

Morphometric Characteristics of Uterine Abnormal Bleeding

Sheikhova Khafiza Kamalovna

Gynecologist of Khorezm Branch of the Republican Scientific Center for Emergency Medical Care, Uzbekistan

Abstract Adenomyosis in women is manifested mainly by the ingrowth of endometrial glands into the myometrium and bleeding in these areas 4-7 times more often than normal during the menstrual cycle. The causes of adenomyosis have not yet been determined by specific criteria; the closest causes are gene mutations. At the same time, this is explained by the fact that during embryonic development, the endometrial glands grow into the myometrium of the uterus. In adenomyosis, the deepest location of the endometrial glands is the branch up to the internal intramural branch of the myometrium, and at the same time this is manifested by a sharp development of vascular weaves in these branches. In our study, we studied the morphometric characteristics of the endometrium in adenomyosis and abnormal bleeding.

Keywords Endometrium, Adenomyosis, Abnormal bleeding, Morphometry, Morphometric pairs

1. Introduction

Abnormal uterine bleeding is a common symptom in women, accounting for 20% of gynecological visits in a two-year period [1].

Dyshomonal changes can cause more bleeding than usual. This condition is especially common among teenagers and premenopausal women. Most dyshomonal changes are more common among overweight women and underweight women. This is especially true in morphofunctional women with a lot of brown adipose tissue in their body, the sharp cumulation of sex hormones causes continuous dysfunctional bleeding from the uterus during menopause [2].

Women with anovulatory uterine bleeding may be given progesterone because they secrete too much estrogen and do not have progesterone to counteract it [3]. Diagnostic scraping from the uterine cavity is also performed for the purpose of diagnosis and treatment. Histology helps to identify endometrial myoma, and adenocarcinoma, atypical hyperplasia, recurrent cystic hyperplasia of the endometrium.

Purpose. The purpose of the study is to assess the condition of the endometrium in women, the morphology of uterine adenomyosis and abnormal uterine bleeding, and to study the set of morphometric characteristics.

2. Material and Methods

Morphological, morphometric and statistical analysis methods were used in the study.

3. Research Results and Their Discussion

Microspecimens prepared from the control group, endometriosis, polyps and endometrial adenocarcinoma were taken for morphometric examination. Microspecimens obtained and prepared from a total of 68 cases of endometriosis $n=21$, endometrial adenocarcinoma $n=24$, endometrial polyp $n=19$ cases and prepared in NanoZoomer (REF C13140-21. S/N000198/HAMAMATSU PHOTONICS/431-3196 JAPAN) scanner is installed. The obtained microimages were processed in the QuPath-0.5.0 software and data were collected on the exact limits and indicators of the magnitudes representing high accuracy and were processed in an automatically programmed system according to the following formula. Comparative numerical data of structural structures of all structures of the endometrium and all studied pathologies were obtained.

Endometriosis, glandular polyp, adenocarcinoma, and control groups were compared and mean sizes were reported. The result of the test is as follows, each of the above-mentioned micropreparation samples were photographed after being scanned, and the sizes of each were presented in a special table. The average statistical analysis results were based on the student-t test, and the confidence level was based on the confidence level around $P \leq 0.01$ and $P \leq 0.05$. average statistical indicators of the obtained results were obtained.

Variational parameters and non-parametric methods of statistics were used, taking into account the arithmetic mean (M), mean square deviations (s), mean standard errors (m), relative sizes (frequency, %) of the studied indicators. The statistical significance of the measurements obtained in the comparison of the mean sizes was determined by the

Student's (t) test, calculating the probability of error (R) in the examination of the general variance (G'-Fisher test) and the distribution norms (by the excess test). Statistical processing was carried out in order to determine the arithmetic mean value and the mean square error of the obtained quantitative data, the reliability index ($R < 0.05$, $R < 0.001$). Statistical significance for qualitative variables was calculated using the χ^2 (chi-square) and z- criteria.

Indicators of any pathologies of the endometrium showed a morphofunctional superiority of all indicators compared to the control group. The obtained magnitudes were compared with each other, compared to the control group, and confirmed by numerical data confirming the level of severity and one of the severe complications, anomalous bleeding.

Currently, in the implementation of modern 3-dimensional multiplex morphometric examinations, 8-12 sections are taken from each sample, scanned on a NanoZoomer (REF C13140-21.S/N000198/HAMAMATSU PHOTONICS /431-3196 JAPAN), and the obtained micrographs are QuPath-0.5.0 - merged in ImageJ software and presented the area of cross-sectional dimensions in X, Y, Z-axes according to the relief of points in a spatial form. The formula of the data obtained for these area units automatically brought ready results according to the direction programmed in the system.

The analysis and numerical indicators of the obtained results are presented and discussed below in the form of a morphogram.

Chronic inflammation of the endometrial glands, due to increased reparative regeneration, occurs in dys hormonal disorders, hyperplasia of glandular cells of the endometrium occurs (remember, hyperplasia is the increase of cells and tissues together with internal and external structures). This process is irreversible, and the morphofunctional hypo- or hyperfunction of the endometrium as a result of morphological adaptation mainly leads to vascular damage and processes related to bleeding [4].

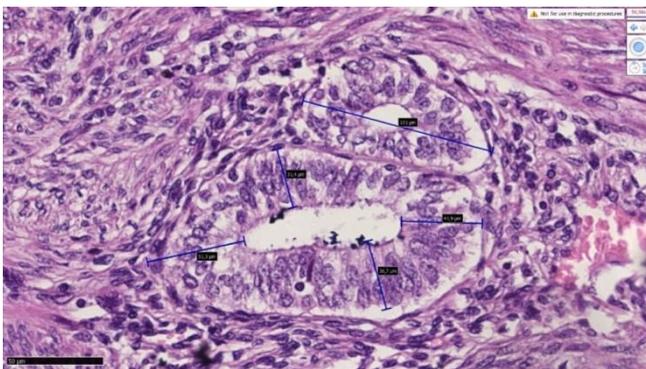


Figure 1. Sample-5. The patient is 35 years old. Endometriosis. A morphogram with measured height and diameter of the endometrial glands in the myometrial space is presented. NanoZoomer (REF C13140-21.S/N000198/HAMAMATSU PHOTONICS /431-3196 JAPAN) has a scanner. Paint G.E. The size is 40x10

Clinically morphologically, patients complain of endometriosis only when bleeding (metrorrhagia-abnormal bleeding from the uterus). As a result, there are quantitative and qualitative changes in the endometrial and myometrial

tissue, the number of vessels in the myometrial and endometrial stroma compared to the control group leads to damage to the endometrium during the menstrual cycle.

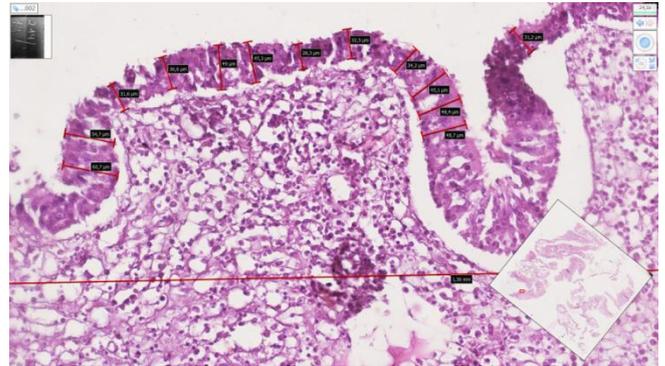


Figure 2. Sample-8. The patient is 38 years old. Glandular fibrotic polyp of the endometrium. Longitudinal dimensions of polyp surface epithelia are given. NanoZoomer (REF C13140-21.S/N000198/HAMAMATSU PHOTONICS /431-3196 JAPAN) has a scanner. Paint G.E. The size is 40x10

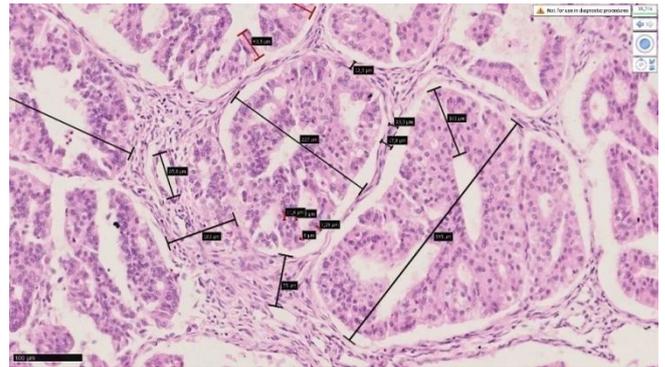


Figure 3. Sample-10. The patient is 39 years old. Endometrial adenocarcinoma. A morphogram of the endometrial glands, measured in height and diameter, is presented. Polymorphism and metaplasia of epithelial cells were preserved in gland epithelia. NanoZoomer (REF C13140-21.S/N000198/HAMAMATSU PHOTONICS /431-3196 JAPAN) has a scanner. Paint G.E. The size is 40x10

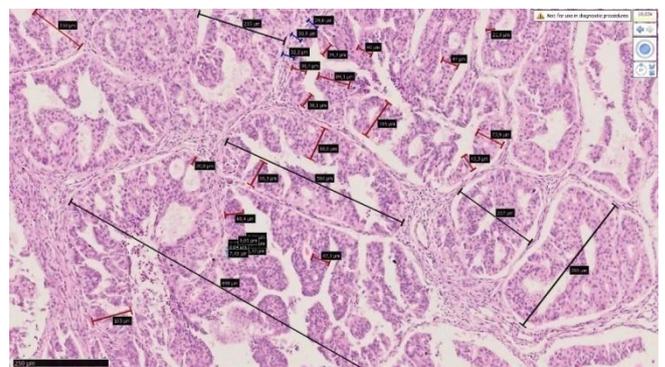


Figure 4. Sample-13 The patient is 36 years old. Endometrial adenocarcinoma. A morphogram of the endometrial glands, measured in height and diameter, is presented. Polymorphism and metaplasia of epithelial cells were preserved in gland epithelia. NanoZoomer (REF C13140-21.S/N000198/HAMAMATSU PHOTONICS /431-3196 JAPAN) has a scanner. Paint G.E. The size is 40x10

In treatment, the answer is obtained by histometry (morphometry) of the structural structures of the tissue using

the field of morphology of evidence-based medicine in addition to standard methods [5]. 10-20 consecutive images of the microsamples were scanned in a NanoZoomer (REF C13140-21.S/N000198/HAMAMATSU PHOTONICS /431-3196 JAPAN). Cellular, vascular, stromal components of the endometrium in the obtained images were measured in μm and the average size indicators were presented in the table.

Therefore, according to the analysis of the data obtained

on the histometric (morphometric) values of cases associated with anomalous bleeding in various diseases of the endometrium, the highest indicators were determined in endometrial adenocarcinoma according to the cellular composition, which confirms the high hypercellular appearance, the tendency to acute damage to the endometrial stroma [5]. In endometrial adenocarcinoma, the size of gland epithelia is $12.24 \pm 1.78 \mu\text{m}$, which is 3.1 times higher than in the control group.

Table 1. The height and thickness of the epithelial cells of the endometrial gland are measured in μm

№		Sizes of endometrial epithelia μm						Average thickness of endometrial gland epithelia		P
		Dome of the uterus		Uterine body		Isthmic cervical area				
		Epithelial height	Epithelial thickness	Epithelial height	Epithelial thickness	Epithelial height	Epithelial thickness			
1	Endometrial polyp (n=13)	41,17±2,25	8,13±1,01	46,25±2,62	8,61±0,75	32,9±1,97	7,23±0,33	40,11±2,27	7,99±0,69	0,01
2	Endometrial adenocarcinoma (n=15)	62,223±10,26	12,33±2,26	66,145±8,95	14,01±1,97	61,132±7,86	10,38±1,12	63,16±9,01	12,24±1,78	0,01
3	Normal quiescent endometrium (n=9)	14,62±1,27	4,31±0,87	18,43±1,02	4,68±0,65	13,21±0,86	3,67±0,42	15,42±1,05	4,22±0,65	0,01

Table 2. The ratio of endometrial gland and stroma areas per brigia is μm^2 (82000 μm^2)

№		The areas occupied by the endometrial gland and stromal area are in μm^2			average thickness	P≤
		Dome of the uterus	Uterine body	Isthmic cervical area		
1	Proportions of atypical hyperplasia stroma and glands (n=17)	2,2:1	1,9:1	1,76:1	1,95:1	
	The area occupied by the endometrial glands	37272,72±216,35	43157,89±256,24	46591,19±275,35	42051,28±249,31	0,01
	The area occupied by the endometrial stroma	44727,28±313,21	38842,11±301,07	35408,81±289,24	39948,72±301,17	0,01
2	The stroma of the endometrial glandular polyp and the area occupied by the glands	7:1	7,8:1	7,2:1	7,33:1	
	The area occupied by the endometrial glands	11714,28±116,08	10512,82±112,68	11388,88±111,29	11205,37±113,35	0,01
	The area occupied by the endometrial stroma	70285,72±112,24	71487,18±129,36	70611,11±134,12	70794,67±125,242	0,01
3	Proportion of endometrial adenocarcinoma stroma and glands (n=15)	1,2:1	1,4:1	0,91:1	1,16:1	
	The area occupied by the endometrial glands	74545,45±116,11	58571,43±124,23	74620,11±121,85	69245,66±120,73	0,01
	The area occupied by the endometrial stroma	7454,55±101,11	23428,57±109,89	7379,89±137,11	12754,33±116,03	0,01
4	Proportion of quiescent endometrial stroma and glands in normal (n=9)	6:1	6,6:1	7:1	6,53:1	
	The area occupied by the endometrial glands	13666,66±525,15	12424,24±325,25	11714,285±645,31	12601,72±498,57	0,01
	The area occupied by the endometrial stroma	68333,34±474,85	69575,76±674,75	70285,71±354,69	69398,28±501,43	0,01

Table 3. The average size of the area occupied by blood vessels and the diameter of blood vessels in various pathologies of the endometrium is μm^2 (82000 μm^2)

№		The vascular area occupied by the blood vessels in the endometrial gland and the average diameter of the vessels in μm^2			Average size	P≤
		Dome of the uterus	Uterine body	Isthmic cervical area		
1	The ratio of the area occupied by blood vessels in the glandular polyp of the endometrium	55,1:1	53,2:1	54,6:1	54,3	
		1488,21 μm^2	1541,35 μm^2	1501,83 μm^2	1511,13 μm^2	
	Minimum diameter of vessels	18,25±1,14	19,01±1,22	18,95±1,35	18,74±1,24	0,01
	The maximum diameter of the vessels	20,21±1,35	21,35±1,07	21,02±1,21	20,86±1,21	0,01
	The average diameter of the vessels					0,01
2	Area ratio of blood vessels in endometrial adenocarcinoma (n=15)	35,5:1	36,4:1	34,9:1	35,6:1	
		2309,85 μm^2	2252,74 μm^2	2349,57 μm^2	2303,37 μm^2	
	Minimum diameter of vessels	12,26±1,01	13,35±1,04	13,01±1,22	12,873±1,09	0,01
	The maximum diameter of the vessels	16,66±0,89	17,35±1,28	17,01±1,16	17,01±1,11	0,01
	The average diameter of the vessels	14,46±0,95	15,35±1,16	15,01±1,19	14,94±1,1	0,01
3	Area occupied by resting endometrial blood vessels, ratio (n=9)	50,5:1	48,2:1	49,3:1	49,33:1	
		1623,76±12,35 μm^2	1701,24±13,01 μm^2	1663,28±14,21 μm^2	1662,27±13,19 μm^2	
	Minimum diameter of vessels	14,25±1,01	15,01±1,05	15,23±1,12	14,83±1,06	0,01
	The maximum diameter of the vessels	19,22±1,35	20,11±1,37	21,12±1,24	20,15±1,32	0,01
	The average diameter of the vessels	16,735±1,18	17,565±1,21	18,175±1,18	17,492±1,19	0,01

In the table above, among the diseases associated with anomalous endometrial bleeding, the type of endometrium rich in vessels, which was identified in endometrial polyps. This is 2.8 times more than the control group in terms of morphofunctionality, which makes it possible to define the glandular type of polyps as the most dangerous among all pathologies of the endometrium from a clinical and morphological point of view. On average, 82,000 μm^2 of the surface, more than half of which was made up of blood vessels, was confirmed by morphometric indicators. This requires a special approach in determining treatment tactics for various polyps of the endometrium in a practical gynecologist.

4. Summary

The above compared evidence and its results lead us to the following conclusions:

1. In uterine endometrial polyp, the area occupied by blood vessels is 545 of the mucosa, and in about half of the processes related to abnormal bleeding, it is the basis for thinking about the polyp.
2. It is characterized by permanent damage to the mucous membrane in various polyps of the endometrium, leading to metaplasia and dysplasia of glandular epithelia.
3. In diseases of the female genital organs associated with abnormal bleeding, it is necessary to always

consider endometrial polyps and take morphometric indicators into account when determining treatment tactics against it.

4. A sharp thickening of the endometrium mainly leads to an increase in gland cells and, in parallel, an increase in vascular networks. This, in turn, confirms the occurrence of processes associated with constant bleeding.

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