

REVIEW

Open Access



Artificial intelligence driven based diagnostics with combined surgical and non-surgical management of uterine fibroids: a narrative review

Manshi Kumari Gupta¹, Sukanya Pattnaik¹ and C. Sudandiradoss^{1*}

Abstract

Uterine fibroids are commonly benign but significantly impact women's health due to undiagnosed asymptomatic progression and lack of awareness. While hysterectomy and myomectomy remain the primary treatments for uterine fibroids, patients need non-surgical alternatives in overall fibroid management. Modern scientific methods such as Artificial Intelligence (AI)-driven diagnostics combined with ancient healing techniques can provide alternative curing methods for affected patients. In this review, we have highlighted three key non-surgical approaches along with molecular basis of uterine fibroid development for futuristic personalized therapies. The non-surgical methods include (i) AI driven diagnostics using 3D Super-Resolution Diffusion-Weighted Imaging (SR-DWI) and support vector machines (SVMs), (ii) Phytochemical-based therapeutics such as curcumin (*Curcuma longa*), resveratrol (*Vitis vinifera*), and epigallocatechin gallate (EGCG, *Camellia sinensis*), (iii) Physical therapies like Yoga and acupuncture. Advanced imaging techniques improve diagnostic accuracy which allows timely intervention. Phytochemicals regulate fibrotic pathways, while yoga and acupuncture alleviate stress and support uterine health, providing a comprehensive non-surgical treatment approach. Additionally, we also describe the molecular basis for uterine fibroid development in terms of germline mutations, epigenetics and signalling pathways which are well correlated with our proposed phytochemical and physical therapies. Overall, we emphasize that the AI driven diagnostics combined with ancient therapeutic approaches offer an adjunctive strategy for effective fibroid management thereby potentially reducing the need for hysterectomy.

Key points

1. This review highlights emerging non-surgical strategies for managing uterine fibroids, including AI-driven diagnostic tools, phytochemical-based treatments, and traditional therapies such as yoga and acupuncture.
2. These approaches offer promising alternatives to surgery, aiming to preserve fertility and improve the quality of life for affected women.
3. The integration of molecular insights with non-invasive therapies supports a more personalized and holistic approach to fibroid care.

*Correspondence:

C. Sudandiradoss

csudandiradoss@vit.ac.in; franklindoss@gmail.com

Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

Keywords Uterine fibroid, Non-surgical, AI/ML, Phytochemical, Acupuncture, Yoga

Introduction

Uterine Fibroids (UFs), also known as uterine leiomyomas or myomas, are benign growths that develop in the muscular wall of the uterus, affecting 70% of women by the age of 50 [1]. The exact cause of uterine fibroids is not fully understood; however, genetic predisposition, hormonal influences—especially estrogen, progesterone and various growth factors are thought to contribute to their development [2]. UF may manifest with symptoms such as heavy menstrual bleeding (menorrhagia), pelvic pain, urinary symptoms, and reproductive dysfunction [3]. Depending on their size and location, UF can interfere with fertility by distorting the uterine cavity, impairing implantation, or causing abnormal uterine contractility [4]. UF significantly impacts a woman's quality of life, causing physical discomfort, psychological distress, and interference with daily activities [1].

Ultrasonography-based estimates suggest that the cumulative incidence of fibroids in women aged 50 or younger is significantly higher in Black women, surpassing 80% compared to approximately 70% in White women. This high level of incidence results in substantial medical costs exceeding \$5.9 billion (and up to \$34.3 billion) annually in the United States alone [1]. In addition to their high prevalence, UF are often linked to various gynaecological disorders, including endometriosis, adenomyosis, infertility, ovarian dysfunction, and, in rare cases, malignant progression to leiomyosarcoma, endometrial cancer, or breast cancer [5]. It is well established that cancer arises due to a combination of genetic and epigenetic alterations [6, 7]. Analyzing molecular signatures can help predict disease progression, facilitating the early identification of high-risk individuals who may require closer surveillance [8]. UF are complex benign tumors with a heterogeneous molecular profile, shaped by genetic mutations, hormonal influences, and epigenetic modifications that contribute to their formation. The primary molecular and genetic subtypes of UF include mutations in the mediator complex subunit 12 (MED12), translocations involving high mobility group AT-hook 1 (HMGA1) or high mobility group AT-hook 2 (HMGA2), and alterations in collagen genes (COL4A5–COL4A6) [9].

Ever since the first hysterectomy was performed, surgery has been the main treatment for symptomatic fibroids. The most common procedures were total abdominal hysterectomy or myomectomy. To make surgery less invasive, mini-laparotomic techniques, including mini-laparotomy-assisted vaginal surgery have also been used [10]. In 1995, a French group introduced a new way to treat fibroids called uterine artery embolization

(UAE) using Ivalon particles. This treatment improved symptoms in 11 out of 16 patients and 10 patients had their menstrual cycles return to normal [11]. In 1999, a large study with 305 patients showed that UAE controlled heavy bleeding in 86% of cases after three months and 92% after one year [12].

An image-guided technique called magnetic resonance imaging (MRI)-guided Focused Ultrasound Surgery has been available for several years. It was approved by the European Medicines Agency (EMA) in 2002 and the US FDA in 2004 [13]. However, since CT and MRI scans are expensive and not widely accessible, ultrasonography remains the primary imaging method for diagnosing uterine fibroids due to its high sensitivity and specificity. Despite its advantages, ultrasound diagnosis of uterine fibroids still faces several challenges. One issue is the difficulty in distinguishing between subserosal and large fibroids or between pelvic and adnexal masses [14]. Another challenge is the lack of standardized imaging views and variations in ultrasound equipment, which affect detection accuracy. Additionally, the accuracy of ultrasound diagnosis depends on the skill and experience of the ultrasonographer [15]. To improve diagnostic accuracy, artificial intelligence (AI) has been used to develop a deep convolutional neural network (DCNN) model that automatically detects uterine fibroids in ultrasound images. This model differentiates between the presence and absence of fibroids and has been both internally and externally validated [16]. Traditional imaging diagnosis relies heavily on the expertise of physicians. However, AI, through machine learning and deep learning, provides better image analysis, consistency, and objectivity, helping improve decision-making in fibroid detection.

Since ancient times, plants and plant-based compounds have played a vital role in traditional medicine and have also been a major source of new drugs in modern pharmaceuticals. Complementary and alternative medicine (CAM) approaches, such as exercise, dietary changes, herbal treatments, and acupuncture, have also been explored for fibroid management. Traditional Chinese Medicine (TCM) formulations, including Gui Zhi Fu Ling Tang (GFLT), have shown potential in reducing fibroid size [17–20]. Holistic strategies that incorporate lifestyle changes, detoxification, and yoga may help alleviate symptoms and enhance the biopsychosocial well-being for women with fibroids [21]. Yoga, in particular, has gained attention as a non-invasive method for managing uterine fibroids, with emerging research suggesting its role in hormonal balance and symptom relief, though more rigorous studies are needed to confirm its effectiveness. This review looks at how herbal treatments

and yoga can help manage uterine fibroids without surgery. Yoga is known to support hormone balance, reduce stress-related inflammation, and ease fibroid symptoms. Natural compounds like curcumin, EGCG, and resveratrol may help slow fibroid growth by affecting key genes and biological pathways. New tools in precision medicine, AI-based diagnostics, and targeted therapies are also improving how fibroids are detected and treated. The review highlights key findings and their clinical value to help bring these approaches into everyday gynecological care.

Molecular-level insights in uterine fibroids: evidence-based non-surgical alternatives

Mutations in specific genes such as Mediator Complex Subunit 12 (MED12) and alterations in High Mobility Group AT-hook 2 (HMGA2) are recognized as biological drivers of uterine fibroid (UF) formation. Of these, MED12 mutations are the most prevalent, occurring in 85% of cases and facilitating abnormal cell proliferation through activation of the (Wnt)/ β -catenin and (TGF- β) pathways [22–25]. On the other hand the HMGA2 aberrations, generally caused by chromosomal alterations at 12q15, promote rapid tumor growth through the activation of Insulin-like Growth Factor (IGF) and Protein Kinase B (AKT) signaling pathways, angiogenesis, upregulation of Estrogen Receptor 1 (ESR1), cyclins D1–D3 (CCND1, CCND2, CCND3), growth factors including Fibroblast Growth Factor 2 (FGF2) and Vascular Endothelial Growth Factor A (VEGFA) [26–30].

A small subset of uterine fibroids also harbors Collagen Type IV Alpha 5/6 chains (COL4A5/COL4A6) deletions, often accompanied by increased Insulin Receptor Substrate 4 (IRS4) expression and SNF2-related CREBBP Activator Protein (SRCAP) mutations that are associated with chromatin remodeling defects [31–33].

Epigenetic changes also play an important role in uterine fibroids. For example, abnormal DNA methylation of genes such as ESR1, Progesterone Receptor (PR), and the tumor suppressors KLF11 and DLEC1 can disrupt hormone sensitivity and affect stem cell differentiation [34–37]. In addition, histone modifications involving the H19/let-7/TET3 pathway increase the expression of pro-fibrotic genes, including Transforming Growth Factor-beta Receptor 2 (TGFBR2), Secreted Protein Acidic and Rich in Cysteine (SPARC), and collagens [38, 39].

At the signaling level, the dysregulation of the Wnt/ β -catenin pathway [40–43] and TGF- β pathway [44–47] promotes proliferation, survival, and extracellular matrix accumulation. Importantly, while uterine fibroids (UFs) exhibit genetic and epigenetic alterations, their transformation into malignancies such as uterine leiomyosarcoma (ULMS) is extremely rare [48–52], breast cancer [53–56], and endometrial cancer [57–60], that can be

fostered by a combination of factors, including alterations in MED12, HMGA2, and Fumarate Hydratase (FH), as well as hormonal and lifestyle factors. Together, these molecular observations provide mechanistic insight and raise the possibility of developing effective, non-invasive therapies to target both systemic and lifestyle factors that promote UF growth.

To systematically summarize these findings, Table 1 provides an overview of the major genetic and epigenetic alterations in UFs, their molecular consequences, and implicated signaling pathways. This table highlights how diverse molecular events converge on common biological mechanisms particularly abnormal cell cycle regulation, extracellular matrix (ECM) remodeling, and hormone sensitivity that collectively drive UF progression.

Medical imaging-based diagnostic and therapeutic in uterine fibroids

Hysterectomy and myomectomy were the surgical modalities of treatment for uterine fibroids; however, these have been substituted lately by different other means of management such as minimally invasive and artificial intelligence interventions. Technological improvement recently introduced non-invasive methods and targeted therapies for fibroid treatment such as promising high-intensity focused ultrasound, percutaneous microwave ablation, or pharmacotherapies that interrupt the multiplication of the fibroid at the molecular level. Novel therapies of uterine fibroids that rely on deep learning models, and machine learning-based diagnostics are changing the way that uterine fibroids are detected and treated. Figure 1 thus illustrates the progressively shifting paradigm in fibroid management and visualizes the integration of Artificial Intelligence and molecular-targeted therapies for precision medicine and non-surgical options.

Artificial intelligence in the diagnosis of uterine fibroids

Artificial intelligence (AI), specifically deep learning (DL), has transformed medical imaging and diagnostics [82]. As a component of DL approach, Deep convolutional neural networks (DCNNs) have turned into advanced computer-aided diagnostic (CAD) tools. In an effort to enhance ultrasound diagnosis of uterine fibroids, a DCNN model has been developed to automatically identify and categorize UFs. This model showed that it could recognize several fibroid masses of different sizes in a single image, identify fibroids, and differentiate between their presence and absence. The model demonstrated its ability to improve diagnostic performance and reduce dependence on senior ultrasonographers by achieving improved sensitivity, specificity and accuracy when compared to junior ultrasonographers [16].

Table 1 Comprehensive Molecular-Level observations in uterine fibroids (UF): Genetic, Epigenetic, Signaling, and oncogenic features with implications for Non-Surgical management

Category	Gene/Pathway	Molecular Features	Functional Consequence in UFs	Clinical/Therapeutic Relevance	EvidenceLevel/Clinical Support	Key References
Driver Mutations	MED12	Hotspot mutations in exon 2 (31–85% of UFs)	Dysregulates Wnt/ β -catenin & TGF- β signaling; promotes proliferation & survival	Biomarker for early UF; potential target for pathway-based therapies	Preclinical/Experimental	[61, 62]
	HMG A2	Chromosomal rearrangement at 12q15; let-7 miRNA regulation	Enhances IGF/AKT pathway, angiogenesis; $\uparrow$ ESR1, CCNDs, VEGFA	Associated with larger, rapidly growing UFs; resistant to GnRH agonists	Clinical observation	[31, 63, 64]
Epigenetic Factors	COL4A5/COL4A6	Xq deletions (~2–4% of UFs) with IRS4 overexpression	Alters ECM composition; linked with diffuse leiomyomatosis	Rare subtype but may benefit from ECM-modulating therapies	Preclinical/Experimental	[31, 33]
	DNA Methylation	Hypermethylation of ESR1, PR, KLF11, DLEC1, KRT19	Silencing of hormone receptors & tumor suppressors; impaired differentiation	Epigenetic drugs (DNMT inhibitors, demethylating diet components) under study	Preclinical/Experimental	[65, 66]
	Histone Modifications (H19/let-7/TET3 axis)	Dysregulated acetylation & methylation marks; $\uparrow$ TET3	Overexpression of TGFBR2, SPARC, collagens $\rightarrow$ fibrosis & ECM accumulation	Modifiable by phytoestrogens (e.g., genistein), diet, yoga-mediated epigenetic regulation	Preclinical/Experimental	[67, 68]
Signaling Pathways	Wnt/ β -catenin	$\uparrow$ Wnt4, Wnt5A/B, Wnt11, Wnt16; $\downarrow$ APC/DKK1/3	Drives stem cell proliferation & hormone-independent growth	Targeting β -catenin or Wnt ligands under research; lifestyle factors may indirectly modulate	Preclinical/Experimental	[69, 70]
	TGF- β	$\uparrow$ TGF- β 1 (fibrosis) and $\uparrow$ TGF- β 3 (ECM synthesis)	Excess ECM, fibrosis, apoptosis resistance	Blocking TGF- β /Smad pathway may reduce UF stiffness; anti-fibrotic diet/yoga may complement	Preclinical/Experimental	[71, 72]
Oncogenic Overlaps	UF $\rightarrow$ ULMS	MED12, HMG A2, FH mutations; $\uparrow$ Ki67, p53, p16	Suggests UF as precursor to ULMS in some cases	Importance of monitoring high-risk UF patients	Preclinical/Experimental	[73–75]
	UF $\rightarrow$ Breast Cancer	Shared estrogen/progestrone pathways; obesity & early menarche links	An adjusted hazard ratio of 1.31 (95% CI 1.10–1.56) breast cancer risk in women with UF	Highlights hormonal & lifestyle factors diet and yoga may reduce risk	Observational/Epidemiological	[76–78]
	UF $\rightarrow$ Endometrial Cancer	Shared genetic loci (5p15.33, 11p13), WT1, TERT	Hormonal imbalance + chronic inflammation $\rightarrow$ risk of EC	Reinforces need for lifestyle-based prevention in high-risk women	Observational/Epidemiological	[79–81]

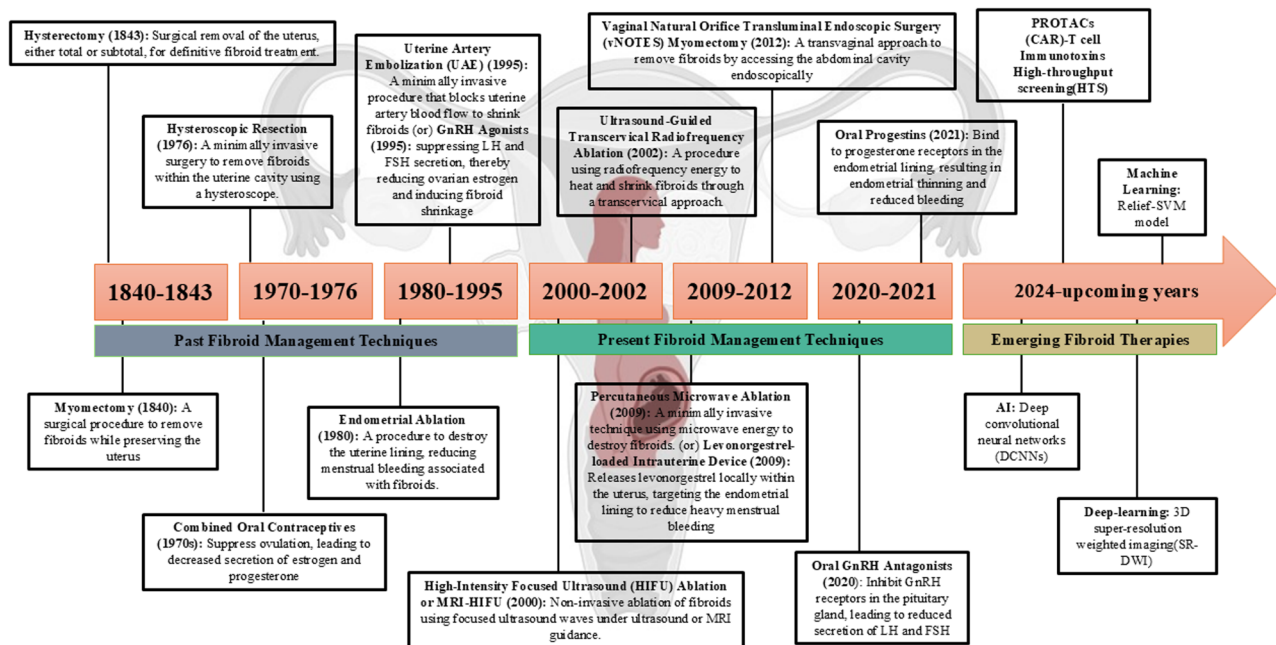


Fig. 1 Illustration of the evolving landscape of uterine fibroid management, highlighting the transition from traditional surgical interventions to modern non-surgical approaches, including pharmacological, lifestyle-based, and complementary therapies. The figure also emphasizes the emerging role of artificial intelligence (AI) and machine learning in guiding personalized treatment decisions, predicting patient outcomes and optimizing non-invasive strategies

Deep learning in segmentation and imaging Recent developments in deep learning hold great potential for enhancing imaging and segmentation methods used in the diagnosis of UFs. This is exemplified in the Deep Learning-Based 3D Super-Resolution Diffusion-Weighted Imaging (SR-DWI) model, which uses generative adversarial networks (GANs) to improve MRI resolution and allow for more precise radiomic feature extraction. With an internal validation AUC of 0.877 and an external validation AUC of 0.800, this model outperformed conventional high-resolution DWI models [83]. Moreover, a high Dice score of 0.95 was achieved by an automatic UF segmentation 3D nnU-Net model referenced against the performances of experienced radiologists for UF segmentation. This methodology makes the monitoring of therapy responses easy through repeatable volumetric measurements with very minimal human effort [84].

Application of machine learning and radiomics in the prognosis of HIFUs With advantages such as higher therapeutic efficacy, shorter recovery time, fewer complications and high-intensity focused ultrasound (HIFU) has gained prominence as a non-invasive treatment for uterine fibroids. Achieving optimal results requires careful preoperative evaluation, where parameters like fibroid size, location and tissue composition along with fertility intentions and imaging-based predictors of treatment response are carefully considered to identify suitable candidates and plan individualized therapy in line

with current clinical and regulatory standards [83]. When combined with multiparametric MRI radiomics characteristics, machine learning models have evolved as crucial tools for predicting the outcome of HIFU therapy [85]. In a study, an AUC of 0.887 and an accuracy of 84.9% were attained by a ReliefF-SVM (Support Vector Machine) model that evaluated T2-weighted and diffusion-weighted MRI characteristics for predicting treatment results. This, in turn, backed the patient selection and thus established a greater accuracy for preoperative assessment. In addition, the imaging and clinical-factor measurements of a radiomics-clinical model demonstrated an AUC of 0.802 in predicting the nonperfused volume (NPV) ratio, which is an important marker of treatment efficacy. The ML techniques might aid the physician in performing more individual-based preoperative assessments, which translate to better and more specific therapy guidelines [86, 87]. Another study indicated that radiomics models employing advanced imaging methods, such as CE-T1WI and T2WI-FS, achieved an AUC of 0.884 in external validation, highlighting their predictive accuracy [88]. Additionally, machine learning models like Random Forest and Multilayer Perceptron were instrumental in predicting postoperative results, including the absorption of necrotic tissue and the recurrence of fibroids, which are vital for determining follow-up plans and improving patient care [89]. Thus, AI, ML, and radiomics have hugely improved the management of the UFs by increasing diagnostic accuracy, enhancing imaging resolution and personaliz-

ing HIFU treatment schemes. These advancements set the stage for precision medicine in the care of fibroids, adding to the optimization of treatment planning and filling gaps in the diagnostic resource. To provide a clearer overview of these advancements, Table 2 summarises the key AI and radiomics models applied in UF diagnosis and prognosis, including dataset characteristics, validation strategies, performance metrics, and clinical implications along with its limitations and population characteristics.

Surgical therapeutics in uterine fibroids

Hysterectomy in uterine fibroids The first successful elective hysterectomy was performed in 1813 by Conrad Langenbeck via the vaginal approach. Today, nearly two centuries later, hysterectomy remains the second most frequently performed surgery among women of reproductive age [94]. Based on recent epidemiological estimates, approximately 80,000 hysterectomies are performed annually in the United Kingdom and over 600,000 in the United States, corresponding to an average rate of 300–400 cases per 100,000 women annually. The majority of these procedures (over 70%) are performed for benign gynecological conditions, including uterine fibroids (33%), menorrhagia (21%), uterine prolapse (28%), and chronic pelvic pain (3%) [15]. In India, the prevalence of hysterectomy is steadily rising, with data revealing that one in every ten elderly Indian women has undergone uterus removal with higher rates observed in rural regions due to limited access to alternative treatments. This upward trend in hysterectomy prevalence across India has prompted a closer examination of its clinical indications and procedural preferences. Pandey et al. (2014) conducted a hospital-based analysis revealing that symptomatic uterine fibroids accounted for 40% of hysterectomy cases, followed by pelvic organ prolapse at 16%, with an overall complication rate of 8.5% [95]. Further regional insights from Maharashtra, as reported by Uikey, Wankhede, and Tajne (2018), demonstrated an even higher prevalence of fibroid-related hysterectomies, comprising 65.33% of case [96, 97]. Here, Fig. 2 illustrates the state-wise distribution of hysterectomy cases across India, highlighting the regional variations in prevalence and a comparative overview of how hysterectomy rates differ between states, reflecting disparities that may arise from variations in healthcare access, awareness levels, socio-economic status, and regional healthcare policies. Such visualization helps in identifying high-burden states and underscores the need for region-specific public health strategies to manage uterine health more effectively. Despite being a common procedure, hysterectomy is not without consequences, women undergoing this surgery may experience early menopause, hormonal imbalances, increased risk of cardiovascular diseases and long-term pelvic dysfunction. The irreversible loss of the

uterus not only impacts physical health but also carries profound psychological and societal implications, making it imperative to reconsider its widespread use, especially when effective non-surgical options exist.

Hysteroscopic management of submucosal fibroids

Hysteroscopic intervention is a key minimally invasive strategy for treating submucosal fibroids, allowing direct visualisation and precise excision of fibroid tissue while preserving the uterine architecture. Compared with conventional open or laparoscopic myomectomy, hysteroscopy generally results in less postoperative discomfort, shorter hospital stays, and faster recovery times. In recent years, laser ablation has gained attention as an alternative or adjunct to conventional resectoscopic techniques, utilising focused energy to remove fibroid tissue accurately while minimising thermal injury to surrounding endometrium [98, 99].

Despite these advantages, hysteroscopic procedures are not entirely risk-free. Complications may include uterine perforation, fluid overload, postoperative adhesions or incomplete fibroid removal. Furthermore, as a relatively recent innovation, laser ablation has limited long-term outcome data, and fibroid recurrence can occur in some patients. Careful patient selection, thorough preoperative imaging, and strict adherence to surgical protocols are therefore essential to mitigate potential risks.

For women in perimenopause, treatment should be tailored to each person's needs by considering their intense clinical symptoms, whether they still wish to have children, their hormone levels, and any other health problems. This personalized approach helps relieve symptoms effectively while avoiding unnecessary or excessive treatments [100, 101]. Additionally, comprehensive patient counselling and shared decision-making allow women to make informed choices regarding surgical versus non-surgical alternatives based on clinical suitability and personal preference.

Overall, hysteroscopic resection and laser ablation provide effective and minimally invasive options for managing submucosal fibroids. However, a careful balance of clinical benefits, potential complications, and patient-specific factors is essential to achieve the most favourable outcomes.

GnRH agonist therapies in uterine fibroids By inducing a state of hypoestrogenism and temporary menopause with amenorrhea, GnRH agonists have been used to shrink fibroids and restore hemoglobin levels in symptomatic women [102–104]. Their prolonged use is limited due to side effects, including hot flashes and bone density reduction [105]. There was a notable improvement in pre- and postoperative hemoglobin levels, along with signifi-

Table 2 Summary of artificial Intelligence-based studies in uterine fibroid detection and prognosis

AI/Method	Dataset/Sample Details	Population Characteristics	Ground Truth Definition	Validation Type	Performance Metrics (with 95% CI if available)	Clinical/Generalizability Notes	Limitations/Biases	Reference
Deep Convolutional Neural Network (DCNN) for ultrasound fibroid detection	3,870 ultrasound images (667 fibroid + 570 non-fibroid controls); training = 2,706; internal = 676; external = 488.	Fibroid: 42.45 ± 6.23 yrs; Control: 39.24 ± 5.32 yrs	Expert radiologist annotation based on ultrasound imaging reports.	Internal and external validation.	Accuracy = 94.72%; Sensitivity = 92.82%; Specificity = 97.05%; CI:NA	AI aided junior sonographers to achieve expert-level performance	Limited data from a single center; possible imaging-parameter bias.	[16]
Attention-based EfficientNetB0 (ultrasound classification)	1,990 ultrasound images (fibroid vs. normal)	Mixed population: inclusion criteria not specified.	Labels confirmed by pathological diagnosis.	Cross-validation (five-fold).	Accuracy = 0.99 (99%); CI:NA	High accuracy using data augmentation for binary classification	No external validation; incomplete population data	[90]
nnU-Net on MRI for uterus/fibroid segmentation	550 MRI scans; training = 440 (80%), validation = 110 (20%).	Uterine fibroid and normal uterus patients; MRI from single institution.	Segmentation masks verified by two expert radiologists.	Internal validation only.	Dice similarity: uterus = 92.55%, fibroid = 95.63%; CI:NA	Enabled 3D reconstruction for HIFU planning	Limited MRI dataset; single-scanner bias.	[91]
3D nnU-Net for uterus segmentation (pre- and post-HIFU MRI)	109 MRI scans (56 pre-HIFU, 53 post-HIFU).	Adult women undergoing HIFU	Segmentation verified by radiologist consensus.	Internal + external validation (hold-out test).	Dice coefficient ≈ 0.95 (mean); hold-out test = 0.92 ± 0.07 (standard) and 0.96 ± 0.02 (HIFU); CI:NA	Enabled quantitative uterine volume assessment	Small cohort; external validation limited	[92]
3D SR-DWI Radiomics model for HIFU prognosis	360 MRI datasets (training = 240; internal test = 60; external test = 60).	Patients undergoing HIFU ablation for fibroids	Post-HIFU clinical outcome and radiologist report.	Internal and external validation.	AUC = 0.868 (SVM); HR-DWI model AUC = 0.805; 95% CI (0.82–0.91).	Outperformed radiologist in HIFU outcome prediction	Requires multicenter validation; interpretability bias	[83]
MRI-radiomics prognostic model (pre- and post-HIFU)	1,055 fibroid patients treated with HIFU and pre/post MRI.	Large data from single-center cohort	Treatment outcomes based labels	Cross-validation (five-fold).	AUC = 0.805; CI:NA	Characterized fibroid heterogeneity for preoperative planning	Retrospective, single-center dataset; limited external validation	[93]

Hysterectomy rates among women 45+ in Rural vs Urban India

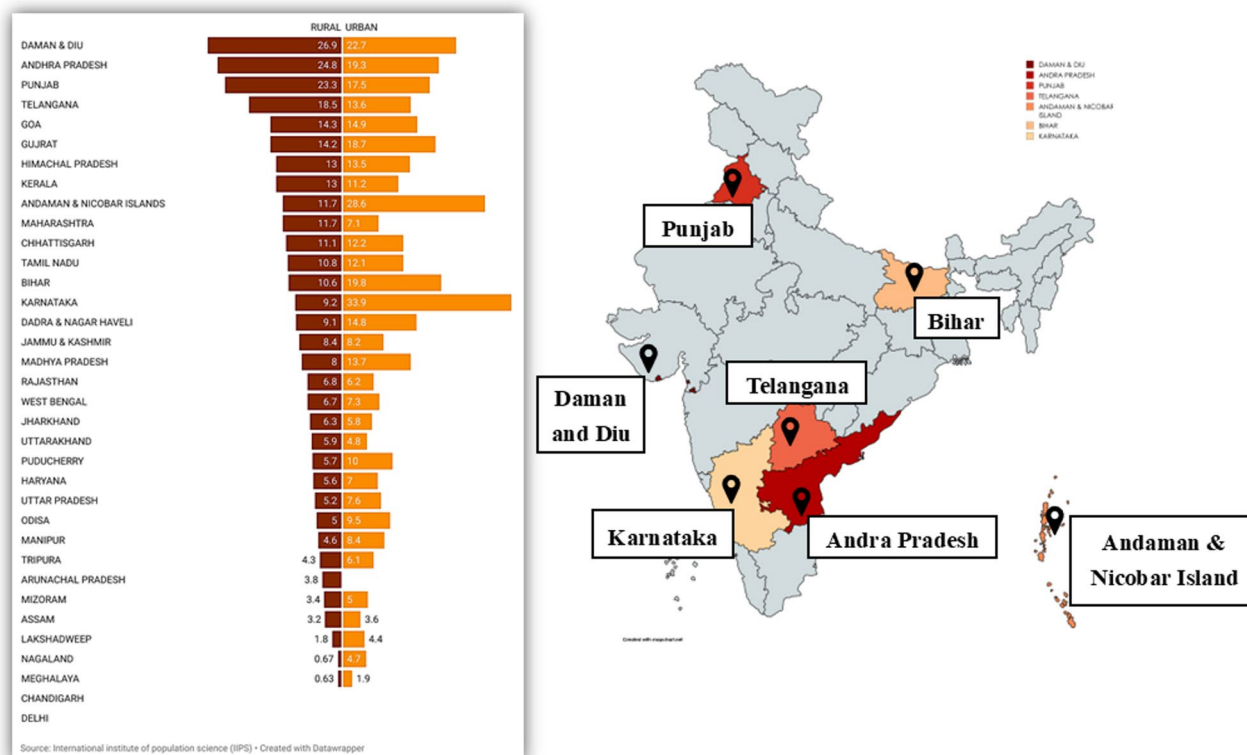


Fig. 2 Visualization of uterine loss due to hysterectomy among women aged 45 years and older across rural and urban regions of India. The data, obtained from the survey, highlights regional and demographic disparities in hysterectomy prevalence. This figure generated using Datawrapper, underscores the differential burden of surgical intervention in fibroid management and emphasizes the need for accessible non-surgical treatment options in diverse settings

cant reductions in uterine volume, gestational size, fibroid volume, and hospital stay duration. Additionally, blood loss and the frequency of vertical incisions decreased for both myomectomy and hysterectomy procedures [106]. Moreover, treatment with GnRH agonists is linked to histological alterations in UFs that can complicate surgical procedures. Preoperative use of leuprolide acetate may lead to myoma degeneration and the loss of the clear boundary between the myoma and myometrium, making the enucleation and removal of myomatous nodules challenging. These myxoid changes can cause the fibroids to become very small and soft, making them difficult to detect, which could result in some fibroids being missed during myomectomy.

Selective progesterone receptor modulator (SPRM) in uterine fibroids Selective progesterone receptor modulators (SPRMs) are a specialized class of synthetic steroids engineered to interact with progesterone receptors (PR) in a highly targeted and tissue-specific manner [107]. These modulators exhibit a distinctive blend of agonistic and antagonistic effects that vary depending on the relative proportions of PR-A and PR-B isoforms within

the tissue. Targeting the fundamental processes behind fibroid development and the symptoms that accompany it, this subtle interaction aids SPRMs in the successful management of UFs [108]. Ulipristal acetate (UPA), a selective progesterone receptor modulator, demonstrates therapeutic efficacy by inhibiting cell proliferation and inducing apoptosis in uterine fibroid cells, leading to fibroid shrinkage and improved control of abnormal uterine bleeding. However, its clinical use has been restricted in several regions following regulatory safety warnings regarding potential liver toxicity, and current guidelines recommend its administration under strict monitoring protocols [109]. Clinical trials, including PEARL III and PEARL IV, as well as the VENUS-II study, have demonstrated UPA's efficacy in managing fibroid symptoms and achieving substantial reductions in fibroid volume over both short-term and extended treatment regimens [110]. These advancements are indeed promising, but it's essential to consider the serious concerns related to the risks of endometrial pathology and liver toxicity that can come with the use of SPRMs. This highlights the importance for further research to holistically understand and manage these risks. More recent SPRMs, such as telapristone

acetate and vilaprisan, are now being developed and offer improved efficacy and safety [111]. These upcoming treatments could improve the options available for managing UFs, giving hope for more effective and precise treatment methods. Offering a focused strategy that enhances prognostic results, SPRMs constitute a substantial development in the handling of UFs. However, continued investigation and clinical evaluation are essential to optimize their application and ensure that their benefits outweigh any potential risks, ultimately advancing patient care in the field of gynecology.

Uterine artery embolization (UAE) and ultrasound-guided radiofrequency ablation (USgRFA) A well-recognized and successful treatment for hypervascular uterine fibroids is uterine artery embolization (UAE), which mainly reduces the size of the fibroid and alleviates associated symptoms [112, 113]. This minimally invasive technique occludes arteries supplying the uterus to effect ischemic infarction in the fibroids, which causes the fibroids to shrink [114]. This treatment offers several benefits, such as a faster recovery time, being less invasive than surgery and no restrictions on the size or number of fibroids that can be treated [115]. Women who need to retain their fertility are usually discouraged from the UAE for possible ovarian function hazards and higher instances of pregnancy-related concerns which may encompass miscarriage, preterm delivery, intrauterine growth restriction (IUGR), malpresentation, abnormal placentation and postpartum hemorrhage [116]. This may indicate that, while UAE does pose threats, it could be an option to be considered for women wishing to conceive in the future, although caution must be exercised. Innovative treatment techniques like ultrasound-guided radiofrequency ablation (USgRFA) are proving to be safer alternatives with effective symptom relief but less complication and possibly lower risk to fertility. The low pain threshold and few side effects of USgRFA make it a viable choice for day surgery settings [117]. It uses the VizAblate System, a combination of intrauterine sonography and radiofrequency ablation. It has been shown safe and effective, even in bigger fibroids [118]. Ultimately, the choice between UAE and other treatments should be guided by individual patient needs, particularly regarding fertility preservation.

Complementary and adjunctive non-surgical approaches (Phytochemicals, Yoga, Acupuncture) **Important phytochemicals in uterine fibroids**

Phytochemicals are biologically active compounds derived from plants, which have always been at the centre of traditional medicine as well as modern pharmacology, providing the means for the discovery of many therapeutic agents against UF. Curcumin is one such

compound that has been known for its antiproliferative and antifibrotic effects on the leiomyoma cells by modulating apoptotic pathways. Isoliquiritigenin induces growth inhibition and apoptosis in human UF cells [119]. Other phytochemicals of therapeutic potential such as apigenin, chlorogenic acid, emodin, ferulic acid, morin, pterostilbene and naringin still await further experimental validation for their role as treatments for UF [120]. Undoubtedly, nerolidol has been found to induce dose-dependent antiproliferative activity in ELT3 leiomyoma cells by modulating the ATM/AKT pathway, downregulating the levels of cyclin-dependent kinases CDK4 and CDK6, and inducing cell cycle arrest at the G1 phase [121]. Also, Epigallocatechin Gallate (EGCG) demonstrated clinical efficacy in reducing the volume of fibroids with an associated reduction in its symptoms devoid of any adverse effects [122]. Curcumin is a possible candidate for therapeutic utilization that inhibits cell proliferation and migration while inducing G0/G1-phase cell cycle arrest and apoptosis through the p38 MAPK/NF- κ B signaling pathway [123]. Dietary phytoconstituents capsaicin, kaempferol, resveratrol, silibinin, and curcumin have shown regulatory effects on the important fibroid-associated pathways, which include Smad 2/3, PI3K/AKT/mTOR, ERK 1/2, and β -catenin, thus indicating their role in the prevention and treatment of UF [124]. Apart from that, quercetin substantially reduces the mRNA and protein levels of collagen 1A1 and fibronectin in leiomyoma cells. Indole-3-carbinol (I3C) manifests similar antifibrotic effects, indicating their value in therapeutic dietary supplementation or localized treatment [125]. Figure 3 shows key phytochemicals and their nutraceutical sources, including fruits, vegetables, and medicinal plants. These bioactive compounds such as flavonoids, polyphenols, and terpenoids are noted for their antioxidant, anti-inflammatory, and hormone-regulating effects, highlighting their role in uterine fibroid management. Because of their diverse mechanisms of action in modulating proliferation, inflammation, angiogenesis, and fibrosis, these phytochemicals show much promise as alternative or adjunctive strategies to UF management. Therefore, continued and stringent preclinical and clinical investigations that will optimize their therapeutic benefit and flatten the path toward inclusion in current treatment regimens for fibroids.

Yoga as an adjunctive therapy for symptom management and physiological regulation in uterine fibroids

Yoga is a holistic mind-body discipline that combines physical postures, breathing techniques and meditation to promote physiological and psychological balance. In recent years, it has gained attention as a complementary therapy for improving health-related quality of life and alleviating symptoms in women with uterine fibroids

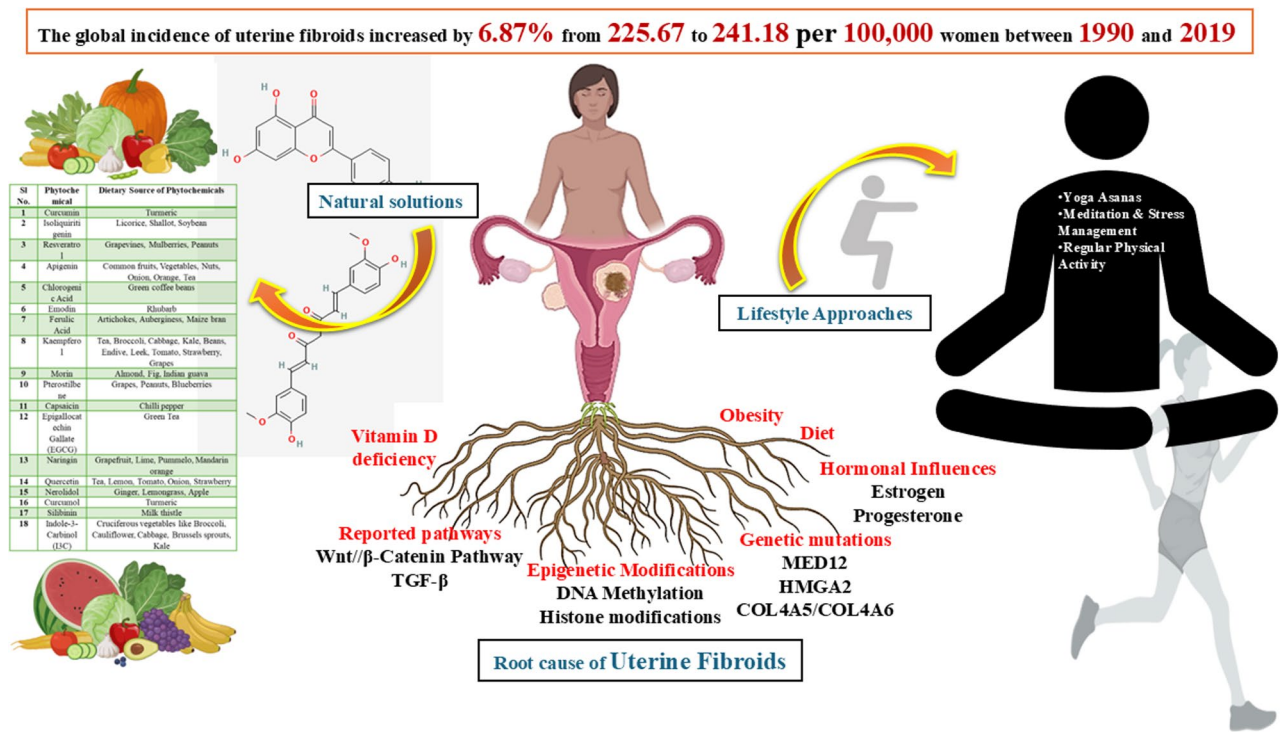


Fig. 3 Illustration of the key etiological factors contributing to uterine fibroid development and their management through non-surgical interventions. The figure highlights hormonal imbalances, genetic predispositions and lifestyle-related triggers as root causes and presents phytochemicals, yoga, and other complementary approaches as potential strategies to mitigate fibroid growth and symptoms. This visualization emphasizes the integration of evidence-based holistic therapies in fibroid management, offering alternatives to invasive surgical procedures

(UF). A clinical study by Baiju et al. (2024) [126] demonstrated that a 90-day structured yoga intervention led to significant reductions in fibroid size, endometrial thickness, and ovarian volume, accompanied by marked improvements in symptom severity and overall quality-of-life scores (UFS-QOL) among reproductive-age women. Although the study was limited by its small sample size and lack of a control group, the findings provide promising preliminary evidence that yoga may beneficially influence fibroid pathophysiology by restoring neuroendocrine balance, reducing systemic inflammation, and improving uterine blood flow through measurable physiological mechanisms.

Further evidence supports yoga’s potential role in modulating reproductive and hormonal health. Cramer et al. (2018) [127], in a systematic review, reported that yoga improves menstrual regularity, pain perception, and psychological well-being in gynecologic conditions such as dysmenorrhea and polycystic ovarian syndrome, both of which share inflammatory and hormonal pathways with uterine fibroids. Complementing this, Yadav et al. (2020) [128] observed that yoga practice may regulate the hypothalamic-pituitary-gonadal (HPG) axis and attenuate stress-induced cortisol secretion, thereby promote uterine homeostasis and reduce hormone-driven fibroid progression. Additionally, regular yoga practice has been

shown to enhance parasympathetic activation and lower oxidative stress, which together improve pelvic circulation and myometrial relaxation key factors in mitigating UF-related symptoms such as pelvic pressure and menorrhagia [129, 130].

Taken together, current evidence suggests that yoga serves as an effective adjunctive approach rather than a primary treatment for uterine fibroids. While direct proof of yoga-induced fibroid regression remains limited, its demonstrated benefits in symptom relief, stress reduction, and endocrine stabilization justify its inclusion as a supportive strategy in UF management. To substantiate these findings, future research should focus on well-designed randomized controlled trials with larger sample sizes and standardized yoga protocols to clarify the magnitude and mechanisms of its therapeutic effects. Further, Table 3 summarizes yoga postures and breathing exercises that have been reported to produce measurable improvements in uterine fibroid parameters, supporting their role as an adjunctive, non-invasive approach in UF management, as evidenced by clinical outcomes documented by P. Sharma et al. (2020) [131].

Acupuncture in uterine fibroids

Acupuncture is one of the cornerstones of Traditional Chinese Medicine (TCM) that has existed for several

Table 3 Yogic practices, duration, and measurable clinical outcomes in the management of uterine fibroids

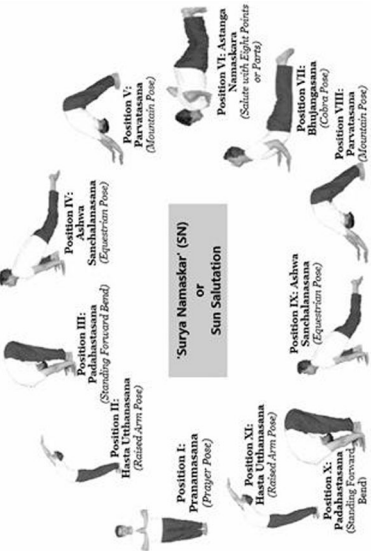
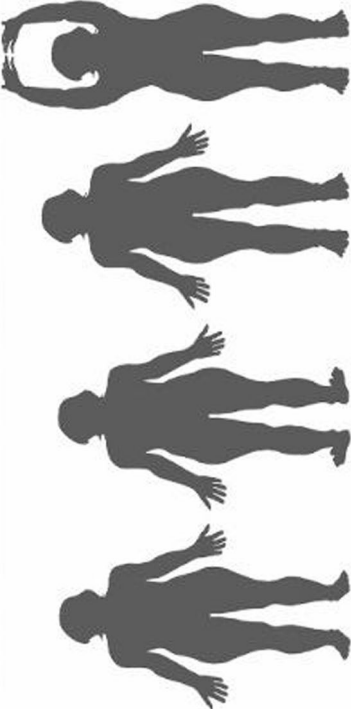
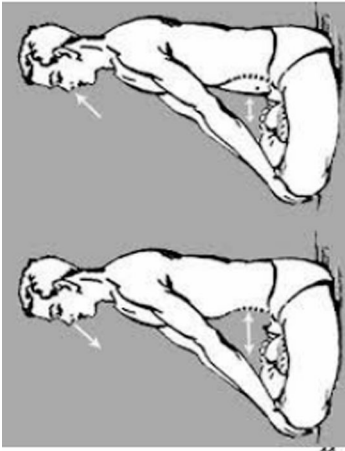
Sl No.	Practice	Representation	Reference	Duration (in mins)	Measurable Clinical Outcome
1	Sun Salutation		[132, 133]	15	Improves endocrine regulation and hormonal balance, potentially reflected in changes to serum oestrogen, progesterone, or cortisol levels relevant to uterine health.
2	Mountain Pose		[134, 135]	1	Alleviates fibroid-associated pain, as observed through reduced scores on validated pain scales (e.g., Visual Analogue Scale, VAS).
3	Triangle Pose		[133, 136, 137]	1 (each side)	Supports hormonal equilibrium and reduces fibroid-related symptoms, which can be monitored via menstrual bleeding scores (e.g., PBAC chart) and patient-reported outcomes.
4	Bridge Pose		[138, 139]	1	Enhances pelvic floor strength and uterine function, measurable through pelvic floor muscle endurance tests or imaging-based uterine contractility assessment.

Table 3 (continued)

Sl No.	Practice	Representation	Reference	Duration (in mins)	Measurable Clinical Outcome
5	Cobra Pose		[138, 140]	1	Decreases pelvic and uterine congestion, often reflected in improved menstrual flow characteristics or reduced pelvic pressure symptoms.
6	Bow Pose		[136, 141]	1	Relieves fibroid-related discomfort, demonstrated by improved quality-of-life indices in fibroid symptom questionnaires (e.g., UFS-QOL).
7	Alternate Nostril Breathing		[133, 142]	25	Stabilises hormonal fluctuations, which may be evidenced through improved FSH/LH ratio and more regular menstrual cycles.
8	Humming Bee Breath		[138, 143]	6	Mitigates inflammation and restores hormonal balance, contributing to symptom relief and measurable improvements in reproductive health outcomes.

millennia in pursuit of either restoring normalcy or curing various ailments, specifically pertaining to reproductive dysfunctions [144]. It is a minimally invasive treatment that targets the root cause of uterine fibroids (UF) rather than just relieving symptoms which makes it more suitable as a complementary therapy, not a primary evidence-based treatment. Also, the acupuncture effectiveness is thought to come from its ability to balance the hypothalamic–pituitary–ovarian (HPO) axis, which plays a key role in maintaining reproductive health [145]. Acupuncture might, thus, relieve endocrine dysregulation associated with the pathogenesis of UF by modulating patterns of secretion of the gonadotropin-releasing hormone (GnRH) and hormone levels [146]. Coupled with its role in increasing uterine perfusion, this opens up a vascular-mediated mechanism of action for acupuncture that could alleviate symptom severity and control fibroid growth [147]. Given that the formation of UFs depends on a complex interplay of estrogen, progesterone, and fibrogenic growth factors, acupuncture may be one of those adjunctive techniques that might provide a therapeutic benefit by re-establishing pelvic neurovascular dynamics and modulating inflammatory cytokine activity [148, 149]. Another dimension of its mechanistic action has been that of signal transduction to connective tissue, into which mechanical signals would flow [150]. Acupuncture shows therapeutic potential and should be used as a complementary approach alongside standard evidence-based treatments. More clinical studies are needed to confirm its long-term effectiveness and to improve treatment protocols. Its ability to support endocrine, vascular, and inflammatory balance highlights its value as an adjunct therapy for UF.

Clinical considerations in non-surgical management of uterine fibroids

Optimal use of non-surgical interventions requires careful patient stratification. Pharmacological therapies are particularly useful for premenopausal women with smaller fibroids or those preparing for fertility, as these agents can suppress estrogen-driven proliferation and control menorrhagia. Another management such as UAE and HIFU are considered for patients with symptomatic fibroids who do not desire immediate pregnancy; however, pre-procedural imaging and fibroid characterization (size, number, and location) are critical to predict efficacy and minimize complications. Regular follow-up with imaging and laboratory assessments is essential to monitor fibroid response, detect regrowth, and manage treatment-related adverse effects. Furthermore, patient comorbidities, accessibility to specialized centers and personal preferences must be incorporated into the decision-making process to ensure individualized therapy.

Limitations and challenges of non-surgical methods in uterine fibroids

The non-surgical management of uterine fibroids includes medications, minimally invasive procedures, lifestyle approaches and newer AI-based tools, each with their own strengths and limitations. Medications such as hormonal therapies and selective receptor modulators can reduce symptoms effectively but they often lead to recurrence once treatment stops and may cause side effects or be unsuitable for some patients. Minimally invasive procedures like uterine artery embolization and high-intensity focused ultrasound can shrink fibroids in a targeted way, but their success depends on factors such as fibroid size, location, blood supply and they may not always resolve symptoms completely. Lifestyle and complementary strategies, including yoga, dietary phytochemicals, and acupuncture, can help improve quality of life and provide symptom relief. However, their benefits are inconsistent, adherence is often difficult and strong clinical evidence is still lacking, meaning they cannot yet be relied on as standalone treatments. Emerging AI-assisted approaches show promise in tailoring treatment and predicting outcomes more precisely, but these remain in early stages, limited by high costs and the need for large-scale validation.

Overall, while non-surgical strategies are expanding, their variable effectiveness, patient-specific challenges, and lack of long-term data mean that treatment must still be carefully individualized. Future progress will rely on well-designed clinical trials, continued research, and the integration of advanced technologies to strengthen non-invasive options and reduce the need for surgery ultimately leading to better outcomes and quality of life for patients.

Conclusion

Uterine fibroids are a significant but frequently overlooked health issue for women, leading to symptoms such as heavy bleeding, pain, fertility problems and emotional distress. Traditional treatment options, such as surgical procedures (e.g., myomectomy, hysterectomy), have serious risks, can result in irreversible changes and are not appropriate in all cases. Within this context, integrative approaches combining emerging technologies and complementary therapies offer a promising yet evolving path forward.

Artificial Intelligence (AI) has begun to show real promise in improving the diagnosis and treatment planning for uterine fibroids. For example, deep convolutional neural networks (DCNN) applied to ultrasound images have permitted junior sonographers to achieve diagnostic accuracy (94–95%) for fibroid visualization comparable to senior radiologists [16]. AI models have also been developed to predict outcomes for patients undergoing

uterine artery embolization and the associated expected symptom relief, achieving moderate predictive performance (area under the curve ~ 0.75–0.87) in small pilot studies [151]. These findings suggest that AI may act as a decision-support tool though large-scale validation and integration into clinical workflows, but it remain prerequisites for broader adoption.

Phytochemicals such as Epigallocatechin gallate (EGCG), curcumin, quercetin, and resveratrol have shown mechanistic results in preclinical models, particularly through modulation of some pathways such as TGF- β , Wnt/ β -catenin, YAP, JNK, and AKT that are implicated in fibroid proliferation and fibrosis [152]. Notably, an early-phase clinical trial of EGCG reported a reduction in fibroid size and symptom relief, though the effect sizes and durability remain uncertain [122]. In addition, a randomized clinical trial using green tea extract (800 mg/day) found a statistically significant decrease in fibroid volume and symptom severity in premenopausal women compared to placebo, without serious adverse effects [119]. Even though these results are encouraging but more rigorous randomized controlled trials are needed to confirm efficacy, optimal dosing, safety and long-term outcomes.

In our review, we found that research focused specifically on women with fibroids is still limited and often based on small studies. A combined approach that uses AI-driven diagnostic tools, evidence-based phytochemicals, and supportive physical therapies appears promising but is still in the early stages of development. While current evidence is preliminary but these methods highlight the potential to move beyond surgery as the primary treatment option, toward more personalized and less invasive care. More well-designed clinical trials and translational studies are needed to confirm their effectiveness, guide clinical use, and ensure patient safety. With ongoing research, this integrated approach could expand treatment options, reduce the overall burden of the disease and improve the quality of life for women living with fibroids.

Acknowledgements

The authors would like to acknowledge the Vellore Institute of Technology, Vellore, for providing the facilities and encouragement to carry out this work.

Authors' contributions

Manshi Kumari Gupta: Conceptualisation, writing original draft and Visualization, Sukanya Pattnaik: Conceptualisation, writing original draft and Visualization and C. Sudandiradoss: Conceptualisation, Investigation, Project administration, Supervision and Writing review and editing.

Funding

The author(s) reported there is no funding associated with the work featured in this review.

Data availability

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

Author details

¹Department of Biotechnology, School of Biosciences and Technology, Vellore Institute of Technology, Vellore, Tamilnadu 632014, India

Received: 17 June 2025 / Accepted: 27 October 2025

Published online: 02 December 2025

References

1. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM (2003) High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol* 188:100–107. <https://doi.org/10.1067/MOB.2003.99>
2. Islam MS, Protic O, Stortoni P, Grechi G, Lamanna P, Petraglia F, Castellucci M, Ciarmela P (2013) Complex networks of multiple factors in the pathogenesis of uterine leiomyoma. *Fertil Steril* 100:178–193. <https://doi.org/10.1016/J.FERTNSTERT.2013.03.007>
3. Bulun SE (2013) Uterine Fibroids, new England. *J Med* 369:1344–1355. <https://doi.org/10.1056/NEJMRA1209993>
4. Pritts EA, Parker WH, Brown J, Olive DL (2015) Outcome of occult uterine leiomyosarcoma after surgery for presumed uterine fibroids: a systematic review. *J Minim Invasive Gynecol* 22:26–33. <https://doi.org/10.1016/J.JMIG.2014.08.781>
5. Devaud N, Vornicova O, Abdul Razak AR, Khalili K, Demicco EG, Mitric C, Bernardini MQ, Gladly RA (2022) Leiomyosarcoma: current clinical management and future horizons. *Surg Oncol Clin N Am* 31:527–546. <https://doi.org/10.1016/J.SOC.2022.03.011>
6. Ting AH, McGarvey KM, Baylin SB (2006) The cancer epigenome - components and functional correlates. *Genes Dev* 20:3215–3231. <https://doi.org/10.1101/GAD.1464906>
7. Vogelstein B, Kinzler KW (2004) Cancer genes and the pathways they control. *Nature* 428:21–28. <https://doi.org/10.1038/nature02877>
8. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH (2012) The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol* 206:211e1–211.e9. <https://doi.org/10.1016/J.AJOG.2011.12.002>
9. Markowski DN, Bartnitzke S, Löning T, Drieschner N, Helmke BM, Bullerdiek J (2012) MED12 mutations in uterine fibroids-their relationship to cytogenetic subgroups. *Int J Cancer* 131:1528–1536. <https://doi.org/10.1002/IJC.27424>
10. Farris M, Bastianelli C, Rosato E, Brosens I, Benagiano G (2019) Uterine fibroids: an update on current and emerging medical treatment options. *Ther Clin Risk Manag* 15:157. <https://doi.org/10.2147/TCRM.S147318>
11. Ravina J, Ciraru-Vigneron N, Lancet JB-T, Arterial embolisation to treat uterine myomata, Elsevier JH Ravina, Ciraru-Vigneron N, Bouret JM, Herbreteau D, Houdart E, Aymard A (1995) undefined, *JJ Merland The Lancet*, 1995-Elsevier (n.d.). <https://www.sciencedirect.com/science/article/pii/S0140673695922822> (accessed March 10, 2025)
12. Hutchins FL, Worthington-Kirsch R, Berkowitz RP (1999) Selective uterine artery embolization as primary treatment for symptomatic leiomyomata uteri. *J Am Assoc Gynecol Laparosc* 6:279–284. [https://doi.org/10.1016/S1074-3804\(99\)80061-9](https://doi.org/10.1016/S1074-3804(99)80061-9)
13. Della Badia C, Karini H (2010) Endometrial stromal sarcoma diagnosed after uterine morcellation in laparoscopic supracervical hysterectomy. *J Minim Invasive Gynecol* 17:791–793. <https://doi.org/10.1016/J.JMIG.2010.07.001>

14. Early HM, McGahan JP, Scoutt LM, Revzin M, Lamba R, Corwin M, Fananapazir G, Sekhon S (2016) Pitfalls Sonographic Imaging Uterine Leiomyoma Ultrasound Q 32:164–174. <https://doi.org/10.1097/RUQ.0000000000000176>
15. Okolo S (2008) Incidence, aetiology and epidemiology of uterine fibroids. *Best Pract Res Clin Obstet Gynaecol* 22:571–588. <https://doi.org/10.1016/j.BP.0B.2008.04.002>
16. Huo T, Li L, Chen X, Wang Z, Zhang X, Liu S, Huang J, Zhang J, Yang Q, Wu W, Xie Y, Wang H, Ye Z, Deng K (2023) Artificial intelligence-aided method to detect uterine fibroids in ultrasound images: a retrospective study. *Sci Rep* 2023 13:113. <https://doi.org/10.1038/s41598-022-26771-1>
17. Yen HR, Chen YY, Huang TP, Chang TT, Tsao JY, Chen BC, Sun MF (2015) Prescription patterns of Chinese herbal products for patients with uterine fibroid in Taiwan: a nationwide population-based study. *J Ethnopharmacol* 171:223–230. <https://doi.org/10.1016/j.jep.2015.05.038>
18. Dalton-Brewer N (2016) The role of complementary and alternative medicine for the management of fibroids and associated symptomatology. *Curr Obstet Gynecol Rep* 5:110–118. <https://doi.org/10.1007/s13669-016-0156-0>
19. Jacoby VL, Jacoby A, Learman LA, Schembri M, Gregorich SE, Jackson R, Kuppermann M (2014) Use of medical, surgical and complementary treatments among women with fibroids. *Eur J Obstet Gynecol Reprod Biol* 182:220. <https://doi.org/10.1016/j.ejogrb.2014.09.004>
20. Rubio EM, Hilton JF, Bent S, Parvataneni R, Oberman E, Saberi NS, Varon S, Schembri M, Waetjen LE, Jacoby VL (2023) Complementary and alternative medicine use among women with symptomatic uterine fibroids. *J Womens Health* 32:546–552. <https://doi.org/10.1089/jwh.2022.0094>
21. (PDF) Management of uterine fibroid with Ayurvedic intervention, (n.d.). http://www.researchgate.net/publication/354697169_Management_of_uterine_fibroid_with_Ayurvedic_intervention (2025)
22. Mehine M, Kaasinen E, Mäkinen N, Katainen R, Kämpjärvi K, Pitkänen E, Heinonen H-R, Bützow R, Kilpivaara O, Kuosmanen A, Ristolainen H, Gentile M, Sjöberg J, Vahteristo P, Aaltonen LA (2013) Characterization of uterine leiomyomas by Whole-Genome sequencing. *N Engl J Med* 369:43–53. https://doi.org/10.1056/NEJMoa1302736/SUPPL_FILE/NEJMoa1302736_DISCLOSURE.PDF
23. Mäkinen N, Mehine M, Tolvanen J, Kaasinen E, Li Y, Lehtonen HJ, Gentile M, Yan J, Enge M, Taipale M, Aavikko M, Katainen R, Virolainen E, Böhling T, Koski TA, Launonen V, Sjöberg J, Taipale J, Vahteristo P, Aaltonen LA (2011) MED12, the mediator complex subunit 12 gene, is mutated at high frequency in uterine leiomyomas. *Science* 334:252–255. <https://doi.org/10.1126/SCIENCE.1208930>
24. Bullerdiek J, Rommel B (2018) Factors targeting MED12 to drive tumorigenesis? *F1000Res*. <https://doi.org/10.12688/F1000RESEARCH.14227.2>
25. Ligon AH, Moore SDP, Parisi MA, Mealiffe ME, Harris DJ, Ferguson HL, Quade BJ, Morton CC (2005) Constitutional rearrangement of the architectural factor HMGA2: a novel human phenotype including overgrowth and lipomas. *Am J Hum Genet* 76:340–348. <https://doi.org/10.1086/427565>
26. Gross KL, Neskey DM, Manchanda N, Weremowicz S, Kleinman MS, Nowak RA, Ligon AH, Rogalla P, Drechsler K, Bullerdiek J, Morton CC (2003) HMGA2 expression in uterine leiomyomata and myometrium: quantitative analysis and tissue culture studies. *Genes Chromosomes Cancer* 38:68–79. <https://doi.org/10.1002/GCC.10240>
27. Peng Y, Laser J, Shi G, Mittal K, Melamed J, Lee P, Wei JJ (2008) Antiproliferative effects by let-7 repression of high-mobility group A2 in uterine leiomyoma. *Mol Cancer Res* 6:663–673. <https://doi.org/10.1158/1541-7786.MCR-07-0370>
28. Mäkinen N, Kämpjärvi K, Frizzell N, Bützow R, Vahteristo P (2017) Characterization of MED12, HMGA2, and FH alterations reveals molecular variability in uterine smooth muscle tumors. *Mol Cancer* 16:1–8. <https://doi.org/10.1186/s12943-017-0672-1/FIGURES/2>
29. Mas A, Cervelló I, Fernández-Álvarez A, Faus A, Díaz A, Burgués O, Casado M, Simón C (2015) Overexpression of the truncated form of high mobility group A proteins (HMGA2) in human myometrial cells induces leiomyoma-like tissue formation. *Mol Hum Reprod* 21:330–338. <https://doi.org/10.1093/MOLEH R/GAU114>
30. Helmke BM, Markowski DN, Müller MH, Sommer A, Müller J, Müller C, Bullerdiek J (2011) HMGA proteins regulate the expression of FGF2 in uterine fibroids. *Mol Hum Reprod* 17:135–142. <https://doi.org/10.1093/MOLEHR/GAQ 083>
31. Mehine M, Kaasinen E, Heinonen HR, Mäkinen N, Kämpjärvi K, Sarvilinna N, Aavikko M, Vähärautio A, Pasanen A, Bützow R, Heikinheimo O, Sjöberg J, Pitkänen E, Vahteristo P, Aaltonen LA (2016) Integrated data analysis reveals uterine leiomyoma subtypes with distinct driver pathways and biomarkers. *Proc Natl Acad Sci U S A* 113:1315–1320. https://doi.org/10.1073/PNAS.15187 52113/SUPPL_FILE/PNAS.1518752113.SD06.XLSX
32. Popp B, Erber R, Kraus C, Vasileiou G, Hoyer J, Burghaus S, Hartmann A, Beckmann MW, Reis A, Agaimy A (2020) Targeted sequencing of FH-deficient uterine leiomyomas reveals biallelic inactivating somatic fumarate variants and allows characterization of missense variants. *Mod Pathol* 33:2341–2353. <https://doi.org/10.1038/s41379-020-0596-Y>
33. Berta DG, Kuisma H, Välimäki N, Räisänen M, Jäntti M, Pasanen A, Karhu A, Kaukomaa J, Taira A, Cajuso T, Nieminen S, Penttinen RM, Ahonen S, Lehtonen R, Mehine M, Vahteristo P, Jalkanen J, Sahu B, Ravantti J, Mäkinen N, Rajamäki K, Palin K, Taipale J, Heikinheimo O, Bützow R, Kaasinen E, Aaltonen LA (2021) Deficient H2A.Z deposition is associated with genesis of uterine leiomyoma. *Nat* 2021 596(596):7872. <https://doi.org/10.1038/s41586-021-03747-1>
34. Moore LD, Le T, Fan G (2013) DNA Methylation and Its Basic Function. *Neuro-psychopharmacology* 38(1):1–38. <https://doi.org/10.1038/npp.2012.1.12>
35. Navarro A, Yin P, Monsivais D, Lin SM, Du P, Wei JJ, Bulun SE (2012) Genome-wide DNA methylation indicates silencing of tumor suppressor genes in uterine leiomyoma. *PLoS ONE* 7:e33284. <https://doi.org/10.1371/JOURNALP ONE.0033284>
36. Sato S, Maekawa R, Tamura I, Shirafuta Y, Shinagawa M, Asada H, Taketani T, Tamura H, Sugino N (2019) SATB2 and NGR1: potential upstream regulatory factors in uterine leiomyomas. *J Assist Reprod Genet* 36:2385–2397. <https://doi.org/10.1007/s10815-019-01582-Y>
37. Maekawa R, Sato S, Yamagata Y, Asada H, Tamura I, Lee L, Okada M, Tamura H, Takaki E, Nakai A, Sugino N (2013) Genome-wide DNA methylation analysis reveals a potential mechanism for the pathogenesis and development of uterine leiomyomas. *PLoS ONE* 8:e66632. <https://doi.org/10.1371/JOURNALP ONE.0066632>
38. Mlodawska OW, Saini P, Parker JB, Wei JJ, Bulun SE, Simon MA, Chakravarti D (2022) Epigenomic and enhancer dysregulation in uterine leiomyomas. *Hum Reprod Update* 28:518–547. <https://doi.org/10.1093/HUMUPD/DMAC008>
39. Di X, Yu L, Moore AB, Castro L, Zheng X, Hermon T, Dixon D (2008) A low concentration of genistein induces estrogen receptor- α and insulin-like growth factor-I receptor interactions and proliferation in uterine leiomyoma cells. *Hum Reprod* 23:1873–1883. <https://doi.org/10.1093/HUMREP/DEN087>
40. Sabeh ME, Saha SK, Afrin S, Islam MS, Borahay MA (2021) Wnt/ β -catenin signaling pathway in uterine leiomyoma: role in tumor biology and targeting opportunities. *Mol Cell Biochem* 476(476):9. <https://doi.org/10.1007/s1101 0-021-04174-6>
41. Mangioni S, Viganò P, Lattuada D, Abbiati A, Vignali M, Di AM, Blasio (2005) Overexpression of the Wnt5b gene in leiomyoma cells: implications for a role of the Wnt signaling pathway in the uterine benign tumor. *J Clin Endocrinol Metab* 90:5349–5355. <https://doi.org/10.1210/JC.2005-0272>
42. Ono M, Yin P, Navarro A, Moravek MB, Coon JS, Druschitz VSA, Serna VA, Qiang W, Brooks DC, Malpani SS, Ma J, Ercan CM, Mittal N, Monsivais D, Dyson MT, Yemelyanov A, Maruyama T, Chakravarti D, Kim JJ, Kurita T, Gottardi CJ, Bulun SE (2013) Paracrine activation of WNT/ β -catenin pathway in uterine leiomyoma stem cells promotes tumor growth. *Proc Natl Acad Sci U S A* 110:17053–17058. https://doi.org/10.1073/PNAS.1313650110/SUPPL_FILE/PN AS.201313650SI.PDF
43. Ono M, Yin P, Navarro A, Moravek MB, Coon JS, Druschitz VSA, Gottardi CJ, Bulun SE (2014) Inhibition of canonical WNT signaling attenuates human leiomyoma cell growth. *Fertil Steril* 101:1441–1449e1. <https://doi.org/10.1016 /J.FERTNSTERT.2014.01.017>
44. Frangiannakis NG (2020) Transforming growth factor- β in tissue fibrosis. *J Exp Med* 217. <https://doi.org/10.1084/JEM.20190103/133821>
45. Protic O, Islam MS, Greco S, Giannubilo SR, Lamanna P, Petraglia F, Ciavattini A, Castellucci M, Hinz B, Ciarmela P (2017) Activin A in inflammation, tissue repair, and fibrosis: possible role as inflammatory and fibrotic mediator of uterine fibroid development and growth. *Semin Reprod Med* 35:499–509. <https://doi.org/10.1055/s-0037-1607265>
46. Ciebiaera M, Włodarczyk M, Wrzosek M, Ślubszewska-Jóźwiak A, Nowicka G, Jakiel G (2018) Ulipristal acetate decreases transforming growth factor β 3 serum and tumor tissue concentrations in patients with uterine fibroids. *Fertil Steril* 109:501–507e2. <https://doi.org/10.1016/J.FERTNSTERT.2017.11.023>
47. Joseph DS, Malik M, Nurudeen S, Catherino WH (2010) Myometrial cells undergo fibrotic transformation under the influence of transforming growth factor β -3. *Fertil Steril* 93:1500–1508. <https://doi.org/10.1016/J.FERTNSTERT.20 09.01.081>
48. George S, Serrano C, Hensley ML, Ray-Coquard I (2018) Soft tissue and uterine leiomyosarcoma. *J Clin Oncol* 36:144. <https://doi.org/10.1200/JCO.2017.75.98 45>

49. Ricci S, Stone RL, Fader AN (2017) Uterine leiomyosarcoma: epidemiology, contemporary treatment strategies and the impact of uterine morcellation. *Gynecol Oncol* 145:208–216. <https://doi.org/10.1016/j.ygyno.2017.02.019>
50. Cree IA, White VA, Indave BI, Lokuhetty D (2020) Revising the WHO classification: female genital tract tumours. *Histopathology* 76:151–156. <https://doi.org/10.1111/HIS.13977>
51. Cui RR, Wright JD, Hou JY (2017) Uterine leiomyosarcoma: a review of recent advances in molecular biology, clinical management and outcome. *BJOG* 124:1028–1037. <https://doi.org/10.1111/1471-0528.14579>
52. Juhasz-Böss I, Gabriel L, Bohle RM, Horn LC, Solomayer EF, Breitbach GP (2018) Uterine leiomyosarcoma. *Oncol Res Treat* 41:680–686. <https://doi.org/10.1159/000494299>
53. Polyak K (2011) Heterogeneity in breast cancer. *J Clin Invest* 121:3786–3788. <https://doi.org/10.1172/JCI60534>
54. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F, Global Cancer Statistics 2020 (2021) GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 71:209–249. <https://doi.org/10.3322/CAAC.21660>
55. Shen TC, Hsiao TC, Hsiao CL, Lin CL, Yang CY, Soh KS, Liu LC, Chang WS, Tsai CW, Bau DT (2017) Patients with uterine leiomyoma exhibit a high incidence but low mortality rate for breast cancer. *Oncotarget* 8:33014. <https://doi.org/10.18632/oncotarget.16520>
56. Wu X, Xiao C, Han Z, Zhang L, Zhao X, Hao Y, Xiao J, Gallagher CS, Kraft P, Morton CC, Li J, Jiang X (2022) Investigating the shared genetic architecture of uterine leiomyoma and breast cancer: a genome-wide cross-trait analysis. *Am J Hum Genet* 109:1272–1285. <https://doi.org/10.1016/j.ajhg.2022.05.015>
57. Oaknin A, Bosse TJ, Creutzberg CL, Giordano G, Harter P, Joly F, Lorusso D, Marth C, Makker V, Mirza MR, Ledermann JA, Colombo N (2022) Endometrial cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol* 33:860–877. <https://doi.org/10.1016/j.annonc.2022.05.009>
58. Javadi K, Ferdosi-Shahandashti E, Rajabnia M, Khaledi M (2024) Vaginal microbiota and gynecological cancers: a complex and evolving relationship. *Infect Agent Cancer* 19:1–12. <https://doi.org/10.1186/S13027-024-00590-7/FIGURES/2>
59. Rowlands IJ, Nagle CM, Spurdle AB, Webb PM (2011) Gynecological conditions and the risk of endometrial cancer. *Gynecol Oncol* 123:537–541. <https://doi.org/10.1016/j.ygyno.2011.08.022>
60. Johnatty SE, Stewart CJR, Smith D, Nguyen A, O'Dwyer J, O'Mara TA, Webb PM, Spurdle AB (2020) Co-existence of leiomyomas, adenomyosis and endometriosis in women with endometrial cancer. *Sci Rep* 2020 10(10):1. <https://doi.org/10.1038/s41598-020-59916-1>
61. Mittal P, Shin YH, Yatsenko SA, Castro CA, Surti U, Rajkovic A (2015) Med12 gain-of-function mutation causes leiomyomas and genomic instability. *J Clin Invest* 125:3280–3284. <https://doi.org/10.1172/JCI81534>
62. Heinonen HR, Pasanen A, Heikinheimo O, Tanskanen T, Palin K, Tolvanen J, Vahteristo P, Sjöberg J, Pitkänen E, Bützow R, Mäkinen N, Aaltonen LA (2017) Multiple clinical characteristics separate MED12-mutation-positive and -negative uterine leiomyomas. *Sci Rep* 2017 7(7):1. <https://doi.org/10.1038/s41598-017-01199-0>
63. George JW, Fan H, Johnson B, Carpenter TJ, Foy KK, Chatterjee A, Patterson AL, Koeman J, Adams M, Madaj ZB, Chesla D, Marsh EE, Triche TJ, Shen H, Teixeira JM (2019) Integrated Epigenome, Exome, and transcriptome analyses reveal molecular subtypes and homeotic transformation in uterine fibroids. *Cell Rep* 29:4069–4085. <https://doi.org/10.1016/j.celrep.2019.11.077/ATTACHMENT/7/BA0C377-3338-4F07-B148-18C80D3A8F5A/MMC7.XLSX.e6>
64. Klemke M, Müller MH, Wosniok W, Markowski DN, Nimzyk R, Helmke BM, Bullerdiek J (2014) Correlated expression of HMGA2 and PLAG1 in thyroid tumors, uterine leiomyomas and experimental models. *PLoS ONE* 9:e88126. <https://doi.org/10.1371/JOURNAL.PONE.0088126>
65. Liu S, Yin P, Xu J, Dotts AJ, Kujawa SA, Coon JSV, Zhao H, Shilatifard A, Dai Y (2020) Bulun, targeting DNA methylation depletes uterine leiomyoma stem cell-enriched population by stimulating their differentiation. *Endocrinology* 161. <https://doi.org/10.1210/ENDOCR/BQAA143>
66. Liu S, Yin P, Xu J, Dotts AJ, Kujawa SA, Coon JS, Zhao VH, Dai Y, Bulun SE (2021) Progesterone receptor-DNA methylation crosstalk regulates depletion of uterine leiomyoma stem cells: A potential therapeutic target. *Stem Cell Rep* 16:2099–2106. <https://doi.org/10.1016/j.stemcr.2021.07.013>
67. Dixon D, Di X, Andrews DMK, Tucker CJ, Yu L, Moore AB, Zheng X, Castro L, Hermon T, Xiao H (2012) A high concentration of genistein down-regulates activin A, Smad3 and other TGF- β pathway genes in human uterine leiomyoma cells. *Experimental & Molecular Medicine* 44:4 44 (2012) 281–292. <https://doi.org/10.3858/emmm.2012.44.4.024>
68. Qiao L, Xia L, Dong Y, Cheng Y, Cao H (2020) Uterine fibroids may play a protecting role against endometrial carcinoma in Chinese women with gynecological diseases. *Biosci Rep* 40:20200350. <https://doi.org/10.1042/BSR20200350>
69. Ali M, Shahin SM, Sabri NA, Al-Hendy A, Yang Q (2020) Activation of β -catenin signaling and its crosstalk with Estrogen and histone deacetylases in human uterine fibroids. *J Clin Endocrinol Metab* 105:e1517–e1535. <https://doi.org/10.1210/CLINEM/DGZ227>
70. Sabeh ME, Saha SK, Afrin S, Borahay MA (2021) Simvastatin inhibits Wnt/ β -catenin pathway in uterine leiomyoma. *Endocrinology*. <https://doi.org/10.1210/ENDOCR/BQAB211>
71. Shen Y, Wu Y, Lu Q, Zhang P, Ren M (2016) Transforming growth factor- β signaling pathway cross-talking with ER α signaling pathway on regulating the growth of uterine leiomyoma activated by phenolic environmental estrogens in vitro. *Tumor Biol* 37:455–462. <https://doi.org/10.1007/S13277-015-3813-4>
72. Chuang TD, Khorram O (2019) Cross-talk between miR-29c and transforming growth factor- β 3 is mediated by an epigenetic mechanism in leiomyoma. *Fertil Steril* 112:1180–1189. <https://doi.org/10.1016/j.fertnstert.2019.07.132>
73. Prat J, Mbatiani 'Nomonde (2015) Uterine sarcomas. *Int J Gynecol Obstet* 131:S105–S110. <https://doi.org/10.1016/j.ijgo.2015.06.006>
74. Mas A, Simón C (2019) Molecular differential diagnosis of uterine leiomyomas and leiomyosarcomas. *Biol Reprod* 101:1115–1123. <https://doi.org/10.1093/BiolREPROD/RYY195>
75. Williams ARW (2017) Uterine fibroids – what's new? *F1000Res*. <https://doi.org/10.12688/F1000RESEARCH.12172.1>
76. Mohan A, Kumar V, Brahmachari S, Pandya B (2022) A study on Clinico-Pathological profile of breast cancer patients and their correlation with uterine fibroids using hormone level and receptor status assessment. *Breast Cancer (Auckl)* 16. https://doi.org/10.1177/11782234221090197/ASSET/IMAGES/LARGE/10.1177_11782234221090197-FIG4.JPEG
77. Chuang SC, Wu GJ, Lu YS, Lin CH, Hsiung CA (2015) Associations between medical conditions and breast cancer risk in Asians: a nationwide population-based study in Taiwan. *PLoS ONE* 10:e0143410. <https://doi.org/10.1371/JOURNAL.PONE.0143410>
78. Yuk JS, Yang SW, Yoon SH, Kim MH, Seo YS, Lee Y, Joo Y, Kim J, Yoon SY, Cho H, Yang K, Gwak G (2023) Association between breast diseases and symptomatic uterine fibroids by using South Korean National health insurance database. *Sci Rep* 2023 13:113. <https://doi.org/10.1038/s41598-023-43443-w>
79. Gallagher CS, Mäkinen N, Harris HR, Rahmioglu N, Uimari O, Cook JP, Shiges N, Ferreira T, Velez-Edwards DR, Edwards TL, Mortlock S, Ruhiglu Z, Day F, Becker CM, Karhunen V, Martikainen H, Järvelin MR, Cantor RM, Ridker PM, Terry KL, Buring JE, Gordon SD, Medland SE, Montgomery GW, Nyholt DR, Hinds DA, Tung JY, Agee M, Alipanahi B, Auton A, Bell RK, Bryc K, Elson SL, Fontanillas P, Furlotte NA, Huber KE, Kleinman A, Litterman NK, McIntyre MH, Mountain JL, Noblin ES, Northover CAM, Pitts SJ, Sathirapongsasuti JF, Sazonova OV, Shelton JF, Shringarpure S, Tian C, Vacic V, Wilson CH, Perry JRB, Lind PA, Painter JN, Martin NG, Morris AP, Chasman DI, Missmer SA, Zonderman KT (2019) C.C. Morton, Genome-wide association and epidemiological analyses reveal common genetic origins between uterine leiomyomata and endometriosis. *Nature Communications* 10:1 10 (2019) 1–11. <https://doi.org/10.1038/s41467-019-12536-4>
80. O'Mara TA, Glubb DM, Amant F, Annibaldi D, Ashton K, Attia J, Auer PL, Beckmann MW, Black A, Bolla MK, Brauch H, Brenner H, Brinton L, Buchanan DD, Burwinkel B, Chang-Claude J, Chanock SJ, Chen C, Chen MM, Cheng THT, Clarke CL, Clendenning M, Cook LS, Couch FJ, Cox A, Crous-Bous M, Czene K, Day F, Dennis J, Depreeuw J, Doherty JA, Dörk T, Dowdy SC, Dürst M, Ekici AB, Fasching PA, Fridley BL, Friedreich CM, Fritschi L, Fung J, García-Closas M, Gaudet MM, Giles GG, Goode EL, Gorman M, Haiman CA, Hall P, Hankison SE, Healey CS, Hein A, Hillemanns P, Hodgson S, Hoivik EA, Holliday EG, Hopper JL, Hunter DJ, Jones A, Krakstad C, Kristensen VN, Lambrechts D, Le Marchand L, Liang X, Lindblom A, Lissowska J, Long J, Lu L, Magliocco AM, Martin L, McEvoy M, Meindl A, Michailidou K, Milne RL, Mints M, Montgomery GW, Nassir R, Olsson H, Orlov I, Otton G, Palle C, Perry JRB, Peto J, Pooler L, Prescott J, Proietto T, Rebbeck TR, Risch HA, Rogers PAW, Rübner M, Runnebaum I, Sacerdote C, Sarto GE, Schumacher F, Scott RJ, Setiawan VW, Shah M, Sheng X, Shu XO, Southey MC, Swerdlow AJ, Tham E, Trovik J, Turman C, Tyrer JP, Vachon C, VanDen Berg D, Vanderstichele A, Wang Z, Webb PM, Wentzensen N, Werner HMJ, Winham SJ, Wolk A, Xia L, Xiang YB, Yang HP, Yu H, Zheng W, Pharoah PDP, Dunning AM, Kraft P, De Vivo I, Tomlinson I, Easton DF (2018) A.B. Spurdle, D.J. Thompson, Identification of nine new susceptibility

- loci for endometrial cancer, *Nature Communications* 9:1–9 (2018) 1–12. <https://doi.org/10.1038/s41467-018-05427-7>
81. Kho PF, Mortlock S, Amant F, Annibaldi D, Ashton K, Attia J, Auer PL, Beckmann MW, Black A, Brinton L, Buchanan DD, Chanock SJ, Chen C, Chen MM, Cheng THT, Cook LS, Crous-Bous M, Czene K, Vivo I, Dennis J, Dörk T, Dowdy SC, Dunning AM, Dürst M, Easton DF, Ekici AB, Fasching PA, Fridley BL, Friedenreich CM, García-Closas M, Gaudet MM, Giles GG, Goode EL, Haiman CA, Hall P, Hankinson SE, Healey CS, Hein A, Hilleman P, Hodgson S, Hoivik E, Holliday EG, Hunter DJ, Jones A, Kraft P, Krakstad C, Lambrechts D, Marchand L, Liang X, Lindblom A, Lissowska J, Long J, Lu L, Magliocco AM, Martin L, McEvoy M, Milne RL, Mints M, Nassir R, Orlov I, Otton G, Palles C, Pharoah PDP, Pooler L, Proietto T, Rebbeck TR, Renner SP, Risch HA, Rübner M, Runnebaum I, Sacerdote C, Sarto GE, Schumacher F, Scott RJ, Setiawan VW, Shah M, Sheng X, Shu XO, Southey MC, Tham E, Thompson DJ, Tomlinson I, Trovik J, Turman C, Berg D, Wang Z, Webb PM, Wentzensen N, Winham SJ, Xia L, Xiang YB, Yang HP, Yu H, Zheng W, Sapkota Y, Steinhorsdottir V, Morris AP, Fassbender A, Rahmioglu N, Vivo I, Buring JE, Zhang F, Edwards TL, Jones S, Dorien O, Peterse D, Rexrode KM, Ridker PM, Schork AJ, MacGregor S, Martin NG, Becker CM, Adachi S, Yoshihara K, Enomoto T, Takahashi A, Kamatani Y, Matsuda K, Kubo M, Thorleifsson G, Geirsson RT, Thorsteinsdottir U, Wallace LM, Yang J, Digna R, Nyegaard M, Low SK, Zondervan KT, Missmer SA, D'Hooghe T, Chasman DI, Stefansson K, Tung JY, Rogers PAW, Nyholt DR, Montgomery GW, Glubb DM, O'Mara TA (2021) Genetic analyses of gynecological disease identify genetic relationships between uterine fibroids and endometrial cancer, and a novel endometrial cancer genetic risk region at the WNT4 1p36.12 locus. *Hum Genet* 140:1353–1365. <https://doi.org/10.1007/s00439-021-02312-0>
 82. Hosny A, Parmar C, Quackenbush J, Schwartz LH, Aerts HJWL (2018) Artificial intelligence in radiology. *Nat Rev Cancer* 18(8):8. <https://doi.org/10.1038/s41568-018-0016-5>
 83. Li C, He Z, Lv F, Liao H, Xiao Z (2024) Predicting the prognosis of HIFU ablation of uterine fibroids using a deep learning-based 3D super-resolution DWI radiomics model: a multicenter study. *Acad Radiol* 31:4996–5007. <https://doi.org/10.1016/j.jacr.2024.06.027>
 84. Theis M, Tonguc T, Savchenko O, Nowak S, Block W, Recker F, Essler M, Mustea A, Attenberger U, Marinova M, Sprinkart AM (2023) Deep learning enables automated MRI-based Estimation of uterine volume also in patients with uterine fibroids undergoing high-intensity focused ultrasound therapy. *Insights Imaging* 14:1–9. <https://doi.org/10.1186/s13244-022-01342-0/FIGURES/4>
 85. Zheng Y, Chen L, Liu M, Wu J, Yu R, Lv F (2021) Prediction of clinical outcome for high-intensity focused ultrasound ablation of uterine leiomyomas using multiparametric MRI radiomics-based machine learning model. *Front Oncol* 11:618604. <https://doi.org/10.3389/FONC.2021.618604>
 86. Wei C, Li N, Shi B, Wang C, Wu Y, Lin T, Chen Y, Ge Y, Yu Y, Dong J (2022) The predictive value of conventional MRI combined with radiomics in the immediate ablation rate of HIFU treatment for uterine fibroids. *Int J Hyperthermia* 39:475–484. <https://doi.org/10.1080/02656736.2022.2046182>
 87. Zheng Y, Chen L, Liu M, Wu J, Yu R, Lv F (2021) Nonenhanced MRI-based radiomics model for preoperative prediction of nonperfused volume ratio for high-intensity focused ultrasound ablation of uterine leiomyomas. *Int J Hyperthermia* 38(1):1349–1358. <https://doi.org/10.1080/02656736.2021.1972170>
 88. Shen L, Huang X, Liu YY, Li QX, Bai SW, Wang F, Yang Q (2024) The value of multi-parameter radiomics combined with imaging features in predicting the therapeutic efficacy of HIFU treatment for uterine fibroids. *Front Oncol* 14:1499387. <https://doi.org/10.3389/FONC.2024.1499387>
 89. Zhang J, Yang C, Gong C, Zhou Y, Li C, Li F (2022) Magnetic resonance imaging parameter-based machine learning for prognosis prediction of high-intensity focused ultrasound ablation of uterine fibroids. *Int J Hyperthermia* 39:835–846. <https://doi.org/10.1080/02656736.2022.2090622>
 90. Xi H, Wang W (2024) Deep learning based uterine fibroid detection in ultrasound images. *BMC Med Imaging* 24:1–8. <https://doi.org/10.1186/s12880-024-01389-Z/TABLES/1>
 91. Wang T, Wen Y, Wang Z (2024) nnU-Net based segmentation and 3D reconstruction of uterine fibroids with MRI images for HIFU surgery planning. *BMC Med Imaging* 24:1–15. <https://doi.org/10.1186/s12880-024-01385-3/FIGURES/10>
 92. Theis M, Tonguc T, Savchenko O, Nowak S, Block W, Recker F, Essler M, Mustea A, Attenberger U, Marinova M, Sprinkart AM (2023) Deep learning enables automated MRI-based estimation of uterine volume also in patients with uterine fibroids undergoing high-intensity focused ultrasound therapy. *Insights Imaging*. <https://doi.org/10.1186/s13244-022-01342-0>
 93. Li C, He Z, Lv F, Liu Y, Hu Y, Zhang J, Liu H, Ma S, Xiao Z (2023) An interpretable MRI-based radiomics model predicting the prognosis of high-intensity focused ultrasound ablation of uterine fibroids. *Insights Imaging* 14:1–12. <https://doi.org/10.1186/s13244-023-01445-2/FIGURES/6>
 94. Taran FA, Brown HL, Stewart EA (2010) Racial diversity in uterine leiomyoma clinical studies. *Fertil Steril* 94:1500–1503. <https://doi.org/10.1016/J.FERTNSTERT.2009.08.037>
 95. Pandey D, Sehgal K, Saxena A, Hebbar S, Nambiar J, Bhat RG (2014) An audit of indications, complications, and justification of hysterectomies at a teaching hospital in India. *Int J Reprod Med* 2014:1–6. <https://doi.org/10.1155/2014/279273>
 96. Shekhar C, Paswan B, Singh A (2019) Prevalence, sociodemographic determinants and self-reported reasons for hysterectomy in India. *Reprod Health* 16:1–16. <https://doi.org/10.1186/s12978-019-0780-Z/TABLES/5>
 97. Uikey P, Wankhede T, T.-I.J. of M (2018) undefined The route of hysterectomy: a comparative study between abdominal hysterectomy (AH), non descent vaginal hysterectomy (NDVH), and laparoscopic assisted vaginal. *GoGale*. Comp Uikey, TM Wankhede, MP TajneInternational Journal of Reproduction, Contraception, Obstetrics and, 2018-go.Gale.Com (n.d.). <https://go.gale.com/ps/i.do?id=GALE%7CA560312485&sid=googleScholar&v=2.1&u=r&linkaccess=abs&issn=23201770&p=HRCA&sw=w> (accessed October 12, 2025)
 98. Vitale SG, Moore O, Riemma G, Carugno J, Yarto ML, Haimovich S (2023) Hysteroscopic laser ablation of symptomatic uterine fibroids: insights from a prospective study. *Climacteric* 26:497–502. <https://doi.org/10.1080/13697137.2023.2205581>
 99. Shifrin G, Engelhardt M, Gee P, Pschadka G (2021) Transcervical fibroid ablation with the Sonata™ system for treatment of submucous and large uterine fibroids. *Int J Gynaecol Obstet* 155:79–85. <https://doi.org/10.1002/IJGO.13638>
 100. Vilos GA, Allaire C, Laberge PY, Leyland N, Vilos AG, Murji A, Chen I (2015) The management of uterine leiomyomas. *J Obstet Gynaecol Can* 37:157–178. [https://doi.org/10.1016/S1701-2163\(15\)30338-8](https://doi.org/10.1016/S1701-2163(15)30338-8)
 101. Vitale SG, Riemma G, Ciebiera M, Cianci S (2020) Hysteroscopic treatment of submucosal fibroids in perimenopausal women: when, why, and how? *Climacteric* 23:355–359. <https://doi.org/10.1080/13697137.2020.1754390>
 102. Lethaby A, Vollenhoven B, Sowter MC (2001) Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids. *Cochrane Database Syst Reviews*. <https://doi.org/10.1002/14651858.CD000547/INFORMAION/EN>
 103. Carr BR, Marshburn PB, Weatherall PT, Bradshaw KD, Breslau NA, Byrd W, Roark M, Steinkampf MP (1993) An evaluation of the effect of gonadotropin-releasing hormone analogs and Medroxyprogesterone acetate on uterine leiomyomata volume by magnetic resonance imaging: a prospective, randomized, double blind, placebo-controlled, crossover trial. *J Clin Endocrinol Metab* 76:1217–1223. <https://doi.org/10.1210/JCEM.76.5.8496313>
 104. Donnez J, Gillerot S, Bourgonjon D, Clerckx F, Nisolle M (1990) Neodymium:YAG laser hysteroscopy in large submucous fibroids. *Fertil Steril* 54:999–1003. [https://doi.org/10.1016/S0015-0282\(16\)53994-6](https://doi.org/10.1016/S0015-0282(16)53994-6)
 105. Moroni RM, Martins WP, Ferriani RA, Vieira CS, Nastri CO, Candido Dos FJ, Reis LG, Brito (2015) Add-back therapy with GnRH analogues for uterine fibroids. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD010854.PUB2/MEDIA/CDR/CD010854/IMAGE_N/NCDD010854-CMP-006-01.PNG
 106. Ichigo S, Takagi H, Matsunami K, Suzuki N, Imai A (2011) Beneficial effects of dienogest on uterine myoma volume: a retrospective controlled study comparing with gonadotropin-releasing hormone agonist. *Arch Gynecol Obstet* 284:667–670. <https://doi.org/10.1007/s00404-010-1732-6>
 107. Rabe T, Saenger N, Ebert AD, Roemer T, Tinneberg HR, De Wilde RL, Wallwiener M (2018) Selective progesterone receptor modulators for the medical treatment of uterine fibroids with a focus on ulipristal acetate. *Biomed Res Int* 2018:1374821. <https://doi.org/10.1155/2018/1374821>
 108. Bouchard P, Chabbert-Buffet N, Fauser BCJM (2011) Selective progesterone receptor modulators in reproductive medicine: pharmacology, clinical efficacy and safety. *Fertil Steril* 96:1175–1189. <https://doi.org/10.1016/J.FERTNSTERT.2011.08.021>
 109. Milewska G, Ponikwicka-Tyszkowski D, Bernaczek P, Lupu O, Szamatowicz M, Sztachelska M, Pilaszewicz-Puza A, Koda M, Bielawski T, Zbucka-Kretowska I, Pawelczyk A, Tomaszewski J, Li X, Huhtaniemi I, Wolczynski S, Rahman NA (2024) Functional evidence for two distinct mechanisms of action of progesterone and selective progesterone receptor modulator on uterine leiomyomas. *Fertil Steril* 122:341–351. <https://doi.org/10.1016/J.FERTNSTERT.2024.02.046>

110. Singh SS, Belland L, Leyland N, von Riedemann S, Murji A (2018) The past, present, and future of selective progesterone receptor modulators in the management of uterine fibroids. *Am J Obstet Gynecol* 218:563–572e1. <https://doi.org/10.1016/j.AJOG.2017.12.206>
111. Small B, Millard CEF, Kisanga EP, Burman A, Anam A, Flannery C, Al-Hendy A, Whirlledge S (2020) The selective progesterone receptor modulator ulipristal acetate inhibits the activity of the glucocorticoid receptor. *J Clin Endocrinol Metab* 105:716–734. <https://doi.org/10.1210/CLINEM/DGZ139>
112. Jonsdottir G, Beermann M, Lundgren Cronsjoe A, Hasselrot K, Kopp H, Kallner (2022) Ultrasound guided microwave ablation compared to uterine artery embolization treatment for uterine fibroids – a randomized controlled trial. *Int J Hyperthermia* 39:341–347. <https://doi.org/10.1080/02656736.2022.2034991>
113. Turtulici G, Orlandi D, Dedone G, Mauri G, Fasciani A, Sirito R, Silvestri E (2018) Ultrasound-guided transvaginal radiofrequency ablation of uterine fibroids assisted by virtual needle tracking system: a preliminary study. *Int J Hyperthermia* 35:97–104. <https://doi.org/10.1080/02656736.2018.1479778>
114. Manyonda I, Belli A-M, Lumsden M-A, Moss J, McKinnon W, Middleton LJ, Cheed V, Wu O, Sirkeci F, Daniels JP, McPherson K (2020) Uterine-Artery embolization or myomectomy for uterine fibroids. *N Engl J Med* 383:440–451. https://doi.org/10.1056/NEJM0A1914735/SUPPL_FILE/NEJM0A1914735_DATA-SHARING.PDF
115. Gao H, Li T, Fu D, Wei J (2021) Uterine artery embolization, surgery and high intensity focused ultrasound in the treatment of uterine fibroids: a network meta-analysis. *Quant Imaging Med Surg* 11:4125. <https://doi.org/10.21037/QIMS-20-1331>
116. Rodríguez J, Isern J, Pons N, Carmona A, Vallejo E, Cassadó J, De Marcos JA, Paraira M, Giménez N, Pessarrodonà A (2021) Pregnancy outcomes after ultrasound-guided high-intensity focused ultrasound (USgHIFU) for conservative treatment of uterine fibroids: experience of a single institution. *Int J Hyperthermia* 38:9–17. <https://doi.org/10.1080/02656736.2021.1908633>
117. Iversen H, Lenz S, Dueholm M (2012) Ultrasound-guided radiofrequency ablation of symptomatic uterine fibroids: short-term evaluation of effect of treatment on quality of life and symptom severity. *Ultrasound Obstet Gynecol* 40:445–451. <https://doi.org/10.1002/UOG.11118>
118. Jones S, O'Donovan P, Toub D (2012) Radiofrequency ablation for treatment of symptomatic uterine fibroids. *Obstet Gynecol Int* 2012:194839. <https://doi.org/10.1155/2012/194839>
119. Islam MS, Akhtar MM, Ciavattini A, Giannubilo SR, Protic O, Janjusevic M, Procopio AD, Segars JH, Castellucci M, Ciarmela P (2014) Use of dietary phytochemicals to target inflammation, fibrosis, proliferation, and angiogenesis in uterine tissues: promising options for prevention and treatment of uterine fibroids? *Mol Nutr Food Res* 58:1667–1684. <https://doi.org/10.1002/MNFR.201400134>
120. Olowosoke CB, Eze CJ, Munir A, Dada OO, Omolabake KE, Oke GA, Mounadi N, Chitita S, Ibsanmi TA (2024) Integrative study of phytochemicals for anti-fibroid agent: A perspective on protein networks, molecular docking, ADMET, simulation, DFT and bioactivity. *Chem Phys Impact* 8:100412. <https://doi.org/10.1016/J.CPHI.2023.100412>
121. Dong JR, Chang WW, Chen SM (2021) Nerolidol inhibits proliferation of leiomyoma cells via reactive oxygen species-induced DNA damage and downregulation of the ATM/Akt pathway. *Phytochemistry* 191:112901. <https://doi.org/10.1016/J.PHYTOCHEM.2021.112901>
122. Islam MS, Parish M, Brennan JT, Winer BL, Segars JH (2023) Targeting fibrotic signaling pathways by EGCG as a therapeutic strategy for uterine fibroids. *Sci Rep* 2023 13:1. <https://doi.org/10.1038/s41598-023-35212-6>
123. Yu YH, Zhang HJ, Yang F, Xu L, Liu H (2023) Curcuminol, a major terpenoid from curcuma rhizoma, attenuates human uterine leiomyoma cell development via the p38MAPK/NF- κ B pathway. *J Ethnopharmacol* 310:116311. <https://doi.org/10.1016/J.JEP.2023.116311>
124. Upadhyay S, Pandey V, Tripathi A, Sahu AN, Rani A, Diwakar A, Chaubey L, Gupta R, Dubey PK (2024) A comparative analysis of phytochemicals versus synthetic drugs/nanomedicines in the treatment of uterine fibroid: a systematic review. *Toxicol Environ Health Sci* 16:21–36. <https://doi.org/10.1007/S13530-023-00198-1/METRICS>
125. Greco S, Islam MS, Zannotti A, Carpinì GD, Giannubilo SR, Ciavattini A, Petraglia F, Ciarmela P (2020) Quercetin and indole-3-carbinol inhibit extracellular matrix expression in human primary uterine leiomyoma cells. *Reprod Biomed Online* 40:593–602. <https://doi.org/10.1016/J.RBMO.2020.01.006>
126. Ka1 B, M2 P, M. S3, Yoga can Inhibit Uterine Fibroid Growth and Improve Health-Related Quality of Life, Nursing A (2024) & Patient Care International Journal 7 <https://academicstrive.com/ANPCIJ/articles/view/1911> (accessed October 11, 2025)
127. Cramer H, Lauche R, Klose P, Lange S, Langhorst J, Dobos GJ (2017) Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. *Cochrane Database Syst Rev* 1. <https://doi.org/10.1002/14651858.CD010802.PUB2>
128. Yadav A, Tiwari P, Dada R (2024) Yoga and lifestyle changes: A path to improved Fertility – A narrative review. *Int J Yoga* 17:10. https://doi.org/10.4103/IJOY.IJOY_211_23
129. Telles S, Singh N, Balkrishna A (2012) Managing mental health disorders resulting from trauma through yoga: A review. *Depress Res Treat* 2012. <https://doi.org/10.1155/2012/401513>
130. Lee MS, Kim JI, Ha JY, Boddy K, Ernst E (2009) Yoga for menopausal symptoms: a systematic review. *Menopause* 16:602–608. <https://doi.org/10.1097/GME.0B013E31818FFFE39>
131. Sharma P, Chhabra R, Singh A, Jogdand RP, Chikitsalya P, Yoga Studio V (2020) P. Sharma Patanajali Chikitsalya Raisnghanagar, Non-surgical approach towards uterine fibroid and ovarian cyst with Yoga practice, INTEGRATIVE MEDICINE CASE REPORTS 1 <https://doi.org/10.38205/imcr.010228>
132. Bandyopadhyay A, Halder K, Pathak A, Kumar B, Saha M (2022) Surya namaskar: as an alternative for aerobic fitness. *Int J Yoga* 15:163–167. https://doi.org/10.4103/IJOY.IJOY_8_22
133. Nalgirkar SP, Vinchurkar SA, Saoji AA, Mohanty SS (2018) Yoga as a therapeutic intervention in the management of dysfunctional uterine bleeding: A controlled pilot study. *J Midlife Health* 9:8–13. https://doi.org/10.4103/JMH.JMH_76_17
134. Rao BH, Gowlikar V, Vooturi S, Benditt DG, Rao HN, Surath M (2022) Tadasana yoga maneuver for preventing Vasovagal syncope recurrences: A pilot study. *JACC Clin Electrophysiol* 8:253–254. <https://doi.org/10.1016/j.jacep.2021.12.007>
135. Saxena R, Gupta M, Shankar N, Jain S, Saxena A (2017) Effects of yogic intervention on pain scores and quality of life in females with chronic pelvic pain. *Int J Yoga* 10:9. <https://doi.org/10.4103/0973-6131.186155>
136. Dhanyal SS, Nandyal SS (2023) Yoga pose annotation and classification by using time-distributed convolutional neural network. *Indonesian J Electr Eng Comput Sci* 32:1639–1647. <https://doi.org/10.11591/IJEECS.V32.I3.PP1639-1647>
137. Ko JKY, Lao TT, Cheung VYT (2021) Pictorial blood loss assessment chart for evaluating heavy menstrual bleeding in Asian women. *Hong Kong Med J* 27:399–404. <https://doi.org/10.12809/HKMJ208743>
138. Nilachal P, Bhavanani AB, Ramanathan M, Mohanakrishnan J, Bhatt A, Srivastava V, Dhanasekaran R (2024) Development of generic yoga therapy protocol for nonspecific chronic low back pain. *Yoga Mimamsa* 56:4–12. https://doi.org/10.4103/YM.YM_74_23
139. Li Q (2022) The effects of yoga exercise on pelvic floor rehabilitation of postpartum women. *J Healthc Eng* 2022:1924232. <https://doi.org/10.1155/2022/1924232>
140. Deepa Y, Aruchunan M, Akshaya Mini T, Akila A (2021) Effect of yoga and naturopathy in a patient with uterine fibroid. *J Integr Health Sci* 9:128–130. https://doi.org/10.4103/JIHS.JIHS_28_21
141. Harding G, Coyne KS, Thompson CL, Spies JB (2008) The responsiveness of the uterine fibroid symptom and health-related quality of life questionnaire (UFS-QOL). *Health Qual Life Outcomes* 6:99. <https://doi.org/10.1186/1477-7525-6-99>
142. Cañete T, Boneu GB, Ramos S, Khalsa DS (2019) Emotional and cognitive improvement with Kirtan Kriya meditation: A pilot study for mild cognitive impairment patients in a Catalan community. <https://doi.org/10.31231/OSF.IO/Y6FKU>
143. Mishra R, Bajpai S, Jha S, Patidar N, Mishra V, Mishra S (2025) Holistic approach to uterine fibroid management (Resistance Training, aerobic exercises and yoga in perimenopausal women). *Int J Sci Technol* 16. <https://doi.org/10.7109/IJSAT.V16.I3.8105>
144. Zhu J, Li J, Yang L, Liu S (2021) Acupuncture, from the ancient to the current. *Anat Rec* 304:2365–2371. <https://doi.org/10.1002/AR.24625>
145. Zhu H, Nan S, Suo C, Zhang Q, Hu M, Chen R, Wan J, Li M, Chen J, Ding M (2019) Electro-acupuncture affects the activity of the hypothalamic-pituitary-ovary axis in female rats. *Front Physiol* 10:451278. <https://doi.org/10.3389/FPHYS.2019.00466/BIBTEX>
146. Ren Y, Zhang J, Wu W, Yuan Y, Wang J, Tang Y, Liao Y, Liu X (2023) Should acupuncture become a complementary therapy in the treatment of uterine fibroid: a systematic review and meta-analysis of randomized controlled trials. *Front Med (Lausanne)* 10:1268220. <https://doi.org/10.3389/FMED.2023.1268220/BIBTEX>

147. Liu W, Wang CC, Lee KH, Ma X, Kang TL (2022) Research methodology in acupuncture and moxibustion for managing primary dysmenorrhea: A scoping review. *Complement Ther Med* 71:102874. <https://doi.org/10.1016/J.CTIM.2022.102874>
148. Li N, Guo Y, Gong Y, Zhang Y, Fan W, Yao K, Chen Z, Dou B, Lin X, Chen B, Chen Z, Xu Z, Lyu Z (2021) The Anti-Inflammatory actions and mechanisms of acupuncture from acupoint to target organs via Neuro-Immune regulation. *J Inflamm Res* 14:7191–7224. <https://doi.org/10.2147/JIR.S341581>
149. Yu WY, Ma LX, Zhang Z, Mu JD, Sun TY, Tian Y, Qian X, Zhang YD (2021) Acupuncture for primary dysmenorrhea: A potential mechanism from an Anti-Inflammatory Perspective, Evidence-Based complementary and alternative medicine 2021. 1907009. <https://doi.org/10.1155/2021/1907009>
150. Zheng MQ, Weng C, Hu W, Shen CQ, Tao Y, Pan ZW (2020) Efficacy assessment of acupuncture in improving symptoms of uterine fibroids: A randomized controlled trial. *Med (United States)* 99:E20016. <https://doi.org/10.1097/MD.00000000000020016>
151. Janghorbani S, Caprio A, Sam L, Lee BC, Sabuncu MR, Lamparello NA, Schiffman M, Mosadegh B (2025) Predicting clinical outcomes and symptom relief in uterine fibroid embolization using machine learning on MRI Features, *AI* 2025. 6(6):200. <https://doi.org/10.3390/AI6090200>
152. Islam MS, Segars JH, Castellucci M, Ciarmela P (2016) Dietary phytochemicals for possible preventive and therapeutic option of uterine fibroids: signaling pathways as target. *Pharmacol Rep* 69:57–70. <https://doi.org/10.1016/J.PHAR.2016.10.013>

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.