

HISTOPATHOLOGICAL CHANGES IN UTERINE LEIOMYOMAS FOLLOWING SELECTIVE PROGESTERONE RECEPTOR MODULATOR THERAPY: A SYSTEMATIC REVIEW AND THEMATIC ANALYSIS

Pathology

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ABSTRACT

Background: Selective progesterone receptor modulators (SPRMs) reduce uterine leiomyoma volume and control abnormal bleeding. This systematic review and thematic synthesis evaluated architectural, cellular and vascular alterations in human uterine leiomyomas following preoperative SPRM exposure. **Methods:** It was conducted as per PRISMA 2020 guidelines. PubMed, Embase, Web of Science, Google Scholar and Scopus were searched from database inception through 2026. Eligible studies evaluated surgical or biopsy leiomyoma specimens post-SPRM therapy using routine light microscopy, special histochemical stains or intact-section morphometry and immunohistochemistry. In vitro models, bulk molecular homogenates, and purely endometrial evaluations were excluded. Two-stage screening was followed by data extraction from included studies. Quality assessment was conducted using Joanna Briggs Institute checklists. A three-stage qualitative thematic synthesis was performed. **Results:** Eight studies with total 346 surgical specimens were included. Thematic synthesis identified three core histopathological domains. First, volume reduction is driven primarily by active enzymatic extracellular matrix degradation rather than diffuse coagulative infarction. Second, smooth muscle myocytes undergo cytomorphological compaction with decreased individual cross-sectional area and increased packing density, while consistently maintaining marked mitotic quiescence (below two mitoses per 10 high-power fields) without cytologic atypia. Third, drug-induced intratumoural vasculopathy can closely simulate smooth muscle tumours of uncertain malignant potential (STUMP), leiomyosarcoma or multilocal cystic neoplasms. **Conclusion:** SPRM-induced fibroid regression represents active matrix proteolysis and cellular compaction rather than ischemic tissue necrosis. Recognizing signature medial myxoid vasculopathy alongside strict preservation of mitotic inactivity prevents the erroneous overdiagnosis of malignancy in patients undergoing surgery following preoperative SPRM exposure.

KEYWORDS

INTRODUCTION

Uterine leiomyomas (fibroids) are the most common benign pelvic mesenchymal neoplasms in women of reproductive age, accounting for substantial morbidity including abnormal uterine bleeding, pelvic pain, and infertility.^[1] Structurally, leiomyomas are characterized by smooth muscle hyperplasia, disordered extracellular matrix (ECM) rich in interstitial collagens (types I and III), fibronectin and proteoglycans, which together constitute up to 50% or more of total tumour volume.^[1]

Progesterone and its receptors (PR-A and PR-B) play a key role in driving leiomyoma cell proliferation and matrix accumulation. Selective progesterone receptor modulators (SPRMs), thus, are the cornerstone for treatment. Published clinical trials have demonstrated that ulipristal acetate (UPA) achieves rapid cessation of heavy menstrual bleeding within days and induces a 30% to 50% volumetric reduction of leiomyoma nodules that frequently persists months after drug discontinuation.^[2]

In diagnostic pathology, attention has focused heavily on the endometrium, establishing consensus guidelines for progesterone receptor modulator-associated endometrial changes (PAEC).^[3] In contrast, the microstructural, degenerative, and vascular modifications occurring directly inside the resected leiomyoma nodule are less clearly understood. Because surgical pathologists are not always informed of a patient's preoperative drug history, drug-altered fibroids exhibiting atypical myxoid degeneration, 'patchwork' fibrosis or irregular cellular packing risk being misclassified as smooth muscle tumours of uncertain malignant potential (STUMP) or low-grade leiomyosarcoma.^[4]

The existing literature assessing intact tissue morphology post-SPRM therapy consists of a focused cohort of fewer than ten dedicated observational, case-control, and surgical trial cohorts. Because these primary studies utilize heterogeneous histological scales, semiquantitative grading systems, and qualitative morphological descriptions, pooled quantitative statistical meta-analysis is neither appropriate nor methodologically valid. Therefore, this study provides a formal systematic review and qualitative thematic synthesis, cataloguing the full histopathological spectrum, cellular dynamics, and diagnostic pitfalls of SPRM-exposed uterine leiomyomas.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement.

Search Strategy

Electronic literature searches were conducted across PubMed/ MEDLINE, Embase, Web of Science, Google Scholar and Scopus from inception through 2026. The search strategy combined MeSH terms and Boolean operators to form a search string like ("Ulipristal" OR "Ulipristal acetate" OR "Asoprisnil" OR "Mifepristone" OR "selective progesterone receptor modulator*" OR "SPRM") AND ("leiomyoma" OR "fibroid" OR "myoma" OR "leiomyomata") AND ("histopatholog*" OR "histolog*" OR "hyalinosis" OR "necrosis" OR "vascular" OR "degeneration" OR "extracellular matrix" OR "collagen" OR "morphometry") NOT ("endometrium" OR "endometrial" OR "PAEC" OR "emergency contraception"). Reference lists of all included papers and relevant gynaecological pathology texts were hand-searched to identify additional eligible reports.

Eligibility criteria

Studies were selected based on the following pre-specified criteria:

- **Population:** Female patients undergoing surgical interventions for symptomatic uterine leiomyomas.
- **Intervention:** Preoperative exposure to an SPRM (e.g., Ulipristal acetate, Asoprisnil, Mifepristone) at therapeutic dosing.
- **Comparator:** Untreated surgical leiomyoma specimens, placebo-controlled surgical cohorts, or internal baseline controls where available.

Outcomes: Documented microscopic tissue alterations assessed on intact tissue sections, including routine Hematoxylin and Eosin (H&E) morphology (e.g., cellularity, mitoses, necrosis, hyalinosis, oedema), special histochemical stains (e.g., Masson's trichrome, Sirius Red), morphometric image analysis and intact-section immunohistochemistry (IHC) targeting structural matrix or vascular markers.

Study Designs: Randomized controlled trials (RCT), prospective or retrospective cohort studies, case-control studies, and detailed clinicopathological case reports/series.

In vitro cell cultures, animal experiments lacking human tissue validation, research relying solely on molecular tests without microscopic tissue examination or focusing entirely on the endometrium rather than the fibroid itself were all excluded. Also, narrative reviews, editorials and conference abstracts lacking complete histological data were not included.

Study Selection and Data Extraction

Two stage screening was performed. Titles and abstracts were inde-

pendently screened against the eligibility criteria, followed by full-text evaluation of candidate studies. Data extraction was performed using a standardized extraction template including: First author, publication year, country, study design, sample size, treatment details, comparator group, histological processing and staining techniques, evaluated histopathological variables and primary morphological and morphometric conclusions.

Quality assessment

Methodological quality was appraised using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists for Cohort, Case-Control, and Case Report studies. The studies with fair and good quality of assessment were included in the result synthesis.

Thematic synthesis

Because the primary endpoints were descriptive histomorphological patterns, qualitative thematic synthesis was performed following the three stage framework established by Thomas and Harden.^[5]

RESULTS

Study Selection

The systematic search identified 218 initial records. Following removal of duplicates (n = 64) and title/abstract screening (n = 154), 22 full-text articles were assessed. Fourteen articles were excluded based on eligibility criteria. Ultimately, 8 primary studies meeting all inclusion criteria, were included. Figure 1 illustrates the PRISMA flow diagram for study selection.

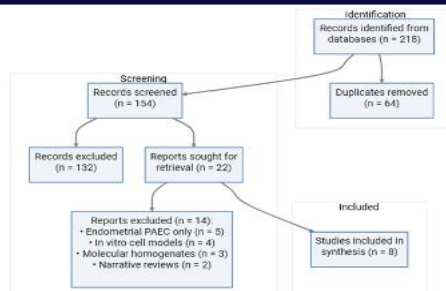


Figure 1. Prisma Flowchart for Study Selection.

Characteristics of Included Studies

The 8 included studies represent 346 surgical tissue specimens obtained from women treated with UPA (n = 7) or Asoprisnil (n = 1). Study designs included randomized placebo-controlled tissue analyses (n = 2), cohort (n = 4), case-control (n = 1) and a detailed diagnostic surgical case report (n = 1). All studies evaluated surgical pathology tissue derived from either myomectomy or hysterectomy specimens. Standard H&E light microscopy was utilized across all studies, complemented by Masson's trichrome (n = 1), Sirius Red (n = 1), computer-assisted morphometric image analysis (n = 3) and intact-section immunohistochemistry (n = 3). Table 1 summarizes the baseline characteristics, staining protocols and primary findings of the included studies.

Table 1. Baseline Characteristics and Quality Assessment of Included Studies

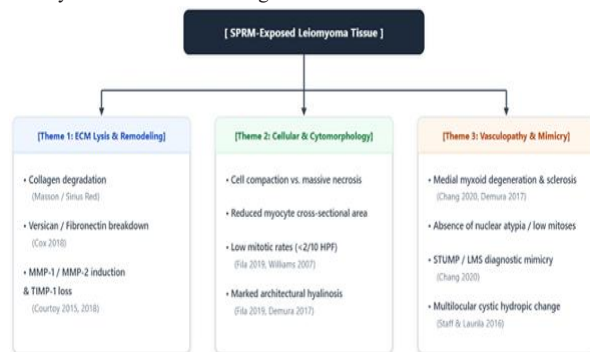
Study and year	Study design	Sample size	Drug regimen	Specimen source	Analytical & Staining methods	Key histopathological findings	Core thematic contribution	Quality assess-
Fila et al. (2019) ^[6]	Case-control	29 (UPA – 14; Control s – 15)	UPA 5 mg/day (1–2 cycles of 3 months)	surgical myomectomy/hysterectomy	Standard H&E light microscopy; semiquantitative scoring (grades 0–3)	Statistically significant moderate hyalinosis (P < 0.05); reduced cellularity; consistently low mitotic index (<2/10 HPF); absence of coagulative tumour necrosis.	Architectural Hyali-nosis & Mitotic Quiescence	Fair
Chang and Latta (2020) ^[7]	Retrospective surgical series	8	UPA 5 mg/day (extended/repeated courses)	surgical myomectomy/hysterectomy	Routine H&E light microscopy	Distinct 'patchwork' plexiform fibrosis; prominent medial myxoid degeneration in intratumoural arteries; hydropic changes mimicking STUMP/ leiomyosarcoma.	Medial Vasculo-pathy & STUMP Diagnostic Pitfalls	Fair
Williams et al. (2007) ^[8]	RCT surgical cohort	129	Asoprisnil (10 mg, 25 mg vs. placebo daily for 3 months)	hysterectomy	Whole-mount H&E histology; computer-assisted image morphometry	Marked compaction of smooth muscle cells; significant reduction in individual myocyte cross-sectional area; lack of coagulative necrosis; arterial wall thickening.	Individual Myocyte Compaction vs. Coagulative Infarction	Good
Cox et al. (2018) ^[9]	Double-blind RCT	16 (UPA – 8, Placebo – 8)	UPA 10 mg/day vs. placebo for 3 months	hysterectomy	Masson's trichrome; intact-section IHC (Versican, Fibronectin, MMP-2, MMP-9)	Significant reduction in collagen bundle density on trichrome (P < 0.05); breakdown of versican and fibronectin architecture; altered interstitial matrix hydration.	ECM Proteoglycan Cleavage	Good
Courtoy et al. (2015) ^[10]	Cohort	59 (UPA – 42, control – 17)	UPA 5 mg/day (1–4 courses)	surgical TMA specimens	Sirius Red polarization; TUNEL; Cleaved-Caspase-3; PCNA IHC	Direct collagen bundle dissolution/lysis; transient early apoptotic peak (cleaved caspase-3); sustained increase in cell packing density (compaction).	Collagen Fibril Dissolution & Apoptosis Timing	Good
Courtoy et al. (2018) ^[11]	Prospective cohort	59 (UPA – 45, control – 14)	UPA 5 mg/day (>1 course)	surgical resection	Intact-section IHC; gelatin zymography (MMP-1, MMP-2, TIMP-1)	Significant induction of active MMP-1 and MMP-2 (P < 0.01) alongside reduced TIMP-1 in responsive tumours; absent matrix enzymatic activation in non-responders.	Enzymatic Regulators of Fibroid Shrinkage	Good
Demura et al. (2017) ^[12]	Cohort	45	SPRM therapy (preoperative administration)	surgical resection	Routine H&E; morphometric area measurement	Microvascular sclerosis; localized focal hyaline matrix replacement; parenchymal smooth muscle volume shrinkage.	Microvascular Sclerosis & Sclerotic Remodelling	Fair
Staff et al. (2016) ^[13]	Surgical clinicopathologic report	1	Repeated intermittent UPA courses (1066 g mass)	Surgical resection	Routine H&E; gross surgical pathology	Multilocular cystic hydropic degeneration; extensive interstitial fluid pooling and vascular remodelling mimicking pelvic malignancy.	Extreme Cystic Hydropic Degeneration Pitfall	Good

Abbreviations

ECM - Extracellular Matrix
H&E – Hematoxylin & Eosin
IHC – Immunohistochemistry
PCNA – Proliferating Cell Nuclear Antigen
RCT – Randomized Controlled Trial
STUMP – Smooth muscle Tumor of Uncertain Malignant Potential
TMA – Tissue microarray
TUNEL – Terminal deoxynucleotidyl transferase dUTP Nick End Labeling

Thematic Synthesis

The qualitative synthesis identified three overarching analytical themes that capture the histomorphological spectrum of SPRM-treated leiomyomas as illustrated in figure 2.



Theme 1: Extracellular Matrix (ECM) Degradation and Collagen Reorganization

A consistent finding across the literature is that SPRM-induced fibroid shrinkage is not primarily mediated by ischemic infarction or massive coagulative tumour cell death. Instead, it is driven by active remodeling and enzymatic degradation of the abundant extracellular matrix. Using specialized connective tissue stains, Courtney et al. (2015) and Cox et al. (2018) independently demonstrated physical thinning, fraying and loss of collagen bundle density within the inter-myocyte matrix of UPA-treated tumours. Intact-tissue IHC revealed architectural cleavage of structural interstitial proteins, specifically versican (VCAN) and fibronectin (FN1).^[9] The degradation of these hydrophilic proteoglycans alters interstitial fluid dynamics and tissue turgor. This matrix dissolution is driven by a localized shift in proteolytic balance. In responsive myomas, UPA administration induces marked cellular expression of active interstitial collagenase (MMP-1) and gelatinase A (MMP-2), coupled with a downregulation of tissue inhibitor of metalloproteinases-1 (TIMP-1).^[11] Particularly, non-responding myomas (20% of clinical cohorts) fail to upregulate these matrix-degrading enzymes, confirming that collagenolysis is the primary structural determinant of volume reduction.

Theme 2: Smooth Muscle Cytomorphology, Compaction and Proliferative Quiescence

The cellular parenchymal compartment responds to SPRM exposure through structural compaction rather than widespread necrosis. Morphometric assessments revealed that following matrix clearance, smooth muscle cells become tightly packed.^[8, 10] The apparent cell density per high-power field (HPF) increases significantly, while the mean individual cross-sectional area of single myocytes shrinks. Cleaved caspase-3 and TUNEL staining indicate that apoptosis occurs primarily as an early, transient wave (peaking within the first few weeks of therapy) rather than a persistent cytotoxic process.^[10] Mitotic activity remains consistently low across all cohorts. To studies reported mitotic counts well below 2/10 HPFs.^[6,8] Moderate-grade architectural hyalinosis is significantly more frequent in UPA-exposed fibroids than in untreated controls ($P < 0.05$).^[6] The ground substance assumes a glassy, eosinophilic, collagen-depleted appearance under standard H&E.

Theme 3: Intratumoural Vasculopathy and Pseudomalignant Diagnostic Pitfalls

The third and most clinically significant theme concerns structural alterations in intratumoural blood vessels and resulting patterns that can mislead surgical pathologists. Intratumoural arterial walls frequently exhibit striking medial hypertrophy, smooth muscle disorganization, and myxoid degeneration of the vascular media.^[7, 8] (Chang & Latta, 2020; Williams et al., 2007). This vasculopathy is accompanied by endothelial swelling and luminal narrowing, occasionally progressing to microvascular sclerosis.^[12] Chronic microvascular ischemia induces focal zones of collapse and replacement fibrosis, described as 'plexiform' or 'patchwork' fibrosis.^[7] These regions feature irregular tongues of collagen separating disorganized smooth muscle fascicles. Because the combination of marked cell compaction, myxoid vascular expansion and ischemic hydropic changes disrupts conventional fibroid architecture, these specimens can be misinterpreted as STUMP or myxoid leiomyosarcoma.^[7] Under extended or repeated courses, localized vascular transudation can induce massive multilocular cystic hydropic degeneration, macroscopically transforming the solid myoma into a cystic pelvic mass that mimics ovarian or peritoneal cystic neoplasms.^[13]

DISCUSSION

This systematic review and thematic synthesis provides a structured analysis of the histopathological changes induced in uterine leiomyomas by SPRMs. While pharmacological evaluations have centred on clinical efficacy and endometrial safety, the surgical pathology literature demonstrates that SPRMs alter the structural, cellular, and vascular composition of the myoma nodule itself.

Biological Mechanism of SPRMs

Medical management of uterine leiomyomas using classical Gonadotropin-Releasing Hormone (GnRH) agonists and newer GnRH antagonists create a hypoestrogenic state that triggers acute devascularization, extensive cellular atrophy, and frequent foci of coagulative infarction.^[14] In contrast, this thematic synthesis shows that SPRM-induced regression follows an active ECM degradation and compaction model.

By selectively modulating progesterone receptors, SPRMs shift the balance between matrix metalloproteinases and their tissue inhibitors.^[15] Progesterone signalling serves as an essential pro-fibrotic driver in fibroid pathogenesis, suppressing collagenase transcription while stimulating ECM deposition through autocrine/paracrine mediators.^[16] SPRM administration interrupts this signalling axis. The upregulation of active MMP-1 and MMP-2, combined with TIMP-1 repression, degrades the dense collagen and proteoglycan scaffold.^[9, 11] As structural versican and fibronectin are cleaved, the high oncotic water-binding capacity of the tumour collapses. Following matrix dissolution, residual smooth muscle cells collapse inward into a compacted arrangement. Because cells are not destroyed en masse, they retain viability in a state of proliferative quiescence,^[6] explaining why clinical tumour shrinkage can persist for months after drug withdrawal without the rebound growth seen with GnRH agonists.

Diagnostic Pitfalls and Differential Diagnosis

The findings synthesized in this review have direct implications for surgical grossing and microscopic interpretation. A pathologist unaware of prior UPA exposure may see high cellular density paired with irregular stromal spaces and suspect an aggressive mesenchymal tumour. However, high-grade leiomyosarcoma requires at least two of the following three Stanford criteria: Marked cytological atypia: Mitotic rate ≥ 10 mitoses per 10 HPFs; True coagulative tumour cell necrosis (abrupt transition between viable and dead cells without interposed granulation tissue or hyalinosis).^[17] As confirmed across all 8 included studies, SPRM-treated fibroids show mitotic quiescence (< 2 mitoses /10 HPF) and lack significant cytological atypia.^[6,8] Their degenerative pattern is predominantly hyalinosis and patchy ischemic collapse, not coagulative necrosis. Prominent medial myxoid change and arterial mural thickening appear to be characteristic morphological signatures of prolonged SPRM exposure.^[7] Identifying these altered vessels helps distinguish drug-associated changes from true neoplastic vascular invasion or de novo myxoid degeneration. As highlighted by Staff et al. (2016), extensive cystic hydropic changes can obscure tissue margins and mimic cystic adnexal masses or STUMP on gross and intraoperative frozen section evaluation.^[18] Clinical history of SPRM use is critical to prevent unnecessary extensive resections in reproductive-aged patients.

STRENGTHS AND LIMITATIONS

This review represents the first PRISMA-compliant thematic synthesis specifically focused on intact leiomyoma surgical pathology post-SPRM exposure. By excluding studies limited to bulk homogenates, it provides concrete architectural and diagnostic morphological data for practicing pathologists. There are certain limitations too. The primary literature is small, largely reflecting the clinical reality that preoperatively treated fibroids are not always biopsied or resected. Differences in cumulative SPRM dosing and varying wash-out intervals introduce morphological heterogeneity that could not be statistically controlled.

CONCLUSION

Preoperative SPRM therapy produces distinct, reproducible histopathological modifications within uterine leiomyomas. Volume reduction is achieved primarily through enzymatic breakdown of the collagenous and proteoglycan extracellular matrix, driven by MMP-1/MMP-2 induction, accompanied by smooth muscle cell compaction rather than diffuse coagulative infarction. Tissue sections typically display marked hyalinosis, proliferative quiescence (mitoses $< 2/10$ HPF) and an absence of clinically significant nuclear atypia. Intratumoural blood vessels frequently show medial myxoid degeneration and

microvascular sclerosis, while stromal collapse can produce patchwork fibrosis and hydropic degeneration that simulate STUMP or malignancy. Pathologists must be routinely informed of preoperative SPRM use, and clinicians should document treatment history on surgical pathology requisitions. Recognizing this drug-induced constellation of findings helps prevent misdiagnosis and ensures appropriate, organ-sparing management for women with uterine leiomyomas.

REFERENCES

1. Munro MG, Tchaikovski SN, Murji A. The epidemiology and pathogenesis of uterine fibroids. *International Journal of Gynecology & Obstetrics*. 2025;171(3):1029-45.
2. Islam MS, Ciavattini A, Petraglia F, Castellucci M, Ciarmela P. Extracellular matrix in uterine leiomyoma pathogenesis: a potential target for future therapeutics. *Human Reproduction Update*. 2018;24(1):59-85.
3. De Milliano I, Van Hattum D, Ket JCF, Huirne JAF, Hehenkamp WJK. Endometrial changes during ulipristal acetate use: A systematic review. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2017;214:56-64.
4. Liu L, Xiao Z, Li Z, Zheng J, Xu X, Zhou H. Uterine smooth muscle tumors of uncertain malignant potential: a 13-year retrospective study. *Front Oncol*. 2024;14:1458968.
5. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol*. 2008;8:45.
6. Fila E, Indraccolo U, Pedriali M, Scutiero G, Borghi C, Greco P. Histological pattern of leiomyomas after ulipristal acetate treatment in women: a case-control study. *Clin Exp Obstet Gynecol*. 2019;46(5):792-6.
7. Chang MC, Latta E. Pathologic Changes in Uterine Leiomyomas After Extended Treatment With Ulipristal Acetate. *Int J Gynecol Pathol*. 2020;39(2):146-51.
8. Williams AR, Critchley HO, Osei J, Ingamells S, Cameron IT, Han C, et al. The effects of the selective progesterone receptor modulator asoprisnil on the morphology of uterine tissues after 3 months treatment in patients with symptomatic uterine leiomyomata. *Hum Reprod*. 2007;22(6):1696-704.
9. Cox J, Malik M, Britten J, Lewis T, Catherino WH. Ulipristal Acetate and Extracellular Matrix Production in Human Leiomyomas In Vivo: A Laboratory Analysis of a Randomized Placebo Controlled Trial. *Reprod Sci*. 2018;25(2):198-206.
10. Courtney GE, Donnez J, Marbaix E, Dolmans MM. In vivo mechanisms of uterine myoma volume reduction with ulipristal acetate treatment. *Fertil Steril*. 2015;104(2):426-34.e1.
11. Courtney GE, Henriët P, Marbaix E, de Coudt M, Luyckx M, Donnez J, et al. Matrix Metalloproteinase Activity Correlates With Uterine Myoma Volume Reduction After Ulipristal Acetate Treatment. *J Clin Endocrinol Metab*. 2018;103(4):1566-73.
12. Demura TA, Revazova ZV, Kogan EA, Adamyan LV. The molecular mechanisms and morphological manifestations of leiomyoma reduction induced by selective progesterone receptor modulators. *Arkh Patol*. 2017;79(3):19-26.
13. Staff SM, Saarelainen SK, Laurila MA. Repeated intermittent use of ulipristal acetate associated with rapid growth and multilocular cystic hydropic degeneration of a uterine fibroid: A case report. *J Case Rep Images Gynecol Obstet*. 2016;2:31-4.
14. Sánchez Martín MJ, Huerga López C, Cristóbal García I, Cristóbal Quevedo I. Efficacy of GnRH antagonists in the treatment of uterine fibroids: a meta-analysis. *Arch Gynecol Obstet*. 2025;311(3):685-96.
15. Rabe T, Saenger N, Ebert AD, Roemer T, Tinneberg HR, De Wilde RL, et al. Selective Progesterone Receptor Modulators for the Medical Treatment of Uterine Fibroids with a Focus on Ulipristal Acetate. *Biomed Res Int*. 2018;2018:1374821.
16. Yang Q, Al-Hendy A. Update on the Role and Regulatory Mechanism of Extracellular Matrix in the Pathogenesis of Uterine Fibroids. *International Journal of Molecular Sciences*. 2023;24(6):5778.
17. Höhn AK, Brambs CE, Hiller GGR, May D, Schmoeckel E, Horn LC. 2020 WHO Classification of Female Genital Tumors. *Geburtschilfe Frauenheilkd*. 2021;81(10):1145-53.
18. Bucuri CE, Ciortea R, Malutan AM, Oprea V, Toma M, Roman MP, et al. Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP): A Systematic Review of the Literature in the Last 20 Years. *Curr Oncol*. 2024;31(9):5242-54.