## Natural history of uterine fibroids during perimenopause and menopause

Michelle Louie<sup>1</sup>, Heidi E. Kosiorek<sup>1</sup>, Reem A. Alsibai<sup>2</sup>, Cherie-Akilah Browne<sup>2</sup>, Sarah Rassier<sup>2</sup>, and Shannon Laughlin-Tommaso<sup>2</sup>

June 5, 2023

## Abstract

Since fibroids are known to be hormonally receptive tumors, it is biologically plausible that fibroids decrease in size after menopause. Patients may opt for more conservative therapy or expectant management if fibroid growth could be predicted[1](#ref-0001). Studies assessing fibroid growth in premenopausal patients have shown that individual tumors in a single uterus grow at different rates and can grow consistently or in short bursts <sup>2</sup>. These variations and the unknown effect of natural menopause make patient counseling difficult. Studies that include only symptomatic menopausal patients or those undergoing treatment can result in selection bias towards fibroids that are increasing in size <sup>3,4</sup>. The objective of our study was to estimate fibroid growth course before and after menopause among women not specifically seeking fibroid treatment. Our hypothesis was that fibroid growth would decline after menopause.

Natural history of uterine fibroids during perimenopause and menopause

Michelle Louie, MD MSCR<sup>1</sup>; Heidi E. Kosiorek, MS<sup>1</sup>, MS; Reem A. Alsibai<sup>2</sup>; Cherie-Akilah Browne<sup>2</sup>; Sarah Rassier MD, MPH<sup>2</sup>; Shannon K. Laughlin-Tommaso, MD<sup>2</sup>

1 Mayo Clinic

Department of Medical and Surgical Gynecology

5777 E. Mayo Blvd, Phoenix, AZ 85054

2 Mayo Clinic

Department of Obstetrics and Gynecology

200 First Street SW, Rochester, MN 55905

Disclosure statement: Michelle Louie is a consultant for Hologic Inc. and Applied Medical. None of the other authors have any conflicts of interest to report.

Source(s) of financial support: None

Corresponding Author:

Michelle Louie, MD MSCR

Mayo Clinic

Department of Medical and Surgical Gynecology

<sup>&</sup>lt;sup>1</sup>Mayo Clinic Hospital

<sup>&</sup>lt;sup>2</sup>Mayo Clinic Department of Obstetrics and Gynecology

5777 E. Mayo Blvd, Phoenix, AZ 85054

- (p) 480-342-0612
- (f) 480-342-2944

Louie.Michelle@mayo.edu

Since fibroids are known to be hormonally receptive tumors, it is biologically plausible that fibroids decrease in size after menopause. Patients may opt for more conservative therapy or expectant management if fibroid growth could be predicted<sup>1</sup>. Studies assessing fibroid growth in premenopausal patients have shown that individual tumors in a single uterus grow at different rates and can grow consistently or in short bursts<sup>2</sup>. These variations and the unknown effect of natural menopause make patient counseling difficult. Studies that include only symptomatic menopausal patients or those undergoing treatment can result in selection bias towards fibroids that are increasing in size<sup>3,4</sup>. The objective of our study was to estimate fibroid growth course before and after menopause among women not specifically seeking fibroid treatment. Our hypothesis was that fibroid growth would decline after menopause.

Patients seeking care at the Mayo Clinic Women's Health Clinic were included in the Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS) study<sup>5</sup> in 2017 and gave consent for use of medical records in research (IRB #11-004280). Primary indications for consultation included hormonal and non-hormonal management of menopausal symptoms and concerns about sexual health including desire and arousal. We performed a retrospective cohort study of participants from the DREAMS study with an intact uterus and [?]2 pelvic ultrasounds with fibroid size measurements. Ultrasounds <3 months apart were excluded. Menopausal status, hormone use, and demographic information were ascertained via chart review. Patients were categorized by menopausal status at their initial ultrasound. Growth rate (%) over 12 months was calculated and we defined a clinically significant change in growth rate as >50% increase or decrease. Patient characteristics and growth rate (%, 12 months) were compared between groups using chi-square test for frequency data and Kruskal-Wallis rank sum test for continuous measures. P values <0.05 were considered statistically significant. R version 4.1.2 was used for statistical analysis.

73 patients met inclusion criteria: 38 premenopausal (median age 43.5, range 24-53), 13 perimenopausal (median age 51, range 44-56), and 22 postmenopausal (median age 56, range 50-74. Three premenopausal and one perimenopausal patient were using hormone medications during the study period. There were no significant differences between groups with respect to race (92% White, p=0.34), ultrasound indication (p=0.12), and interval between scans (median 2 years, p=0.65). Median diameter of the largest fibroid on second scan decreased with menopausal transition, from 2.5 cm in premenopausal patients to 2.3 cm in perimenopausal patients to 1.7 cm in postmenopausal patients (p=0.04). 12-month fibroid growth rate was stable (median 0%), and not different between groups (p=0.84) [Figure 1]. 35 (92.1%) of premenopausal, 12 (92%) of perimenopausal, and 21 (95.4%) of postmenopausal participants had a decrease or no clinically meaningful change in 12-month growth rate. 3 (8%) of premenopausal, 1 (8%) of perimenopausal, and 1 (5%) of postmenopausal participants had a greater than 50% increase in growth rate.

In our cohort of patients presenting for menopausal or sexual health concerns, we did not observe clinically significant fibroid growth during perimenopause or menopause. 12-month fibroid growth rate appears to stabilize with menopausal status, with less variability for menopausal patients compared to peri- or premenopausal patients. Due to the very low proportion of patients using hormone therapy, no further analysis of the effect of hormone therapy was completed. Our cohort was chosen to attempt to capture the natural history of fibroids through the menopausal transition and aid in counseling the asymptomatic patient. Future studies of larger and more diverse groups would help to determine the natural history of large fibroids and the effect of hormone therapy and patient characteristics such as race, ethnicity, weight, and medical comorbidities.

References

- 1 Borah, B. J., Nicholson, W. K., Bradley, L. & Stewart, E. A. The impact of uterine leiomyomas: a national survey of affected women.  $Am\ J\ Obstet\ Gynecol\ 209,\ 319\ e311-319\ e320,\ doi:10.1016/j.ajog.2013.07.017\ (2013).$
- 2 Peddada, S. D. *et al.* Growth of uterine leiomyomata among premenopausal black and white women. *Proc Natl Acad Sci U S A* 105, 19887-19892 (2008).
- 3 Shen, Minghong MD1,2; Duan, Hua MD, PhD1; Chang, Yanan MD1; Wang, Sha MD1. Growth of surgically confirmed leiomyomas in postmenopausal women: analysis of the influencing factors. Menopause 28(11):p 1209-1213, November 2021. | DOI: 10.1097/GME.00000000001846
- 4 Cohen Rassier, Sarah L. MD, MPH; Louie, Michelle Y. MD; Hopkins, Matthew R. MD; Stewart, Elizabeth A. MD; Laughlin-Tommaso, Shannon K. MD. Letter to the Editor re Shen et al. Menopause 29(8):p 999, August 2022. | DOI: 10.1097/GME.0000000000002043
- 5 Faubion SS, Kapoor E, Kling JM, Kuhle CL, Sood R, Rullo JE, Thielen JM, Shuster LT, Rocca WA, Hilsaca KSF, Mara KC, Schroeder DR, Miller VM. Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS): A cohort profile. Maturitas. 2018 Jan;107:44-49. doi: 10.1016/j.maturitas.2017.09.013. Epub 2017 Oct 5. PMID: 29169579.

## Figure Legend:

Figure 1: Distribution of the 12-month growth rate by initial menopause status. Displayed is a boxplot; horizontal line is the median, top and bottom of the box are the 25th and 75th percentiles. Outliers are shown as points outside the box and whiskers.

