"THE FDA'S REVIEW OF THE DATA ON OPEN POWER MORCELLATION WAS INADEQUATE"
WILLIAM H. PARKER, MD
(AUDIO; NOVEMBER 2014)

Why is traditional open myomectomy acceptable if power morcellation isn't?

The actions taken by the US Food and Drug Administration (FDA) and medical device companies to limit use of power morcellation have effectively led to a halt in the use of minimally invasive surgery for removal of large uterine fibroids. This would seem to leave open laparotomy as the only viable choice for the conservative removal of these benign tumors in women who choose to retain their uterus for personal, cultural, or childbearing reasons. Or does it?

Any open myomectomy of an intramural or subserosal myoma involves an incision into the uterine serosa and muscularis, thus exposing the surface of the tumor to the peritoneal environment. The mass is then grasped with penetrating instruments and manipulated free of its myometrial attachments with other instruments such as forceps, scissors, and electrocautery devices. Suction instruments are freely employed over the operative field. The gloved digits of the surgeon are frequently used to bluntly dissect the tumor from the surrounding myometrial bed.

Because of the desire to maximize future fertility potential by minimizing adhesions, frequent irrigation is considered by most reproductive surgeons to be a necessary part of good surgical technique. Irrigation hydrates the tissues and carries away blood, but it can be counted on to disperse countless cells from the exposed surface of the tumor. After resection, the tumor is removed from the operative field and handed

NOVEMBER 2014

off, usually to the gloved hand of an assistant who will be handling all of the tools that are used from that point forward. If an abscess is a "dirty case" from the standpoint of the spread of infection, then any myomectomy is a potentially "dirty case" from the standpoint of the spread of neoplasia. Given the fundamental nature of this procedure, there seems to be no way to do a "clean" myomectomy.

Since any form of myomectomy involves at least as much manipulation of the tumor mass as morcellation, it should be at least as likely as morcellation to spread aberrant cells. An inadvertent exposure of the unprotected surface of a leiomyosarcoma at the time of a traditional open myomectomy is not different in any essential way from the exposure of the surface of the same tumor at the time of a myomectomy followed by any type of morcellation.

It is logical then that if morcellation can be proscribed by regulation and litigation, myomectomy itself will be proscribed on the exact same lines of reasoning.

Despite the widespread use of either abdominal or minimally invasive myomectomy over the last 75 years, disseminated uterine leiomyosarcoma is now and always has been a rare disease. This fact has always been accounted for in our risk assessments of leiomyoma surgeries. In addition, there is no scientific evidence that power morcellation, nonpowered morcellation, or abdominal myomectomy without morcellation has ever been causative in the spread of even one patient's leiomyosarcoma. Leiomyosarcoma is by definition capable of disseminating by itself.

No medical authority would recommend total hysterectomy for every patient with any myoma, based on the possibility that any individual patient might be harboring a uterine cancer that can spread. This is, however, the exact evolutionary endpoint of the reasoning of the FDA and our legal system. The device companies are to be the deep pockets of the morcellation lawsuits and physicians will be the deep pockets of future myomectomy lawsuits. Gynecologists have always considered risk/reward factors in decisions regarding myomectomy and morcellation. We have an obligation to defend the reproductive rights of our patients. Lawyers, regulators, and even the corporations that dominate the medical device market are motivated by other concerns.

The practice of modern medicine aggressively challenges clinical decision-making based solely on anecdotal evidence. It has done so for well over a century now. It is one of the few standards that still unites good doctors under the battered and tattered umbrella of our professionalism. Our challenge as modern physicians is to stand fast against our new regulatory masters (as well as

their former and future law partners) with their grave misunderstandings of the very character of gynecologic decision-making.

Michael C. Doody, MD, PhD
Knoxville, Tennessee

"THE EXTRACORPOREAL C-INCISION TISSUE EXTRACTION (EXCITE) TECHNIQUE"
MIREILLE D. TRUONG, MD, AND ARNOLD P. ADVINCULA, MD (VIDEO; NOVEMBER 2014)

Awesome video!

I tried this technique as outlined in the video—totally awesome! It worked really well! Thanks to the surgeons who came up with it!

Ravindhra Mamilla, MD
Thief River Falls, Minnesota

"HOW USEFUL IS RANDOM BIOPSY WHEN NO COLPOSCOPIC LESIONS ARE SEEN?"
ANDREW M. KAUNITZ, MD (EXAMINING THE EVIDENCE; OCTOBER 2014)

Additional clarification would be appreciated

According to Dr. Kaunitz's summary of the findings of Huh and colleagues,[1] the population group included women with low-grade squamous intraepithelial lesions (LSIL) or high-grade squamous intraepithelial lesions (HSIL) (ie, anything above atypical cells of undetermined significance [ASCUS]), along with women who tested positive for human papillomavirus (HPV) 16/18, regardless of cytology.

It would have been useful to have the LSIL and HSIL populations (independent or dependent of HPV status) broken down into subgroups.

The expert commentary does not indicate whether the 2.7% of biopsy-proven cervical intraepithelial neoplasia (CIN) 2 and CIN 3 were predominantly confined to women with HSIL or equally prevalent in the LSIL population.

Without this information, I am not convinced that LSIL requires a random biopsy when colposcopy is adequate and normal, regardless of HPV status.

Jonathan Kew
Maitland, New South Wales, Australia

Reference

1. Huh WK, Sideri M, Stoler M, Zhang G, Feldman R, Behrens CM. Relevance of random biopsy at the transformation zone when colposcopy is negative. Obstet Gynecol. 2014;124(4):670–678.

Are we reverting to past practices?

For someone who has done colposcopy for about 35 years, I find the conclusions of Huh and colleagues nonsensical. If the squamocolumnar junction is visible and an endocervical curettage is done, this is adequate. Performing random biopsies takes us back to the days before we had the colposcope. I was there, and I'm not proud of how we handled abnormal Pap results.

Another issue: If you find severe dysplasia on random biopsy in a 40-year-old woman, how and what do you treat? Is this a case of treating the lab and not the patient? Or is this a case of inadequately trained gynecologists and/or pathologists?

Anton Strocel, MD
Grand Blanc, Michigan

›› Dr. Kaunitz responds

I thank Dr. Kew and Dr. Strocel for their interest in this commentary on the value of random biopsies during colposcopy when lesions are not visualized. Dr. Kew is correct that the authors did not separate findings in women with low-grade versus high-grade intraepithelial cytology. Dr. Strocel refers to the value of clinical experience when performing colposcopy. Both the current article by Huh and colleagues,[1] as well an earlier high-quality report by Gage and colleagues,[2] point out that, even in skilled hands, colposcopy is not as sensitive in detecting CIN as we have believed in the past. These reports present convincing evidence that, regardless of clinical experience, when no lesion is seen at the time of colposcopy, performing one or two random biopsies substantially increases diagnostic yield of clinically actionable (CIN 2 or worse) disease.

References

1. Huh WK, Sideri M, Stoler M, Zhang G, Feldman R, Behrens CM. Relevance of random biopsy at the transformation zone when colposcopy is negative. Obstet Gynecol. 2014;124(4):670–678.
2. Gage JC, Hanson VW, Abbey K, et al. Number of cervical biopsies and sensitivity of colposcopy. Obstet Gynecol. 2006;108(2):264–272.

"CONJUGATED ESTROGEN PLUS BAZEDOXIFENE—A NEW APPROACH TO ESTROGEN THERAPY"
ANNE A. MOORE, DNP, APN
(CASES IN MENOPAUSE; OCTOBER 2014)

Why not encourage soy intake?

Thanks for an interesting discussion on conjugated estrogen/bazedoxifene (CE/BZA; Duavee). I note that:

- CE/BZA is manufactured by Pfizer
- Dr. JoAnn Pinkerton, who is interviewed by Anne Moore, DNP, APN, is affiliated with Pfizer, and
- CE/BZA costs $120 per month.

Since menopausal symptoms are caused by the decreased production of ovarian estradiol, why not prescribe estradiol 0.5–1 mg, which costs only $4 monthly?

Another point to consider: Over several decades of providing care to ethnically diverse women, my observation is that Japanese/Korean and Latina women report far fewer hot flushes than their white sisters.

CONTINUED ON PAGE 24

CONTINUED FROM PAGE 14

I believe that it is because of their soy and yam intake. I personally eat about 0.25 lb of tofu per week. It can be diced for salad or soup or served with soy sauce, ginger, and bonito (fish) flakes. It can also be crushed and mixed with lean ground beef, pork, chicken, or turkey to make lean, healthy meatloaf.

Tofu is rich in phytoestrogens, lowers cholesterol, and promotes local soy farmers—a win-win situation.

Yasuo Ishida, MD
St. Louis, Missouri

›› Dr. Barbieri responds

Dr. Ishida raises an important issue of managing conflicts of interest in medical publications. Dr. Ishida notes that, in the past, Dr. Pinkerton was supported by Pfizer, the company that manufactures (CE/BZA, Duavee). Dr. Ishida also points out that, in a recent OBG Management article, Dr. Pinkerton provided her clinical perspective on the use of CE/BZA in practice.

Often, with a new medication, the physicians with the most expertise in using it have helped with key clinical trials. The results of these trials provide the basis for FDA approval of the medication. Prior to FDA approval of a drug, only experts involved in the clinical trial have first-hand experience with the new treatment.

Dr. Pinkerton is an internationally respected expert in the field and provided a balanced overview of CE/BZA and how it might be used in practice. Dr. Pinkerton disclosed that she personally receives no current support from Pfizer, but that she was supported by Pfizer years ago.

This potential conflict of interest was reported in the article.

›› Dr. Pinkerton responds

I am proud to serve as a key researcher, consultant, and writer for publications exploring the newest hormonal option for menopausal women—CE/BZA. All of my contracting and fees for my research and consulting with Pfizer have been paid through the University of Virginia, not to me personally. This allows me to be involved in innovative women's health research and disseminate results without the same conflicts as those who receive reimbursements directly from Pfizer. My relationship to any pharmaceutical company with which I am involved is always through my university and disclosed on every paper, presentation, and talk that I give.

The best way to learn about the pros and cons of a product is to be involved in the sentinel research, to

CONTINUED ON PAGE 45

This space has purposely been left blank.

CONTINUED FROM PAGE 24

have access to all data, including adverse effects, and to be able to evaluate who might be the best candidates for a new product in women's health.

Although oral estradiol is inexpensive, women with a uterus also need a progestogen to protect against uterine cancer. *It appears that the combination of estrogen and synthetic progestins carry a greater risk of breast cancer than estrogen alone. Estradiol is also available as a patch, gel, lotion, and ring but, again, needs to be paired with a progestogen if a woman has a uterus.*

This new drug is well established in published randomized clinical trial data *as an effective alternative to traditional estrogen-progestogen therapy (EPT) in symptomatic postmenopausal women with a uterus. Results from Selective Estrogens, Menopause, and Response to Therapy (SMART)[1] randomized controlled trials (RCTs) have shown improvements in symptoms similar to those seen with EPT. These include a reduction in hot flash frequency and severity; a reduction in night sweats, with fewer sleep disruptions; and bone loss prevention. The effects on total cholesterol (an increase in triglycerides) and the drug's mild effect on vulvovaginal atrophy (VVA) also are similar to those observed with EPT. The drug has a neutral effect on breast tenderness, breast density, and the risk of breast cancer.[1,2] It also protects against endometrial hyperplasia and cancer and increases amenorrhea rates. VTE and stroke risks are expected to be similar to traditional oral hormone therapy (HT). The major benefit of CE/BZA, compared with traditional EPT, is the lack of significant breast tenderness and changes in breast density or vaginal bleeding often seen with traditional EPT.[3]*

As for the benefits of soy for menopausal women, *clinical data imply that phytoestrogens and soy foods may be of benefit for postmenopausal women. According to a recent review article by Messina[4] (an international authority on phytoestrogens), isoflavone supplements relieve menopausal hot flashes if they have enough of the isoflavone genistein. Soy has shown benefits with regard to ischemic heart disease—by lowering low-density lipoprotein (LDL) levels and providing a source of omega fatty acids. However, no clear effect has been seen with soy for the prevention of bone loss. The effect on breast cancer risk is unclear. Soy binds to estrogen receptors, which could be harmful. However, soy may bind preferentially to estrogen-receptor beta, thus acting more SERM-like or protective, particularly if given during childhood or adolescence.*

For any woman, the decision about using a food source, such as tofu, or isoflavone-rich supplements, such as one containing equol, should be based on a discussion with her clinician regarding her individual needs and the risks and benefits of all options.

In our Midlife Clinic at University of Virginia, we discuss over-the-counter products, lifestyle and dietary changes, and nonhormonal and hormonal options with our patients to help them identify the best choices.

References

1. Pinkerton JV, Harvey JA, Pan K, et al. Breast effects of bazedoxifene-conjugated estrogens: a randomized controlled trial. Obstet Gynecol. 2013;21(5):959–968.
2. Harvey JA, Pinkerton JV, Baracat EC, et al. Breast density changes in a randomized controlled trial evaluating bazedoxifene/conjugated estrogens. Menopause. 2013;20(2):138–145.
3. Pinkerton JV, Pickar JH, Racketa J, Mirkin S. Bazedoxifene/conjugated estrogens for menopausal symptom treatment and osteoporosis prevention. Climacteric. 2012;15(5):411–418.
4. Messina. Soy foods, isoflavones, and the health of postmenopausal women. Am J Clin Nutr. 2014;100 (Suppl 1):423S–430S.

This space has purposely been left blank.