Leiomyoma therapeutic options: is it now prime time for stratified medicine?

We have now entered the era of stratified medicine. The right medicine for the right patient provides optimal outcomes. The goals are three-fold when treating women with symptomatic leiomyoma. First, we must determine which groups of patients would benefit most from a specific therapy. Second, we must comprehend the patient's perspective and determine which symptom(s) interferes most with her quality of life. Finally, when possible, we must offer the most minimally invasive therapy that treats the symptom(s) that affect her and preserve fertility if that is a goal. Having outcomes-based research that allows us to stratify women based on risk factors will provide our patients the confidence that new treatment options will be effective in women like themselves. Nationally, the Patient Centered Outcomes Research Institute has recognized the paucity of high-quality clinical trials and the need to study diverse populations in uterine fibroids.

Uterine leiomyomas are the most common pelvic tumor in premenopausal women. Fortunately, for most women, fibroids are present and a passenger but do not create problems. When symptomatic, the burden of fibroid-related disease is greatest among women of the African diaspora, 80% of which are affected. Women of African descent have larger fibroids, earlier onset of symptoms, heavier or prolonged menses, and anemia as well as increased rates of hospitalization, higher rates of myomectomy, and greater risk of hysterectomy. Lower health-related quality-of-life scores, higher absenteeism from work, and interference with physical activities and relationships are reported (1). Black women have less access to nonsurgical options, and when markedly symptomatic they have demonstrated decreased self-esteem and poorer body image.

Ulipristal acetate is a selective P receptor modulator that is being evaluated in women with symptomatic leiomyoma. Current well-designed randomized controlled trials that assess ulipristal acetate efficacy include very few women of African ancestry (2). Therefore, the results from these studies may not be generalizable to black women. Patients enrolled in clinical trials for novel treatments of uterine fibroids must be ethnically diverse to determine whether there are the differences in treatment outcomes by race or ethnicity.

In this prospective observational cohort study by Murji et al. (3), 5 mg of ulipristal acetate was used to treat two groups of women with symptomatic leiomyoma who self-identified as black or white. Both groups of women were provided with the uterine fibroid symptoms quality of life questionnaire and a health-related quality of life total score, and they provided an Aberdeen bleeding score before receiving ulipristal acetate for 3 months. Murji et al. noted that black women had a higher disease burden (younger age, larger uteri) than the white women with comparable perception of symptom severity. After undergoing treatment with ulipristal acetate, white women had a higher rate of improvement in bleeding scores and higher rates of amenorrhea and were more satisfied with the therapy based on a 5-point Likert scale compared with black women. This is a unique study that equally included women of African descent and Caucasian women to investigate the effects of a novel treatment for uterine fibroids. Not only were the authors successful in recruiting these women, their retention rates for the 3 months' study duration were high. In this trial, inclusivity was achieved by enrolling comparable numbers of ethnically diverse women. Their findings demonstrate how therapeutic outcomes might be affected by race and ethnicity, thus upholding the tenets of stratified medicine.

There are a few limitations to this study that are notable. First, the FIGO classification system (4) for abnormal uterine bleeding (AUB) was not used in this study to identify the subclassifications of leiomyoma. This system was established in 2011 and adopted by the American College of Obstetricians and Gynecologists; it provides a uniform communication tool among researchers and clinicians. The subclassification system describes the unique location of uterine fibroids including the intracavity, submucosal, transmural, and subserosal locations. Standardization of fibroid location is a prerequisite in clinical trials and must be used to improve categorization and to compare outcomes. Second, the inclusion criteria for selecting pelvic imaging were not specified in this study. Among women with AUB, saline infusion sonography (SIS), 3-dimensional (3D) transvaginal ultrasound (TVUS), 3D-SIS, and pelvic magnetic resonance imaging (MRI) are more sensitive in detecting intracavitary lesions than TVUS. While TVUS is more routinely used, it is less sensitive in evaluating endometrial pathology and fails to detect one out of six intracavitary lesions. We advocate the use of imaging that provides the greatest sensitivity in evaluating the endometrium. Most intracavitary fibroids can be treated with hysteroscopic myomectomy and provide excellent resolution of heavy menstrual bleeding, circumventing the use of prolonged medical therapy. The treatment response of women with large subserosal leiomyoma may be different than that of women with intracavitary lesions.

At the conclusion of the study, post-treatment pelvic imaging would have been informative. If studied, racial differences in uterine volume may have been detected with this dosage. Additionally, pelvic MRI would have been ideal in the qualitative assessment of characteristic changes of fibroids including necrosis, calcification, or degenerative changes that may result from ulipristal acetate. This information could be used to further correlate with patient satisfaction and long-term outcomes. Lastly, different validated questionnaires were used pre- and post-treatment. This makes it difficult to compare all the specific domains of patient outcomes following therapy with ulipristal acetate.

We applaud the efforts of Murji et al. (3) to recruit women from the African diaspora in their research protocol. These women bear the greatest fibroid-related symptoms compared with Caucasian women. It's a herculean feat, and few studies have been able to achieve this enrollment profile. This should serve as an excellent example and motivation for future researchers to make greater efforts to include women of African descent when studying leiomyoma.

The National Institutes of Health delineate strategies and guidance to aid in the recruitment and retention of minority and underrepresented individuals into clinical trials (5). Their recommendations are practical and clinically useful. Certainly, for future clinical trials, women of African descent who bear the greatest fibroid burden must be included in significant numbers. We must be patient centric. The importance of including racial diversity in clinical trials is that it will help determine whether outcomes are the same for black women and white women. More importantly, it will help researchers determine what our patients really want and what outcomes are clinically significant and important to them. We endorse the use of the FIGO classification of uterine fibroids in all trials. Future leiomyoma studies must be inclusive to reap the benefits of stratified medicine.

Linda D. Bradley, M.D.
Ndeye-Aicha Gueye, M.D.
Department of Obstetrics and Gynecology, Women's Health Institute, Center for Menstrual Disorders, Fibroids and Hysteroscopic Services, Cleveland Clinic, Cleveland, Ohio

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