001;81(4):885-896.
4. Johnson N, Cornes P. Survival and recurrent disease after postoperative radiotherapy for early endometrial cancer: systematic review and meta-analysis. *BJOG*. 2007;114(11):1313-1320.
5. Rose PG, Sommers RM, Reale FR, Hunter RE, Fournier L, Nelson BE. Serial serum CA 125 measurements for evaluation of recurrence in patients with endometrial carcinoma. *Obstet Gynecol*. 1994;84(1):12-16.

“HOW TO IMPROVE OUTCOMES IN GESTATIONAL DIABETES—FOR MOTHER AND BABY”

E. ALBERT REECE, MD, PHD, MBA
(MARCH 2011)

Management of GDM isn’t always straightforward

I have several questions regarding some points in Dr. Reece’s article:

A 1-hour postprandial finger-stick glucose level of 130 mg/dL was mentioned as the cutoff for initiation of treatment. Is that cutoff the more widespread and accurate limit (rather than 140 mg/dL at 1 hour)? Do we have trials supporting this change?

I did not notice any mention of hemoglobin A1c (HbA_{1c}) in the article. Most clinicians use an HbA_{1c} level of 6% and below as the goal for gestational diabetes mellitus (GDM). However, I had a patient

whose HbA_{1c} consistently remained below 5%, but her fingerstick glucose exceeded 140 mg/dL at 1 hour more than 50% of the time, so I treated that hyperglycemia.

Do we have guidelines or data addressing the question of whether it is postprandial high glucose levels that are responsible for the morbidities of GDM rather than the average level, i.e., HbA_{1c}? Before HbA_{1c} came into use, I think that most of us treated the glucose level determined by fingerstick, even if the 3-hour test was negative, if the history and suspicion of GDM suggested that we should.

I hope that Dr. Reece can enlighten us on these points.

Dennis Fito, MD
Liberal, Kan

» Dr. Reece responds

Traditionally, a 1-hour postprandial blood glucose level ≥ 140 mg/dL has been used as the cutoff for the diagnosis of GDM. However, the ongoing management of a woman given a diagnosis of GDM is a different issue. In the typical management scheme, to which I believe Dr. Fito is referring, if a patient is able to maintain her blood glucose level below 130 mg/dL on diet alone, then no further medical intervention is necessary other than third-trimester measurement of fetal abdominal circumference.

However, if a woman with previously diagnosed GDM has a fasting plasma glucose level ≥ 95 mg/dL or a 1-hour postprandial glucose level ≥ 130 mg/dL, after attempts have been made to control her blood sugar using dietary management, then insulin or another type of antihyperglycemic therapy should be initiated.

There is ample evidence that women who have glucose challenge test results of 130 to 139 mg/dL are at increased risk of perinatal morbidity

and, therefore, need to be managed more aggressively than they have traditionally been managed.^{1,2}

As for HbA_{1c}, it is a valuable tool for monitoring glycemia over a period of time, but it is not currently recommended for the screening or diagnosis of diabetes, including GDM. Because HbA_{1c} levels are not influenced by daily fluctuations in the blood glucose concentration but reflect the average glucose level over the previous 6 to 8 weeks, it is not surprising that Dr. Fito found a discrepancy between a patient's HbA_{1c} readings and the fingerstick readings.

The HbA_{1c} level is useful for monitoring the effects of diet, exercise, and drug therapy on blood glucose in diabetic patients. If the HbA_{1c} level is less than 7% of total hemoglobin, it means the patient is being managed well. Indeed, it has been demonstrated that the complications of diabetes can be delayed or prevented if the HbA_{1c} level can be kept close to 7% or below.³

References

1. Cheng YW, McLaughlin GB, Esakoff, TF, Block Kurbisch I, Caughey AB. Glucose challenge test: screening threshold for gestational diabetes mellitus and associated outcomes. *J Matern Fetal Neonatal Med.* 2007;20(12):903-908.
2. Gumus II, Turhan NO. Are patients with positive screening but negative diagnostic test for gestational diabetes under risk for adverse pregnancy outcome? *J Obstet Gynaecol Res.* 2008;34(3):359-363.
3. Lapolla A, Dalpra MG, Fedele D. Pregnancy complicated by diabetes: what is the best level of HbA_{1c} for conception? *Acta Diabetol.* 2010;47(3):187-192.

“FDA WARNS: DON'T USE TERBUTALINE FOR PRETERM LABOR”
(WEB EXCLUSIVE; FEBRUARY 2011)

Terbutaline has a long history in obstetrics

What is the Level-1 evidence that brought the FDA to the conclusion that terbutaline is unsafe for preterm labor? The drug has been used by many physicians for decades without

any untoward events in the communities in which I have practiced—namely, in New York, New Jersey, and Connecticut. The dosages we used were less than those used by an internist and the duration of use was typically short.

Charles Bowers Jr, MD
Springfield, NJ

» The editors respond

According to the FDA, “The decision to require a Boxed Warning and Contraindication is based on the FDA’s review of post-market safety reports of heart problems and even death associated with terbutaline use for obstetric indications, as well as data from medical literature documenting the lack of safety and effectiveness of terbutaline for preventing preterm labor, and animal data suggesting potential risks. Based on this information, the FDA concluded that the risk of serious adverse events outweighs any potential benefit to pregnant patients for either prolonged use of terbutaline injection beyond 48–72 hours or use of oral terbutaline for prevention or treatment of preterm labor.¹

“These changes to the drug labeling are consistent with statements from the American College of Obstetricians and Gynecologists discouraging use of terbutaline for preventing preterm labor.”¹

Note, however, that it is acceptable to use terbutaline for the management of patients who have preterm labor while they are completing a course of glucocorticoids (48 hours), and for the acute treatment of tachysystole when the fetal heart rate tracing is abnormal.

Reference

1. FDA warns against certain uses of asthma drug terbutaline for preterm labor [news release]. U. S. Food and Drug Administration; February 17, 2011. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm243840.htm>. Accessed April 14, 2011.