07 - Fibroid Focus

Gyan - Vahini

From

FOGSI, Food Drugs & Medicosurgical Equipment Committee July - 2025

Common condition.

Uncommon clarity.

— Dr. Asha Jain

Editor & Chairperson, FOGSI FDMSE Committee

Message From Dr. Sunita Tandulwadkar

Dr. Sunita Tandulwadkar

President FOGSI-2025

Fibroids are one of the most common gynecological conditions affecting women, yet their influence reaches far beyond a clinical diagnosis. They impact quality of life, fertility, and pregnancy outcomes, making their understanding a matter of both medical and public health importance in India.

This book brings together a comprehensive view of fibroids, beginning with their epidemiology and burden in Indian women, and moving through genetic and molecular causes, classification, and clinical presentation. It then explores the wide spectrum of treatment—from hormonal therapy to advanced surgical approaches including hysteroscopy, laparoscopy, and robotic surgery. The effect of fibroids on fertility and pregnancy is discussed with clarity, reflecting the true significance of this condition.

Equally commendable is the focus on future directions. Newer advances such as gene editing, targeted therapies, and the application of artificial intelligence in diagnosis and treatment planning highlight the exciting possibilities ahead.

As President of FOGSI, I am proud to see this scholarly yet practical volume being offered to our fraternity. I am confident it will serve as a valuable resource for gynecologists, students, and researchers committed to advancing women's health.

I congratulate the editors and contributors for their dedication in bringing science, clinical expertise, and innovation together in this book. May it inspire continued progress in improving the lives of women with fibroids and further strengthen our mission: **Swasth Nari**, **Samruddha Vatan**—a healthy woman for a prosperous nation.

Dr. Sunita Tandulwadkar
President, FOGSI

Message from Dr Abha Singh

Dr. Abha Singh
Vice President FOGSI-2025

It is my privilege to introduce Fibroid Focus, an e-magazine that mirrors FOGSI's ethos of nurturing futures—safe mother, safe child—even before conception. The carefully selected sixteen chapters address questions our patients ask every day: Why did I develop fibroids? What are my non-hormonal options? Can I preserve fertility? How safe is a pregnancy with fibroids? What lies ahead if surgery is not feasible? By spanning preventive strategies such as lifestyle modification and vitamin D, through contemporary interventions like UAE, HIFU and RFA, to visionary concepts of targeted gene therapy, this compendium equips clinicians across practice settings. I particularly applaud the inclusion of health-economic perspectives, often overlooked yet critical in counselling women who balance family priorities with financial constraints. To our young colleagues, I say: use these pages as a springboard for innovation—whether in refining minimally invasive techniques, researching nutraceutical efficacy, or harnessing AI for personalised care. To our seniors, I invite mentorship—sharing pearls that only experience can polish. My heartfelt appreciation goes to Dr Sunita Tandulwadkar for unwavering presidential guidance, Dr Suvarna Khadilkar for operational excellence, and Dr Asha Jain for her indefatigable leadership that converted vision into a vibrant digital reality. May this issue stimulate thoughtful dialogue and, ultimately, kinder, smarter fibroid management for every Indian woman.

Warm Regards,

Dr Abha Singh
Vice President North Zone Fogsi

Message from Dr Suvarna Khadilkar

Dr. Suvarna Khadilkar
Secretary General FOGSI-2025

A high-quality scientific resource is only as strong as its structure, and this issue exemplifies disciplined curation. Beginning with the burden of disease and genetic insights, progressing through FIGO classification, pharmacological and procedural advances, and culminating in health-economics and futuristic therapies, the chapters follow a logical, learner-friendly sequence. Such intentional flow reflects the hallmark of the Food, Drugs and Medicosurgical Equipment Committee, whose yearly e-magazines have become trusted touchstones for busy practitioners. I commend Dr Asha Jain, her editorial board and each chapter author for delivering content that is evidence-anchored yet eminently readable in Indian English. Importantly, medico-legal pearls, quality-of-life data and cost considerations have been woven in—essentials for ethically sound counselling in our diverse socio-economic landscape. As Secretary General, I recognise the countless hours behind each reference check, image permission and layout iteration. Your diligence strengthens FOGSI's commitment to continuous professional development. I encourage members to integrate these recommendations into standard operating protocols, audit outcomes and share feedback, enabling iterative improvement of future editions. Let this publication remind us that scholarly exchange is a living process—one that thrives on critique, collaboration and compassionate application at the bedside. Congratulations to all involved.

With best and warm wishes,

Dr. Suvarna Khadilkar
Secretary General, FOGSI

Dr. Asha Jain
Chairperson
FOGSI FDMSE Committee

FOREWORD

I write this foreword with a sense of practical optimism. Uterine fibroids affect more than one-third of Indian women of reproductive age, yet patient pathways remain uneven—from delayed recognition in remote districts to overtreatment in urban practice. The Food, Drugs and Medicosurgical Equipment (FDMSE) Committee therefore resolved that our July 2025 e-magazine would be devoted entirely to fibroids, translating evidence into everyday decision-making.

My first debt of gratitude is to our leadership at FOGSI. President **Dr Sunita Tandulwadkar** encouraged the committee to keep the content relevant to office practice and future-ready. Secretary-General **Dr Suvarna Khadilkar** guided us on maintaining academic rigour without jargon. Vice-President In-charge **Dr Abha Singh** reminded us to foreground affordability and access, themes central to "Nurturing Futures: Safe Mother, Safe Child." Their steady counsel kept the project on course despite tight timelines and an overflowing clinical calendar.

A publication stands or falls on the quality of its authors. I am pleased to record that seventeen colleagues accepted our invitation and met every deadline with professional discipline. The chapters unfold in a deliberate sequence, and the credit for that coherence belongs to the writers themselves: **Dr Himleena Gautam** on epidemiology; **Dr Purvi Agrawal** on molecular underpinnings; **Dr Rimpi Singla** on non-hormonal symptom control; **Dr Ginny Gupta** on hormonal therapy; **Dr Sreedevi Vellanki** and **Dr M Chandra** on selective progesterone-receptor modulators and oral GnRH antagonists; **Dr Prabhdeep Kaur** for nutraceuticals and lifestyle; **Dr Deepti Gupta** on hysteroscopic procedures; **Dr Sugandha Goel** on laparoscopic and robotic myomectomy; **Dr Jyothi G. S.** on interventional radiology; **Dr Neetha George** on medicolegal aspects of hysterectomy; **Dr Vishnupriya K M N** on fertility; **Dr Varuna Pathak** on pregnancy outcomes; **Monica Umbardand** on health economics and quality of life; **Dr Renu Jain** on device innovation; and **Dr Priyanka Rai** on gene editing, targeted therapy and artificial intelligence. With my own contribution on FIGO classification and advanced imaging, we cover the complete arc from pathogenesis to future horizons.

Each author respected the committee's editorial brief: keep references current, avoid repetition, use Indian English, and embed actionable points. Their tables and flow-charts were cross-checked for accuracy; images were captioned for easy insertion into presentations; and every statement about drugs or devices was verified against CDSCO and DCGI approvals as of June 2025. The result is a compact resource that a postgraduate can revise in one sitting and a senior consultant can search for a quick protocol check before surgery.

Some insights emerged repeatedly during editing. First, the gap between diagnosis and definitive treatment is narrowing because point-of-care ultrasound is now standard in even tier-2 cities, yet counselling about non-surgical options remains weak. Second, we need multicentre Indian data on long-term outcomes of oral GnRH antagonists; current evidence is extrapolated largely from European cohorts. Third, cost-effectiveness analyses must shift from procedure-centric to woman-centric matrices, factoring time off work, social support and mental health. Finally, the ethical horizon is expanding: gene editing raises profound questions about germline intervention that our fraternity cannot ignore. These themes cut across chapters, and I encourage readers to engage with them in departmental audits and journal clubs.

I close with a simple request. Please do not let this document sit in your downloads folder. Use it to update clinic handouts, refine surgical consent, mentor juniors and inform policy debates in your local society meetings. If even one woman avoids an unnecessary hysterectomy or receives timely myomectomy because of information gleaned here, our collective effort will have been worthwhile.

On behalf of the entire editorial and review team, I thank **Dr Sunita Tandulwadkar**, **Dr Suvarna Khadilkar** and **Dr Abha Singh** once again for their unwavering support. I congratulate every author for intellectual honesty and punctuality. I also acknowledge the silent hands- Bhupendra Sahu, who converted Word files into this polished e-publication.

May this issue of Fibroid Focus inform, clarify and, above all, improve the care we offer to every Indian woman who entrusts us with her reproductive health.

Dr Asha Jain
Editor, FDMSE E-Magazine

"Know Your Numbers" is an ambitious health initiative.

- This project seeks to gather vital health data- Weight, Blood pressure, Blood Sugar Level with HbA1C, and Hemoglobin level -from women across India.
- By focusing on these key health indicators, the project aims to foster a proactive health management culture among women.
- The data collected will be instrumental in identifying prevalent health issues early and promoting interventions that can significantly reduce the incidence of che diseases.
- This initiative not only emphasizes the importance of regular health monitoring but also strives to empower women with the knowledge and tools needed to take charge of their health, ensuring they lead longer, healthier lives.
- Collect key health data: weight, blood pressure, blood sugar, HbA1C, and hemoglobin from women across India.
- Encourage proactive health management for early identification of prevalent health issues.
- Promote timely interventions to reduce chronic disease incidence.
- Empower women with knowledge and tools for better health and longevity.
- Gather vital health data: weight, blood pressure, blood sugar (HbA1C), and haemoglobin levels from women across India.
- Foster proactive health management among women.
- Identify prevalent health issues early and promote timely interventions.
- Reduce the incidence of chronic diseases through regular monitoring.
- Empower women with knowledge and tools for healthier, longer lives.

SURVEY FOR KNOW YOUR NUMBER (KYN) PROJECT

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Epidemiology & Burden of Uterine Fibroids in Indian Women

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Fibroids, also known as leiomyomas or myomas, are benign growths arising from the myometrium of uterus. These develop from myometrial stem cells and are clonal in origin. The cause of the fibroids is unknown, but it is effected by estrogen and progesterone which proliferate tumor growth. They may be single or multiple and negatively affect the reproductive system, causing various symptoms and deteriorating the women's quality of life[1,2].

Incidence & prevalence- It has been postulated that fibroids occur in over 70% of women by the age of menopause. Prevalence varies from 4.5% to 68.6%. They are estimated to be clinically apparent in 25% of women of reproductive age and cause severe symptoms in approximately 25% of women requiring to seek treatment. However, the actual incidence and prevalence of uterine leiomyomas are likely to be underestimated because in many women it is asymptomatic, or symptoms develop insidiously, and therefore remains undiagnosed. These undetected cases of fibroids effect the epidemiological data and evidence on associated factors to reflect severe disease[3,4]. In some studies, 15% prevalence rate has been found in asymptomatic young woman aged 18–30 years with a significantly increased prevalence in Black women[5].

Burden of the disease – Fibroids can cause a range of severe and chronic symptoms. The most common presenting symptom is heavy menstrual bleeding, which can lead to anaemia, fatigue and painful periods. Other symptoms include non-cyclic pain, abdominal mass, dyspareunia or pelvic pressure, and bladder or bowel dysfunction resulting in urinary incontinence or retention, pain or constipation[3,4]. Symptoms from fibroids can lead to missed workdays and reduced productivity, impacting the woman's income and overall economic well-being. This can also affect mental health. The cost of treating uterine fibroids depends on size, number, symptoms, age of women, wish of childbearing etc. Thus, costs of treatment can vary widely, depending on the type of treatment (medications, surgery, etc.). These also add to financial burden on the family[6].

Effect of age- Fibroids have never been reported before menarche with very few cases reported in adolescent age group. Prevalence is highest in the age group of 30-50years Women between 41-60 years of age have 10 times higher risk of developing fibroids as compared to 21-30 years of age, due to the various hormonal changes and myocyte mutations in each menstrual cycle over the reproductive years[7,8].

Racial and ethnic variations- Black women have higher prevalence of 18.5% compared to 10% prevalence in Whites between the age of 18-65years[9]. By the age of 50 years, the cumulative incidence is approximately 70% in white women and more than 80% in black women based on ultrasound detection of fibroids. The incidence is around 3 times higher in Blacks and 2 times higher in Hispanic women as compared to Whites[10,11].

African Americans are more likely to be diagnosed with uterine fibroids at an earlier age, and have larger, multiple and more rapidly growing fibroids, with more severe symptoms. The reasons for these differences may be differential expression of genes and micro-RNAs as well as differences in diet, physical activities, stress, use of beauty products, environmental and occupational exposures between these races[9,11].

Studies have shown that incidence in Caucasian women is around 40% by age 35, and almost 70% by age 50. The data was similar in Italy, while the incidence was lower among the Swedish women[1]. Various studies on the risk in Asian women have shown conflicting results, with some showing risk similar to Blacks and some showing similar to Caucasians. A review has shown that Eastern Europe, Tropical Latin America, Brazil and India experience the greatest uterine fibroid burden[12].

Trend in India- In India, various studies have shown prevalence ranging from 4.5% to 70% in 30-50years age group. Study has showed that there is difference in incidence in women of rural India (37.65%) and urban India (24%) [13,14].

Risk factors- Fibroids do not have a specific aetiology. However, various risk factors have been found to play role in the development of fibroids apart from racial and ethnic. These are[2,3,6,11,15,16] -

a] Age- With increasing age, the chances of having fibroids significantly increases. In African American women incidence is 60% below 45years, which is 80% at ≥50years. In white women, 40% of <35years have fibroids and 70% of >50years have fibroids.

b] Family history-Various studies have shown a familial predisposition of fibroids, with a risk ranging from 8-70%. Risk of developing myomas can be upto 2.5times higher in first degree relatives of women having myomas and can be almost 2times more in monozygotic twins as compared to dizygotic twins.

c] Early menarche- This leads to increased exposure to reproductive hormones causing higher mutations in genes controlling myometrial proliferation.

d] Parity- nulliparous women have higher risk of developing fibroids than multiparous ones.

e] Hypertension- Hypertension increases the risk by 5 times.

f] Obesity- High BMI, higher waist-to-hip ratios and fat percentage of >30% increase risk of having fibroids. Obese with type2 DM also has higher risk.

g] Dietary factors- green vegetables, fruits, fish and yogurt reduce risk of developing fibroids. Consumption of ham, beef have shown to increase risk, whereas consumption of dairy products has shown conflicting associations in various studies.

h] Vitamin D deficiency – this is strongly associated with higher risk of fibroids.

i] Lifestyle factors- Reduced physical activity, increased stress and caffeine intake may increase fibroid risk. Alcohol, mostly beer intake is associated with fibroid risk in dose dependent manner.

j] Environmental exposure-

[i] Endocrine-disrupting chemicals(EDCs)- these compounds can alter functioning of the endocrine system and have been found to have positive association with fibroids. These are found in various beauty products, water bottles, beverages canned foods, pesticides etc. and include Bisphenol A(BPA), benzophenone-3, triclosan, triclocarban, parabens, phtalates etc. Prenatal exposure to DES, which is an EDC, increases risk by around 2fold.

[ii] Air pollution- Chronic exposure to air pollution increases risk of fibroids.

k] Contraceptive pills- Early use of OCPS at 13-16years of age have shown positive association than those who were not exposed at that age. Obese postmenopausal women using HRT have also shown to have higher risk.

Conclusion-

Fibroids are the most common benign neoplasm of women. They can be asymptomatic, but can cause mild to severe symptoms affecting quality of life and increasing physical, mental, psychological and financial burden. With increasing age, fibroids can increase in number and size. In India, rural population has higher incidence of fibroids than urban population. Multiple risk factors are associated with fibroids, out of which some are modifiable. Awareness regarding the epidemiology and risk factors are needed among the healthcare providers.

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Genetic and Molecular Pathogenesis of Uterine Fibroids

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Introduction

Uterine fibroids, or leiomyomas, are benign smooth muscle neoplasms of the myometrium and represent the most common tutors of the female reproductive tract. Affecting up to 70% of women by the age of 50, fibroids contribute significantly to gynaecologic morbidity, including abnormal uterine bleeding, infertility, and pelvic pressure symptoms. While traditionally considered hormonally driven, advances in genomic and molecular profiling have identified key driver mutations and epigenetic mechanisms central to fibroid pathobiology. This chapter present, synthesis of the molecular pathways underlying fibroid development, with particular focus on MED12, HMGA2, fumarate hydratase (FH) deficiency, and progesterone signalling.

1. Genetic Architecture of Uterine Fibroids

Fibroids exhibit a clonal origin, typically arising from a single mutated myometrial smooth muscle cell. Cytogenetic analyses have revealed recurrent chromosomal rearrangements, the most common involving chromosomes 12 and 14, often affecting the HMGA2 locus, and mutations in the MED12 gene on chromosome Xq13.1. Integrative genomic studies suggest that approximately 80–90% of fibroids harbour one of several mutually exclusive molecular alterations, supporting the existence of distinct pathogenetic subtypes [1].

2. MED12 Mutations: The Most Prevalent Driver

MED12 (Mediator complex subunit 12) mutations are present in approximately 70% of fibroids \[2]. Most mutations cluster in exon 2 and result in altered transcriptional regulation by disrupting the mediator complex function, which integrates signals from transcription factors to RNA polymerase II.

Mechanism of Action: MED12 mutations lead to aberrant recruitment of transcriptional machinery, deregulating Wnt/β-catenin signalling and other growth-related pathways. Recent evidence implicates altered chromatin accessibility and enhancer-promoter interactions in fibroid pathogenesis.

Clinical Significance: MED12-mutant fibroids tend to be multiple, smaller, and are more common in reproductive-aged women. Importantly, these mutations are rarely found in malignant uterine smooth muscle tumours, supporting their role in benign pathogenesis.

3. HMGA2 Overexpression and Chromosomal Rearrangements

High-mobility group AT-hook 2 (HMGA2) is a non-histone chromatin remodelling protein encoded on chromosome 12q15. HMGA2 rearrangements or overexpression define another key molecular subtype of fibroids.

Mechanism: HMGA2 promotes cell proliferation by modulating chromatin architecture and facilitating the transcription of growth-promoting genes. Its overexpression is commonly associated with translocations involving chromosome 12 and leads to disruption of its 3' untranslated region (UTR), resulting in escape from miRNA-mediated repression.

Clinical Profile: HMGA2-positive fibroids are typically large, solitary, and found in younger women. They exhibit increased mitotic activity and greater fibrotic content than MED12-mutant tumours [1,3].

4. Fumarate Hydratase (FH) Deficiency and Hereditary Leiomyomatosis

A minority of fibroids arise due to biallelic inactivation of the FH gene, especially in the context of hereditary leiomyomatosis and renal cell cancer (HLRCC) syndrome.

Mechanism: Loss of FH leads to accumulation of fumarate, which acts as an oncometabolite. Fumarate inhibits α-ketoglutarate-dependent dioxygenases, leading to epigenetic dysregulation via histone and DNA hypermethylation. This results in a pseudo-hypoxic state, stabilization of HIF-1α, and activation of angiogenic and proliferative pathways.

Histological Clues: FH-deficient fibroids show prominent nucleoli with peri nucleolar halos, eosinophilic inclusions, and atypia. Immunohistochemical loss of FH or 2-succinyl-cysteine (2SC) positivity aids in diagnosis.

Clinical Relevance: FH mutations are associated with increased risk of aggressive renal cancers and warrant genetic counselling.

5. Progesterone Signalling and Steroid Receptor Pathways

Despite distinct genetic drivers, almost all fibroids exhibit hormone-dependent growth, particularly in response to progesterone.

Pathway Overview: Progesterone binds to its receptor (PR), activating downstream effectors such as STAT3 and Bcl-2, which promote anti-apoptotic and proliferative effects. Progesterone also modulates ECM production via TGF-β and promotes angiogenesis through VEGF.

Cross-Talk with Genetic Pathways: MED12 and HMGA2 mutations appear to sensitize fibroid cells to progesterone signalling, amplifying their growth potential. Gene expression profiling demonstrates upregulation of PR co-activators in MED12-mutant fibroids.

Therapeutic Implication: Targeting PR using selective progesterone receptor modulators (SPRMs) like ulipristal acetate can suppress fibroid growth, though long-term safety remains under investigation [3].

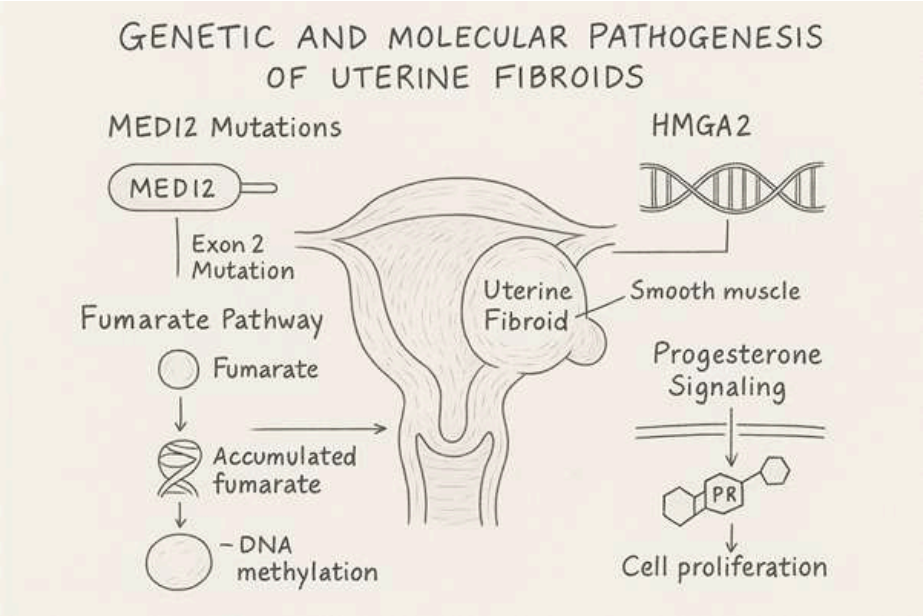
6. Epigenetic and Transcriptomic Landscapes

Beyond mutations, fibroid pathogenesis is shaped by epigenetic dysregulation, including altered DNA methylation, histone modifications, and non-coding RNA networks.

Key Features:

- Hypermethylation of tumour suppressor genes
- Upregulation of miR-21 and downregulation of miR-200 family
- Changes in enhancer landscape contributing to cell-type specific gene expression

Single-cell transcriptomics has revealed heterogeneity in fibroid cellular composition, highlighting the role of fibroblasts, immune cells, and extracellular matrix in tumour progression [3].



Conclusion

The pathogenesis of uterine fibroids is a mosaic of distinct yet intersecting genetic, epigenetic, and hormonal pathways. MED12 mutations, HMGA2 rearrangements, and FH deficiency represent major molecular drivers, each with unique clinical and biological profiles. These alterations interface with oestrogen and progesterone signalling to drive tumour growth and heterogeneity. Understanding these mechanisms provides a rational framework for targeted therapies and precision medicine approaches in fibroid management.

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FIGO Leiomyoma Classification & Advanced Imaging

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Introduction

Uterine leiomyomas (fibroids) are the most common uterine neoplasm and a frequent cause of abnormal uterine bleeding, pelvic pain and pressure, subfertility, and bulk-related symptoms. Because symptoms and therapeutic options depend strongly on the lesion's relationship to the endometrium and serosa, a precise location-based description is central to clinical decision-making. The International Federation of Gynaecology and Obstetrics (FIGO) classification provides a shared language between imaging and the operating theatre, allowing gynaecologists, interventional radiologists, and sonologists to align treatment with anatomy. This chapter emphasises how FIGO sub classification—supported by ultrasound (US) and magnetic resonance imaging (MRI)—translates into practical surgical and interventional choices, drawing particularly on Tu et al. (MRI focus) and Palheta et al. (ultrasound reporting and surgical planning).

Why classification matters in practice

- **Counselling and route selection.** Submucosal lesions (FIGO 0–2) drive bleeding and reproductive complaints and are usually amenable to hysteroscopic management, while intramural/subserosal lesions (FIGO 3–7) more often require laparoscopic/open myomectomy or hysterectomy depending on burden and reproductive goals. A mislabelled lesion can escalate the surgical route unnecessarily or, conversely, set up an incomplete resection.
- **Risk anticipation.** Pedunculated fibroids (FIGO 0 and 7) risk prolapse or torsion; intramural lesions with marked submucosal extension risk fluid overload and uterine wall injury during hysteroscopy; pedunculated subserosal masses may mimic adnexal pathology unless bridging vessels are recognised on imaging.
- **Team communication.** A compact report that conveys number, dominant lesions, exact FIGO types, relationships to mucosa/serosa, and coexistent pathology (e.g., adenomyosis) saves theatre time and avoids intra-operative surprises.

FIGO Leiomyoma Classification—Clinical and Surgical Utility

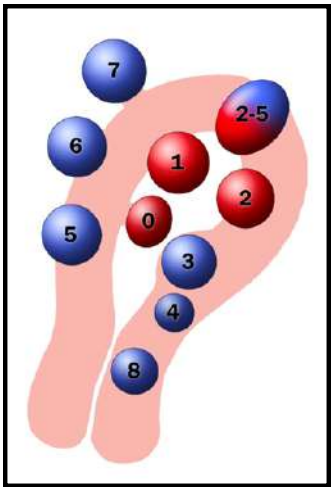

Table 2 FIGO fibroid classification system

Group	Type	Description
Submucosal	0	Pedunculated intracavitary
	1	< 50% intramural (≥ 50% submucosal)
	2	≥ 50% intramural (< 50% submucosal)
Other	3	100% intramural, contacting endometrium
	4	100% intramural, no endometrial or subserosal contact
	5	Subserosal, ≥ 50% intramural
	6	Subserosal, < 50% intramural
	7	Pedunculated subserosal
	8	Non-myometrial location: e.g., cervical, broad ligament, parasitic
Hybrid	X–X	Both submucosal and subserosal components. First number designates the submucosal component and second number designates the subserosal component

Submucosal group (Types 0–2)

- **Type 0 (intracavitary pedunculated).** A mucosa-based fibroid on a narrow stalk prolapsing or mobile within the cavity. Clinically, it is a prime cause of heavy bleeding and cramping. Utility: Typically treated by hysteroscopic polypectomy/myomectomy; preoperative imaging should document stalk origin and calibre to anticipate bleeding and completeness of resection. Post-procedure expulsion may occur after embolization; hence operator awareness of expulsion/infection risk is important.

- **Type 1 (≥50% submucosal, <50% intramural).** These protrude into the cavity but retain a shallow intramural base. Utility: Usually suitable for single-stage hysteroscopic resection. Reporting must include maximal diameter, base width, distance from internal os, and any cavity distortion to plan loop size, energy, and fluid monitoring.

- **Type 2 (<50% submucosal, ≥50% intramural).** Deeper base with smaller intracavitary component. Utility: May need a staged hysteroscopic approach or preoperative medical shrinkage; careful assessment of residual myometrium between fibroid and serosa is important for safety. Surgeons should be alerted to wall thickness and vascularity to mitigate perforation and postoperative rupture risks in future pregnancy.

Other (intramural/subserosal) group (Types 3–7)

- **Type 3 (100% intramural with endometrial contact).** No intracavitary component but abuts the endometrium and may cause bleeding. **Utility**: Not suitable for hysteroscopic resection; laparoscopic/abdominal myomectomy is typical when symptomatic. Reporting should specify the area and length of endometrial contact to correlate with bleeding pattern.
- **Type 4 (completely intramural).** Classic bulk-symptom fibroid. **Utility**: Route depends on size, number, and distribution. Intramural vascularity and degeneration patterns on imaging guide blood loss precautions and choice of energy devices.

- **Type 5 (subserosal with ≥50% intramural component) and Type 6 (subserosal with <50% intramural). Utility**: Laparoscopic myomectomy is standard when feasible. Differentiation of Types 5 vs 6 helps predict dissection depth and myometrial closure strategy. Documenting proximity to serosa, relation to round ligament and uterine vessels, and presence of bridging vessels supports safe port placement and dissection.
- **Type 7 (pedunculated subserosal). Utility**: Risk of torsion and infarction; careful search for the pedicle's uterine origin is essential. Imaging that confirms bridging vessels and a claw sign at the uterine interface prevents misdiagnosis as an adnexal tumour and reduces inappropriate oophorectomy.

Type 8 (other locations). Cervical, broad ligament, parasitic, and extrauterine leiomyomas. **Utility**: Preoperative localisation of feeding vessels and adjacent organ relationships is crucial. MRI can depict cervix involvement and parametrial planes; surgeons should anticipate distorted ureteric course and plan ureteric identification.

Hybrid types (e.g., 2–5). Lesions spanning mucosa to serosa. Utility: The hyphenated code conveys the extent on either side; for example, a 2–5 indicates ≥50% intramural with both submucosal and subserosal components. Surgical planning often requires staged or combined approaches; reports should indicate dominant direction of growth, cavity distortion, and serosal contour bulge.

Group	Type	Description
Submucosal	0	Pedunculated intracavitary
	1	< 50% intramural (≥ 50% submucosal)
	2	≥ 50% intramural (< 50% submucosal)
Other	3	100% intramural, contacting endometrium
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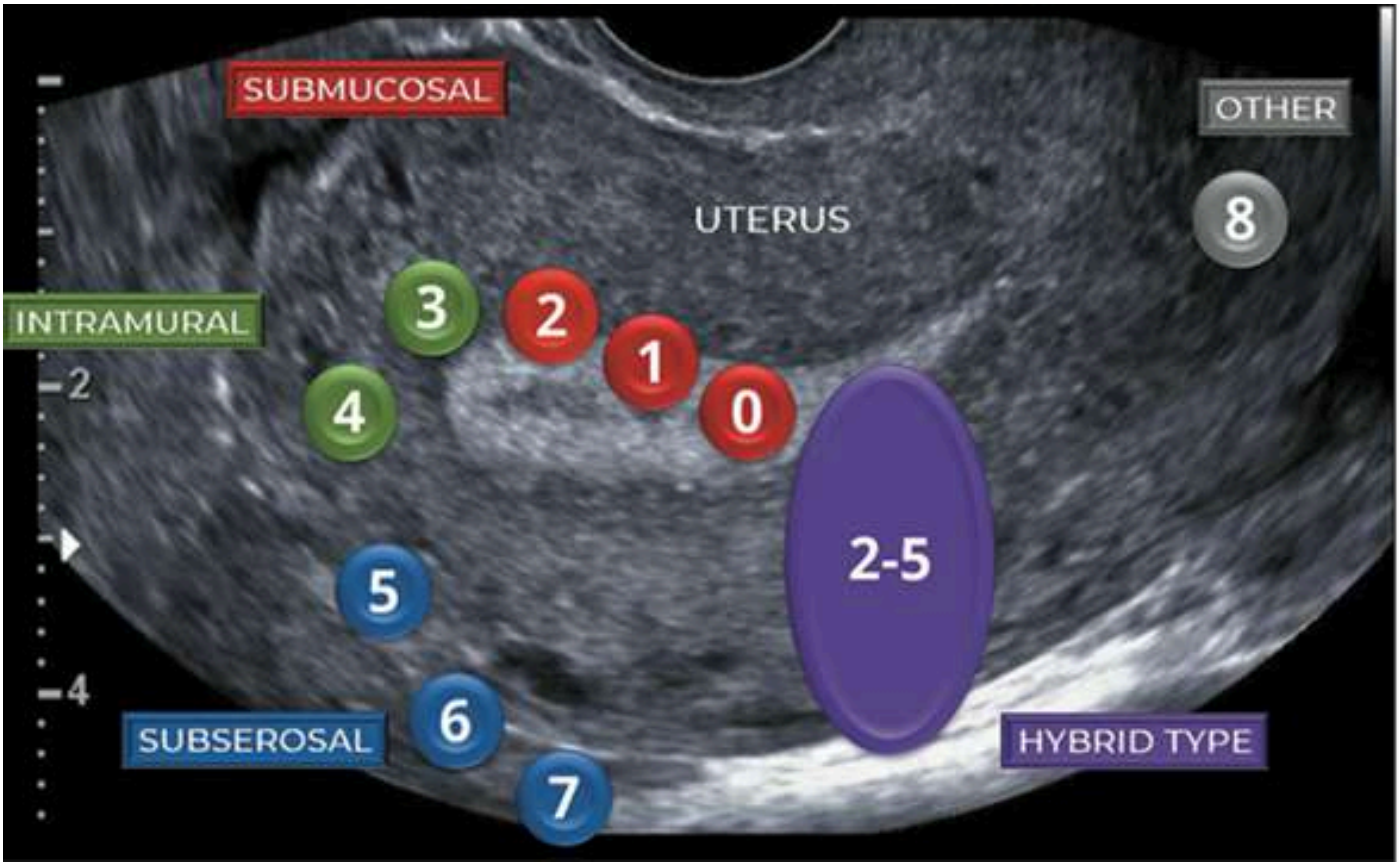
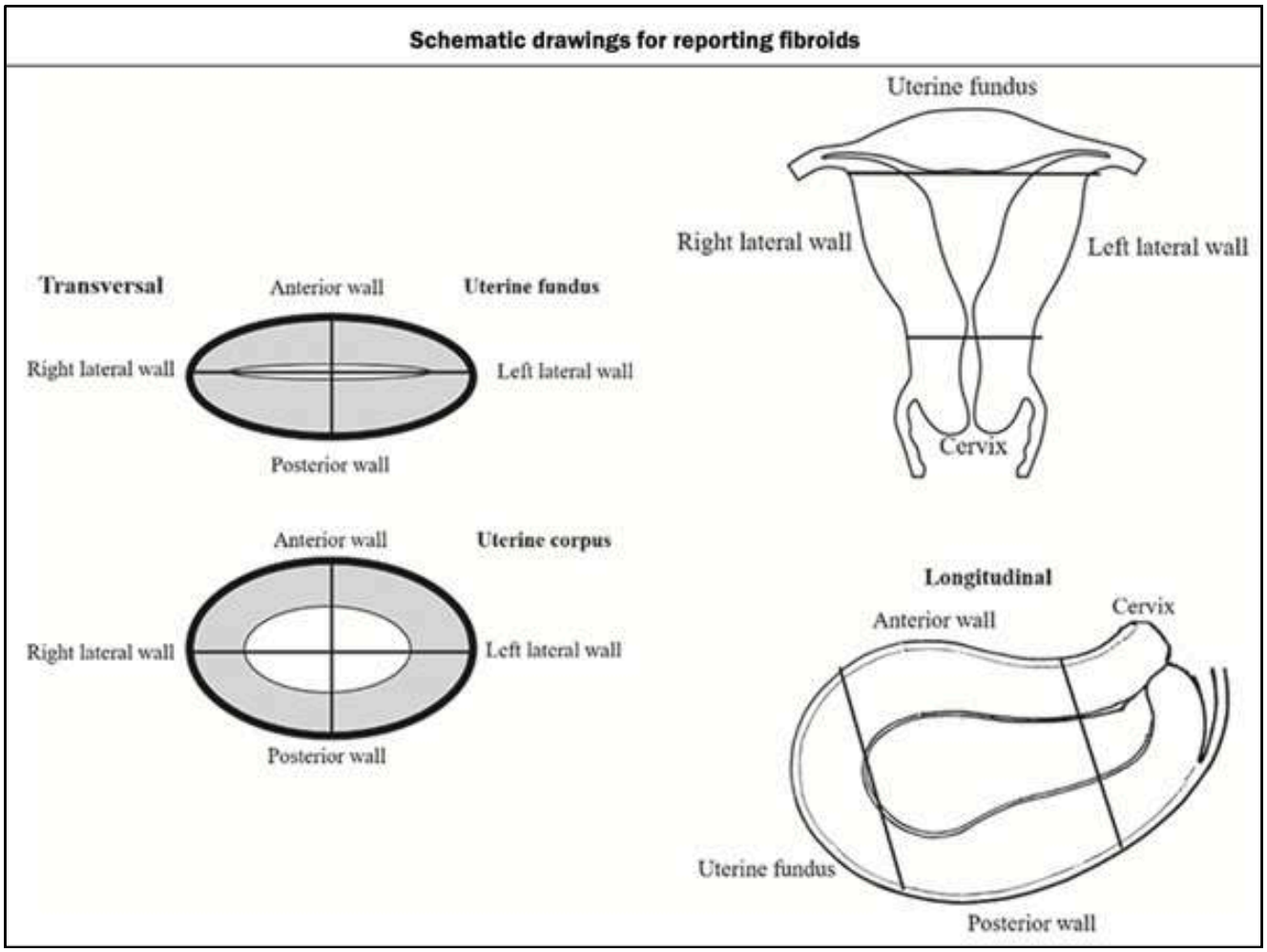
Ultrasound: First-line Characterisation with a Surgical Lens (Palheta et al.)

Ultrasound remains the initial and often definitive modality for triage. Palheta et al. propose a structured, illustrated transvaginal US report built around preoperative needs. Key elements include:



1. **Uterine metrics.** Longitudinal, anteroposterior, and transverse dimensions with calculated volume; uterine version and flexion for hysteroscopic access planning.
2. **Number and dominance.** Estimated total number and up to four largest nodules with individual measurements and FIGO types; when >4 are present, identifying dominant lesions ensures realistic surgical time planning.
3. **Precise location.** Anterior/posterior, fundal, right/left, and segment (corpus vs isthmus/cervix), along with distance to endometrium and to serosa; these distances help judge feasibility of hysteroscopic resection (submucosal reach) and risk to serosa.
4. **Endometrial relationship.** Degree of cavity involvement, base width, and angle of indentation for submucosal lesions; SIS improves mapping for types 0–2.
5. **Serosal relationship.** Surface bulge and pedicle for subserosal lesions; look for bridging vessels to confirm uterine origin when morphology suggests adnexal mass.
6. **Vascularity.** Colour/Power Doppler pattern (peripheral rim, intralesional flow). Hypervascular fibroids may respond better to embolization and are at higher bleeding risk intra-operatively.
7. **Texture and degeneration.** Echogenicity, shadowing (edge or fan-shaped), cystic changes suggestive of hydropic/myxoid change, and calcifications; these influence instrument choice and resection time.
8. **Coexistent pathology.** Adenomyosis (globular uterus, myometrial cysts, junctional zone disruption), endometrial polyps, or deep endometriosis, all of which may alter route and counselling.



Implications for the surgeon

- A **Type 1** submucosal fibroid with a narrow base, adequate distance from the serosa, and modest vascular rim is a good candidate for single-stage hysteroscopic resection.
- A **Type 2** lesion with a broad base and thin overlying serosa should prompt discussion of staging, preoperative medical therapy, or alternative routes to reduce perforation and postoperative uterine wall weakness.
- A **Type 7** subserosal mass with clear bridging vessels on US avoids misclassification as an adnexal tumour—preventing unnecessary salpingo-oophorectomy.
- Mapping **multiple lesions** and identifying the **dominant symptomatic culprit** (e.g., the FIGO 3 fibroid abutting the endometrium) rationalises operative priorities and fluid management plans.

MRI: Added Value Beyond Ultrasound (Tu et al.; Gomez et al.; Liu et al.)

When to escalate to MRI

- Markedly enlarged, multi-fibroid uteri when US field of view is limited.
- Indeterminate relationship to endometrium/serosa after US or SIS (e.g., hybrid lesions).
- Pre-embolization planning (vascularity, degeneration) or MR-guided focused ultrasound planning.
- Differentiation from adenomyosis or adnexal neoplasms; confirmation of uterine origin via bridging vessels and claw sign.

Core MRI features with surgical relevance (Tu et al.)

- **Signal characteristics.** Conventional leiomyomas are T1 isointense and T2 hypointense relative to myometrium; a T2-hyperintense rim may reflect peripheral oedema or venous/lymphatic congestion. These features help separate typical fibroids from mimics.

- **Degenerations and subtypes that change the plan.**
  - **Cellular leiomyoma:** Often T2 hyperintense with avid enhancement and mild diffusion restriction; can mimic malignancy but remains well circumscribed—anticipate soft tumour texture and vascularity during resection.
  - **Hydropic/myxoid change:** Marked T2 hyperintensity with cystic spaces and hypoenhancing mucinous regions; expect gelatinous tissue, longer morcellation time, and potential fluid shifts.
  - **Apoplectic/hemorrhagic change:** T1 hyperintense foci and nonenhancing necrotic centres; anticipate friable tissue and bleeding risk.
  - **Lipoleiomyoma:** Fat signal across sequences; generally incidental and rarely needs intervention.

- **Bridging vessels and pedicles.** Curvilinear flow voids on T2 and a claw sign on post-contrast images confirm uterine origin of pedunculated masses and direct surgeons away from adnexal surgery (critical for Type 6–7).
- **Hybrid mapping.** Multiplanar imaging precisely demonstrates mucosal and serosal interfaces, helping codify hyphenated types (e.g., 2–5) and set realistic operative sequencing.

Organ-axial T2-weighted imaging (Liu et al.)

Aligning high-resolution coronal images parallel to the uterine long axis and oblique axial images perpendicular to it improves depiction of cavity distortion, base width, and endometrial/serosal interfaces compared with standard body-axial planes. In practical terms, this alignment enhances confidence in FIGO staging against surgical findings and helps quantify indentation angles and depths that predict feasibility of hysteroscopic resection. Teams should request organ-axial acquisition when FIGO mapping is decisive for the route.

Structured MRI reporting and the clinical question (Tordjman et al.)

Structured reports that explicitly incorporate the FIGO code and a checklist of key features reliably transmit the information surgeons need—uterine position/size, number of nodules, individual lesion sizes and locations, enhancement patterns, presence of degeneration, myometrial thickness overlying submucosal bases, and any coexistent adenomyosis. Such reports reduce back-and-forth clarification, shorten image review time, and increase the proportion of cases where a management plan can be made from the report alone.

Practical Operative Pearls by FIGO Type (Integrating US and MRI)

- **Type 0.** Confirm stalk implantation site and calibre; plan for vasopressin infiltration and loop control; anticipate expulsion if prior embolization; ensure infection counselling.

- **Type 1.** Measure base width and cavity indentation at US or MR; ensure adequate wall thickness to avoid perforation; consider preoperative cervical preparation to ease hysteroscopic access.

- **Type 2**. Quantify residual myometrium to serosa on MR; discuss staging and postoperative uterine integrity with patients desiring future pregnancy; consider preoperative shrinkage to reduce intramural bulk.

- **Type 3.** If bleeding is disproportionate to cavity findings, map the contact area with endometrium; hysteroscopy is diagnostic only—definitive treatment is laparoscopic/abdominal myomectomy or hysterectomy when indicated.

- **Type 4.** For large intramural lesions, MRI assessment of degeneration informs blood loss strategies; anticipate multilayer closure to restore uterine architecture.

- **Type 5/6.** Define serosal relation and intramural depth to plan enucleation plane; look for nearby vascular pedicles; in posterior fundal lesions, port placement may need adjustment to avoid bowel adhesions.

- **Type 7.** Confirm uterine origin (bridging vessels/claw sign) and torsion risk; plan vascular pedicle control early; avoid traction that might avulse the pedicle during laparoscopy.

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- **Type 8.** Cervical/broad ligament lesions demand ureteric identification strategies; MRI mapping of parametrial planes is especially helpful.

- **Hybrid** (e.g., 2–5). Stage the plan: hysteroscopic relief of intracavitary component followed by laparoscopic enucleation of the subserosal component, or vice versa, depending on symptoms and access; MRI clarifies which component dominates.

Distinguishing Fibroids from Mimics and Malignancy (Tu et al.)

Although leiomyomas are benign, differentiating them from smooth muscle tumours of uncertain malignant potential and leiomyosarcoma is pivotal. MRI red flags for malignancy include a rapidly enlarging mass in a postmenopausal patient, high T2 signal intensity with heterogeneous or irregular nonenhancing necrotic areas, infiltrative margins, and marked diffusion restriction. Yet overlap exists—cellular and hydropic leiomyomas can be T2 hyperintense with variable diffusion metrics. Thus, correlation with clinical context and lesion circumscription is essential, and indeterminate cases warrant multidisciplinary review or biopsy as per institutional pathways. From a surgical standpoint, suspicious features shift consent, route, and containment strategies.

Leiomyoma Category	Histologic Features	MRI Findings
Conventional	Intersecting fascicles of bland spindle cells with cigar-shaped nuclei are found without atypia, necrosis, or mitotic activity	Circumscribed borders Homogeneous Isointensity or low signal intensity on T1W images Low signal intensity on T2W images Early homogeneous enhancement, similar to myometrial enhancement Low signal intensity on ADC maps
Leiomyoma subtypes		
Cellular	Compact smooth muscle cells without intervening collagen	Circumscribed borders Signal intensity higher than that of myometrium on T2W images Marked avid early enhancement Mild diffusion restriction and lower ADC levels than those of typical leiomyomas
Lipoleiomyoma	Benign smooth muscle proliferation associated with mature adipocytes	Circumscribed borders Signal intensity similar to subcutaneous fat signal intensity with all pulse sequences, with no diffusion restriction or central enhancement
Apoplectic leiomyoma	Sudden hemorrhagic infarction leading to coagulative necrosis	Circumscribed borders Peripheral rim of low signal intensity on T2W images and high signal intensity on T1W images due to obstructed veins Lack of contrast enhancement, particularly within the central portion of the mass
Hydropic leiomyoma	Edematous stroma that causes compartmentalization of the smooth muscle cells, resulting in cystic spaces with acellular centers	Circumscribed borders Cystic spaces with well-defined areas of markedly high signal intensity on T2W images and low signal intensity without enhancement on T1W images
Myxoid leiomyoma	Interspersed abundant myxoid matrix	Circumscribed borders Low signal intensity on T1W images High signal intensity on T2W images Areas of heterogeneous enhancement within hypoenhancing mucinous lakes
Leiomyoma degeneration		
Hyaline degeneration	Smooth muscle tumor cells are surrounded by a zone of hyalinized fibrous tissue	Circumscribed borders Areas of hyaline degeneration that are typically isointense on T1W images, have low signal intensity on T2W images, and have less enhancement than the myometrium

Note.—ADC = apparent diffusion coefficient, T1W = T1-weighted, T2W = T2-weighted.

Putting it all together: A FIGO-focused Reporting Template (US and MRI)

Header: Uterine orientation (AV/RA, flexion), uterine size (three diameters and volume), endometrial thickness and uniformity, adnexae overview.
Lesion inventory (up to four dominant; additional as 'others'):

1. **Lesion ID (A, B, C…); FIGO type; site** (anterior/posterior, fundal, right/left, segment); size (three diameters).
2. **Endometrial relationship:** distance to cavity, base width, indentation depth/angle (submucosal types), length of mucosal contact (Types 3).
3. **Serosal relationship:** distance to serosa, surface bulge, pedicle features (for Types 6–7); presence of bridging vessels.
4. **Internal characteristics:** echotexture/T2 signal, degeneration (cystic, haemorrhagic), calcifications.
5. **Vascularity/enhancement:** Doppler pattern (US); early homogeneous/heterogeneous enhancement (MRI).
6. **Adjunct findings:** adenomyosis features; deep endometriosis nodules, hydrosalpinx.

Impression (surgical summary): Concise list of dominant symptomatic lesions with FIGO codes, proposed routes (hysteroscopic vs laparoscopic/open vs interventional), technical cautions (thin serosal bridge over Type 2, pedicle for Type 7, high vascularity), and suggestions for sequence (if hybrid).
This style—advocated in the US domain by Palheta et al. and mirrored in structured MRI by Tordjman et al.—streamlines planning and documentation while making the radiology report an operative roadmap rather than a catalogue of measurements alone.

Frequently Asked Clinical Scenarios

- **Heavy bleeding with a 'normal' cavity scan**. Look for FIGO 3 lesions that press on but do not enter the cavity; these can be occult at blind biopsy yet symptomatically relevant.
- **Suspected fibroid 'ovarian mass'.** For a mobile adnexal-appearing mass, seek bridging vessels (US Doppler or MR flow voids) and a claw sign; correct identification prevents adnexal surgery.
- **Infertility with multiple fibroids.** FIGO 0–2 lesions merit priority due to cavity effects; intramural lesions that do not distort the cavity may be watched unless large or strategically placed. A combined US+MR approach can isolate the culprit lesion to treat while preserving uterine integrity.
- **Perimenopausal growth.** Reassess with MRI when growth is rapid or imaging features are atypical; surgical planning should incorporate oncologic precautions if malignancy cannot be excluded.

Conclusion

FIGO subclassification transforms imaging into actionable surgical and interventional decisions. In everyday practice:

- **Use ultrasound** to triage, quantify base and wall relationships, document vascularity, and classify clearly using FIGO—particularly for submucosal and pedunculated subserosal lesions.
- **Use MRI** when anatomy is complex, when hybrid or large lesions distort landmarks, or when differentiation from mimics is required. Organ-axial T2-weighted acquisitions heighten staging accuracy, while structured MRI reports that embed FIGO codes and surgical checklists raise decision quality.
- **Communicate in FIGO shorthand** in the impression and theatre brief, highlight risks (thin serosa over Type 2; torsion for Type 7; high vascularity; degeneration), and align routes to anatomy and patient goals.

A disciplined FIGO-based approach—grounded in the imaging strengths of US and MRI—improves safety, reduces operative time, and preserves reproductive outcomes where desired.

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Non-hormonal medical management of fibroids

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Introduction:

Uterine fibroids are the most common benign **pelvic tumors**, affecting >60% of women aged 30–44 years. Abnormal uterine bleeding and heavy menstrual bleeding are the most common symptoms. Heavy menstrual bleeding interferes with physical, social, and emotional well-being. Anemia and its consequences, such as weakness and fatigue, also affect the quality of life (1).

Mechanism of bleeding in fibroids (2)

- Enhanced vascularization: Fibroids lead to increased expression of angiogenic factors, like vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF) and platelet-derived growth factor (PDGF), and endothelin-1. This increased and aberrant angiogenesis results in immature and fragile vessels, prone to haemorrhage.
- The increase in the surface area of the endometrium and the size of the uterine cavity
- Dilated blood vessels on the surface caused by compression of veins by fibroids. The hemostatic actions of platelets and fibrin plugs may be overwhelmed by the enlarged diameter of vessels
- Impaired myometrial contractility
- Hemostasis appears to be altered by a TGF-induced cascade of cytokines, causing defective endometrial decidualization and reduced hemostasis

Management:

Management of fibroids depends on symptoms, their severity, the number, size, and localization of fibroids, and the desire for fertility or to preserve the uterus, irrespective of fertility goals. Hence, counseling is important for tailoring the best individualized treatment plan. Different surgical, medical, or radiologic treatment options should be discussed with the patient, depending on their presentation and choices. Most of the women presenting with AUB prefer to avoid surgery, and many desire to preserve the uterus. The last 2 decades have witnessed a shift toward more conservative interventions. The following are the non-hormonal medical options mainly for symptomatic relief.

Nonsteroidal anti-inflammatory drugs (1)

The NSAIDs decrease both menstrual bleeding and dysmenorrhea. They act by inhibiting cyclooxygenase, thus reducing prostaglandin synthesis at the endometrial level, and reducing the prostacyclin to thromboxane ratio. Data on the efficacy of NSAIDS in the management of heavy bleeding due to fibroids is limited. NSAIDs are less effective than tranexamic acid. However, these are often used as first-line drugs in the management of patients who do not wish to undergo hormonal treatment. NSAIDs have been shown to reduce menstrual blood flow by 20–46% when used alone.

Tranexamic acid

Tranexamic acid inhibits fibrinolysis by reversibly blocking lysine-binding sites on the plasminogen molecule. It slows down the breakdown of blood clots and reduces inflammation, which helps to prevent prolonged bleeding and pain. Hence, it only provides symptomatic relief from bleeding but has no direct effect on fibroids. It is available in oral or intravenous formulations. It is effective in controlling bleeding in acute as well as chronic settings, improving the quality of life. It can be used independently or in conjunction with an NSAID during menstruation. It is effective in reducing menstrual blood loss by 26%–50% (1). Usual dose is 1.3 g three times daily for up to 3-5 days per cycle. Tranexamic acid is generally well tolerated, and there is no evidence suggesting an increased risk of thromboembolic events, even in patients at high risk (3).

In one double-blind, placebo-controlled study, 115 women with heavy menstrual bleeding who received tranexamic acid had a significantly greater reduction in menstrual blood loss of −69.6 mL (40.4%) compared with −12.6 mL (8.2%) in the 72 women who received placebo (P<.001), and a meaningful reduction in menstrual blood flow (defined as 36 mL or higher). The maximum daily dose used in the study was 3.9 g. Women treated with tranexamic acid experienced significant improvements in limitations in social and physical activities, work, and self-perceived menstrual blood loss (P<.01) (4).

Vitamins and supplements

It has been hypothesized that Vitamin D could inhibit fibroid growth. In a recent randomized controlled trial, no statistically significant decrease in the fibroid volume was observed in a group that received Vitamin D for 12 weeks. However, a significant increase in the fibroid volume was observed in the placebo group, implying that Vitamin D consumption may inhibit fibroid growth (5). Similarly, the green tea extract, epigallocatechin gallate, has been shown to inhibit and potentially lead to the apoptosis of fibroid cells. A randomized pilot-controlled clinical study demonstrated that patients who received epigallocatechin gallate had a significant reduction in fibroid volume and associated HMB compared with the placebo group (6). Such studies are limited, and no recommendations can be made without further investigation.

Management of anemia due to heavy bleeding

Simultaneous treatment of anemia resulting from menstrual blood loss is equally important to improve quality of life. Iron deficiency anemia (IDA) resulting from blood loss can be treated either orally or intravenously. Oral iron supplementation is generally used to treat IDA. Intravenous iron is recommended for severe anemia, in non-responders to oral iron, or in cases where a rapid rise in hemoglobin level is required before surgery. Intravenous iron has been shown to lead to a greater increase in hemoglobin and ferritin levels than oral iron

Initial evaluation of the patient with acute AUB should include a prompt assessment for signs of hypovolemia and potential hemodynamic instability. If the patient is hemodynamically unstable or has signs of hypovolemia, intravenous access with a single or two large bore intravenous lines should be initiated rapidly as should the preparation for blood transfusion and clotting factor replacements.

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Hormonal treatments for Uterine Fibroids

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Hormone therapy is a non-surgical approach to managing uterine fibroids. Hormone therapies play a significant role in treating uterine fibroids by altering the hormonal influences that affect their growth and associated symptoms.

Understanding the connection between hormones and fibroids

- Fibroids are sensitive to the female reproductive hormones, estrogen and progesterone.
- Estrogen promotes the growth of fibroid tissue, and higher levels, such as during pregnancy, can lead to their enlargement.
- Progesterone also contributes to fibroid growth by enhancing cell survival and promoting vascular changes that improve blood supply to the fibroids. Types of hormonal treatments

1. GnRH agonists (Gonadotropin-Releasing Hormone Agonists):

• **How they work:** These medications, like leuprolide acetate and goserelin, reduce the production of estrogen and progesterone by temporarily putting the body into a menopause-like state.

• **Benefits:** This can shrink fibroids, alleviate heavy bleeding, reduce pelvic pain, and improve anemia caused by blood loss.

• **Limitations:** GnRH agonists are typically used for short durations (up to six months) due to potential side effects like hot flashes, vaginal dryness, and bone loss. Fibroids may regrow after treatment stops.

2. GnRH antagonists

• **How they work:** These medications, like elagolix and relugolix, directly block GnRH receptors, suppressing the production of LH and FSH without the initial flare-up effect of GnRH agonists.

• **Benefits:** They can significantly reduce menstrual bleeding associated with fibroids.

• **Limitations:** They don't shrink fibroids. They can be used for longer periods (up to two years) when combined with add-back therapy (low-dose estrogen and progestin) to lessen side effects like hot flashes and bone loss.

3. Selective progesterone receptor modulators (SPRMs)

• **How they work:** SPRMs, such as ulipristal acetate, target progesterone receptors in the uterus.

• **Benefits:** They can inhibit fibroid growth and alleviate symptoms like heavy bleeding. Short-term use has been shown to improve quality of life, reduce menstrual bleeding, and increase the rate of amenorrhea (no periods).

• **Limitations:** SPRMs can cause benign progesterone associated endometrial changes (PAECs), which are typically reversible upon discontinuation. Concerns about potential liver toxicity have led to restrictions on their use in some areas.

4. Progestin-releasing intrauterine devices (IUDs)

• **How they work:** These devices release a synthetic form of progesterone (progestinlevonorgestrel) directly into the uterus.

• **Benefits:** They primarily target the endometrium and can help control heavy bleeding, but they don't typically shrink the fibroids themselves.

• **Limitations:** They are not suitable for all women, especially those with very large fibroids that may alter the shape of the uterus, making IUD insertion difficult or in some cases the IUD may be prone to expulsion due to anatomy distortion by the myoma [like in submucous myomas distorting the cavity]

• **Not suitable if uterine volume is in exces of 200cc**

5. Hormonal birth control pills

• **How they work:** Combination pills (estrogen and progestin) or mini-pills (progestin only) can help regulate menstrual cycles and reduce heavy bleeding.

• **Limitations:** Birth control pills don't typically shrink fibroids, and in some women, they may even cause the fibroids to grow larger. They can also have side effects like water retention, headaches, and breast tenderness.

Important notes

• Hormone therapy generally provides symptom relief and can shrink fibroids mostly temporarily. Currently, GnRH agonists and SPRMs are most effective in volume reduction, but they are not a cure and fibroids may regrow after treatment stops.

• The effectiveness and suitability of each hormonal treatment can vary depending on the individual patient's symptoms, fibroid characteristics, and other factors.

• It's essential to discuss the specific situation with a patient (i.e., according to FIGO classification of her myoma/s, her complaints, whether fertility is an issue or heavy menstrual bleeding or other complaint) to determine the most appropriate treatment plan for the fibroid/s

• Hormone therapy in fibroids may be used as a bridge to menopause .

• Hormone therapy may alleviate symptoms before surgery in fibroids .

• Potential side effects with hormone therapy need discussion beforehand with patient

• Regular monitoring including pelvic exams and imaging is recommended during hormone therapy.

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Selective Progesterone Receptor Modulators &Oral Gnrh Antagonists In Treatment Of Fibroids

Author:- Dr. Sreedevi Vellanki
Vijaywada AP

Uterine fibroids are monoclonal tumours arising from uterine smooth muscle cells and myometrial fibroblasts. These tumours, although benign, are commonly associated with abnormal uterine bleeding, bulk symptoms and reproductive dysfunction. Being hormone sensitive they occur more frequently during reproductive years and are rarely seen before menarche. Traditionally, surgery has been the mainstay of management for symptomatic UF, with either myomectomy for fertility preservation, or hysterectomy . Nonsurgical conservative interventions include uterine artery embolization, focused energy delivery systems, and radio frequency myolysis. Until recently, medical management for UF symptoms has been limited to oral contraceptives, LNG IUS, progestins, NSAIDS, tranexamic acid, danazol, and GnRh agonists.

Recently a new class of medication called SPRMs has shown promise for treatment of women with fibroids. The class of SPRMs includes various drugs such as mifepristone, ulipristal acetate and asoprisnil. SPRMs can cause benign changes to the endometrium that are not related to cancer and are not precancerous. It has been discovered that progesterone and PRs are required for cellular proliferation and fibroid growth. Compared to the surrounding myometrium, fibroids express elevated levels of both types of PR: PR-A and PR-B. Progesterone and its receptors therefore represent potential targets for inhibiting UF growth. SPRMs are designed to compete at the PR binding site in a tissue-specific manner. Binding of the SPRM to the PR leads to a mix of agonistic and antagonistic effects. The relative strength of these opposing effects may be related to the proportions of PR-A and PR-B in the particular tissue and the SPRM's specific affinity for each receptor isoform. By acting on PRs throughout the reproductive system, SPRMs induce several effects that assist in bleeding control and fibroid shrinkage. These include direct antiproliferative ,proapoptotic ,antiangiogenic and antifibrotic effects on leiomyoma cells; endometrial changes that reduce bleeding; and inhibition of the pituitary gland's luteinizing hormone surge, resulting in anovulation and subsequent amenorrhea.

SPRMs may be used in the following indications:

1.Women who decline surgery or UAE.
2.Surgery or UAE are not suitable.
3.Surgery or UAE have failed.

1.ULIPRISTAL ACETATE [UPA] : UPA is a synthetic SPRM with predominant inhibitory action on PR.A dose of 5mg od can be used for 3 month course up to 4 courses with 2 months break in between two courses. Monitor LFTs before starting UPA, monthly for first two courses and once before each new course, 2-4 weeks after treatment is stopped and when clinically indicated. Do not initiate UPA if ALT/AST exceeds twice the upper limit of normal. UPA is contraindicated in women with underlying liver disease and should not be used for women waiting for surgery as bridging therapy.

PAEC [Progesterone associated endometrial changes]are benign and reversible changes seen in 60% of women treated with 3 months of UPA and are completely reversible within 6 months after cessation of treatment. Intermittant treatment is advised to allow the women to menstruate during the off period which helps in reversal of changes. In March 2020,the license for UPA 5mg was suspended by the European Medicines Agency and its Pharmacovigilance Risk Assessment Committee due to drug induced liver injury [DILI] requiring Liver Transplant in 5 cases.The suspension was lifted in February 2021 but with RESTRICTED USE as the incidence of DILI was lower than DILI caused by Paracetamol.

2 trials established the safety and efficacy of UPA as compared to either placebo (PEARL I) or the GnRHa leuprolide acetate (PEARL II). Across these 2 trials, UPA was superior to placebo and noninferior to leuprolide acetate on key clinical end points. The most common adverse events with UPA were headache and breast tenderness, although these did not occur significantly more often than with placebo in PEARL I. Moderate to severe hot flashes were reported in 11% of patients in PEARL II compared to 40% of patients treated with leuprolide acetate ($P < .001$), albeit without add-back therapy.The VENUS-I trial was designed to reflect the US population and satisfy US Food and Drug Administration requirements. Similar to PEARL I, VENUS-I compared 5- and 10-mg UPA doses to placebo, but in a population consisting of 69% African American patients. Preliminary results showed that UPA was superior to placebo for rate of amenorrhea and time to amenorrhea. Furthermore, 3 months of UPA reduced the impact of UF symptoms on patients' daily activities compared to the baseline evaluation. The PEARL III and IV data and preliminary findings from VENUS-II demonstrated that repeated courses of UPA are safe and effective at maintaining long-term control of fibroid symptoms, with a therapeutic effect lasting for at least 3 months beyond treatment cessation.

2.MIFEPRISTONE [RU-486] : This is the original PR modulator prescribed for medical management of HMB. Dose is 10-25 mg od or 50 mg alternate days for 3 months. The drug causes endometrial atrophy and amenorrhea and raises hemoglobin. But the effect of Mifepristone on volume of fibroid is debatable.
Several other SPRMs have been studied in UF, notably Asoprisnil, Telapristone acetate and Vilaprisan. As a class, the SPRMs have been shown to be effective for improving QoL, decreasing menstrual blood loss, and achieving amenorrhea. There have been 2 randomized trials evaluating asoprisnil from 5-20 mg per day. These studies showed that asoprisnil is able to suppress uterine bleeding in a dose dependent manner in patients with UF. Its clinical development was halted in 2007 due to a change in priorities by its developer. Telapristone acetate is another SPRM that has shown promise in animal models and preliminary clinical research; its development was briefly suspended in 2009 due to liver toxicity concerns but has now restarted, using a lower dose. Vilaprisan is a novel SPRM currently in the late stages of clinical development.

ORAL GnRh ANTAGONISTS IN TREATMENT OF FIBROIDS.

Novel gonadotrophin releasing hormone (GnRh) antagonist treatments have recently been developed in combination with hormonal add-back therapy, as an oral treatment option for women suffering from uterine fibroids.

Registration trials assessing the GnRH antagonist combination preparations with Relugolix, Elagolix and Linzagolix have assessed treatment efficacy for fibroid-related heavy menstrual blood loss in comparison to placebo. These agents competitively block the GnRH receptors causing rapid dose -dependant decrease in gonadotropin and subsequent suppression of ovarian steroid hormones. The action starts within 24 hrs and is easily reversible on discontinuing the drug due to its short half-life and there is no initial flare effect.Due to the risk of hypoestrogenic effects and bone loss,GnRh antagonist therapy may be combined with an addback therapy with 1mg Estradiol and 0.5mg norethindrone acetate once daily.

Elagolix

Elagolix is a non-peptide gonadotropin-releasing hormone (GnRH) receptor antagonist. It works by suppressing the pituitary secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to a reduction in ovarian hormone production. It is primarily used for managing moderate to severe pain associated with endometriosis and uterine fibroids.

Indications

-Moderate to severe pain associated with endometriosis -Management of heavy menstrual bleeding due to uterine fibroids in premenopausal women

Contra-Indications

-Pregnancy (Category X) -Severe hepatic impairment -Known hypersensitivity to Elagolix or its components.

Special Precautions :Monitor for signs of bone loss; supplement with calcium and vitamin D if necessary. -Caution in patients with cardiovascular risk factors due to possible lipid changes. -Not recommended for use in women with osteoporosis.

Side Effects

Common: Hot flashes, headache, nausea, fatigue, and insomnia

Serious: Bone density reduction, hepatic enzyme elevation, and mood disturbances Rare: Allergic reactions

Drug Interactions:

Potent CYP3A4 inhibitors or inducers may alter Elagolix plasma concentrations. -Avoid co-administration with drugs highly dependent on CYP3A4 for clearance.

Trials- Elaris UF-1and Elaris UF-2 evaluated the safety,tolerability and efficacy of 6 month Elagolix treatment with dosage of 300 mg twice daily either alone or in combination with hormonal add-back therapy. Later Elaris UF EXTEND study was carried out for another 6 months[upto 12 months total]of elagolix 300mg twice daily with hormonal add back therapy.Results showed that total 12 months of combination treatment still sustained MBL reduction while no new safety concerns were associated with an additional 6 months.

RELUGOLIX:

Relugolix is an orally active nonpeptide GnRH-receptor antagonist that is suitable for daily use. It competitively binds to pituitary GnRH receptors, blocking the binding and signaling of endogenous GnRH and thus leading to reversible, dose-dependent decreases in gonadotropin concentrations and subsequent suppression of ovarian estradiol and progesterone production. In previous phase 3 trials involving Japanese women with symptomatic fibroids, relugolix at a dose of 40 mg led to improvements similar to those observed with leuprolide acetate with regard to heavy menstrual bleeding, anemia, and pain and to a significant reduction in pain as compared with placebo. To achieve efficacy, minimize hypoestrogenic side effects, and preserve bone mineral density, relugolix combination therapy (consisting of 40 mg of relugolix, 1 mg of estradiol, and 0.5 mg of norethindrone acetate) was developed as a once-daily treatment for maintaining estradiol levels within the physiologic range of the early follicular phase of the menstrual cycle, with the addition of a progestin to mitigate the unopposed estrogen action that could lead to endometrial hyperplasia.

Two replicate international, double-blind, randomized, placebo-controlled, phase 3 trials (LIBERTY 1 and LIBERTY 2) were conducted to assess the efficacy and safety of once-daily relugolix combination therapy in women with fibroid-associated heavy menstrual bleeding. A delayed relugolix combination therapy regimen, which consisted of relugolix monotherapy for 12 weeks followed by 12 weeks of relugolix combination therapy, in an additional group of participants to assess the benefit and safety of the addition of estradiol and norethindrone acetate was evaluated. In these trials, once-daily relugolix combination therapy resulted in a substantial reduction in heavy menstrual bleeding in women with uterine fibroids, with resolution of anemia, a reduction in pain, and reduced distress related to bleeding and pelvic discomfort, while preserving bone density and minimizing the incidence of hot flashes associated with relugolix monotherapy.

Uterine fibroids have an impact on women's lives due to their high prevalence, physical symptoms, their consequences on patients' emotional and psychological well-being and loss of work productivity. The choice of therapeutical approaches varies depending on several factors, and therefore should be applied individually. Currently, there is an unmet need for good, reliable, uterine-sparing options.

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Nutraceuticals, Vitamin D, and Lifestyle Interventions in Uterine Fibroids: A Non-Pharmacological Perspective

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Introduction

Uterine fibroids (leiomyomas) are the most common benign tumors in women of reproductive age, with an estimated incidence of 20–40% in this population (Stewart E A etal , 2017). Although often asymptomatic, fibroids can cause significant morbidity, including heavy menstrual bleeding, pelvic pain, and infertility. While surgical and pharmacological interventions remain the mainstay of treatment, increasing interest has emerged in non-pharmacological approaches. Among these, nutraceuticals, Vitamin D supplementation, and lifestyle interventions have shown promise in both prevention and management of uterine fibroids.

Nutraceuticals and Fibroid Management

Nutraceuticals—bioactive compounds derived from food sources—have gained popularity due to their antioxidant, anti-inflammatory and anti-proliferative properties.

1. Epigallocatechin Gallate (EGCG)

EGCG, the most abundant catechin in green tea, has shown significant potential in reducing fibroid volume and symptom severity. Studies suggest that EGCG inhibits fibroid cell proliferation, induces apoptosis, and reduces expression of fibrosis-related proteins (Zhao et al., 2010). In a randomized controlled trial by Roshdy et al. (2013), green tea extract significantly reduced fibroid size and improved quality of life compared to placebo.

2. Curcumin

Curcumin, the active component of turmeric, exerts potent anti-inflammatory and anti-proliferative effects. It has been found to inhibit the growth of leiomyoma cells and modulate pathways involved in cell cycle regulation and apoptosis (Akarapon Sukonthanonta et al 2015). Though clinical data is limited, in vitro studies show promising results for fibroid suppression.

3. Resveratrol

Resveratrol, a polyphenol found in grapes and red wine, has demonstrated anti-fibrotic and anti-proliferative effects. It inhibits estrogen-induced proliferation of uterine fibroid cells and promotes apoptosis (Islam MS et al 2014). Resveratrol may also modulate angiogenesis, which is crucial in fibroid growth.

4. Omega-3 Fatty Acids

These essential fatty acids possess anti-inflammatory properties and may influence estrogen metabolism. While direct evidence in fibroids is limited, higher omega-3 intake is associated with reduced inflammation and a lower risk of hormone-related disorders, suggesting a potential role in fibroid prevention (Andrea tenelli et al,).

5. Vitamins A, C, and E

These antioxidant vitamins help reduce oxidative stress, which is implicated in fibroid pathogenesis. Vitamin A regulates cell differentiation and proliferation, while vitamins C and E scavenge free radicals that could otherwise promote fibroid growth (Iwona Szydłowska et al 2022).

6.Vitamin D and Uterine Fibroids

Vitamin D has emerged as a key factor in fibroid development and progression. Several observational studies have reported an inverse relationship between serum Vitamin D levels and fibroid prevalence.

Mechanisms of Action

Vitamin D acts through the vitamin D receptor (VDR), which is expressed in fibroid tissue. Its anti-fibrotic, anti-proliferative, and pro-apoptotic effects are well-documented. Specifically, Vitamin D:

Inhibits fibroid cell proliferation.
Downregulates expression of transforming growth factor-beta (TGF-β), a key mediator in fibrosis.
Reduces extracellular matrix (ECM) production, which is crucial in fibroid development (Halder et al., 2012).

Clinical Evidence

A study by Sabry et al. (2013) found that women with low serum 25(OH)D levels were significantly more likely to have fibroids. In a pilot study, Al-Hendy et al. (2016) demonstrated that Vitamin D3 supplementation (50,000 IU weekly) reduced fibroid size over 12 weeks. Although more extensive trials are needed, these findings support the potential of Vitamin D as a non-invasive treatment option.

Supplementation Guidelines

Although optimal dosing varies, many clinicians recommend 1,000–4,000 IU/day for women with fibroids, especially in those with documented deficiency. Regular monitoring of serum 25(OH)D levels is advised.

Lifestyle Interventions

Lifestyle choices significantly impact hormonal balance and inflammation, both of which are central to fibroid development. Adopting healthy behaviors can play a preventive and therapeutic role.

1. Diet and Nutrition

Diet influences fibroid risk through estrogen metabolism, inflammation, and oxidative stress.

Beneficial Foods:

Fruits and vegetables: Rich in antioxidants and phytoestrogens; reduce oxidative stress and modulate estrogen activity.

Whole grains and legumes: High in fiber; aid in estrogen elimination via the gut.

Dairy products: Some studies suggest a protective role due to calcium and vitamin D content.

(Islam M.S., Segars J.H.,2017)

Foods to Avoid:

Red and processed meats: Associated with higher estrogen levels and increased fibroid risk.

High-glycemic index foods: Promote insulin resistance and inflammation, potentially exacerbating fibroid growth (Chiaffarino et al., 1999).

2. Physical Activity

Regular exercise helps maintain a healthy weight and reduce estrogen levels (Donna Day Baird et al2006). A cohort study by Wise et al. (2006) found that women engaging in regular physical activity had a 30% lower risk of developing fibroids compared to sedentary individuals.

3. Weight Management

Obesity is a known risk factor for uterine fibroids due to increased peripheral aromatization of androgens to estrogens in adipose tissue. Maintaining a normal BMI helps reduce estrogenic stimulation of fibroid growth.

4. Stress Reduction

Chronic stress elevates cortisol, which can disrupt reproductive hormone balance. Stress management techniques such as yoga, meditation, and mindfulness can help restore hormonal equilibrium and potentially mitigate fibroid symptoms (Dr R Pavithra et al 2024).

Conclusion

The integration of nutraceuticals, vitamin D supplementation, and lifestyle interventions offers a promising, low-risk approach to the management of uterine fibroids. While not a replacement for medical or surgical treatment, these strategies can complement conventional therapies, especially for women seeking fertility preservation or symptom relief without invasive procedures. Further clinical research is warranted to establish standardized protocols and confirm long-term outcomes.

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Hysteroscopic Myomectomy and office procedures

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Background

Uterine fibroids or leiomyomas are most common benign tumours of female genital tract being found in almost 80% women. Majority of them are asymptomatic. Certain risk factors increase the likelihood of development of fibroids like African race, genetic predisposition, family history, alcohol consumption, obesity, unopposed estrogen exposure, hypertension and vitamin D deficiency. Submucous myomas represent about 5-10% of all myomas.

Clinical presentation

Fibroids can have varying presentation from being completely asymptomatic to presenting with lump in abdomen, pain in abdomen, heavy menstrual bleeding, abnormal uterine bleeding, dysmenorrhea, poor reproductive outcomes and subfertility. Clinical symptoms and examination findings depend on size and location of fibroids. Submucous myomas often present with menstrual abnormalities, subfertility and adverse reproductive outcomes.

Evaluation and assessment

After detailed history and thorough clinical examination, first line of investigation to confirm the diagnosis is transvaginal ultrasound.

Ultrasound

TVUS is low cost, easily accessible, and accurate. On ultrasound myomas typically appear as well circumscribed, hypo-echoic masses and submucous may appear as thickened endometrium. They need to be differentiated from endometrial polyps. Submucous myomas are often hypoechoic with peripheral vascularity, whereas endometrial polyp is often echogenic with feeding vessel. 3D USG combined with saline infusion sonography (SIS) gives fairly accurate information about number of myomas, cavitary indentation, myoma mantle and distance from serosa; all of which play important role in deciding choice of surgery and route.

Hysterosalpingography (HSG)- gives cavitary outline and tubal patency. However, does not give any opinion about fibroid topography or overlying myoma mantle.

MRI- MRI is not routinely indicated in uterine fibroids but can aid in certain difficult cases where > 4 fibroids are present, fibroid in difficult/ atypical location like cervical or broad ligament, where uterine volume is >375 $cm^{3,}$

Classification

The two main classifications used for categorising fibroids are the ESGE classification developed by Wansteker et al in 1993 and the STEP-W classification proposed by Lasmar in 2005.

Image 1 showing ESGE classification for submucous myomas.

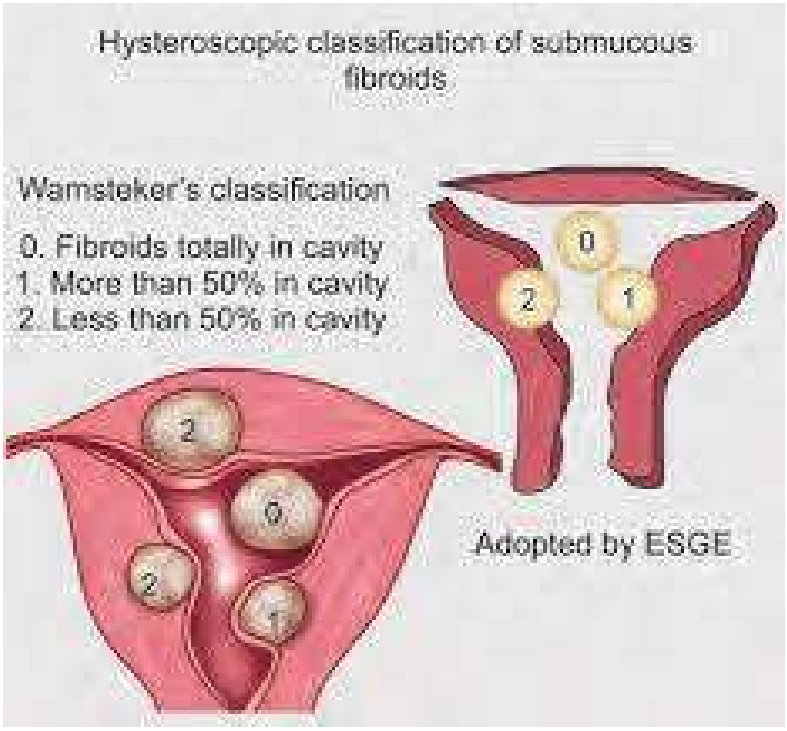
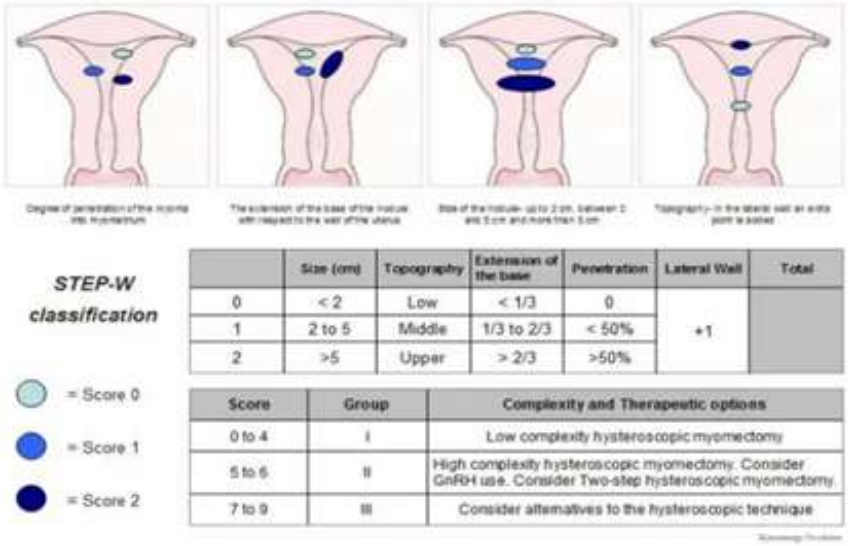


Image 2 showing STEP- W classification by Lasmar that takes into account degree of penetration of fibroid into myometrium, size of nodule, extension of base of myoma, wall of origin.



	Size (cm)	Topography	Extension of the base	Penetration	Lateral Wall	Total
0	< 2	Low	< 1/3	0	+1	
1	2 to 5	Middle	1/3 to 2/3	< 50%		
2	>5	Upper	> 2/3	>50%		

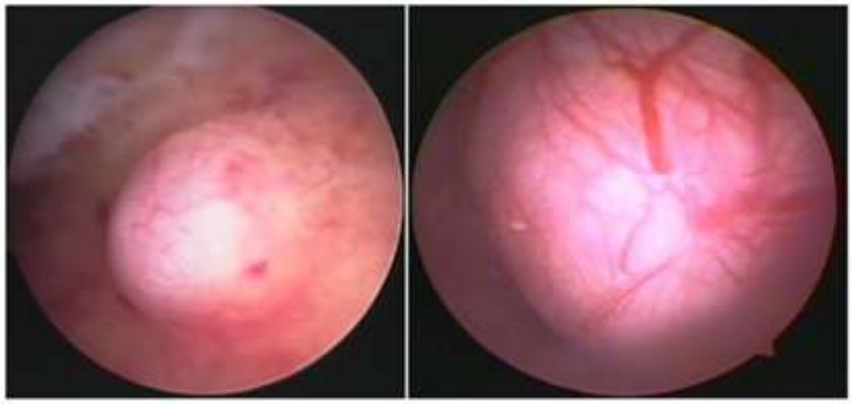
Score	Group	Complexity and Therapeutic options
0 to 4	I	Low complexity hysteroscopic myomectomy
5 to 6	II	High complexity hysteroscopic myomectomy. Consider GnRH use. Consider Two-step hysteroscopic myomectomy
7 to 9	III	Consider alternatives to the hysteroscopic technique

Hysteroscopic myomectomy

Traditionally for submucous myomas also, treatment options included hysterectomy or abdominal myomectomy. Hysteroscopic myomectomy was first reported in 1976, nearly 5 decades ago by Neuwirth and Amin. It is now the standard approach for management of isolated/ predominantly submucous symptomatic myomas. Hysteroscopic myomectomy is a trans cervical procedure which is minimally invasive.

Benefits of this procedure include symptom relief, early postoperative recovery, early ambulation, minimal need for analgesics and lower morbidity. Owing to technical improvements and widespread availability hysteroscopic myomectomy has increased manifold.

Image 3 showing hysteroscopic appearance of submucous myoma.



Indications

Symptomatic woman with submucous myoma

Desirous of preserving menstrual/ fertility function.

Contraindications

Active pelvic inflammatory disease, fever, tubo ovarian abscess or hydrosalpinx, cervical cancer, suspected pregnancy

Prerequisites

Preoperative preparation

Best planned in follicular phase when pregnancy is ruled out, endometrium is thin, and chances of bleeding are less.

GnRH agonists may reduce myoma size by 30-50% and decrease endometrial vascularity as well, but routine preoperative use is not recommended. GnRH agonist pre-treatment maybe useful in selected cases with multiple myoma, myoma > 3 cm, myoma mantle < 8 mm, located close to cornu.

Instrumentation

Rigid telescope with operating channel, mechanical instruments like scissor and grasper, loop resectoscope for electrosurgical slicing, mechanical tissue removal system, fluid management system

Anaesthesia- small type 0 fibroid maybe addressed in office setting, however regional anaesthesia is preferred as patient is more comfortable, and consciousness levels can be monitored.

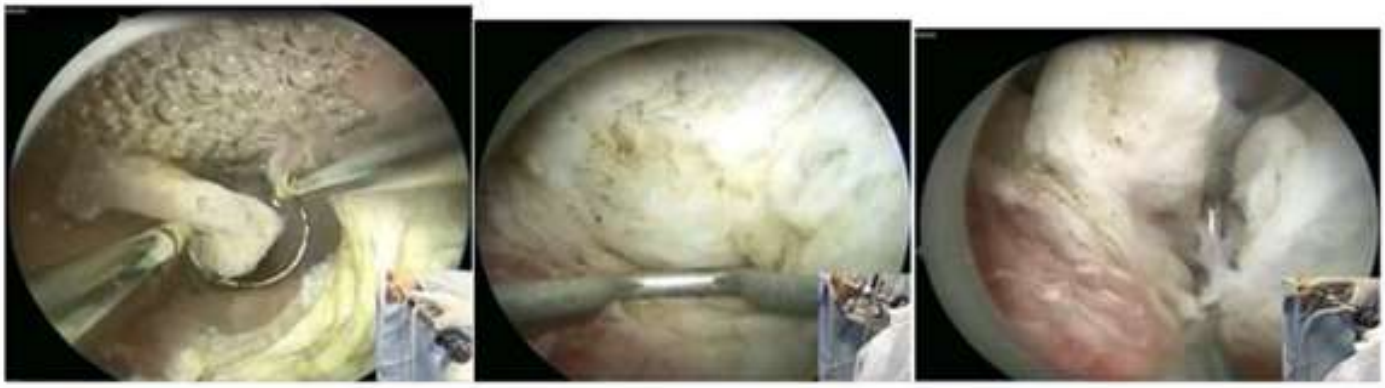
Dilute vasopressin (20 units/ I ampoule in 200 ml normal saline), 5 cc may be injected into cervical stroma at 11,2,4,7 o clock positions respectively.

Avoid overzealous cervical dilatation as it can increase risk of cervical laceration and cause fluid leak resulting in poor pressures and visualisation.

Techniques

Slicing technique

- Incremental and systematic excision of myoma in segments
- Excision started at surface and progressing towards base.
- Slicing/ shaving movement takes place during backward/ return movement of the loop.
- Segments removed intermittently from uterine cavity.
- Resection is stopped when fasciculate structure of myometrium is visualized.
- This method allows for treating bigger nodules, removal of myoma pieces from cavity, simultaneous haemostasis and volumetric reduction.
- Disadvantages include risk of perforation, surgical interruption for removal of fragments and potential damage to surrounding endometrium/ myometrium.



- Speed of loop affects balance between coagulation and cutting effect, slower speed favouring coagulation and faster speed cut.

Resection of pedicle

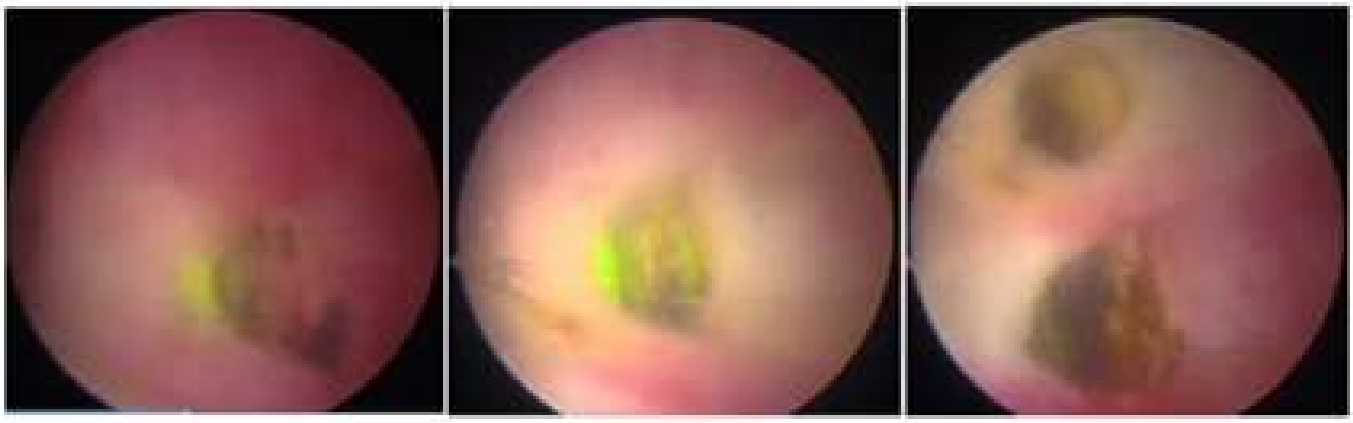
- Small pedunculated myoma
- Pedicle cut with scissor or electrosurgical loop.
- Detached myoma maybe extracted with forceps.

Hysteroscopic Morcellation

- Now hysteroscopic Tissue retrieval systems are available or TRS.
- Primary brands used are Myosure, Truclear and Symphion
- Utilized mainly for type 0 and 1 myomas.
- Simultaneous excision by swift blade and aspiration of tissue fragments in tissue trap takes place.
- Advantage is ease of use, shorter learning curve, reliance on only mechanical energy.

Laser myolysis

- Laser application causes myolysis leading to myoma destruction or delayed expulsion.
- Mainly diode laser is used with 5 fr fibre, with combinations of two wavelengths 980nm and 1470 nm.



Radiofrequency ablation

- Additional USG guided myolysis technique.
- Uses radiofrequency ablation handpiece connected to special intrauterine USG probe.
- Myolysis using laser/ radiofrequency does not give tissue specimen for pathology.

OPPIuM technique

- Office Preparation of Partially Intramural Myoma Technique
- Aim to downgrade type I and type II myomas to facilitate easy and safe resection subsequently.
- First sitting- office procedure, incision made on endometrial mucosa covering myometrium till the pseudo capsule.
- Follow up hysteroscopy after 2 menstrual cycles- myoma often becomes grade 0 making removal easy.

Caution & Complications

- Amongst all hysteroscopic procedures, myomectomy has highest number of complications with reported complications in 0.3-28% cases. Fluid intravasation and uterine perforation are commonest reported complications.

- Cervical lacerations can take place during dilatation/ instrumentation. Foley/ tamponade or local suturing usually suffice.
- Uterine perforation- if energy source was being used, then immediate laparoscopy should be done to rule out abdominal organ injuries. Procedure should be abandoned.
- Uterine bleeding- pre procedure dilute vasopressin and simultaneous coagulation of vessels maybe done to reduce likelihood.
- Fluid overload
- Infections
- Air embolism
- Postoperative adhesions
- Myomas situated on opposing walls should never be resected simultaneously as it increases the likelihood of adhesion formation.

Post operative recovery.

Patient may experience slight spotting for 2-4 wk. after surgery.
Menstrual hygiene should be maintained.
Sexual intercourse may be resumed after 7 days.
Douching is not recommended.

In case of grade 0 myoma, pregnancy maybe attempted after 1 month and in broad base/ large intramural component myomas, after 6-8 weeks following surgery.

Infertility/ amenorrhea post-surgery should be evaluated hysteroscopically to rule out post-surgery endometrial synechiae.

Key points-

- Hysteroscopic myomectomy is standard of care for submucous myoma. This procedure can give excellent results but is also a more challenging hysteroscopic procedure with higher complication rates.
- Meticulous attention to patient evaluation, preoperative planning, preparedness, appropriate procedure, performed correctly can give good results.

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LAPROSCOPIC AND ROBOTIC MYOMECTOMY

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INTRODUCTION

Uterine leiomyomas are very common, occurring in up to 80 % of reproductive-aged women [1]. Over half of women with uterine leiomyomas are symptomatic, with the majority presenting with abnormal uterine bleeding, bulk symptoms, pelvic pain, recurrent pregnancy loss, and even infertility thereby posing a significant health burden [2], [3] Management of uterine leiomyomas can be organized into four different categories: expectant, medical, interventional, and surgical. For those who are symptomatic and desiring fertility-preservation or simply a uterine-sparing procedure, myomectomy is the principal intervention [4]. The primary surgical techniques used in myomectomy are open surgery, laparoscopic surgery, and, recently, robot-assisted ("robotic") surgery.

Informed Consent before myomectomy: KNOW BEFORE YOU GO

- The general risks and complications associated with laparoscopic and robotic surgery must be explained to patients before surgery. All cases who undergo myomectomy are required to have a caesarean section at the time of giving birth after undergoing this surgery.

- Another important issue is the case of unexpected malignancy. There is a possibility of the scattering of tumour cells resulting in poor survival outcome.

There is also the risk of rupture of the uterus during pregnancy. If there are a large number of fibroids or if the fibroids are in the areas that are difficult to access, there is a possibility of not being able to perform hemostasis and subsequent need for hysterectomy.

- **Preoperative Evaluation and Treatment**

Preoperative suppressive therapies such as danazol or gonadotropic-releasing hormone agonists (GnRH), may enable restoration of a normal haematocrit, decrease the size of myomas. GnRH agonists have negative side effects such as the development of a pseudo-menopausal hypoestrogenic state and are associated with a possible increased risk of myoma recurrence. In addition, studies have also shown that agonist therapy can soften myomas, obscuring the cleavage plane between the fibroid and the pseudo capsule, making the surgery more difficult with increased bleeding.

Role of imaging: Fibroid Mapping "REVEAL THE UNSEEN"

- The FIGO classification system is useful for uniform and consistent classification of fibroids. To be able to manage these fibroids, it is vital to understand their number, site, size and character. It is much more relevant if we want to opt for non-surgical management methods including Uterine Artery Embolization (UAE) Options for Fibroid mapping

- 2D & 3D Ultrasonography (preferably TVS-USG is the initial investigative modality for diagnosis of uterine fibroids. Small fibroids up to few mm can also be identified. Transvaginal USG is better suited to identify smaller fibroids, while transabdominal route is better for large fibroids. (5)

- The 3D technology involves capturing serial sequential 2D images in three different planes: axial, horizontal and perpendicular, which is then converted into volume data. It can be stored and analyzed in different angles and arbitrary planes. This allows for better reproducibility, as well as ease of review of the stored data by a second reviewer. 3D -USG captures coronal view of the uterus and helps in delineating extension of fibroid within the myometrium and endometrial cavity, differentiating it from adenomyoma and adenomyosis

- MRI: The MRI seems to be superior to 2D US, SIS and diagnostic hysteroscopy. MRI can identify fibroids as small as 5 mm; their precise location including cervical and parasitic and the extent and type of degeneration and views of the endomyometrial junctional zone (EMJ)

- MRI possesses the highest sensitivity and specificity (88– 93 %, 66–91 %, respectively) among all modalities and for differentiating fibroids from focal adenomyosis. Subserosal fibroids may be differentiated from solid ovarian masses by Bridging vascular sign. The diagnostic clue is that the mass is separate from the ovary and a feeding vessel can be demonstrated arising directly from the uterus.

ROBOTIC SURGERY IN GYNAECOLOGY

Gynaecologic surgery has traditionally been taught through laparotomy or a vaginal approach. During laparotomy, the surgeon has the benefit of depth perception and haptic feedback from the resistance of tissue. The human wrist affords 6 degrees of freedom for intra-abdominal suturing.[6]

The advent of laparoscopy created a minimally invasive alternative to laparotomy for cases that cannot be performed vaginally. Laparoscopy has evolved significantly over the last decades, with improved hand instrumentation, electrosurgical devices, and high-intensity light sources.[7]Advantages of laparoscopy over laparotomy include decreased postoperative pain, a shorter hospital stay, faster return to normal activities, better cosmetic results, and less blood loss.[8,9] This represents an enhancement along the continuum of laparoscopic technological advances. Robotic instrumentation provides 7 degrees of freedom: 3 degrees provided by the robotic arms (insertion, pitch, yaw) and 4 degrees from the "wristed" instruments (pitch, yaw, roll, and grip).[6]This improves dexterity and enables the surgeon to manipulate and dissect tissue in a delicate, controlled fashion. Robotic technology may improve efficiency, accuracy, ease, and comfort associated with the performance of laparoscopic operations such as hysterectomies for benign and malignant indications, myomectomies, tubal reanastomoses, complex endometriosis surgery, and sacrocolpopexies.[7]Cited advantages of robotic technology over conventional laparoscopy include absence of tremor, a 3-dimensional image, superior instrument articulation, downscaling of movements, and comfort for the surgeon.

Robot setup times by the operative room staff, operative times for use of robot, total operative times, and perioperative outcome were analysed. The learning curve was defined as the number of cases required to stabilize operative time to perform the various procedures.

Comparison of Robotic (and Robot-Assisted), Open, and Laparoscopic Myomectomy

Laparotomy has long been the standard surgical approach to myomectomy because it allows easy access to the uterus for the removal of large fibroids. However, it usually requires a large incision and, compared with minimally invasive surgery, is associated with longer hospitalization, considerably higher levels of postoperative analgesia, and increased morbidity.[10]

Moreover, second-look laparoscopic studies examining adhesion formation after an open myomectomy have demonstrated the presence of adhesions. Patient who underwent robot-assisted laparoscopic myomectomy had significantly decreased estimated blood loss, complication rates, and length of stay, but the operative times were significantly longer in the robotic group.

It does not offer insight into the level of expertise of the robotic myomectomy teams compared with the standard laparoscopic myomectomy teams. The learning curve is a fundamental variable to be addressed when comparing proficiency levels and complication rates of robotic procedures.

LIMITATION

Some of the major limitations include surgical system and specialized equipment costs, the need for personnel training, the learning curve associated with learning a new surgical technique and extended operative time. There is also a lack of tactile feedback during the procedure, which may lead to breakage of suture or applying excessive traction on the myoma resulting in breaching and compromising the endometrial cavity, which is an undesirable outcome. Port placement in robotic surgery is another limitation as the ports are larger than the typical conventional laparoscopic ports and they are placed higher on the abdomen. This higher port placement will make possible conversion of robotic to laparoscopic myomectomy more challenging if needed. The use of the robot system is also limited due to its size. Any position changing requires undocking and re-docking the robot which will result in even more added surgical time.[11] These aspects can all have a great impact on the cost-effectiveness of robotic surgery.

CONCLUSION

In myomectomy there are three important steps—enucleation, repair, and extraction. Each of them requires advanced skills. Laparoscopic suturing and knot tying are important prerequisites for attempting this kind of surgery. We need to continually train ourselves in basic laparoscopic skills like suturing, knot tying, and needle driving using a dry box to achieve the level required to manage this kind of surgery safely. To achieve healthy wound healing, accurate intracorporeal suturing is vital.

It is very likely that the different techniques will continue to coexist in the future, and that open, laparoscopic, robotic, and robot-assisted myomectomy will be performed based on the clinical scenario and surgeon expertise. More research is needed to define preoperative factors that make one approach superior to another for a given clinical situation, both in terms of patient outcomes and cost effectiveness.

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INTERVENTIONAL RADIOLOGY: UAE, HIFU & RFA

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Introduction

The advent of interventional radiology (IR) has significantly transformed the therapeutic landscape of benign gynaecological pathologies, especially uterine fibroids. With an increased emphasis on fertility preservation, shorter recovery times, and patient-centric care, procedures like Uterine Artery Embolization (UAE), High-Intensity Focused Ultrasound (HIFU), and Radiofrequency Ablation (RFA) offer compelling alternatives to traditional surgical approaches. These modalities align with the modern gynecologist's pursuit of minimally invasive and uterus-conserving treatment strategies.

This chapter delineates the principles, indications, and practical considerations of UAE, HIFU, and RFA, with an emphasis on device availability, radiation exposure, informed consent, and disposable resource utilization, particularly relevant in the Indian healthcare setting.

Uterine Artery Embolization (UAE)

Principle and Indications

UAE involves transcatheter occlusion of uterine arteries using embolic agents to induce ischemic infarction of fibroids. Indications include symptomatic uterine leiomyomas, adenomyosis, arteriovenous malformations, and refractory postpartum haemorrhage. UAE offers symptom relief in ~85-90% of cases.

Device Availability

In India, UAE is performed in most tertiary care institutions equipped with digital subtraction angiography (DSA) suites. However, access is uneven across public hospitals. Availability of trained interventional radiologists is a rate-limiting factor in non-metro areas.

Radiation Considerations

UAE involves moderate to high radiation doses depending on fluoroscopy duration and technique. According to the Society of Interventional Radiology, typical dose-area product (DAP) ranges between 50–200 Gy.cm^2. Optimization strategies include:

- Low-dose pulsed fluoroscopy
- Collimation and beam filtration
- Real-time dose monitoring

Though radiation is largely within permissible thresholds, counselling women desiring future fertility is critical.

Consent Essentials

- Risk of premature ovarian failure, especially in women >40 years
- Potential need for repeat procedures or conversion to surgery
- Post-embolization syndrome

- Impact on fertility remains inconclusive

The landmark RCT by Manyonda et al. (NEJM 2020) compared UAE and myomectomy, showing similar quality-of-life outcomes but higher reintervention rates in the UAE group.

Disposables Utilized

- 4–5F angiographic catheters (e.g., Cobra, Simmons)
- Hydrophilic guidewires
- Embolic materials: Polyvinyl alcohol (PVA), calibrated microspheres
- Sheaths, syringes, contrast media
- Sterile draping kits and flushing systems

High-Intensity Focused Ultrasound (HIFU)

Principle and Indications

HIFU is a non-invasive thermoablative technique that uses converging ultrasound waves to raise the temperature of fibroid tissue to 60–90°C, inducing coagulative necrosis without damaging surrounding myometrium. MRI-guided and ultrasound-guided systems are available.

Common indications include solitary or few intramural/subserosal fibroids <10 cm, with favorable acoustic windows.

Device Availability

HIFU availability is currently restricted to select urban centers in India. Systems like Chongqing Haifu JC200, Sonalleve, and INSIGHTEC ExAblate are used, requiring significant infrastructural investment. Lack of public-private partnerships hinders wider adoption in the government sector.

Radiation Profile

HIFU is entirely radiation-free, offering an excellent option for reproductive-age women. MRI-guided HIFU poses no ionizing exposure but adds to procedural cost and duration.

Consent Essentials

- Not all fibroids are amenable (calcified, pedunculated, deeply posterior)
- Longer procedural time (~2–3 hours)
- May require multiple sessions
- Risk of skin burns, thermal injury, nerve damage (rare)
- Limited long-term fertility outcome data

The **NICE IPG770 (2022)** recommends HIFU for fibroids with proper patient selection and institutional experience.

Disposables Utilized

- Acoustic coupling gel pads
- Degassed water tanks (if required)
- Disposable bed covers and probe protectors
- Gowns and sterile barriers

Radiofrequency Ablation (RFA)

Principle and Indications

RFA employs needle electrodes to deliver alternating current-induced thermal energy to fibroid tissue, usually under laparoscopic or transvaginal ultrasound guidance. Ablation temperatures reach ~100°C.

RFA is suitable for women with moderate-sized symptomatic fibroids desiring uterine preservation, especially those unfit for surgery.

Device Availability

RFA is increasingly available in private hospitals across India. Commercial systems include the Acessa ProVu™, Celon (Olympus), and STARmed Viva RF. Equipment costs are moderate, but single-use probes drive up per-case expense.

Radiation Profile

RFA is typically performed under USG or laparoscopic visualization, avoiding radiation. In oncology contexts (e.g., liver or kidney tumors), CT-guidance may involve radiation exposure.

Consent Essentials

- Fertility outcomes are under-studied
- Requires general anesthesia
- Potential for fibroid recurrence or incomplete ablation
- Limited access in rural settings

The 2023 review by Brucker et al. (Obstet Gynecol) reaffirmed RFA as a safe, uterus-sparing alternative with good patient satisfaction and low complication rates.

Disposables Utilized

- RF probes (monopolar or bipolar)
- Generator electrodes and grounding pads
- Laparoscopic access instruments
- Smoke evacuation filters
- Sterile consumables

Comparative Summary

Parameter	UAE	HIFU	RFA
Invasiveness	Minimally invasive (endovascular)	Non-invasive	Minimally invasive (lap/USG)
Radiation Exposure	Moderate	None	None (usually)
Anesthesia Requirement	Local/Regional	None/Conscious sedation	General

Device Availability	Moderate	Low	Moderate
Disposable Burden	High	Low	Moderate
Impact on Fertility	Inconclusive	Possibly favorable	Unknown
Time to Recovery	3–7 days	1–2 days	3–5 days
Long-term Data	Extensive	Growing	Emerging

Challenges in Implementation (Indian Context)

- **Infrastructure gaps:** Absence of DSA suites or HIFU-compatible imaging platforms in district hospitals.
- **Cost barriers:** High cost of disposables and capital equipment; limited insurance coverage.
- **Training limitations:** Scarcity of trained IR specialists and cross-disciplinary collaboration.
- **Patient awareness:** Myths around infertility and poor understanding of IR procedures persist.
- **Regulatory gaps:** Absence of national guidelines on selection criteria and procedural standards.

Conclusion

UAE, HIFU, and RFA represent the vanguard of fibroid management in a fertility-conscious, minimally invasive era. Each modality presents unique benefits and limitations, with appropriate patient selection being the cornerstone of success.

Multidisciplinary collaboration among gynaecologists, radiologists, and anaesthesiologists, along with strategic investments in training and infrastructure, is imperative. India's healthcare system stands to benefit significantly from expanding access to IR procedures, particularly for women in resource-constrained regions.

As we advance, outcome registries, long-term fertility data, and cost-effectiveness studies will further consolidate the role of interventional radiology in routine gynaecologic practice.

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Hysterectomy For Fibroids -Indications And Medicolegal Pearls

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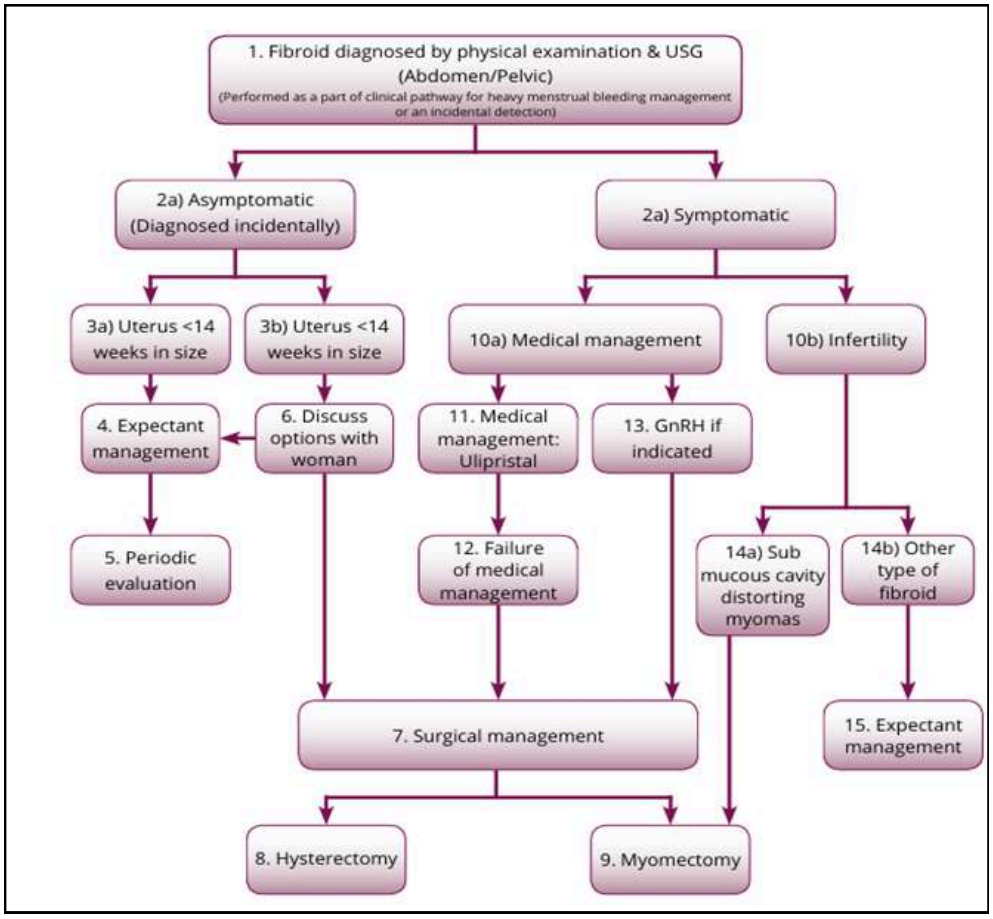

Hysterectomy is considered when Leoimyoma when coexists with the following

Symptomatic fibroids not amicable to medical or conservative management and patient is not keen on fertility or menustrual function
Uterine size >14 week

Coexisting problems like
Adenomyosis
Abnormal uterine bleeding
chronic pelvic pain/pelvic inflammatory disease (PID)
Uterovaginal prolapse (UV prolapse)
Endometriosis
Precancerous lesions of cervix
Premalignant conditions of uterus (atypical endometrial hyperplasia)
Malignant tumors of uterus and cervix
Gender affirming surgery

GTD family completed in selected cases esp when not tolerating Mtx /uncontrolled bleeding
Uterine transplant after CS
PPH

Specific indications related to type of hysterectomy:
NDVH:
Hysterectomies should be routinely done by the vaginal route esp when less than 16 week and depends on the surgeons expertise .

TAH:
When hysterectomy via vaginal route is contraindicated and LAVH appears risky or very difficult esp
Uterus 20 weeks size or greater
Adnexal pathology
Invasive cancer
Multiple surgeries on uterus previously
Adhesions
If adnexal pathology is suspicious of malignancy or frozen study at laparoscopy or VH suggests possible or doubtful
Malignancy
Advanced endometriosis
Excessive vaginal narrowing

LAVH:
LAVH is indicated when laparoscopic assistance can undo contraindication or the hindrance to perform VH
Uterine fibroids, adenomyosis, and dysfunctional uterine bleeding with uterine size greater than 12–14 weeks size or
broad ligament fibroid, or uterine volume more than 300 cc.

coexisting problems like
Benign ovarian cyst, tubal, and/or ovarian mass (non-malignant and non-tuberculous)
Endometriosis
Pelvic adhesions
PID
Chronic pelvic pain
Occasionally, oophorectomy or salpingo-oophorectomy

MEDICOLEGAL ASPECTS OF HYSTERECTOMY
Hysterectomy, or the surgical removal of the uterus, in India is subject to specific medicolegal considerations and guidelines, particularly due to concerns surrounding unnecessary procedures, especially in younger women and marginalized communities.

1. Informed Consent

- Mandatory: Valid and informed consent is crucial for any medical procedure, including hysterectomy.
- Comprehensive Information: Patients must be fully informed about:

o The indications for the procedure (medical necessity).
o Alternative treatment options (medical and non-surgical).
o The risks and benefits associated with the surgery.
o Potential complications during and after the procedure.
o Long-term consequences, including potential for early menopause if ovaries are removed.
o Impact on quality of life after the operation.

- Voluntary and Comprehensible: The consent process must ensure the patient's decision is voluntary and that they fully understand the information presented, tailored to their age, mental status, and intellectual abilities.
- Documentation: Clear and comprehensive documentation of the informed consent process is vital for legal protection and accountability.

2. Appropriate indications and alternatives

- Hysterectomy as a last resort: FOGSI guidelines and court pronouncements emphasize that hysterectomy should be considered a last resort, after exploring and exhausting all other reasonable medical and non-surgical treatment options.
- Focus on treatment pathways for common conditions: Guidelines highlight specific treatment pathways for conditions that commonly lead to hysterectomy, such as:

o Abnormal Uterine Bleeding
o Vaginal Discharge
o Lower abdominal pain/Pelvic Inflammatory Disease (PID)
o Abnormal looking cervix (requiring evaluation and treatment to rule out malignancy, not necessarily hysterectomy)
o Uterocervicovaginal Prolapse

- Emphasize non-surgical alternatives: FOGSI actively promotes alternatives like LNG IUS (Levonorgestrel intrauterine system) for managing heavy bleeding as a non-surgical option.

3. Auditing and monitoring of hysterectomies

- Focus on prevention: Guidelines stress the importance of robust monitoring mechanisms to prevent unnecessary procedures.
- Audit Committees: District and State level committees are mandated to audit hysterectomy cases, particularly for women under 40 or in cases where no clear indication or prior treatment history is documented.
- Data Collection and Analysis: Hospitals are required to submit monthly data on hysterectomies, including patient demographics, indications, and chosen surgical routes.
- Addressing Concerns: Audits should also investigate discrepancies between indicated conditions and histopathology reports, as well as instances of severe morbidity or mortality.

4. Addressing medicolegal risks

- Potential for Negligence Claims: Doctors face increasing scrutiny regarding the appropriateness of hysterectomy decisions.
- Inadequate Information & Unjustified Procedures: Failure to obtain proper informed consent or performing a hysterectomy without sufficient medical justification can lead to allegations of medical negligence and battery.
- Court Rulings and Guidelines: The Supreme Court of India and the Ministry of Health & Family Welfare have issued guidelines and directions to address these concerns, focusing on proper regulation and monitoring.
- Focus on Documentation and Transparency: Thorough documentation of the entire medical process, from diagnosis and counseling to surgical procedure and follow-up care, is crucial to demonstrate adherence to guidelines and mitigate legal risks.

The Federation of Obstetric and Gynaecological Societies of India (FOGSI) plays a significant role in formulating policy statements and guidelines for its members to ensure ethical and appropriate practices related to gynecological care, including hysterectomy.

In conclusion, the performance of hysterectomy in India is increasingly regulated, emphasizing informed patient choice, adherence to guidelines, comprehensive documentation, and diligent monitoring to prevent unnecessary procedures and minimize medicolegal issues.

Government of India launched "Guidelines to prevent Unnecessary Hysterectomies in October-2022. The guidelines have already been circulated to all state/UTs for strict compliance of the guidelines including setting of Hysterectomy Monitoring Committee at State/UTs and District level. The National Hysterectomy Monitoring Committee (NHMC) has been formed under the Chairpersonship of Additional Secretary & Mission Director, NHM, Ministry of Health and Family Welfare, Government of India (c)& (d) As per the National Family Health Survey-5 (2019-21), the percentage of hysterectomy in Private health facilities has increased by 2.3% from 67.3% in NFHS-4 (2015-16) to 69.6% in NFHS-5 (e) & (f) Government of India has issued direction vide DO.No.H.11016/21/2019-MCH on dated 4th October 2022 to all State/UTs for strict compliance to the "Guidelines to prevent Unnecessary Hysterectomies" both in public and Private hospitals.

The action points in this regard are as follows;

The State/District Nodal Officer to facilitate to capture and analyses the data on hysterectomy in both public and private hospitals in the prescribed data collection form. State/District to issue necessary orders to both public and private sectors to submit a line list of all women who underwent hysterectomy every month At district level, both public & private facilities must submit, line list of women who underwent hysterectomy which includes following parameters like her age, Parity, Occupation, Indication of hysterectomy, previous medical/surgical history, Hysterectomy route, past treatment history etc. The State/District nodal officer will also be responsible for audit of the data on regular basis of Hysterectomy cases, where age of the patients are less than 40 years Arrange necessary trainings and sensitization sessions for both public and private sector professionals Apart from this, State level committee to meet every 6 months to review the district level data to ensure that unnecessary hysterectomies can be avoided

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Fibroids & Fertility

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Introduction:

A global analysis of infertility trends shows that the global age standardized prevalence rate of female infertility (agnostic of cause) increased at 0.68%. [1] Parallelly the uterine fibroid showed a 0.27% increase in age specific incidence rate. 52 out of 88 countries worldwide showed significant increase in fibroid incidence for the reproductive age group. [2] The sync in increases of incidence of infertility and fibroid incidence lays the foundation for the need for this discussion.

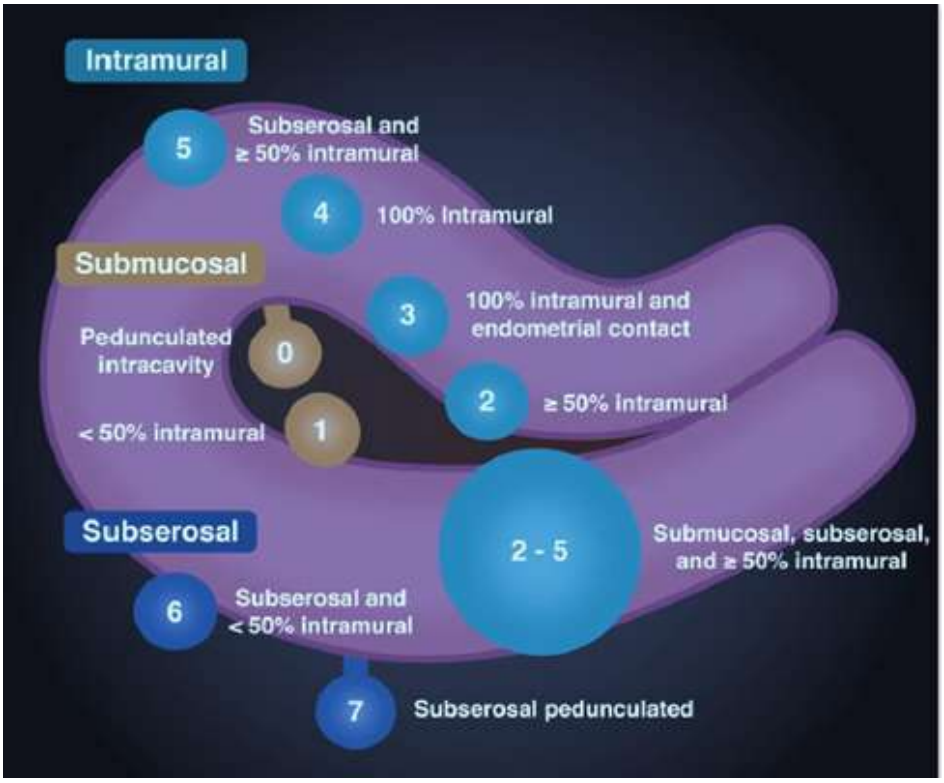


Figure 1. Fibroid nomenclature – FIGO.

A review of the terminology used to describe fibroids is important for clarity (figure 1)

Location specific impact of fibroids

·A 63% reduction and in clinical pregnancy rates 68% risk of miscarriage with Types 0,1,2 fibroids (compared to no fibroids) have been confirmed.

- Types 6,7 fibroids have no (or very little) impact on fertility.
- There are difficulties in ascertaining the fertility impact of fibroids with types 3,4,5

- Secondary analyses of individual studies have shown conflicting data regarding the relationship between intramural fibroids and fertility.
- Results of prior studies which included fibroids not distorting cavity and fibroids distorting cavities are now considered less relevant.
- Bias and confounding factors (retrospective nature of studies, other comorbidities, age, male factor etc) are difficult to sort out.
- One methodologically superior systematic review meta-analysis (Wang et al) which investigated fibroids not disturbing cavity (but excluding subserosal) confirmed reduction in live birth (relative risk of 0.82, p value 0.005) and clinical pregnancy rates (relative risk 0.86, p value 0.005).
- A reduction in pregnancy outcomes does not necessarily mean that surgical correction is beneficial.

How do fibroids affect fertility?

Figure 2. Mechanisms of fibroid related infertility

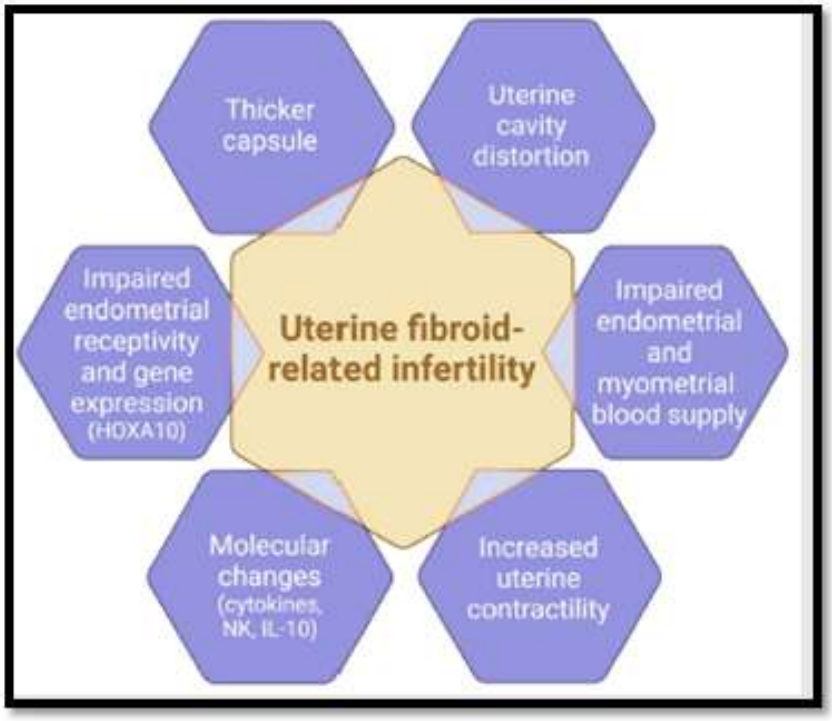
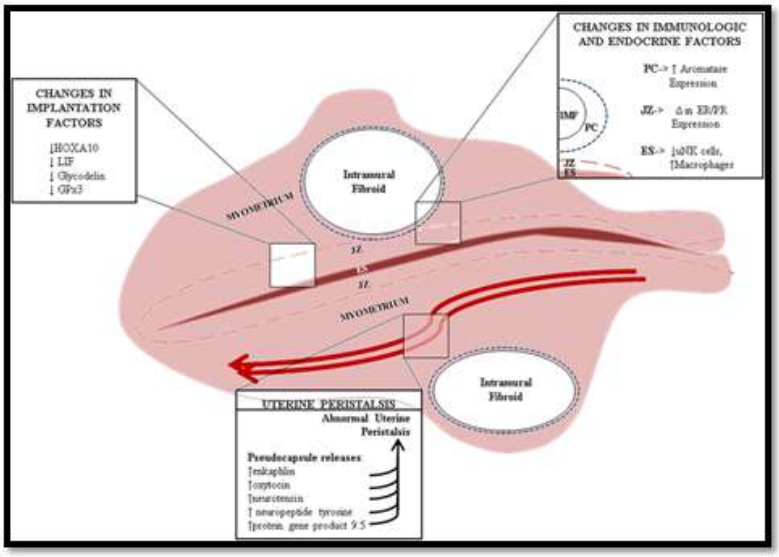


Figure 3. Mechanisms of fibroid related infertility



The pathophysiology of fertility problems in the context of fibroids are summarized in figures 2 and 3. These can be classified as stated below.

Alteration in implantation factors

- HOXA 10 (a homeobox-containing transcription factor that is essential for embryonic uterine and adult endometrial development during each menstrual cycle) alteration affects endometrial receptivity.
- Glycodelin (a glycoprotein that affects cell proliferation, differentiation, adhesion, and motility) reduction causes implantation problems.
- Fibroid induced alteration / thickening / disruption of the Uterine junctional zone (inner third of myometrium immediately adjacent to the endometrium) can lead to infertility/ early pregnancy loss.

Uterine myometrial peristalsis

- Myometrial contractions are expected to be minimum during implantation windows (upto 7 days post-ovulation) but presence of fibroid may alter this.
- Uterine myometrial peristalsis (observable by MRI analysis) showed demonstrable reduction after myomectomy,
- Pseudocapsule of the fibroid (which marks the boundary of the fibroid) are rich in neovascularization molecules like endogloin, CD34 and other molecules like tyrosine, neurotension and protein gene product 9.5, all which are known to induced myometrial contractions.

Immunological alterations

- Alteration in Uterine natural killer cells (uNK) and macrophages (a commonly noted feature in fibroids) contributes to implantation failure.
- Alteration in the estrogen receptor-progesterone receptor concentration gradient can also get altered affecting early pregnancy outcomes.
- Localized changes in aromatase expression owing to fibroid presence alters fertility outcomes.

MANAGEMENT OF FIBROIDS

There is a great deal of heterogeneity in the studies which have analyzed impact of surgical options (myomectomy) on pregnancy rates. Discussing all the relevant studies which have seemingly conflicting results and differ subtly is beyond the purview of this chapter. ASRM summary statements and recommendations and unanswered questions are presented below.

SUMMARY OF EVIDENCE STATEMENTS

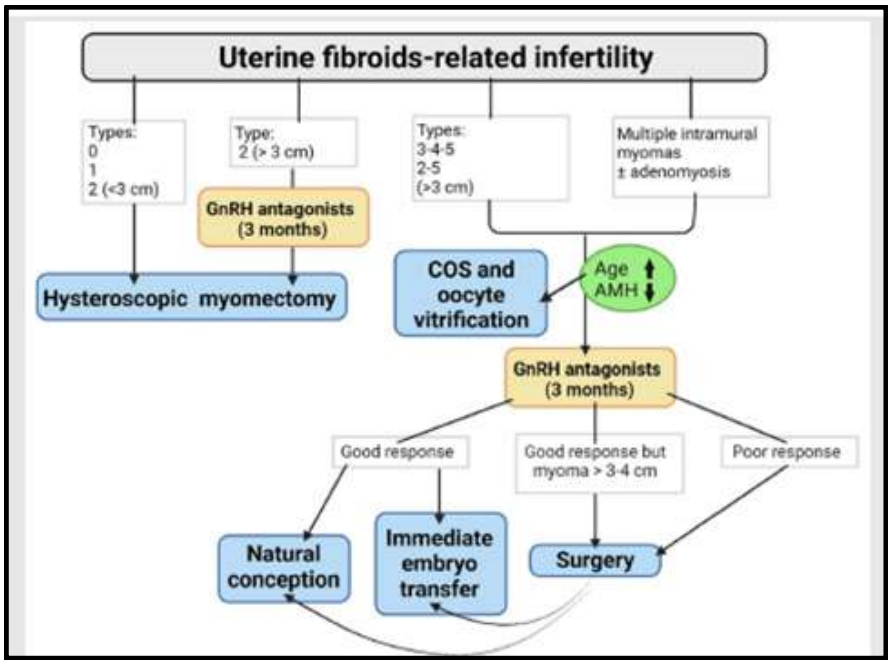
- There is insufficient evidence to conclude that myomas reduce the likelihood of achieving pregnancy with or without fertility treatment. (Grade C)
- There is insufficient evidence that removal of subserosal fibroids improves fertility. (Grade C)
- There is fair evidence that myomectomy does not impair reproductive outcomes (clinical pregnancy rates, livebirth rates) following ART. (Grade B)
- There is insufficient evidence that myomectomy (laparoscopic or open) reduces miscarriage rates. (Grade C)
- There is fair evidence that hysteroscopic myomectomy for submucosal myomas improves clinical pregnancy rates. (Grade B)
- There is insufficient evidence to conclude that hysteroscopic myomectomy reduces the likelihood of early pregnancy loss in women with infertility and a submucous fibroid. (Grade C)

RECOMMENDATIONS FOR SURGICAL MANAGEMENT

- In asymptomatic women with cavity-distorting myomas (intramural with a submucosal component or submucosal), myomectomy (open or laparoscopic or hysteroscopic) may be considered to improve pregnancy rates.
- Myomectomy is generally not advised to improve pregnancy outcomes in asymptomatic infertile women with non-cavity–distorting myomas. However, myomectomy may be reasonable in some circumstances, including but not limited to severe distortion of the pelvic architecture complicating access to the ovaries for oocyte retrieval.
- It may be reasonable to accept the SOGC guideline in this respect wherein surgery is indicicated for Infertile women with large (>5 cm) Type II submucosal fibroids or Type II fibroids with <1 cm between the external surface of the fibroid and uterine serosa.

Way forward

Despite the lack of high level evidence, there is always a need for an algorithmic approach, which is presented below.



UNANSWERED QUESTIONS AND FUTURE RESEARCH ITEMS

- What is the impact of leiomyomas on fecundability?
- Does the degree of cavity distortion impact the benefit of myomectomy? Better assessment of the cavity in clinical trials is needed.
- What is the true impact of intramural fibroids with no submucosal component on reproductive outcomes?
- What is the value of myomectomy on ART outcomes?

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Pregnancy with Fibroids – Maternal and Perinatal Outcomes

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Introduction

Uterine fibroids are common benign tumours in women of reproductive age, with a pregnancy prevalence of 1.6% to 10.7%.[1] Diagnosis may be missed, especially for fibroids under 5 cm, due to limitations in clinical and ultrasound detection during pregnancy. The physiological thickening of the myometrium during pregnancy being responsible for diagnostic dilemmas. As more women delay childbirth, fibroids during pregnancy are increasingly encountered. In women undergoing infertility treatment, fibroid incidence ranges from 12% to 25%, making this a growing clinical concern.[2]

Fibroid-Related Symptoms and Pathophysiology in Pregnancy

Only 10–20% of fibroids become symptomatic during pregnancy, with pain—typically from red degeneration or torsion—being the most common presentation, especially in fibroids >5 cm during the late first or early second trimester. Less commonly, symptoms include pelvic pressure, vaginal bleeding, or fibroid impaction. Rapid fibroid growth may outpace its blood supply, causing necrosis, ischemia, and prostaglandin release, resulting in pain. Though fibroids may grow modestly during pregnancy (about 12% in volume), most show minimal change postpartum, with around 7.8% decreasing in size during puerperium. [3,4]

Maternal Outcomes in Pregnancy with Fibroids

1. First trimester complications

Miscarriage: Fibroids are linked to an increased risk of spontaneous miscarriage, with number and location being more significant than size. Higher risk is seen with multiple fibroids, those distorting the endometrial cavity, and those located in the uterine corpus, particularly submucosal or intramural types. Klatsky et al. reported an Øadjusted odds ratio of 1.68 (95% CI: 1.23–2.31) for miscarriage in such cases. Proposed mechanisms include increased uterine contractility, compression effects, and impaired placental blood supply.[5]

First trimester screening.: Fibroids are known to interfere with normal placental implantation. The possible turnover of the fibroid cells may have an effect on the genetic screening tests. The effect on either genetic biochemical screening result values or fetal cell-free DNA testing on the fetal fraction is not well known.

2. Antepartum Complications

- **Hemorrhagic Complications in Pregnancy:** Bleeding in early pregnancy is more likely when the placenta implants near a fibroid, especially with multiple fibroids. Submucosal, retroplacental, and intramural fibroids within 2 mm of the endometrial cavity or larger than 200 cm^3 are independent risk factors for placental abruption, likely due to ischemia and decidual necrosis from impaired blood flow. Fibroids also double the risk of placenta previa, even after accounting for previous uterine surgeries. Additionally, prolapse of a pedunculated fibroid through the cervix may mimic antepartum hemorrhage, requiring careful differential diagnosis.

- **Preterm labor:** Mechanical irritation and increased uterine irritability may contribute to preterm labor. Multiple fibroids and those in contact with the placenta are considered independent risk factors for preterm labor, especially with fibroids bigger than 5 cm. [6,7] The obstetrician's tendency to plan cesarean myomectomy may also influence the rate of preterm deliveries.

- **PPROM:** Fibroids do not seem to increase the risk of preterm premature rupture of membranes. In fact, various studies suggest a decreased risk of PPROM in women with fibroids.

- **Fetal growth restriction:** Women with fibroids are at slightly increased risk of delivering a growth-restricted infant, especially when fibroids impinge on placental implantation zones.

- **Preclampsia:** Fibroids in early pregnancy may impair trophoblast invasion, potentially contributing to preeclampsia later. However, it remains unclear whether fibroids directly increase the risk of developing preeclampsia.

3. Labor and Delivery:

·Fibroids are associated with an increased risk of malpresentation, obstructed labor, and cesarean delivery, although the incidence of labor dystocia remains relatively low. Large, multiple, and lower uterine segment fibroids interfere with effective uterine contractions and increase uterine tonus due to reduced oxytocinase activity. This limits fetal positioning and raises the risk of breech presentation or cephalopelvic disproportion. Cesarean delivery rates increase almost three fold compared to those without fibroids.

- **Post partum Hemorrhage:** Fibroids may distort the uterine architecture and interfere with myometrial contractions leading to uterine atony, postpartum hemorrhage and eventually puerperal hysterectomy.

- **Morbidly adherent Placenta:** Adherent placenta may be found in cases of the placenta implanting over the submucous myoma, or myomectomy scar. Retained placenta is more common in all women with fibroids compared with control subjects, regardless of the location of the fibroid.

- Rare complications of fibroids with pregnancy include DIC, cervical pregnancy, hemoperitoneum, uterine inversion, urinary retention or L5 radiculopathy.

Perinatal Outcomes

NICU admissions are higher due to prematurity, LBW, respiratory distress syndrome, hyperbilirubinemia, or birth asphyxia following obstructed labor. No consistent link exists between fibroids and congenital anomalies or perinatal mortality, though large submucosal fibroids may cause fetal deformities like dolichocephaly, torticollis, or limb defects.

Management of fibroids in pregnancy

- Management of fibroids in pregnancy depends upon the period of gestation and symptoms. Asymptomatic fibroids are managed conservatively.

- Fibroid pain in pregnancy is usually managed conservatively with rest, hydration, and analgesics. Acetaminophen is the first-line treatment, opioids; injectable or patches may be added if needed. NSAIDs like ibuprofen can be used before 32 weeks but should be limited due to risks like ductus arteriosus closure, oligohydramnios, and platelet dysfunction. Prolonged NSAID use (>48 hours) in the third trimester requires caution.

- **Myomectomy during pregnancy.** Antepartum myomectomy in the first or second trimester has shown comparable obstetric and neonatal outcomes to conservative management, though cesarean delivery is more common due to rupture concerns. Indications include intractable pain, large or rapidly growing fibroids, torsion, or compression of adjacent organs.

- **Uterine artery embolization:** a conservative modality for the treatment of symptomatic fibroids, is absolutely contraindicated in pregnancy and in women desiring future fertility.

Cesarean Myomectomy: Risks and Emerging Evidence:

Once avoided due to hemorrhage risks, cesarean myomectomy is now considered safe in selected cases when performed by skilled teams. Zhao et al.'s meta-analysis of over 5,000 cases showed no significant rise in blood loss, hysterectomy, or hospital stay with adequate precautions.[9] Advantages include smaller myometrial incision due to a lower uterus-to-fibroid ratio, easier enucleation and suturing due to softer gravid myometrium, and enhanced hemostasis from physiological uterine contractions with or without added oxytocics. Additional benefits reduced need for repeat surgeries and anesthesia. Proper case selection, surgical expertise, and preparedness for complications are essential for favorable outcomes and cost-effective care.

Indications of Caesarean Myomectomy:

1. Fibroids obstructing the uterine incision or interfering with delivery or uterine closure.
2. Large subserosal or pedunculated fibroids at risk of torsion postpartum.
3. Symptomatic fibroids causing significant pressure symptoms.
4. Patients for whom future surgery poses increased risk.
5. Limited access to follow-up care or difficulty returning for a second surgery.
6. Patient request for removal of known fibroid during caesarean.
7. Postpartum risks of retaining fibroids: atonic PPH, subinvolution, and uterine inversion with fundal fibroids.

Surgical Considerations and Technique

Before surgery, obtaining detailed informed consent is essential. Instrument selection depends on surgical expertise, fibroid features, and institutional resources. Prepare caesarean, hysterectomy, and blood loss management trays in advance. Common instruments include Metzenbaum/Mayo scissors, myoma screws, Bonney clamps, and Green-Armytage forceps. Techniques like uterine tourniquets, electrocautery, uterine artery ligation, and oxytocin help reduce bleeding. Avoid myomectomy if the placenta lies beneath the fibroid; decisions must prioritize maternal safety.

Steps of Performing CM: -

1. Administer general anesthesia to manage potential hemodynamic instability and prolonged surgery.
2. Insert two 16-gauge IV cannulas before induction.
3. Give 1000 mg tranexamic acid IV pre-induction.
4. Perform cesarean using the Munro-Kerr technique; use an upper segment incision if a fibroid obstructs the lower segment.
5. Deliver the baby before proceeding with myomectomy, unless fibroid removal is essential for delivery.
6. Avoid incising directly over fibroids during hysterotomy whenever possible.
7. Actively manage the third stage of labor.
8. Infuse 20–30 units of oxytocin in 500 mL dextrose at 60–90 drops/min.
9. Exteriorize the uterus for better access.
10. Repair the uterine incision promptly.
11. Infiltrate the fibroid capsule with diluted vasopressin (20 units in 500 mL saline).
12. Temporarily occlude uterine artery flow using a Penrose drain or bilaterally ligate uterine arteries if required.
13. Perform intracapsular myomectomy using blunt/sharp dissection and myoma screw; avoid entering the uterine cavity.
14. Reapproximate the myometrium in layers; close serosa with herringbone/baseball stitch.
15. Apply anti-adhesive gel.
16. Place a wide-bore drain in the pouch of Douglas and close the abdomen in layers.
17. If bleeding continues, ligate internal iliac arteries or proceed to hysterectomy.
18. Monitor blood loss and provide fluid/blood replacement as needed.
19. Insert 800 mg rectal misoprostol postoperatively and continue oxytocin infusion for 24 hours.

Surgical Advances in Cesarean Myomectomy: Hemorrhage reduction during cesarean myomectomy is achieved using high-dose oxytocin, uterine tourniquets, electrocautery, and bilateral uterine artery ligation. Modern tools have enhanced safety—vessel sealing devices like LigaSure and Harmonic Scalpel reduce blood loss and duration, while hemostatic agents (Floseal, Surgicel, Gelfoam) limit suturing. Barbed sutures enable efficient closure, and ultrasound guidance aids in locating deep fibroids. Despite these advances, risks include intraoperative bleeding, pelvic organ injury, longer operative time, postpartum hemorrhage, blood transfusion, ileus, extended hospitalization, or the need for reoperation if complications arise.

Drug Safety in Pregnancy with Fibroids

1. Analgesics: as discussed above
2. Tocolytics: Nifedipine is relatively safe and commonly used for uterine irritability. Magnesium sulfate is reserved for neuroprotection and preterm labor. Progesterone helps suppress myometrial activity and prevent preterm labor. Indomethacin should not be used beyond 32 weeks.
3. Tranexamic Acid: Safe for antenatal and intraoperative bleeding; no teratogenic risk reported.
4. Uterotonics: Oxytocin, misoprostol, and carboprost manage uterine atony, with close monitoring due to altered fibroid-affected myometrium response.

Conclusion

Pregnancy with fibroids requires individualized care, including vigilant antenatal monitoring, personalized obstetric planning, and selective surgical intervention. Cesarean myomectomy is increasingly safe with experienced surgeons. Ensuring drug safety and incorporating updated guidelines are essential to achieving optimal maternal and perinatal outcomes in these complex pregnancies.

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Health Economics and Quality of Life in Uterine Fibroid Management

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Introduction

Uterine fibroids (leiomyomas) are common benign tumors among reproductive-age women, significantly affecting both physical and psychological health. Their management must align with national policies that balance clinical effectiveness, health economics, and quality of life (QoL). In this chapter, we critically analyze health economic concerns—including cost per QALY for therapies like GnRH antagonists and medical device procurement policies—in direct alignment with ICMR and Ministry of Health and Family Welfare (MoHFW) guidelines, and cite all relevant national protocols.

Epidemiology, Burden, and National Context

The prevalence of uterine fibroids among Indian women is substantial, with studies estimating rates up to 11.35%—with excessive bleeding and fibroids being the principal cause for hysterectomy in India [1].The impact on work productivity and overall QoL underlines the necessity for economically sustainable, guideline-directed management.

Clinical Management Framework: National Guidance and Indian Council of Medical Research (ICMR) Guidelines

Blanket use of hysterectomy is discouraged. Less invasive options (medical management, uterine artery embolization) prioritized according to symptoms, age, and fertility preferences [2][3]. Medical therapies: First-line options include tranexamic acid, LNG-IUS, and oral progestogens. Recent protocols acknowledge newer therapies such as GnRH antagonists for selected cases [2].Surgical management: Reserved for cases where other modalities fail, with clear advice to avoid hysterectomy in women under 35 whenever possible [2][3].

MoHFW Standard Treatment Guidelines:

MoHFW reaffirms that: Not all fibroids necessitate surgical intervention; observation remains appropriate for asymptomatic women or those with small fibroids [4][5].Long-term safety, cost burden, and patient values must be considered in selecting therapy.

Health Economic Evaluation in Fibroid Management

Cost-Effectiveness and QALY

QALY (Quality-Adjusted Life Year) is the central metric in health economics, integrating both survival duration and health-related quality of life. Cost per QALY assists policymakers in assessing the value and sustainability of various treatment options.

GnRH Antagonists

International analyses (NICE, UK) estimate cost-effectiveness ratios for oral GnRH antagonists like relugolix between £2,795–£5,808 per QALY gained compared to GnRH agonists, factoring in reduced need for invasive procedures and improved adherence. Indian-specific economic data remain limited but follow similar trends due to growing local availability and adaptation into national protocols [2][6].

Cost-utility gains stem from: Decrease hospitalization, lost from work,Non-invasive administration (oral route).

National Policy on Economic Evaluation

Current Indian guidelines do not mandate QALY reporting, but progressive integration is recommended for all new therapies and medical devices as per ICMR and MoHFW policy statements [7][2][4].

Quality of Life: Assessment and Outcomes

QoL Measurement Tools: Standard Tools advocating validated as VAS and disease-specific questionnaires —embedded within clinical audits [2][1]. Evidence shows significant improvements in VAS scores post-intervention, particularly after myomectomy, embolization medical therapy [1].

Impact of Fibroid Therapies on QoL

Indian and global studies report that effective management of fibroids—especially with agents like GnRH antagonists or LNG-IUS—markedly increases patient-reported QoL and work productivity [8][6].

Device Procurement Policies: Indian National Guidelines

MoHFW Procurement and Maintenance Guidance

MoHFW's comprehensive policy for medical equipment, including for fibroid therapies, underscores:

A lifecycle-based approach for warranty and maintenance: National recommendations advocate a 2-year warranty plus 8 years Comprehensive Maintenance Contract (CMC) for most high-value equipment, with adjustments for lower-value items [9]. Rate contracts for consumables—preferably with a minimum two-year duration—ensure cost containment and supply continuity [9]. Transparent procurement protocols: All purchases must comply with General Financial Rules (GFR), with competitive tenders and electronic tracking/pilot asset tagging systems [9][10]. Specific guidelines for device procurement for institutions, ensuring accessibility to advanced therapeutic modalities (e.g., for minimally invasive surgery, embolization [9].

Policy Area	National Recommendation
Warranty + CMC	2 years warranty + 8 years CMC [9]
Consumables	≥2-year contracts, OPEX for proprietary
Procurement Process	GFR compliant, competitive tendering [10]
Asset Tagging & Tracking	Electronic/tag-based pilot projects [9]
Device Lifecycle Selection	Per institutional equipment list [9]

Integration with Regulatory Standards

All medical devices for fibroid management in India are regulated under the Drugs & Cosmetics Act, 1940 and the Medical Devices Rules, 2017, as enforced by the CDSCO, ensuring quality and safety standards are met for procurement and use

Incorporating Health Economics into Clinical Decision-Making

Indian national guidelines increasingly urge clinicians to evaluate clinical efficacy and economic sustainability when adopting new medical technologies. Device procurement and new drug adoption require demonstration of value (cost per QALY) and integration with local health systems, aligning with MoHFW's vision of sustainable, equitable health infrastructure[9][4][7].

Key Recommendations and Future Directions

Treatment Individualized: no universal hysterectomy, promote medical/minimally invasive options whenever feasible.

Decisions should be personalized considering the cost-benefit ratio. - Move toward QALY-based evaluations: Particularly necessary with newer drugs and advanced medical devices. Procurement Policy Adherence: Strict compliance with MoHFW procurement, maintenance, and tracking guidelines is mandatory for all public hospitals.

Expand Indian Data: Ongoing need for large-scale, country-specific studies of costs, outcomes, and real-world QALY/QoL results.

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Device Innovations for Fibroid Ablation

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BACKGROUND

Uterine leiomyomas , also known as myomas or fibroids, are benign smooth-muscle tumors that form in the myometrium and have a low risk of becoming malignant. They affect around 70% of women of reproductive age, and are the most prevalent reason for gynecologic surgery. Many women are asymptomatic; however, uterine fibroids produce clinically significant symptoms in around 25% of women. Pelvic discomfort, dysmenorrhea, menorrhagia, urinary frequency, dyspareunia, and subfertility are the most common symptoms.

Conservative medical therapy with nonsteroidal anti-inflammatory drugs, contraceptive steroids, and gonadotropin-releasing hormone (GnRH) agonists is the first line of treatment and may be all that is necessary for the majority of women with symptoms. However, for women with continued or worsening symptoms, interventional or surgical therapies are necessary.

These have historically included uterine artery embolization (UAE), myomectomy, and hysterectomy. Uterine fibroids are still the most common reason for hysterectomy worldwide. For women who wish to start a family, myomectomy is the treatment of choice. On the other hand, surgical procedures are linked with a high risk of short and long-term morbidity, necessitate a hospital stay, and take weeks to recover. Despite the excellent clinical outcomes of these procedures, their invasive nature and associated risks and complications are undesirable to a significant subset of women. Thus, there remains significant demand for a noninvasive option for treatment of symptomatic uterine fibroids refractory to medical therapy.

MAGNETIC RESONANCE-GUIDED FOCUSED ULTRASOUND SURGERY (MRGFUS)

Introduction

Magnetic resonance-guided focused ultrasound surgery (MRgFUS) is an alternative to myomectomy that is without a surgical incision or any major complication. It is a non-invasive technique that causes immediate coagulative necrosis in 1–3 s and can be performed under either magnetic resonance imaging (MRI) guidance or ultrasound guidance and in a well circumscribed area measuring a few mm in diameter.

This system combines MRI and focused ultrasound to form a “closed-loop therapy and feedback system” that enables the physician to adjust treatment parameters and control the treatment, helping to maintain a high level of safety and efficacy. An MRI scanner is used for 3D imaging of anatomical and thermal mapping, which permit high-resolution visualization of the patient's anatomy for planning of treatment, and quantitative information on the change in tissue temperature to monitor and control the treatment. Therapeutic focused ultrasound (FUS) energy on a specific point is where sound waves converge and produce the highest energy to heat and ablate the tissue within the body without damaging the tissue along the beam path.

There are four factors that are important in patient selection: Number of fibroids; Fibroid volume; Fibroid intensity and Subcutaneous fat layer. The guideline recommends treating patients with up to six fibroids and not more than 4 cm in size. A large fibroid volume may not be completely ablated in a single session and may require a second treatment. Patients who have a total fibroid volume of more than 500 cm^3, or a hyper-intense fibroid on T2 weighted imaging are suggested to be pre-treated with a GnRH analogs for 3 months in an effort to reduce the size and vascularity of the fibroid. Hyper-intense fibroids (type 3), which represent vascularization, fluid-rich tissues, or degeneration are more resistant to heating and may show poor energy absorption, thus are not suitable for MRgFUS. A thick fat layer might result in beam aberration. The majority of the fibroid mass should be no more than 12 cm depth away from the skin line, as this is the upper limit of the scanner.

Indications

- Definitive diagnosis of the uterine fibroid(s) or adenomyosis as the source of symptoms;
- Lesion(s) clearly visible on non-contrast MRI;
- Patient is able to fit into MRI unit;
- Patient can tolerate the procedure under conscious sedation or no sedation; the treatment does not require general anesthesia;
- Patient is able to communicate sensations to the physician during the procedure.

Exclusion criteria

- Hemoglobin <10 mg/dL;
- Patient has hemolytic anemia;
- Patient has unstable cardiac status.
- Patient has severe cerebrovascular disease (multiple CVA or CVA within 6 months);
- Patient is on anti-coagulation therapy or has an underlying bleeding disorder;
- Evidence of uterine pathology other than leiomyoma;
- Patient has an active pelvic infection;
- Patient has an undiagnosed pelvic mass outside the uterus;
- Patient's weight >110 kg;
- Patient with extensive longitudinal abdominal scarring in an area of the abdomen directly anterior to the treatment area;
- Patient with standard contra-indications for MR imaging such as non-MRI compatible implanted metallic devices;

Advantages

- Non-invasive without the trauma of surgery;
- Outpatient procedure, no hospitalization;
- Fast recovery, women generally return to normal activity within days;
- Quality of life, most patients report a significant relief from symptoms during the weeks following treatment;
- Safe, minimal side effects with no drugs;
- Uterine-sparing, maintains natural hormonal function;
- May be considered in patients who seek fertility sparing options.

Complications

Device-related complications in magnetic resonance–guided focused ultrasound surgery.

Device-related serious complication	Number of cases reported
Second/third degree skin burns	13%
Bowel injury	1%
Nerve injury	<0.1%
Bladder wall injury	<0.1%

Additional reported treatment-related side effects include abdominal pain, lumbar pain, fever, significant bleeding, and vaginal discharge.

Post-treatment outcome

Follow up NPV

To assess the respond on MRgFUS, follow up MRI measuring NPV is done at least 3 months post-treatment. Higher NPVs are associated with greater efficacy. A type 1 fibroid has the best energy absorption and thus produces a larger reduction in fibroid volume.

Quality of life

A systematic review based on UFS-QOL showed that patients who underwent MRgFUS with larger NPV had improvement of severe symptoms and overall quality of life.

Fertility

Promising post-MRgFUS results are described in patients with uterine fibroids who wish to conceive. MRgFUS is safe and does not increase the rate of spontaneous abortions or pregnancy complications.[33] Some authors found that vaginal delivery is preferable post-MRgFUS as there is no surgery involved, no adhesion found and thus no risk of uterine wall rupture during gestation and delivery.

RADIOFREQUENCY ABLATION (RFA)

Radiofrequency thermal ablation (RFA) is a minimally invasive technique for conservative treatment of symptomatic fibroids which represents a promising alternative to standard surgical myomectomy.

RFA generates thermal effects (60°C–80°C) causing apoptosis of tissue cells by thermal coagulation and formation of vascular thrombosis in the blood vessels supplying the fibroid, which causes ischemic necrosis and atrophy along with inactivation of the estrogen and progesterone receptors within the fibroid owing to the thermal effect resulting in prevention of hormonal-dependent tissue proliferation.[2]

Different access techniques are available, including percutaneous, laparoscopic, hysteroscopic and trans cervical/transvaginal approaches. All the different access routes can be performed as a single surgical step or combined with each other when the position of the fibroids to be treated allow the use of the same electrode through different routes.

The overall advantages of myolysis in respect to surgical resection include reduced morbidity (operating time, blood loss, and length of hospital stay), preservation of the endometrial cavity, real-time imaging guidance, and the feasibility of undertaking as an outpatient procedure.

LAPAROSCOPIC RADIOFREQUENCY ABLATION (LRFA)

Indications include treatment of intramural, subserosal, submucosal and transmural fibroids in symptomatic premenopausal women. It is not recommended for pedunculated fibroids with a stalk <50% of the total myoma diameter. Also, patients with a history of pelvic or cervical malignancy, prior treatment of fibroids should be excluded from treatment. The ideal condition for treatment would be a fibroid volume <300 cm^3 and a maximum diameter <6 cm.

TRANSVAGINAL RADIOFREQUENCY ABLATION (TRFA)

Transvaginal radiofrequency ablation (TRFA) is a more recent technique for radiofrequency myolysis using a vaginal ultrasound guided approach. A 16–17 gage-thick 30–35 cm-long electrode with fixed or flexible active tip exposureis inserted through an ultrasound guider on the transvaginal probe used for the fibroid identification and treatment . TRFA is normally performed in an outpatient setting and is associated with mild-moderate pain and limited use of analgesics.

PROCEDURE-RELATED COMPLICATIONS

TRFA is reported to be associated with very low intra-operative and peri-operative complications. Nonspecific procedure-related are anesthesiologic complications and procedure related complications are estimated to be 1.78% and include infection (3.2%), intestinal heat injury requiring surgery (1.69%) and vaginal discharge (15%) were also found. Pelvic organ thermal injury including intestine and bladder is a rare but serious complication: ablative energy spread to surrounding intestinal loops, especially after laparoscopic RFA, can lead to rectouterine fistula, intestinal necrosis, and need for demolitive surgery.

TECHNIQUE EFFICACY OUTCOME

Radiofrequency ablation has been shown to offer targeted treatment of fibroids, with size reduction of fibroids, and improvement of symptoms and quality of life, while maintaining a safe profile with few complications and low reintervention rates. Compared to uterine artery embolization and magnetic resonance image–guided HIFU, RFA is shown to have significantly greater reduction in mean fibroid volume

CONCLUSION

Uterine fibroids are a common pathologic entity causing many women to seek treatment. MR-HIFU has emerged as the only non-invasive treatment option in patients who have failed conservative and medical therapy. This modality has been shown to be safe, feasible, and effective in reducing symptoms in women with symptomatic fibroids amenable to treatment. The therapy is ideal for a subset of women; however, careful clinical selection is important for safety and good outcomes.

Radiofrequency ablation represents a valuable tool in tailoring treatment solutions along with conventional surgical and non-surgical techniques in managing fibroid-related symptoms. Transvaginal radiofrequency ablation offers quick and safe procedures in a day-surgery setting reducing the overall costs related to hospitalization and conventional surgery.

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Future Horizons: Gene Editing, Targeted Therapy & AI

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Uterine fibroids are among the most common gynaecologic conditions, affecting many women during their reproductive years. While treatment has traditionally relied on medical therapy and surgery, advances in digital medicine, molecular biology, and AI are now driving a shift toward more personalized and less invasive care.

Genetic Landscape of Uterine Fibroids

Fibroids are clonal tumours arising from the smooth muscle cells of the myometrium. High-throughput sequencing by Mehine et al. revealed distinct pathogenic pathways in leiomyoma formation, supporting an emerging molecular classification.(1) Multiple gene mutations have been implicated, including:

- **MED12** (Mediator Complex Subunit 12)hotspot mutations and **HMGA2** (High Mobility Group AT-hook 2) overexpression: MED12 hotspot mutations, found in up to 70% of fibroids, occur on chromosome Xq13 and affect the Mediator complex, a key regulator of transcription via Cyclin C–CDK8, linking it to various oncogenic pathways. HMGA2 overexpression, present in ~10% of cases, often coexists with MED12 mutations or HMGA1 (6p21) rearrangements. Together, MED12 and HMGA2 abnormalities account for 80–90% of all leiomyomas, highlighting their central role in fibroid pathogenesis. (2)

- **COL4A5/6** (Collagen Type IV Alpha 5 Chain) and **FH** (fumarate dehydratase) mutations: Somatic deletions in the COL4A5–COL4A6 locus, previously linked to Alport syndrome with diffuse leiomyomatosis, were uniquely found in uterine leiomyomas. These deletions leads to high IRS4 overexpression, suggesting an oncogenic role in this leiomyoma subtype.(2)
  Though not yet standard in clinical care, genetic profiling may soon guide treatment in cases of rapid growth, recurrence, or atypical fibroid presentations.

CRISPR and Beyond: The Future of Gene Editing in Fibroids

In vitro fibroid models are limited by early loss of MED12-mutant cells due to poor proliferation in 2D cultures. CRISPR knock-in technology overcomes this by enabling precise gene editing. Buyukcelebi et al. introduced the Gly44 MED12 mutation into myometrial cells, leading to enhanced 3D growth and metabolic changes, especially in the tryptophan–kynurenine pathway. When implanted in vivo, these cells formed fibroid-like lesions, providing a model for studying pathogenesis and targeted therapies. Though not yet in clinical use, CRISPR-Cas9 and newer tools like base and prime editing are advancing preclinical research.(3)

- Silence MED12 mutations in fibroid cell lines: A study used CRISPR/Cas9 and lentiviral shRNA (short hairpin RNA) models targeting MED12 that demonstrated reduced fibroid cell proliferation and ECM production, confirming its role in fibroid pathogenesis and opening non-hormonal therapy avenues.(4)

- Inhibit fibroid growth by targeting estrogen/progesterone receptors: A 2004 study by Al-Hendy et al. showed that direct uterine delivery of an adenovirus encoding a dominant-negative estrogen receptor effectively blocked estrogen signaling and halted fibroid growth in mice. Separately, EC313, a novel SPRM (selective estrogen receptor modulator) significantly reduced fibroid size, ECM content, and hormone receptor levels in human fibroid xenografts implanted in immunodeficient mice.(5)

- In vivo delivery of CRISPER: CRISPR/Cas9 ribonucleoproteins delivered via electroporation into the uterine cavity of mice successfully induced endometrial cancers by editing tumor suppressor genes such as PTEN and p53. This demonstrates the feasibility of targeted in vivo gene editing in uterine tissue, laying a promising foundation for fibroid-specific interventions aimed at minimizing surgical needs and preventing recurrence.(6)

Emerging Targeted Therapies for Uterine Fibroids

- **mTOR (mammalian target of rapamycin) inhibitors**- mTOR inhibitors, with anti-proliferative and anti-angiogenic properties, are under evaluation for fibroid suppression. In one study, Rapamycin exposure caused irreversible growth arrest in primary fibroid cells, though hTERT (human telomerase reverse transcriptase)-immortalized cells reversed this effect which highlighted mTOR's role in fibroid cell proliferation and senescence. (7)

- **Anti – Fibrotic Agents:** These agents target fibroid stiffness and volume by altering ECM dynamics and fibrosis-related signaling pathways (e.g., TGF-β, YAP/TAZ).

Table 1 : Anti-Fibrotic Agents Targeting Uterine Fibroids

Agent	Mechanism of Action	Effect on Fibroids	Model/System
Clostridium histolyticum collagenase(8)	Breaks down ECM collagen	↓ Fibroid stiffness by 46%,	Preclinical
Verteporfin(9)	Inhibits YAP/TAZ signaling → ↓ fibrotic gene expression	↓ Fibronectin, versican, activin A, SMAD2	Fibroid cell cultures
Halofuginone(10)	Inhibits TGF-β1 signaling	↓ Collagen synthesis, ECM production	In vitro and mouse models

Pirfenidone(11)	Anti-fibrotic; inhibits collagen gene expression	↓ Fibroid and myometrial cell proliferation	Early-stage studies
EGCG (Epigallocatechin Gallate, Green Tea Extract)(12)	Natural inhibitor of proliferation and ECM synthesis	↓ Fibroid cell growth, ↓ collagen and fibronectin	In vitro

Artificial Intelligence in Fibroid Diagnosis & Management :-

Deep convolutional neural networks (DCNNs) and architectures like YOLOv3 and MobileNet-V2 significantly improve real-time fibroid detection, enhancing sensitivity and specificity even in junior practitioners as seen in a study by Huo et al. (13) Their study used deep learning model DCNNs that mimic the visual cortex to detect image patterns, while Chiappa et al. applied radiomics to convert scans into quantitative data for clinical decision-making beyond visual assessment.(14) Radiomics and AI models applied to ultrasound and MRI aid in distinguishing benign from malignant uterine lesions and assist in fibroid mapping and FIGO classification for fertility-sparing surgeries.

Table 2 comparing the Radiomics feature with DCNN model :

Aspect	**Chiappa et al. (2021)**	**Huo et al. (2023)**
Goal	Classify sarcomas vs fibroids using ultrasound radiomics	Enhance fibroid detection by junior sonographers using deep learning
Sample Size	70 patients (20 sarcomas, 50 fibroids)	1237 patients, 3870 ultrasound images
Technique	Manual radiomics feature extraction + Machine learning classifiers via TRACE4	Deep Convolutional Neural Network (DCNN) trained on raw images
Performance	Accuracy: 85%, Sensitivity: 80%, Specificity: 87%, AUC: 0.86	Accuracy: 94.7%, Sensitivity: 92.8%, Specificity: 97%
Strengths	High interpretability, feature-level control	Large sample size, high real-time detection capabilities
Limitations	Single-center, small sample, generalizability concerns	"Black box" nature; no malignancy differentiation

Wen et al. used the nnU-Net deep learning model for automated MRI segmentation of uterine fibroids and the uterus, achieving high Dice scores (95.6% for fibroids, 92.6% for uterus). This accuracy supports precise 3D planning for high-intensity focused ultrasound (HIFU), where sub-millimeter targeting is critical to protect surrounding tissues.(15)

AI in Clinical Decision-Making

- XGBoost-based model A retrospective study of 1,000 HIFU-treated fibroid cases used LASSO (Least Absolute Shrinkage and Selection Operator) feature selection and five ML(machine learning) algorithms, incorporating MRI features, skin-to-target distance, and platelet count that aided preoperative selection.(16)

- Multiparametric MRI + ML predicting immediate non-perfused volume ≥90% (NPV≥90%): In a separate cohort (n=73), mpMRI-based analysis before HIFU identified GBM as the top-performing classifier (AUC=0.95, accuracy=0.92), with key predictors including ADC ratios, T2 signal, and subcutaneous fat thickness.(17)

- AI-guided MRI instance segmentation assisting laparoscopic myomectomy: In a 73-patient cohort, mpMRI (multiparametricMRI) prior to HIFU showed gradient boosting (GBM) as the best predictor (AUC=0.95, accuracy=0.92), with ADC ratios, T2 signal, and subcutaneous fat thickness as key features.(18)

A Case Scenario

Patient: 34-year-old woman, nulliparous, symptomatic multiple fibroids (largest 4.5 cm). A liquid biopsy detected a MED12 gene mutation and an AI-enhanced MRI revealed a high fibrotic ECM.

Personalized, Tech-Driven Treatment Plan:

- **AI-based 3D MRI segmentation (using nnU-Net)** created a detailed fibroid map.

- She received **Selective Progesterone Receptor Modulator (SPRM) therapy** for 3 months, targeting her fibroid type based on molecular profiling.

- A **robot-assisted laparoscopic myomectomy** was performed to remove the fibroids while preserving fertility.

- A **post-operative AI prediction model (XGBoost-based)** analyzed surgical and genetic data, predicting <10% recurrence risk over 5 years.

Challenges & Ethical Considerations

Gene editing, targeted therapy, and AI tools are transforming fibroid care but face key challenges. Gene editing risks off-target effects and germline changes, limiting it to research. Targeted therapies offer non-surgical options but are costly, less accessible, and lack long-term data. AI tools enhance imaging and planning but depend on high-quality data and raise concerns around privacy, bias, and limited usability in low-resource settings.

Future Directions

- **CRISPR-based gene therapy** for fibroid prevention in high-risk women
- **AI-integrated robotic surgery** with fibroid-specific navigation
- **Wearable sensors** and mobile apps for continuous symptom monitoring
- **Single-cell genomics** to map fibroid heterogeneity and tailor treatment

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THANK YOU