

THE TREATMENT AND EVOLUTION OF CERVICAL CANCER

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Abstract: The purpose of this study is to establish the evolution of cervical cancer after applying a conventional treatment. Materials and methods. The study was performed on a number of 1249 patients who were suspected of having cervical neoplasia, and who were monitored between 2006-2010 in „Elena-Doamna” Clinical Hospital of Obstetrics and Gynecology in Iași, the Military Hospital Galați, the County Hospital Galați and the Emergency Hospital Buzau. Results and discussions. The study proved the effectiveness of the conservative treatment for the patients who were diagnosed using cytology, colposcopy, biopsy and histopathology, with or without HPV viral infection. Conclusions. The patients with an early diagnose have a 15% higher surviving probability. The patients who responded to the conservative preoperative treatment well are more likely to survive than the patients who did not respond favourably to the conservative preoperative treatment.

INTRODUCTION

The activity of early detection of cervical carcinoma is not well organized yet, and that is why we can see that in everyday practice most cases come to the doctor when the cancer is already in a relatively advanced stage, which requires complex laborious interventions and generally having unsatisfying results. When the disease is detected in due time and treated accordingly, the results are very good and lead to a decrease in the specific mortality and make it possible to avoid the mutilating surgical procedures. This way the doctors are able to accomplish the modern medicine goal - *biologic healing of the disease without the physical and/or psychic mutilation of the patient* (1, 4, 6, 7).

According to the data supplied by the Computer and Sanitary Statistics Centre in Romania, over 66% of the new cases of cancer that were detected in 2005 are between 35 and 55 years old, and about 70% of the deaths caused by cervical cancer are registered for women aged between 45 and 70 (11).

Cervical neoplasia is a serious chronic disease of great medical and social importance, with a severe evolution when detected in its advanced stages, being one of the most complex and difficult problems of human pathology (8).

A cytologic result - type H-SIL (High Grade Squamous Intraepithelial Lesion) shows a significant risk for the patient in cause of getting a pre-invasive cervical lesion or even invasive cancer. According to some studies that were analyzed when the recommendations Bethesda 2001 were made - regarding the conduct when meeting H-SIL cytology, the chance for a patient with H-SIL cytology to have a CIN II/III (cervical intraepithelial neoplasia) biopsy of confirmation is around 70-75%, and the chance to have invasive cancer is about 1-2% (10).

THE PURPOSE OF THE STUDY

The purpose of this study is to establish the evolution of cervical cancer after applying a conventional treatment.

The study tries to establish some correlations between elements of epidemiology and the histologic diagnosis for every batch of cases, underlining the risk factors that are frequently met in cervical neoplasia.

We want to see the clinico-progressive particularities according to the pathogenic mechanism, associated comorbidities, doctor addressability, precocity of diagnosis and establishing of treatment and we will decide the prognostic factors involved in causing cervical cancer.

MATERIAL AND METHODS

The batch to be studied was made of 1249 patients, all monitored for suspicion of cervical neoplasia in „Elena-Doamna” Clinical Hospital of Obstetrics and Gynaecology Iași.

The criteria to be met for being accepted in this group: a deteriorated health state; suspicion of cervical neoplasia; free consent of the patient; willingness to come back for a subsequent medical check-up; access to a telephone and emergency transportation; willingness to support/have a surgical procedure if the medication fails to have positive results; lack of allergic reactions to the substances used in the study.

The conservative conduct is represented by the fact that patients repeat the cytology when admitted into the batch (the initial cytology was made before this moment).

That is why, the traditional conduct which is recommended as optimum in the case of an H-SIL cytology consists of performing a colposcopy associated after that with the cervix evaluation/examination.

The purpose of all these steps is to see if:

- There is or there is not a lesion that can be colposcopically identified which is also susceptible of suggesting changed cells that correspond to an H-SIL cytology;
- The colposcopy is or is not satisfactory
- The immediate diathermal excision is suitable or not for the case.

RESULTS AND DISCUSSIONS

The share of the patients who were treated in a conservative manner shows the following aspects (tab. I):

Table I. Statistical differences for the patients with a conservative treatment according to the epidemiologic characteristics and diagnosis

Parameters analyzed	Conservative treatment				Statistical significance
	yes		no		
	n	%	n	%	
Age group					
< 45 years old	568	30.1	329	17.5	$\chi^2=6.36$; GL=1; p=0.012
≥ 45 years old	681	36.1	307	16.3	
Area of origin					
Urban	921	48.9	536	28.4	$\chi^2=26.07$; GL=1; p=0.000003
Rural	328	17.4	100	5.3	
Marital status					
Married	857	45.5	519	27.5	$\chi^2=35.41$; GL=1; p<0.001
Single	392	20.8	117	6.2	
Viral testing					
HPV (+)	89	4.7	45	2.4	$\chi^2=0.0$; GL=1; p=0.956
HPV (-)	1160	61.5	591	31.4	
Cytologic examination					
High degree	848	45.0	412	21.9	$\chi^2=1.71$; GL=1; p=0.191
Reduced degree	401	21.3	224	25.3	
Colposcopic examination					
Yes	272	14.4	87	4.6	$\chi^2=17.40$; GL=1; p=0.00003
No	977	51.8	549	29.1	
Biopsy					
Yes	704	37.3	154	8.2	$\chi^2=174.36$; GL=1; p<0.001
No	545	28.9	482	25.6	
Histopathologic examination					
Yes	707	37.5	138	7.3	$\chi^2=206.21$; GL=1; p<0.001
No	542	28.8	498	26.4	

- 54.5% patients are over 45 years old;
- 73.7% patients come from cities or towns (urban area);
- 68.6% patients are married;
- for 67.9% of the patients treated in a conservative manner the cytodiagnosis was high in degree;
- 21.8% of the patients had colposcopy performed;
- biopsy was performed for 56.4% of the patients treated in a conservative way;
- 56.6% of the patients treated in a conservative manner were histopathologically diagnosed

The effectiveness of the conservative treatment for the patients diagnosed by cytology, colposcopy, by biopsy and histopathology, with or without viral infection with HPV, is shown by drawing the ROC curve (tab. II, fig. 1).

Table II. Comparative analysis of accuracy according to the conservative treatment

Diagnostic	VPP (%)	VPN (%)	Sensibility (%)	Specificity (%)	Accuracy	p
HPV (+)	7.1	7.1	13.1	3.7	8.4	0.956
H-SIL	67.9	64.8	79.1	50.7	64.9	0.191
Colposcopy	21.8	13.7	33.1	8.2	20.6	0.00003
Biopsy	56.4	24.2	59.4	22.0	40.7	<0.001
Histopathology	56.6	21.7	58.7	20.3	39.5	<0.001

ROC curve shows better accuracy of the treatment after establishing the cytologic diagnosis of high degree (64.9%) and also in the case of biopsy (40.7%). The statistical analysis according to the HPV viral infection, for the patients treated in a conservative manner, did not lead to any significant conclusions that could allow the extrapolation of results.

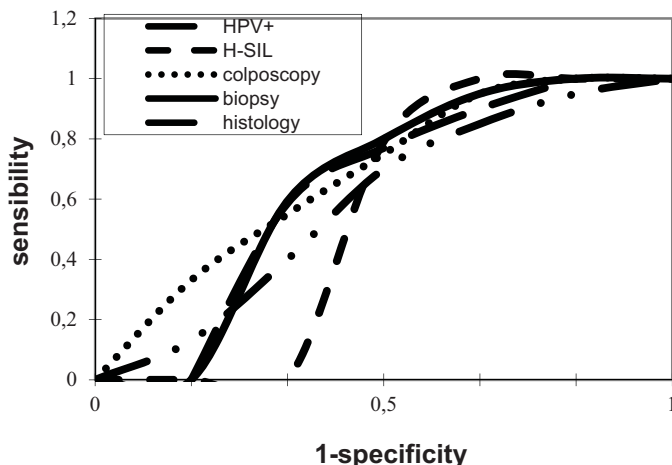


Figure 1. ROC curve - the assessment of conservative treatment effectiveness

The evolution of cases with cervical neoplasia diagnosis

Usually the colposcopic evaluation, following immediately after an H-SIL cytology leads easily to the identification of the high degree cervical or vaginal lesion, the positive predictive value of the colposcopy being really high in this situation (4, 5, 6, 9).

But there are situations when the high degree cervical or vaginal lesion cannot be identified **colposcopically**. So, after the colposcopy and the evaluation of the endo-cervix the following clinical situations can occur:

-There is a cyto-colpo-histologic discordance where we have:

- H-SIL type cytology
- a satisfactory colposcopy, but one that does not identify the presence of a lesion
- negative biopsy or showing changes that would qualify for CIN I at most;

-it is advisable to review the cytologic and histologic smear whenever this is possible and also to perform the colposcopic examination.

-There is a cyto-colposcopic discordance where we have:

- H-SIL type cytology
- unsatisfactory colposcopy, that does not identify the presence of a lesion
- negative biopsy or showing changes that would qualify for CIN I at most;

-it is recommended to reassess the cytologic and colposcopic results and it is imperative to also have a histologic evaluation.

According to **neoplasia staging** you will notice the following aspects (fig. 2):

- for the patients diagnosed in stage II, the probability of survival decreases in the first year after being diagnosed to 65%, after 2 years it decreases to 30% and is theoretically null after 7 years from the moment when it was diagnosed;
- for the patients diagnosed in stage III, the probability of survival decreases in the first year after being diagnosed to 60%, after 3 years it decreases to 30% and is theoretically null after 6 years from diagnosis;
- for the patients diagnosed in stage IV, the probability of survival decreases in the first year to 50%.

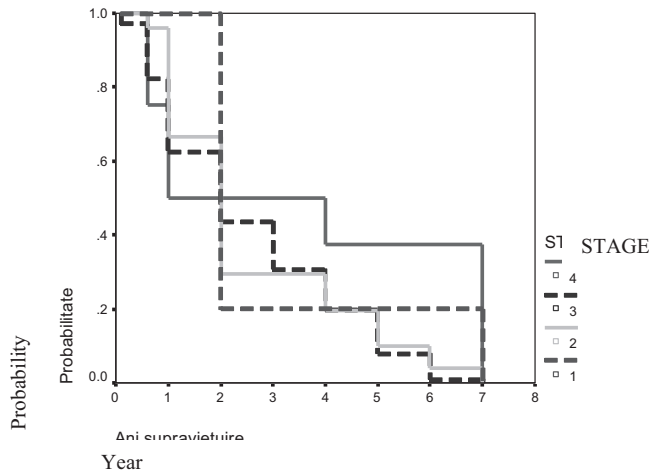


Figure 2. Survival of the patients with cervical neoplasia according to staging

The patients who responded the conservative pre-operative treatment are more likely to survive when compared to the patients who did not respond favourably to the conservative pre-operative treatment; the latter have a probability of survival of at most 5 years after being diagnosed with cervical neoplasia (fig. 3).

The probability of survival decreases to about 45% in the first year after diagnosis for the patients with post-operative complications (fig. 4).

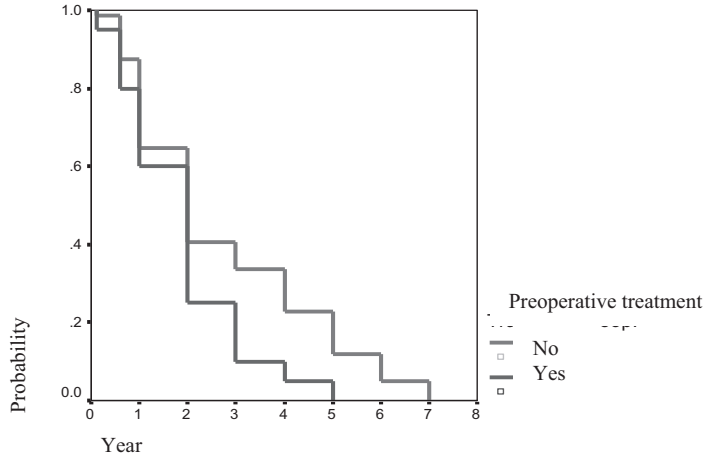


Figure 3. Survival of the patients with cervical neoplasia according to the conservative preoperative treatment

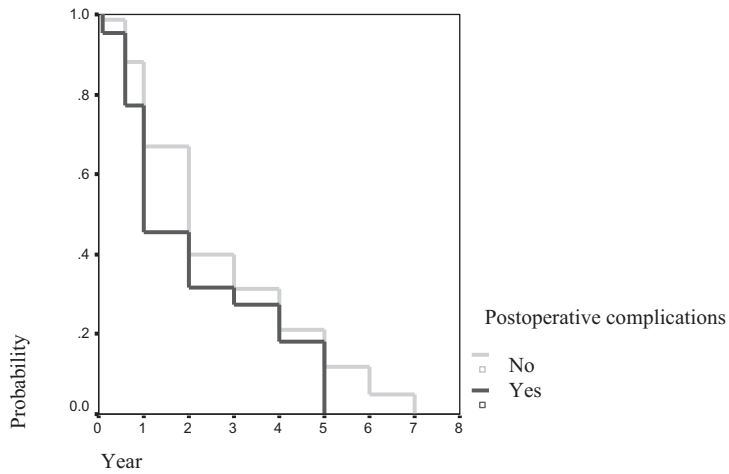


Figure 4. Survival of the patients with cervical neoplasia according to the postoperative complications

CONCLUSIONS

The conservative conduct is represented by a repeated cytology when the patients are admitted into the batch of study (the initial cytology is performed before this moment). The patients benefited from colposcopy and biopsy only if the repeated cytology suggested more severe changes.

The immediate colposcopy, followed by biopsy when needed, represents an aggressive manner of therapeutic conduct.

The sorting of HPV (Human immunodeficiency virus) was used in association with a cytologic result in order to appreciate its effectiveness in selecting the patients with atypical squamous cells with an undetermined significance that need colposcopy. If the cytology showed more severe changes or if it found the presence of a high oncogenic risk HPV, the patients were directed towards colposcopy.

The patients who were early detected have a 15% higher survival probability. The patients who responded to the preoperative conservatory treatment have a higher survival probability than the patients who did not respond favourably to the preoperative conservative treatment.

The comparison of the three methods allowed us to find out:

- the effectiveness of each of the conduct options in early detection of the serious changes that can progress to cancer;
- how acceptable each of the conduct options is for the patients;
- which is the ratio cost/effectiveness corresponding to each option.

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