Translational Frontiers: Innovation in fibroid treatments for the 21st century

The critical first step in generating translational therapies is having a strong scientific foundation. The scientific infrastructure on which to build innovative fibroid therapies is sparse. Why are we so far behind in fibroid research? There are many reasons there was no "Framingham Fibroid Project" to set the stage for new treatments today. My aim is to highlight some of the areas where we need to focus attention to overcome this historic disadvantage.

Some of the reasons are common to many fields of inquiry. Over the last half of the 20th century we have had better control over mortality and can instead focus on disease processes that cause morbidity. Focusing first on myocardial infarctions and then on arrhythmias and sudden death, the mortality from heart disease has decreased significantly. With mortality issues better controlled, the focus can shift to improving quality of life with chronic conditions such as congestive heart failure and prevention of cardiovascular disease by controlling hypertension, hypercholesterolemia and smoking.

While there was clearly some mortality from fibroids, the number of events was few. However, as the shift occurred to studying morbidity we fell behind on the science. Much more is known even today about the biology of a vascular smooth muscle cell in an atherosclerotic plaque than is known about uterine myocytes and the transformed myocytes we know as leiomyomas. We also need to consider primary and secondary prevention in addition to treatment.

However many factors other than science come into play. First, the fact that uncontrollable menstrual bleeding is a difficult topic to discuss socially clearly plays a role. Even as discussion of sensitive topics such as erectile dysfunction and urinary incontinence have become commonplace in our culture, women have been reluctant to discuss this socially embarrassing problem. It is likely that the since this disease affects women exclusively and minority women in particular, elements of sexism and/or racism may have played a role in the deceased attention to this disease.

Finally other lifestyle issues have played a role in focusing attention toward minimally invasive therapies. When the typical women had her children in her 20's and then developed fibroids in her 30's and had a hysterectomy in her 40's the impact of hysterectomy on her life was less severe than if she delayed childbearing until her 40's. This is compounded by the fact that parity appears in many studies to be protective against the development of fibroids. Additionally, if you go back to the 50's and 60's when effective contraception was difficult to obtain, the benefit of hysterectomy as contraception played a role in this therapy's popularity.

From the point of view of industry, the primary question is always, "What is the market for this drug or device?" I believe we have been vastly underestimating this by citing only the women who currently undergo surgical therapies and often by citing only hysterectomy data.

The cost of hysterectomy is the most commonly quoted number for the costs of myomas. As we all know, hysterectomy numbers represent diseases other than myomas and we need to capture the fibroid specific information. We need to estimate the costs of all types of myomectomies, uterine artery embolization (UAE), and newer forms of therapies as they develop. Additionally we need to look at the costs of sanitary products and try to factor in the overuse by women with leiomyoma-related menorrhagia. Many women in my practice use adult diapers for protection, and common wisdom has this product supporting the economic importance of urinary incontinence.

Finally, there are a huge number of currently unmeasured costs for leiomyomas. While there has been one study estimating the work loss with menstrual abnormalities, many women adjust their entire work-life around their menses. Many conventional treatment modalities such as oral contraceptive pills, progestins and medicated IUD's are currently being used for control of myoma symptoms. Additionally an array of alternative and complimentary therapies is used for this indication.

Most importantly, we are currently treating only "end-stage" disease. Because we lack early intervention many women have significant symptomatology long before they become candidates for our available therapies.

How do we approach innovation? The first way is to test therapies already marketed for a different indication that show promise for leiomyomas. The use of interferons and agents for treatment of acromegaly will be discussed in this section.

Secondly, how do we approach novel agents and yet not expose patients to significant risks? In this section we will primarily focus on the introduction of MRI-guided focused ultrasound therapy starting with safety studies and continuing through data supporting FDA-approval of the associated technology. Particular emphasis will be placed on issues surrounding novel therapies, both interventional and medical, on women who have not completed their families.

In addition, we will discuss the process of myoma recurrence and how this affects all therapies. We will end by discussing changes that would foster innovation in this field.

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