Clinical Management of Leiomyoma

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KEYWORDS

• Fibroids • Leiomyoma • Pathophysiology • Clinical management • Research

KEY POINTS

- Uterine leiomyoma, benign monoclonal tumors, afflict an estimated 60% of reproductive-aged women, with higher rates among African American women.
- Leiomyomas are associated with significant medical costs, impaired fertility potential, obstetric complications, and gynecologic morbidity.
- Currently, the effective clinical management of leiomyoma is limited by the fact that hysterectomy is the only cure.
- New methods of diagnosis, medical and surgical treatments, as well as interventional radiology and treatment methods are being examined.

INTRODUCTION

In this section, the demographic characteristics and costs of leiomyoma are examined to provide the reader with a brief review of the scope of the problem.

Uterine leiomyomas are exceedingly common, with 60% of reproductive-aged women being affected, and 80% of women developing disease during their lifetime.[1] More than 600,000 hysterectomies are performed annually, and fibroids are the leading indication for hysterectomy in the United States.[2] The annual costs associated with fibroids are estimated at 4 to 10 billion dollars. Estimated lost work-hour costs ranged from $1.55 to 17.2 billion annually. Obstetric outcomes that were attributed to fibroid tumors resulted in a cost of $238 million to $7.76 billion each year.[3]

In addition to the gynecologic complications associated with leiomyoma, fibroids are associated with 10% of cases of infertility. In a little less than 5% of patients, leiomyomas are the only cause of infertility.[4] Among women undergoing assisted

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reproductive technologies, there is clinical evidence to support an association of cavity distortion by submucosal and intramural leiomyoma and of decreased implantation rates after embryo transfer. The clinical data have been considered compelling enough to support a recommendation of myomectomy before IVF.[5] Recent leiomyoma investigations have elucidated previously unknown demographic factors. The age of onset of disease, for example, has been demonstrated to occur at a younger age based on ultrasound evaluations in asymptomatic women. In a recent study of African American and Caucasian women less than 30 years of age, the overall prevalence of leiomyoma based on transvaginal ultrasound was 14.9%. Leiomyomas were more common among African American women than Caucasian women (25.6% vs 6.9%).[6] These findings challenge the traditional dogma that fibroids are uncommon in women under the age of 30.

Age at menarche has also been shown to be an important demographic characteristic that can help identify women at risk for the development of leiomyoma. In a large epidemiologic study of 5023 women screened by ultrasound, early age at first menses had a positive association with fibroid size, type, and location, with a stronger association noted for multiple fibroids.[7] These findings are consistent with earlier studies that identified early age at menarche as a risk factor for the development of leiomyomas.[8]

Obesity has been shown to be a risk factor for fibroid development and may partially explain the increased incidence of leiomyoma among groups that have a high rate of obesity. In a retrospective cohort study, 50% of women with fibroids were found to be obese and 16% were morbidly obese compared with a 25% rate of obesity and a 7.2% rate of morbid obesity in the general population.[9] In a more recent publication, the risk of uterine fibroid development was reported to be 3 times greater for women who weigh more than 70 kg, compared with women who weigh less than 50 kg.[10] Given the increasing incidence of obesity in the United States, an associated increase in the incidence of leiomyoma can be anticipated.

Like pregnancy, family history has been a subject of debate. A recent study suggested that self-reported family history may not be a reliable marker for a high risk of leiomyoma development. In a study of 1072 women (660 African American, 412 Caucasian), self-reported family history of fibroids was not found to be a useful tool for identifying high-risk women.[11]

In summary, some of the most common demographic risk factors include African American race, obesity, and age at menarche. Other factors, such as parity and family history, remain a subject of debate. Additional epidemiologic factors, such as diet, particularly vitamin D deficiency, and environmental toxins, are the subject of ongoing investigations. Further research is needed to identify additional demographic characteristics that are associated with fibroid development. This information will be helpful in counseling patients about their risk of disease. As effective prophylactic treatments are developed, prospective intervention may be possible.

PATHOPHYSIOLOGY

In this section, the pathophysiology of leiomyoma, including molecular mechanisms and genetics, is discussed. In examining the gross appearance of leiomyoma as well as the molecular structure, it has become clear that these benign tumors are composed of altered collagen fibrils, resulting in an altered extracellular matrix (ECM) compared with adjacent myometrium. The distorted ECM is thought to contribute to the increased rigidity of leiomyoma compared with normal myometrium. This understanding of the ECM in the context of a dynamic uterine muscle has led to