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Association between Vaginal Ultrasound and the Histopathological Analysis in the Diagnosis of Endometrial Hyperplasia and Uterine Cancer

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Abstract

Introduction: Uterine cancer represented by the endometrial cancer is the most common form of cancer for adult woman with a tendency to increase due to the high life expectancy for woman. An early diagnosis of endometrial cancer increases proportional for correct treatment like in all cases of cancer.

Material and Methods: During a year a study was conducted about the value of the vaginal ultrasound of 112 woman with pre- and post-menopause bleeding making an association with the results of the histopathological analysis obtained from the uterine curettage biopsy.

Results: A increased thickness of the endometrium higher than 8mm was found in endometrial cancer, endometrial hyperplasia and glandular cystic hyperplasia.

Conclusion: There was a statistically significant association ($p<0.001$) between the endometrium thickness and the histopathology analysis results. The differences obtained between the thickness of the endometrium in endometrial cancer and endometrial hyperplasia have no statistically significant association ($p=0.31$) though there is a statistically significant association ($p=0.0036$) between endometrial hyperplasia and proliferative endometrium.

Keywords: Endometrial cancer; Ultrasound; Endometrial hyperplasia; Histopathological analysis; Diagnosis

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Introduction

Female genital cancer is one of the major concerns for gynecologist form all around the world. If in the 1980s the main concern was the cervical cancer in the last 30 years interest shifted towards the uterine cancer due to its high incidence and the difficulties for an early diagnostic and therapy, not only due to the sever comorbidities that appear in elderly woman. Today uterine cancer is the 2nd most common female genital cancer after breast cancer. Through the years the incidence between cervical cancer and endometrial cancer changed from 9:1 to 2:1 in favor of the cervical cancer to 1:3 in favor of uterine cancer. The ratio changed due to early diagnosis of precancerous lesions of the cervix and due to higher life expectancy in woman [1-4].

The positive diagnosis for endometrial cancer is based on the symptomatic triad: Obesity, hypertension and diabetes which is associated with bleeding in pre- and post-menopause.

The Gold standard for the diagnosis for endometrial cancer is the histopathological exam after diagnostic dilation and curettage.

During the 1980s the ultrasound examination became one of the best screening tests for endometrial cancer due to the evolution of the ultrasounds [5,6] (Figures 1-4).

Materials and Methods

A number of 112 patients in pre or post menopause which underwent and diagnostic dilation

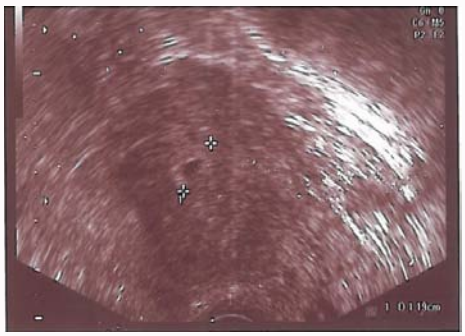

Figure 1: Vaginal US, Glandular cystic hyperplasia.

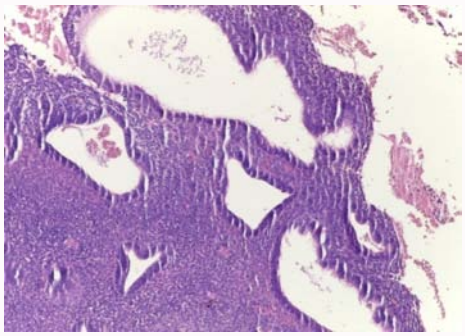

Figure 2: Glandular cystic hyperplasia Hex100.

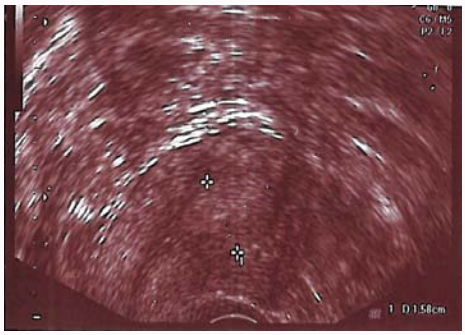

Figure 3: Endometrial hyperplasia.

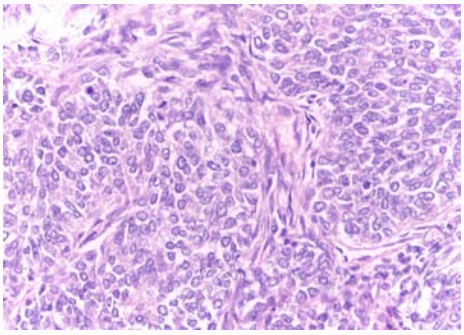

Figure 4: Endometrial endometrioid adenocarcinoma.

and curettage during one year were taken into account for our study. The results from the histopathological analysis were correlated with the thickness of the endometrium which was measured by ultrasound. An Voluson 730 with a 7.5 mm HZ vaginal probe was used, measurements were made for a longitudinal section. The biopsy results were classified in 6 groups after a study by Szabo [7,8].

1. Endometrial cancer
2. Endometrial hyperplasia
3. Glandular cystic hyperplasia
4. Endometrial polyp
5. Proliferative endometrium
6. Atrophic endometrium

We can consider this procedure like a screening method for the adenocarcinoma so we can do an early detection and adopt a good and early treatment so we can have a better prognostic [9-12].

Results

The average age in the study lot was 59 years 9 months and 3 days. The cases were classified in groups according to the results of the histopathology analysis and the thickness of the endometrium.

Table 1 and 2 show the endometrial thickness resulting from the ultrasound examination for the six groups of histopathological results, seen from two perspectives: As a continuous numerical value (expressed with range, mean, and standard deviation) and as a rank value (expressed as six disjoint ranking intervals), respectively.

The endometrial thickness was compared for the patients with endometrial cancer *vs.* those with endometrial hyperplasia, but statistical significance was not reached for the present sample of cases ($t=1.04$, $df=44$, $p=0.31$).

On the other hand, the endometrial thickness was significantly different for the cases with glandular cystic hyperplasia compared to the patients with a proliferative endometrium ($t=3.094$, $df=44$, $p=0.0036^{**}$).

Endometrial cancer and the hyperplasia of the endometrium were considered as pathological so we further compared the variations and changes in the endometrium separately within this group of cases and the benign ones (i.e., endometrial polyps, proliferative activity or atrophy). Sensibility and specificity were calculated.

Table 3 and 4 show the results of independence statistical testing for the pathology and the benign group, respectively. The Monte-Carlo method was applied for the *Chi-square* test. For both groups, results proved a very significant association between the histopathological examination results and the ultrasound results regarding the endometrial changes.

From this study results that an endometrium with a thickness smaller than 4 mm excludes any pathological lesion in our study in 9.82% of the cases. All cases of endometrial cancer had a thickness of tales 8 mm in 30.35% of the cases.

Statistical analysis

Statistical analysis was performed using the R package (www.r-project.org). Continuous variables were expressed either as minimum - maximum range with sub-intervals of values or as mean values with standard deviation; while categorical data were synthesized as counts with percentages. For the statistical tests, a 0.05 (i.e., 5%) level of significance was considered, with 0.95 (i.e., 95%) confidence level for the estimates.

The parametric t-test was employed for comparing mean values

Table 1: Ultrasound examination results expressed as a continuous numerical variable, for the six groups of histopathological groups.

No.	Results of the histopathological examination	Cases		Range	Mean ± Std. dev.
		No.	%	min-max	
1	Endometrial cancer	34	30.35	8-22 mm	15.5 ± 7 mm
2	Endometrial hyperplasia	12	10.71	8-18 mm	13.7 ± 4.3 mm
3	Glandular cystic hyperplasia	28	25	6-24 mm	10.4 ± 5.5 mm
4	Endometrial polyp	14	12.5	6-14 mm	9.3 ± 4.3 mm
5	Proliferative endometrium	18	16.07	2-10 mm	5.7 ± 4.7 mm
6	Atrophic endometrium	6	5.35	1-8 mm	4.6 ± 1.2 mm
7	TOTAL	112	99.98	1-23 mm	11.1 ± 10.9 mm

Table 2: Ultrasound examination results expressed as a rank variable, for the six groups of histopathological groups.

Results of histopathological examination	Thickness of the endometrium [mm]						TOTAL
	4	5-7	8-10	11-15	16-20	>20	
Endometrial cancer	0	0	6	14	8	6	**34**
Endometrial hyperplasia	0	0	2	6	4	0	**12**
Glandular cystic hyperplasia	0	7	9	10	1	1	**28**
Endometrial polyp	0	4	6	4	0	0	**14**
Proliferative endometrium	7	8	3	0	0	0	**18**
Atrophic endometrium	4	2	0	0	0	0	**6**
TOTAL	**11**	**21**	**26**	**34**	**13**	**7**	**112**

Table 3: Association between the ultrasound examination and histopathological results, for the pathology group.

Results of histopathological examination	Thickness of the endometrium [mm]				
Total 74 cases	5-7	8-10	11-15	16-20	>20
Endometrial cancer	0	6	14	8	6
Endometrial hyperplasia	0	2	6	4	0
Glandular cystic hyperplasia	7	9	10	1	1

Test *Chi-square* with Monte-Carlo method (10000 replicates) → p=0.0019**

Table 4: Association between the ultrasound examination and histopathological results, for the benign group.

Results of histopathological examination	Thickness of the endometrium [mm]			
Total 38 cases	4	5-7	8-10	16-20
Endometrial polyp	0	4	6	4
Proliferative endometrium	7	8	3	0
Atrophic endometrium	4	2	0	0

Test *Chi-square* with Monte-Carlo method (10000 replicates) → p=0.0031**

in two independent samples. For testing independence between the histopathological examination and the ultrasound results, the *Chi-squared* test did not meet the validity condition, therefore the Monte-Carlo method was applied, with 1,000 replicates each time.

Discussion

The transvaginal ultrasound is the most common used exploration in gynecology and in oncogynecology alongside the CT and MRI.

The ultrasound exam has an important value in the exploration of the endometrium, the measurement of the endometrial thickness being the most useful and objective value.

The endometrial hyperplasia is a specter of morphological and biological changes of the endometrial glands which include variable aspects from normal tissue to *in situ* carcinoma.

WHO and ISGC in the pursuit for a better evaluation of the endometrial hyperplasia in relation to the endometrial cancer introduced a new term. Atypical cells are a better indicator for the progress towards carcinoma.

The evolution from hyperplasia to carcinoma in our study had the incidence of: Simple endometrial hyperplasia 1%, complex endometrial hyperplasia 3%, atrophy simple endometrial hyperplasia 8%, atrophy simple endometrial hyperplasia 29%. It is difficult to define the limit between in situ carcinoma and atypical sever endometrial hyperplasia. It can be appreciated in those cases in which the thickness of the endometrium is bigger than 10 mm [13-17].

Associating endometrial hyperplasia with bleeding during the climax with the symptomatic triad of the uterine cancer increases the chances of an early diagnosis. In those conditions ultrasound evaluation of the endometrium has an important value in the diagnostic of endometrial cancer.

Conclusion

1. Ultrasound exam is a cheap investigation that tighter with

a clinical exam can be used as useful screening test for uterine cancer through the measuring of the endometrial thickness in pre- and post-menopause.

2. A value smaller than 5 mm in post menopause exclude and precancerous lesion and endometrial cancers.

3. Vaginal ultrasound can diagnose endometrial polyps which can be the cause for post-menopause bleeding in 12% of our cases.

4. Vaginal ultrasound can specify the local extension of the endometrial carcinoma visualizing the location of the tumor, its biometric invasion as well as whether or not the cervix is included; there was a statistically significant association ($p<0.001$) between the endometrium thickness and the histopathology analysis results.

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