MORPHOLOGICAL STRUCTURE OF THE MUSCULAR LAYER OF THE UTERUS IN WOMEN OF MIDDLE REPRODUCTIVE AGE

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Abstract: The myometrium - the muscular wall of the uterus is a structurally *complex organ whose morphological organization is central to female reproductive function. In women of middle reproductive age (25–40 years), the myometrium undergoes dynamic structural changes under the influence of hormonal, cellular, and extracellular matrix (ECM) factors. This review synthesizes current evidence on the histological layering of the myometrium, the cellular composition and ultrastructure of smooth muscle cells (SMCs), the organization of the junctional zone (JZ), the role of the ECM, vascularization, innervation, and hormonal receptor distribution. A comprehensive understanding of myometrial morphology is essential for elucidating the pathogenesis of uterine disorders including adenomyosis, leiomyoma, and infertility. Recent advances in single-cell transcriptomics and high-resolution imaging have substantially refined our understanding of myometrial architecture and cellular heterogeneity.*

Keywords: *myometrium; smooth muscle cells; junctional zone; uterine morphology; reproductive age; extracellular matrix; hormonal receptors; adenomyosis.*

Introduction

The uterus is a hollow muscular organ of the female reproductive system whose wall comprises three principal layers: the endometrium (inner mucous layer), the myometrium (middle muscular layer), and the perimetrium (outer serosal layer). The myometrium constitutes the largest proportion of uterine volume and is composed primarily of smooth muscle cells [1]. It provides the contractile force essential for menstruation, blastocyst implantation, and parturition. In women of middle reproductive age generally defined as 25 to 40 years the myometrium is in its most functionally active state, responding to cyclic fluctuations in ovarian steroids and undergoing continuous morphological adaptation [2].

Despite being historically regarded as a homogeneous mass of smooth muscle, modern imaging modalities particularly T2-weighted magnetic resonance imaging (MRI) and advances in molecular biology have revealed a highly differentiated zonal architecture within the myometrium [3]. The identification of the junctional zone (JZ) as a structurally and functionally distinct subendometrial layer has transformed the understanding of uterine physiology and pathology [4]. Recent progress in single-cell transcriptomics, organoid systems, and quantitative morphometry has further clarified the cellular heterogeneity, stem cell biology, and ECM dynamics of this tissue [6, 7].

This review provides a comprehensive morphological description of the myometrium in women of middle reproductive age, covering its layered organization, cellular constituents, ECM composition, vascular and neural supply, and hormonal receptor expression, with reference to literature published in the last five years (2021–2026).

Aim of the study: To analyze the morphological structure of the uterine muscular layer in women of middle reproductive age, with emphasis on zonal architecture, smooth muscle cell ultrastructure, extracellular matrix composition, and hormonal receptor distribution, based on current literature (2021–2026).

Materials and Methods

Study design and sample collection: The study was conducted on myometrial tissue samples obtained from women of middle reproductive age (25–40 years), classified according to WHO criteria [13]. The main group consisted of myometrial specimens collected during elective surgical procedures myomectomy or hysterectomy performed for medical indications. The control group comprised autopsy materials from women of corresponding age who died as a result of accidental causes, with no history of gynecological or hormonal disorders. Inclusion criteria were: age 25–40 years, absence of hormonal disorders in the medical history, and chronic somatic diseases in remission. All procedures were conducted in accordance with ethical standards and with informed consent [2].

Histological processing: Tissue samples were immediately fixed in 10% neutral buffered formalin for 24 hours. Following standard dehydration through ascending alcohol concentrations, specimens were embedded in paraffin blocks. Serial sections of 5–7 μm thickness were prepared using a rotary microtome. The following staining protocols were applied: hematoxylin and eosin (H&E) for general morphological assessment; Van Gieson stain for differentiation of connective tissue and muscle fibers; and Masson's trichrome for visualization of collagen fibers and assessment of fibrosis [4, 8].

Morphometric analysis: Quantitative assessment of myometrial parameters was performed using a Leica DM2000 light microscope equipped with a digital camera and ImageJ image analysis software. The following parameters were measured in five standardized fields per section: myocyte nuclear volume and shape; thickness of muscle bundles; muscle-to-connective tissue ratio (morphometric index); and density and wall thickness of blood vessels (arteries and veins) [2, 4].

Statistical analysis: All numerical data were processed using descriptive and inferential statistics in Microsoft Excel and SPSS Statistics v.26.0. Mean values (M) and standard error of the mean (±m) were calculated for all parameters. Between-group differences were assessed using Student's t-test. Results were considered statistically significant at $P < 0.05$.

Results

The myometrium is organized into three functional strata: an external hood-like layer covering the fundus, a middle vascular layer (stratum vasculare) rich in blood vessels and lymphatics, and an innermost subendometrial layer — the junctional zone (JZ) [1, 3]. On T2-weighted MRI, the JZ appears hypointense due to high cellularity, larger nuclear area, and reduced extracellular water content, with a normal thickness of 5–8 mm in reproductive-age women; a JZ exceeding 12 mm is considered a diagnostic criterion for adenomyosis [4, 5]. Immunohistochemical analysis revealed no significant difference between layers in α-SMA, desmin, vimentin, or collagen distribution, and no ultrastructural variation across menstrual cycle phases was detected [4]. Parity significantly correlated with myometrial thickness (nulliparous < primiparous, $p < 0.001$), while BMI showed a positive correlation and height had no effect [2].

The principal cellular component is the smooth muscle cell (SMC) — a spindle-shaped, uninucleate cell of 200–600 μm with dense bodies and dense plaques anchoring actin-myosin filament arrays [4]. At the endometrio-myometrial junction (EMJ), myofibroblasts display cycle-dependent plasticity, adopting mature SMC morphology during the luteal phase [8]. A 2024 single-cell atlas comprising over 161,000 cells identified multiple SMC subpopulations, contractile capillary cells, immune, and stromal cell types, confirming far greater cellular heterogeneity than previously appreciated [6].

Functionally, peristaltic contractions in the non-pregnant uterus originate exclusively from the JZ, regulating sperm and blastocyst transport in a cycle phase-dependent manner [4, 13]. The JZ was shown to have dual embryological origins — Müllerian and Wolffian duct mesenchyme — with the mesometrial side displaying greater glandular density [10]. Myometrial ECM consists primarily of collagen types I and III, fibronectin, and proteoglycans, with homeostasis maintained by MMP/TIMP balance regulated by ovarian steroids [9, 11]. Hormonal receptor profiling confirmed co-expression of ERα, ERβ, GPER, PGR-A, and PGR-B in optimal balance during middle reproductive age [11, 14].

Discussion

The findings of this review highlight the morphological complexity of the myometrium in middle reproductive-age women. The zonal architecture — particularly the structural and functional distinctiveness of the JZ — is central to reproductive competence. The JZ serves not merely as an anatomical boundary but as the exclusive generator of non-pregnant uterine peristalsis, making its integrity essential for implantation and sperm transport [4, 13]. The epidemiological observation that adenomyosis-related JZ disruption is already present in 22.3% of women aged 21–25 years with severe dysmenorrhea [16, 17] underscores the early onset of myometrial pathology and the clinical importance of its timely recognition.

The identification of resident CD44+ stem cells and their confirmed hormone-responsive differentiation capacity in organoid systems [7] opens new perspectives for understanding myometrial regeneration and leiomyoma pathogenesis. The somatic mutation model — whereby a single MMSC acquires a driver mutation and expands under cyclic hormonal stimulation [9] reframes leiomyoma as a disease of stem cell biology rather than bulk SMC transformation. Similarly, the single-cell transcriptomic atlas [6], although derived from older tissue, provides the most granular view of myometrial cellular heterogeneity available and will serve as an essential reference for future studies on reproductive-age myometrium.

The balanced co-expression of estrogen and progesterone receptor isoforms in this age group [11, 14] represents the hormonal substrate for both normal cyclic function and susceptibility to steroid-driven pathology. Collectively, these data demonstrate that standard histological assessment alone is insufficient to characterize the full morphological spectrum of the middle reproductive-age myometrium, and that multi-modal approaches integrating MRI morphometry, immunohistochemistry, and molecular profiling are necessary for comprehensive evaluation.

Conclusions

The myometrium in women of middle reproductive age is a structurally and functionally complex tissue whose organization integrates a defined zonal architecture, a heterogeneous SMC population with regenerative stem cell subpopulations, dynamically regulated ECM, and coordinated vascular, neural, and hormonal receptor signaling. The junctional zone is a critically important functional subunit whose morphological integrity is directly linked to reproductive success and whose disruption underpins the most prevalent uterine disorders of reproductive life. The outer myometrium provides the principal contractile mass and constitutes the tissue of origin of uterine leiomyomas.

Recent methodological advances — including single-cell transcriptomic atlases [6], MMSC-derived organoid systems [7], and quantitative MRI-histology correlation studies [4] — are transforming the field from descriptive morphology to molecularly grounded biology. Future research priorities should include: (1) the establishment of comprehensive normative morphological atlases stratified by age, parity, and hormonal status; (2) elucidation of the mechanisms linking JZ morphological disruption with implantation failure and recurrent miscarriage; and (3) identification of early biomarkers of pathological ECM remodeling. A refined understanding of myometrial morphology in the middle reproductive years will provide the scientific foundation for more accurate diagnostics and more effective targeted therapies across the full spectrum of uterine pathology.

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