



## Histological and morphometrical features of endometrial polyposis complicated with uterus bleeding.

*Review and clinical tadermoid cyst*

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### ABSTRACT

**E**ndometrial polyposis is a condition that affects the lining of the endometrium or the uterus and it is seen in 1–17% of women in their reproductive years. The symptoms are often uterine bleeding which can occur as menorrhagia and the polyps can be sessile or pedunculated. This pathology can also arise in women who are in the post-menopausal phase and the exact pathogenesis of the pathology is not known but there are theories that shed light on how this may occur. We conducted a study in which we took 70 surveyed women with endometrial polyps which were complicated by uterine bleeding to determine their morphological types and identify the relationship between the types of polyps and the frequency of uterine bleeding.

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### INTRODUCTION

An endometrial polyp, otherwise known as uterine polyposis is a pathology that occurs in women of varying ages. Endometrial polyps are benign neoplasms with a low risk of malignancy [1, 23]. The statistics show that it occurs less often in women of 25 to 35 years of age and as for women who have approached menopause, the statistics have been contradictory. The prevalence of this pathology occurs mostly among women within the ages of 40 to 50 [1]. The exact prevalence of endometrial polyps is unknown, but Dreisler et al. Reported that 82% of women had asymptomatic course of endometrial polyps. And the prevalence of polyps that have been implicated in about 50% of cases of abnormal uterine bleeding and 35% of infertility [15–16, 24, 25, 26].

Regarding the etiology of polyps is the most recognized theory is that the occurrence of endometrial polyps is linked to hormonal changes in the body. This hormonal change refers to the changes in estrogen levels, especially estrogen-alpha levels in the endometrium. The occurrence of the polyps have been related with nelevated levels of estrogen rates as the levels of estrogen found in the polyps on examination is higher than the normal endometrial estrogen levels [17–19]. This shows that there is a connection between elevated estrogen levels and development of polyps. Furthermore, the estrogen receptors are seen to be concentrated in the endometrial polyp which is more so than in the endometrium. Another hormone that is affected is the progesterone, which is seen to be in lower rates in the polyp than it is in the endometrium [1, 3]. The progesterone receptors A and B are less concentrated in the stroma as well as the estrogen receptors and this can be a leading factor in why the stroma doesn't shed its lining during menstrual circle as the other parts of the endometrium does [27]. Another etiological factor and risk factor can be considered the use of Tamoxifen. Tamoxifen is a synthetic drug that is a selective modulator of estrogen receptors and is used to prevent and treat breast cancer and because of its estrogen-like effects contribute to polyps [5, 28]. Also the general effect of the drug is to inhibit apoptosis as well and this aids the growth of the polyps and prevents its shedding during normal menstrual circles. Another risk factor is the hormone replacement therapy that is done

in postmenopausal women. This is a treatment plan for women who have reached menopause so as to manage the symptoms associated with menopause [3, 17–19].

Microscopically, endometrial polyps consists of endometrial glands, stroma and blood vessels and it can be single or multiple, sessile or pedunculated and have size range from millimeters to several santimeters. Usually the prevalence of stromal or glandular component polyps are divided into the following histological types: basal or glandular, fibrous and glandular fibrous polyps and also adenomatous polyp which is associated with a high risk of malignancy. The morphology of the glandular component is different. For example, the glands may be functioning or not, have normal histology, or be cystically altered, etc.. [2, 7–9, 11]

Although the risk of endometrial polyps low malignancy (except adenomatous polyps, which are predictors of malignant transformation), they are one of the causes of pathological conditions such as abnormal uterine bleeding and infertility. The prevalence of the pathology of EP in the population of women with infertility is put anywhere between 3% and 38% and this is in cases with primary infertility. In cases with secondary infertility, the statistic is a bit lower as it is placed at 1.8% to 17% [4, 6, 10]. The one of the most common symptoms that can be associated with endometrial polyps is an abnormal uterine bleeding. The statistics show that about 68% of premenopausal and post-menopausal women with the incidence of EP, presented with bleeding [5]. Of the women in the premenopausal group, about 15–50% presented with this complication and in women with post-menopausal EP, there was about 30% of bleeding complications [5, 12–14].

Histopathological studies of polyps in women with uterine bleeding revealed certain morphological changes, as the development of venous hyperemia and apical necrosis due to stugnation in the stroma of the polyp, the superficial location of blood vessels in the polyp or thinning of the vessel walls [29].

**STUDY DESIGN**

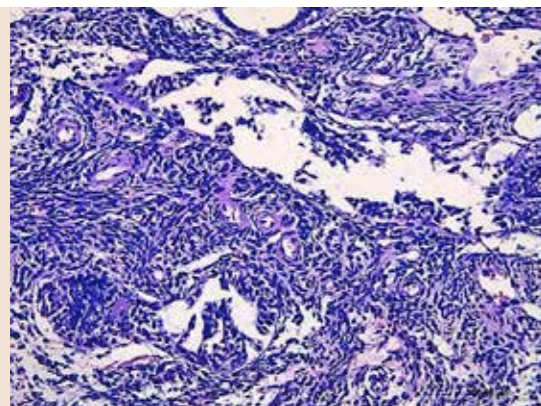
To compare histological features of polyps that were complicated with uteral bleeding and those than not, retrospective study was performed. 70 cases of endometrial polyps were included in the study and composed 4 groups – group 1 – basal polyps without bleeding (n=17), basal polyps with bleeding (n=17), glandular-fibrous polyps without bleeding (n=18), glandular-fibrous polyps with bleeding (n=18). Main clinical indicators are shown in the table 1.

Morphometric evaluation included estimation of the number of vessels in the histological slides (magnification x200, microscope Leica ...) and measurement the thickness of the vessels. For this reason, free software Image J was used. Statistical analysis was performed using SPSS IBM Statistics v. 24.0. Study groups were compared according the values of mean ± standard deviation, median, number of positive indicator in group, statistical difference were calculated with non-parametric tests such as Mann-Whitney criterion (for two independent samples) and Kruskal-Wallis 1-way ANOVA (for more than two independent samples).

**RESULTS**

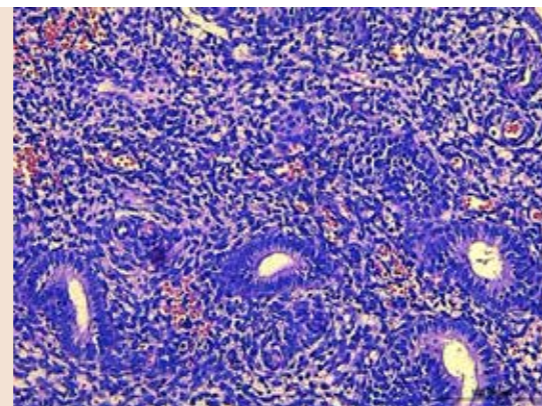
All cases inside groups demonstrated typical histological features that are shown and described in figures 1–4.

**Figure 1.** Basal type endometrial polyp without bleeding



Tissue consists of an immature endometrium with glands lined with proliferative epithelium without signs of hormonal transformation. Glands in polyps are located chaotically, have various form and size, with lack of vertical orientation. The stroma of polyps is compact, consists of the same type of spindle-shaped cells that form tufts. The stroma is poor in collagen fibers. Vessels are small, with relatively thin walls, are arranged in chains and are located in a strip of connective tissue.

**Figure 2.** Basal type endometrial polyp with bleeding



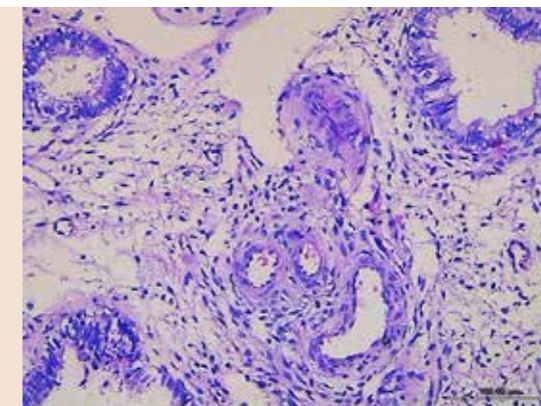
Tissue consists of an immature endometrium with glands of indifferent or proliferative type without signs of hormonal transformation. Glands in polyps are located chaotically, have a different shape and size, with no signs of vertical orientation. The stroma of polyps is compact, consisting of the same type of round or spindle-shaped cells that form tufts. The stroma is poor in collagen fibers, with signs of edema and hemorrhage. A significant number of small vessels with walls of different thickness is determined. The vessels are arranged in chains and surrounded by connective tissue layers.

**Table 1.** Clinical characteristic of study groups.

Parameter	Group				p-value
	Basal polyps without bleeding (n=17)	Basal polyps with bleeding (n=17)	Glandular-fibrous polyps without bleeding (n=18)	Glandular-fibrous polyps with bleeding (n=18)	
Age, years					
Mean±SD	29,86±3,21	35,3±10,9	48,17±12	45,5±12,9	<0.001*
Median	31	35	47,5	41	
Primary diagnosis of endometrial polyps n (%)	7 (41,2%)	4 (23,5%)	10 (55,6%)	3 (16,7%)	0,41
Menstrual irregularities n (%)	3 (17,6%)	8 (47%)	3 (16,7%)	3 (16,7%)	0,012*
Menopause n (%)	0 (0%)	0 (0%)	5 (27,8%)	2 (11%)	0,031**

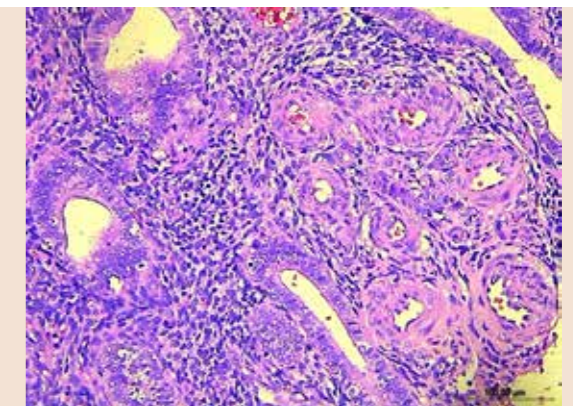
Positions with statistically significant differences are marker in bold.  
 \* – Independent-Samples Mann-Whitney U Test  
 \*\* – Independent-Samples Kruskal-Wallis Test

**Figure 3.** Glandular-fibrous polyp without bleeding



Tissue consists of structures represented by glands of various shapes and sizes and fibrous or fibrous-edematous stroma. The glands are uneven, have signs of hormonal transformation and partially retain their vertical orientation. In polyps there is a decrease in the number of stromal cells, uneven distribution of blood vessels. Blood vessels are arranged in balls, have thickened walls. In some cases, polyps have a vascular-stromal leg.

**Figure 4.** Glandular-fibrous polyp with bleeding



Tissues consists of structures represented by glands of various shapes and sizes and a stroma with a fairly compact arrangement of spindle-shaped cells, which often form tufts. There is collagenization of the stroma, signs of edema and hemorrhage. The glands are uneven, have signs of hormonal transformation and partially retain their vertical orientation. In polyps there is an uneven distribution of blood vessels. Blood vessels are located in balls with a large number of arteries, which have significantly thickened walls. In some cases, polyps have a vascular-stromal leg.

**Table 2** shows the distribution of morphometric parameters among the study groups.

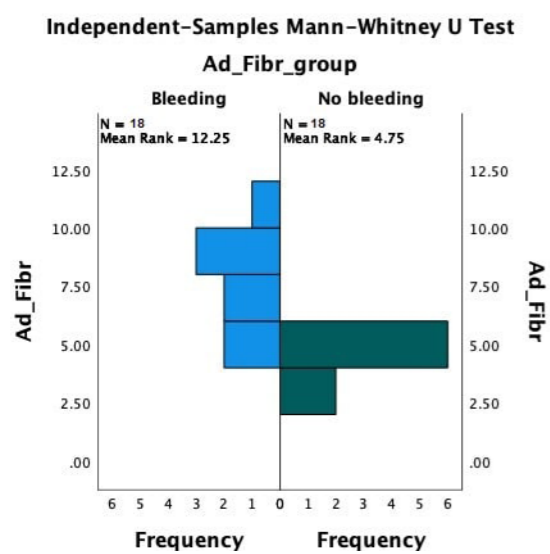
Parameter	Group				p-value
	Basal polyps without bleeding (n=17)	Basal polyps with bleeding (n=17)	Glandular-fibrous polyps without bleeding (n=18)	Glandular-fibrous polyps with bleeding (n=18)	
Number of vessels					
Mean±SD	5,3±1,1	5,57±1,81	4,2±0,76	7,38±1,92	<b>&lt;0,001*</b>
Median	5	5	4	7,5	
Wall thickness, µm					
Mean±SD	5,1±1,73	7,6±2,2	10,78±3,87	16,56±7,11	<b>&lt;0,001**</b>
Median	5	7	10	15	

Positions with statistically significant differences are marked in bold.  
 \* – Independent-Samples Mann-Whitney U Test  
 \*\* – Independent-Samples Kruskal-Wallis Test

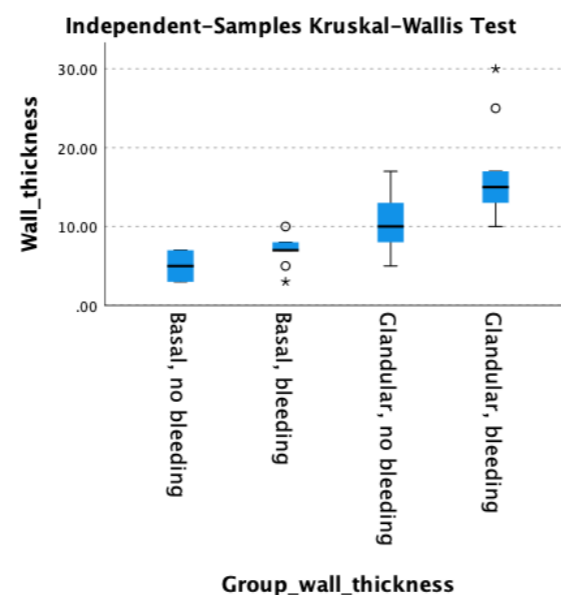
Figure 5 shows distribution and ranks of the number of vessels in Glandular-fibrous polyps without bleeding and Glandular-fibrous polyps with bleeding groups.

Figure 6 shows box plot demonstrating distribution of vascular wall thickness among all groups.

**Figure 5.** Number of vessels in glandular polyps groups.



**Figure 6.** Box plot of the distribution of vascular wall thickness among all groups.



**DISCUSSION**

In our study, we considered the morphometric parameters of the vessels of uterine polyps and composed 4 groups – group 1 – basal polyps without bleeding (n=17), basal polyps with bleeding (n=17), glandular-fibrous polyps without bleeding (n=18), glandular-fibrous polyps with bleeding (n=18)

The data we obtained indicate an increased number of vessels and vascular wall thickness in the group of patients with bleeding.

During the formation of uterine polyps, the process of angiogenesis takes place, because the polyp as an element of epithelial hyperplasia must have a blood supply that will provide oxygen and nutrients. Excessive or insufficient vascular growth contributes to numerous disorders. In many diseases associated with angiogenesis, there is a defective formation of the vascular bed and increased vascular fragility, which can cause abnormal uterine bleeding. [31]

In contrast to the well-ordered and highly regulated processes underlying normal menstrual cycle hemostasis and menstruation, abnormal endometrial bleeding reflects derangements in these physiological processes

Endometrial polyps often present as metrorrhagia. Little is known about the mechanism for such bleeding but increased polyp MMP and cyclo-oxygenase production have been noted [32]. Microvascular density also appears increased [33]. These findings suggest that aberrant angiogenesis may also play a role in polyp-associated abnormal endometrial bleeding. Thus, polyp-associated dilated, fragile superficial endometrial vessels would be prone to intermittent bleeding as seen in LTPOC treated endometria. [30]

The study of vascular morphology provides answers to the questions of abnormal uterine bleeding. Further research will provide opportunities to prevent their occurrence and reappearances, which often follow after treatment.

**CONCLUSION**

Endometrial polyps are a benign disease with minimal mortality, but the complications they cause can be fatal. In our study, we were

able to evaluate the morphometric aspects of vascular polyps and shed light on the causes of abnormal uterine bleeding. In the future, this study may be useful for professionals struggling with this pathology.

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