

HOSPITAL PHYSICIAN®

OBSTETRICS AND GYNECOLOGY BOARD REVIEW MANUAL

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The *Hospital Physician Obstetrics and Gynecology Board Review Manual* is a peer-reviewed study guide for residents and practicing physicians preparing for board examinations in obstetrics and gynecology. Each manual reviews a topic essential to the current practice of obstetrics and gynecology.

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Uterine Leiomyoma

Editor:

Matthew F. Davies, MD, FACOG

Associate Professor, Department of Obstetrics and Gynecology, Chief, Division of Women's Health, Director, Obstetrics and Gynecology Residency Program, Pennsylvania State University, Milton S. Hershey Medical Center, Hershey, PA

Contributors:

Gina M. Northington, MD

Fellow, Division of Urogynecology and Reconstructive Pelvic Surgery, University of Pennsylvania, Philadelphia, PA

Lily A. Arya, MD, MS

Assistant Professor, Department of Obstetrics and Gynecology, Director, Urogynecology and Reconstructive Surgery Fellowship Program, University of Pennsylvania, Philadelphia, PA

Table of Contents

Introduction	2
Risk Factors and Pathogenesis	2
Clinical Presentation and Diagnosis	4
Treatment	8
References	10

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Uterine Leiomyoma

Gina M. Northington, MD, and Lily A. Arya, MD, MS

INTRODUCTION

Uterine leiomyoma (also referred to as myoma, fibromyoma, or fibroid), the most common benign neoplasm of the female reproductive tract, represents the clonal expansion of a cell within the myometrium of the uterus. These benign tumors occur in up to 30% of symptomatic reproductive aged women, with the true prevalence estimated to be as high as 70%.^{1,2} The incidence peaks in the fourth decade and declines after menopause.³⁻⁵ Uterine leiomyoma is the leading indication for hysterectomy (abdominal and vaginal), accounting for approximately one third of all procedures performed annually in the United States.^{4,6} Symptoms and treatment options for uterine leiomyoma span a continuum from no symptoms with expectant management to severe pain with hysterectomy. This manual begins with a review of factors that contribute to increased risk for and pathogenesis of uterine leiomyoma. This is followed by a case-based discussion of the clinical symptoms, evaluation, and optimal treatment of uterine leiomyoma.

RISK FACTORS AND PATHOGENESIS

RISK FACTORS

The etiology of uterine leiomyoma is most likely multifactorial, as no single factor has been shown to be causative. Multiple risk factors have been identified through epidemiologic studies largely based on the theory that leiomyomas result from excessive estrogen and, to some degree, progesterone exposure. The most widely studied factors include age at menarche, parity, race, family history, and infertility. As most of these factors have some impact on estrogen and/or progesterone exposure, it is difficult to determine their precise influence on leiomyoma tumorigenesis.

Age at Menarche

Age at menarche is inversely associated with risk of uterine leiomyoma.⁷⁻¹⁰ Menarche occurring at age 10 years or older was associated with a 50% increase in risk for leiomyoma confirmed by hysterectomy com-

pared with menarche occurring at age 12 years or older.⁹ Two large prospective cohort studies show that age at menarche is related to risk of uterine leiomyoma as a monotonic, dose-response relationship.^{9,10} This relation suggests that early age at menarche and leiomyoma share a common etiology.¹¹ An alternate explanation is that early age at menarche results in an increased cumulative exposure to estrogen and progesterone and a higher lifetime number of cell divisions in the myometrium, thereby increasing the probability of cellular mutation.⁹ In any case, the biologic explanation for this relationship requires further study.

Parity

Nulliparity has also been implicated as a risk factor for uterine leiomyoma. It has been hypothesized that pregnancy reduces the amount of unopposed estrogens.¹² Studies have reported a reduction of risk ranging from 20% to 50% in women who have delivered at least 1 child.^{8,10,12,13} Although some studies show that the magnitude of risk reduction increases with each term delivery when compared with nulliparous women, other studies do not show any evidence of an association.^{12,14}

Increased risk of uterine leiomyoma with a diagnosis of infertility has also been demonstrated.^{7,9,12} Faerstein's study⁷ was the first to show evidence of an association between submucosal uterine leiomyoma and infertility or nulliparity. Healy¹⁵ also demonstrated that implantation rates were significantly lower in women with intrauterine and submucosal fibroids, even when there was no deformation of the uterine cavity. However, it remains unclear whether infertility or nulliparity is part of the causal pathway or if early subclinical leiomyoma, in fact, leads to infertility.¹⁶

Race

The epidemiologic evidence consistently supports the association between race and uterine leiomyoma. The proposed biologic basis includes genetic factors and an increased endogenous estrogen exposure.¹⁷ The risk among African-American women has been reported to be between 3 and 9 times that among Caucasian women.^{2,3,7} In a large US prospective cohort study of nurses, peak incidence was shown to occur at an earlier age in African-American women than in Caucasian