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Review

Diagnostic Approach for Precancerous and Early Invasive Cancerous Lesions of the Uterine Cervix

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A B S T R A C T

Invasive cervical cancer is second most common female cancer worldwide with about 493 000 new cases per year. About 273 000 women die from cervical cancer each year, 85% of which take place in developing countries. Cervical cancer has a slow progress, from pre-invasive cervical intraepithelial neoplasia (CIN) to invasive phases, meaning that the disease can be diagnosed while in the phase of pre-invasive lesion, and treated successfully thanks to the regular screening of asymptomatic women (the Pap smear). The authors review new possibilities of early detection of cervical cancer with emphasis on colposcopy. The role of colposcopy is discussed among possibilities of early diagnosis. The authors discuss additional diagnostic procedures for preinvasive lesions of the uterine cervix like DNA cytometry, (flow cytometry). This method can point to dysplasia which can progress to severe stages, such as HSIL (High grade Squamous Intraepithelial Lesion). If the level of chromosomal disturbance is higher (aneuploidy), it is more probable that HSIL will develop. Laser screening of cells extracted with modern cytologic screening LBC (Liquid Base Cytology) enables us to automatically measure ploidy (chromosome regularity, or irregularity) and PCR provides analysis of HPV types. These methods are recommended for a routine check-up of borderline cervical lesions in order to anticipate ones likely to regress or progress.

Key words: *colposcopy, cervical cancer, Cervical Intraepithelial Neoplasia (CIN)*

Introduction

According to the 2003 yearbook, 313 new cases of cervical cancer (13.7/100000) and 493 cases of Cervical Intraepithelial Neoplasia (CIS) in Croatia were discovered[1]. Although the cervical cancer mortality rate is on the decrease, 100 women still die every year[1]. Cervical cancer is second most common female cancer worldwide with about 493 000 new cases per year, and it is most common female cancer in Africa, Asia and South America[2]. About 273 000 women die from cervical cancer each year, 85% of which take place in developing countries[2]. There were 12 800 new cases and 4 600 fatal outcomes in the US during the year 2000. Mean age of cervical cancer patients is 51.4 years, with an almost equal distribution in age groups 30 to 39 years and 60 to 69 years[3]. In Croatia, in the age groups between 25–39 years and 50–64 years, a decreasing trend of cervical cancer incidence is observed. An increase of cervical cancer incidence over the last 20 years has been observed in the age-groups 40–44 and 45–49 years[4].

Cervical cancer has a slow progress, from pre-invasive intraepithelial neoplasia (CIN) to invasive phases, which means that the disease can be diagnosed while in the phase of pre-invasive lesion, and treated successfully thanks to the regular screening of asymptomatic women (the Pap smear).

In developed countries, most cases of cervical cancer are diagnosed among women without the regular Pap smear. Unfortunately, in developing countries, the screening of asymptomatic women is often not available.

In addition to this sad fact, attitudes towards this disease and the lack of public health education make the situation even worse.

This is the population in which we can find patients with cervical cancer in advanced phases, when the disease has spread into the bladder, the rectum, the nerve pathways of the pelvis, or the bone.

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Radiotherapy and palliative care are often insufficient in these countries, so many patients die as outcasts, suffering from extreme pain and bearing the stench of the vaginal secretion. These are mostly women who have children who still depend on them, so their deaths cause severe dysfunctions in the family.

Cervical Cancer Symptoms

Abnormal vaginal bleeding is the most common symptom of invasive cervical cancer. Among sexually active women, the symptoms include postcoital bleeding, although one must not dismiss both the intermenstrual and the postmenopausal bleedings.

In comparison with endometrial cancer, which is rather quickly manifested by bleeding, cervical cancer among women who are not sexually active is asymptomatic until it reaches an advanced stage.

The large tumor mass is often infected, so there is a stench vaginal discharge present, even prior to vaginal bleeding.

Pretorius and colleagues[5] report that in advanced stages of the disease the first signs can be the following: pelvic pain; pressure – that is tenderness in rectal or bladder regions; occasional discharge of urine or faeces through vagina. The report includes 81 patients with the diagnosis of cervical cancer: 56% of them had vaginal bleeding as the first symptom of the disease, 28% had an abnormal Pap smear, 9% suffered from pain, 4% had vaginal discharge, and 4% had no symptoms.

It should be mentioned that small tumors, meaning the earlier stages of the disease, were found among patients with an abnormal Pap smear.

Diagnostic Procedures

Making an early diagnosis of cervical cancer can present a challenge for the following reasons:

a) its frequent asymptomatic nature,
b) if there is no possibility of a gynaecological examination in speculas for distinguishing the source of the disease in the endocervical canal or under the ectocervical epithelia,
c) because of a fairly high percentage of false-negative Pap smear results, even among regular patients.

Gynecologic Examination in Cervical Cancer Diagnosing

In speculas the primary lesion is seen as: exophytic (Figure 1), endophytic, ulcerative, or polipoid. If the tumor is growing under the epithelium or in the endocervical canal, ectocervix can seem intact macroscopically.

The direct spread into the vagina is visible, but the infiltration can be subepithelial and possible only with obliterated vaginal vaults or the presence of cervical stenosis.

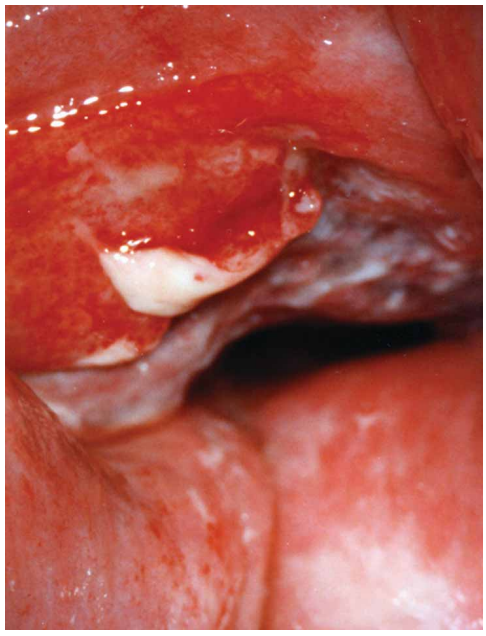

Fig. 1. Invasive cervical cancer.

In later stages the visualization of the cervix can be difficult. During manual palpation, the cervix feels indurated (except in pregnancy), and enlarged.

The size of the cervix can best be measured by rectal examination, which is necessary to estimate the spread of the disease on the parametrium, as well. MRI helps us get more precise information on the spread of the disease and thus the stage of the disease. Additional physical examination must include: the palpation of the liver, of the supraclavicular and inguinal lymph nodes, in order to rule out metastatic disease.

Complementary contemporary radiology techniques in the assessment of cervical volume as well as the ultrasound diagnostics must be taken in mind.

Tissue sampling for patohistological verification is an inevitable part of diagnostic protocol. Any tumor mass or ulceration calls for histological analysis, in this case for the so-called punch biopsy (*excisio probatoria cervicis*). Any unusually indurated or enlarged cervix needs to be analysed through biopsy and/or endocervical abrasion.

TABLE 1
SUGGESTED PROTOCOL ON THE TREATMENT OF PATIENTS WITH THE ABNORMAL PAP SMEAR DEPENDING ON THE COLPOSCOPIC FINDING

	Satisfactory finding	Unsatisfactory finding
Minor change	• Control for 6 month	• Repeat PAP smear • HPV test • Control colposcopy
Major change	• Biopsy + PHD	• Biopsy + PHD
IC suspected	• Biopsy + PHD	• Biopsy + PHD

Both satisfactory and unsatisfactory colposcopic findings deal with thorough visibility of the uterine portio, SCJ- squamocolumnar

Cytological Test in Diagnosing Cervical Cancer

Cytological diagnosis of conventional cervicovaginal smear or Pap test is one of the most efficient screening tests known to date, which has been credited with the significant decline in the incidence and mortality of cervical carcinoma in the world. The measures of cervical cytology availability as a screening test are its sensitivity, specificity, predictive value and diagnostic accuracy. The sensitivity of cervical screening in Croatia is 90.0%, specificity 98.6%, positive predictive value 92.3%, negative predictive value 98.1% and overall diagnostic accuracy 97.2%[6]. The main objection to conventional cytology as a screening test refers to its low sensitivity, false positive and false negative results. In the last few decades new techniques of cervical cytology sampling and processing such as liquid-based cytology (LBC), have been developed. The advantages of LBC over conventional smear are reduced rate of inadequate samples and false negative findings, higher rate of abnormal cytology findings detected and significantly shorter time needed for analysis of a specimen prepared by LBC method[6].

Human Papillomavirus Testing

There are clear benefits for the use of HPV DNA testing in the triage of equivocal smears, low-grade smears in older women and in the post-treatment surveillance of women after treatment for CIN[7]. However, there are still issues regarding how best to use HPV DNA testing in primary screening. Primary screening with Hybrid Capture((R)) 2 (HC2) generally detects more than 90% of all CIN2, CIN3 or cancer cases, and is 25% relatively more sensitive than cytology at a cut-off of abnormal squamous cells of undetermined significance (ASC-US) (or low-grade squamous intraepithelial lesions (LSIL) if ASC-US unavailable), but is 6% relatively less specific[7]. In countries where cytology is of good quality, the most attractive option for primary screening is to use HPV DNA testing as the sole screening modality with cytology reserved for triage of HPV-positive women. Established cytology-based programmes should also be gradually moving towards a greater use of HPV DNA testing to improve their efficacy and safely lengthen the screening interval. The greater sensitivity of HPV DNA testing compared to cytology argues strongly for using HPV DNA testing as the primary screening test in newly implemented programmes, except where resources are extremely limited and only programmes based on visual inspection are affordable[7].

The Role of Colposcopy

Colposcopy is necessary if the gynecologist finds no unusual features of the cervix in the patient with symptoms or an abnormal Pap smear. On the other side if a firm diagnosis cannot be set after the biopsy, diagnostic cone biopsy is recommended. Colposcopic detection of microinvasive cancer depends on its size and location (Figure 2). The gynaecologist can miss smaller lesions, although the probability of stromal invasion increases with the level of lesion spread on the surface. If the microinvasive cancer is entirely within the endocervical canal, the ectocervix can seem alright during colposcopy. Signs of microcancers of the ectocervix are atypical blood vessels prone to bleeding.

Atypical blood vessels are located unusually and randomly, they differ in diameter, and often change direction, forming sharp angles. Intercapillary distance is larger and changeable (Figure 2).

The colposcopy enlarges the picture of the early invasive cancer and shows the surface and the atypical blood vessels. In these cases of IA1–IB1 thorough colposcopy may enable to find scribble shaped border between ill uterine cervix and rather health vaginal coupole tissue. It is important in planning the size of upper third vaginal tissue involvement in radical hysterectomy removal, thus leaving middle and lower third of the vaginal tissue health and able to bring endovaginal irradiation source when needed.

Endophytic tumors often look like erosions. When enlarged, papillary surface and atypical blood vessels are visible. Keratosis can mask the colposcopical finding of an underlying lesion, which is the reason why biopsy is necessary. Due to our colposcopic experience uterine cervix adenocarcinoma has no distinctive features. We can spot all vascular changes that have been described so far.

Histology

In the presence of a satisfactory examination, colposcopically directed punch biopsy becomes the gold stan-

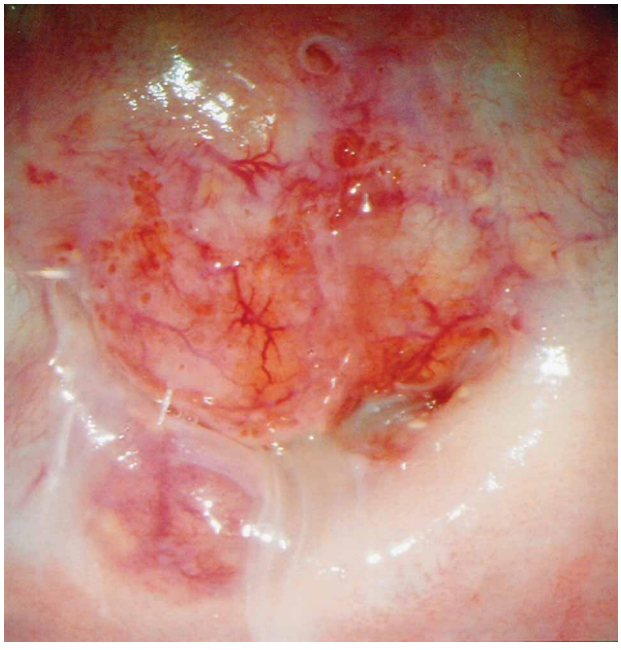

Fig. 2. Microinvasive cervical cancer.

dard of diagnosis. All women with a smear showing high grade Squamous Intraepithelial Lesion (HSIL) should have material submitted for histology. Women with a smear showing Low grade Squamous Intraepithelial Lesion (LSIL) and who have no abnormalities detected by colposcopy should have repeat smear preformed; if it is normal, it is safe to follow-up citologically. In low grade SIL (LSIL) immature basal type cells occupy lower third of the epithelium. Histological abnormalities associated with LSIL are a result of proliferation of basal and parabasal cells in the infected epithelium[8]. The resultant hyperplasia can be highly variable and take many forms but is most commonly characterized by papillomatosis and acanthosis. In high grade SIL (HSIL) immature basal-type cells occupy more than the lower third of the epithelium. In addition there is nuclear crowding, pleomorphism and loss of the normal cell polarity[8].

Flow Cytometry

Additional diagnostic procedure for preinvasive lesions of the uterine cervix is DNA cytometry, (flow cytometry). This method can point to dysplasia which can progress to severe stages, such as HSIL (High grade Squamous Intraepithelial Lesion). If the level of chromosomal disturbance is higher (aneuploidity), it is more probable that HSIL will develop.

Laser screening of cells extracted with modern cytologic screening (LBC) enables us to automatically measure ploidity (chromosome regularity or irregularity) and PCR analysis of HPV types. These methods are recommended for a routine check-up of borderline cervical lesions in order to anticipate ones likely to regress or progress. DNA cytometry of targeted excision samples from sites selected by colposcopy presents a challenge.

Here is a common dilemma: the claim of the expert clinician that CIN ll is biologically closer to dysplasia levis (CIN l) and that it requires no aggressive approach, and the answer that this is only possible after the neoplastic potential of the lesion is confirmed by flow cytometry technique. It is only after this procedure that we can decide on the follow-up or ablation techniques!

Until this becomes the practice, we are left with cytological analysis, which is to be made two months after the biopsy (biopsy forceps, or diathermic loop), which is described in the protocol for premalignant lesions[9,10].

On the basis of the follow-up cytological analysis, repeated colposcopies and complete revisions tell us what to do next.

Basic Directives

Colposcopy classifications and achievements varied from Graz 1975 to Barcelona 2002 as follows:

Graz classification[11] stated that aceto-white epithelium makes an abnormal colposcopic finding, Rome classification[12] stated that such epithelium is almost patognomonic for HPV infection, and can be more or less visible, with or without clear borders, while Barcelona classification[13] points out all of the above including the statement that aceto-whitening can appear quickly and slowly disappear, or slowly appear and disappear quickly. This is related to the intensity of the disruption of intracellular chromatine in HPV infected cells.

Colposcopic classification which points to normal and abnormal colposcopic images of various stages of abnormality and availability of transformation zone is complemented by cytological classification[14] and patohistological classification[8].

These are the prerequisites for the collaboration of the gynaecologist, the cytologist and the pathologist, in order to achieve the best results through establishing protocols for diagnostics and treatment.

Protocol for diagnostics and treatment of premalignant lesions of the cervix and lower genital tract is a corner stone we hadn't had and which was created from 1996 to 2000, and at last established at the conference celebrating 75 years of colposcopy in clinical practice in Croatia.

The protocol has become a landmark for all of us who delved into the comprehensive subject of preinvasive cervical lesions[9,10]. At clinical training courses in colposcopy and early diagnostics and prevention of neoplastic changes in the lower genital tract the theoretical practice

TABLE 2
EXISTING PROTOCOL ON TREATMENT OF PATIENTS WITH ABDORMAL PAP SMEAR AND UNSATISFACTORY COLPOSCOPIC FINDING OR WITH MICROINVASCIVE CARCINOMA OF SQUAMOS CELLS ON PROBATORI EXCISION

Status of the excision of microinvasion up to 5 mm or less	Recommendations
Margins clear, ECC negative, stage IA1 with no spread to lymphovascular area:	• cone biopsy if the patient wants to preserve fertility
	• repeat cone biopsy
Margins and/or ECC positive dysplasia	• modified radical hysterectomy
	• if conization not appropriate, then perform hysterectomy +/– pelvic lymphadenectomy
Stage IA1 with invasion into lymphovascular area	• pelvic lymphadenectomy + conisation, or radical trachelectomy (for fertility reasons)
	• modified radical hysterectomy and pelvic lymphadenectomy

Adopted from Hacker, 2000[16], ECC/endocervical curretage, LVSI – lympho vascular space invasion

ends with the protocol, and then we present a series of colposcopic images in order to entice discussion on possible gravity of lesions and patohistological verification.

Our great interest in the issue led us to the introduction of those ablation and destruction procedures which will spare the cervix and hence the reproductive system of our patients, and their health as a whole.

The cytologic and colposcopic protocol that we established for the follow-up after classic probatory excision by forceps (Kevorkian, Thomas Gaylor) or after probatory excision by loop decreases the number of unnecessary cold knife cones and diathermic cones by loop.

In cases of persistent cytologic abnormalities, after biopsy, and a second colposcopic examination, it could be easier to decide on one of such procedures in order to preserve the gynaecological and reproductive health.

We must point out that is necessary to inform the patient that diathermic cone biopsy (LETZ) and classic cone biopsy with scalpel did remove the site of a potentially more severe change, but at the same time we must point that the responsibility lies both in the hands of the woman and her partner, in order to ensure that such situation does not repeat in the future.

What if the Disease Progresses?

The collaboration of the gynaecologist, the cytologist, and the pathologist implies that the current state of a patient needs to be discussed on several levels: the stage of the initial invasion, the sample on which the initial invasion was discovered, age and parity of the patient. After we consider these levels, we can decide on further treatment of the patient.

Common Questions in Colposcopic Practice

The earlier the cervical cancer is diagnosed, the better the chances are of successful treatment. Here are some basic issues in our everyday clinical, and gynaecological and oncological practice. I will also take into consideration those patients in advanced stages of this disease.

A) The approach to the treatment of microinvasive planocellular cervical cancer IA1 diagnosed after LETZ biopsy or classic test excision by forceps. What if the patient is a nulliparous, or if she had a baby once, or more times?

B) The approach to the treatment of microinvasive planocellular cervical cancer IA2 diagnosed after LETZ biopsy or after classic test excision by forceps. What if the patient is a nulliparous, or if she had a baby once, or more times?

C) The approach to the treatment of microinvasive planocellular cervical cancer IA1 diagnosed after LETZ biopsy or after classic cone biopsy by scalpel. What if the patient is a nulliparous, or if she had a baby once, or more times?

D) The approach to the treatment of microinvasive planocellular cervical cancer IA2 diagnosed after LETZ cone biopsy or after classic cone biopsy by scalpel. What if the patient is a nulliparous, or if she had a baby once, or more times?

What about the grey area? How to treat patients with stromal invasion of more than 5 mm, the spread larger than 7 mm, and the change still not visible to the naked eye? Do they already belong to the IB1 group or not? What about reproduction? What if the finding is an incidental finding at hysterectomy, or at a diagnostic cone biopsy, or at one of the mentioned excohleation of the cervical canal or probatory excisions?

All of the above requires thorough studying taking in mind FIGO classification as the most acceptable for all those involved in cervical cancer diagnosis and treatment[15] (Figure 3).

Importance of Continuous Medical Education

Colposcopic diagnostic accuracy depends upon a practitioner's proficiency. Therefore, not only a well structured initial training but also a continuous practice with proper clinical feedback is necessary. The European colposcopy training programs in 2004 reached the consensus on a structure of a program. It is recognized that training must involve actual colposcopic experience that is supervised by a trainer in a recognized centre. The trainer and the experience received must meet certain standards in terms of workload and case-mix. It has been agreed that in EFC-recognized training programs trainees would see a minimum of 100 patients[17].

Multidisciplinary Approach to Cervical Cancer Prevention

Cervical cancer prevention strategies should be directed from secondary to primary prevention. Two prophylactic human papillomavirus (HPV) vaccines have been shown to be highly effective and are now recommended for use in many countries. As a result, primary prevention of cervical cancers that are attributable to HPV types 16 and 18 is now possible. Although this has been enthusiastically embraced, it brings new challenges. Other aspect of a primary prevention is education in sexually responsible behavior. Considering the lowering age of first sexual intercourse one should make every effort to establish multidisciplinary teams (physicians, psychologists, teachers…) and appropriate settings for such an education.

Conclusion

Numerous questions and answers were brought up during the postgraduate clinical training course »Diagnostics, Treatment and Prognosis for Preinvasive Lesions and Carcinoma of the Cervix« held at the Ob/Gyn

Clinic in University clinical center Zagreb, on 7 and 8 April 2006.

Critical scientific and practical thinking and the participation of gynaecologists, pathologists, cytologists, radiologists and epidemiologists established firm foundations for a comprehensive insight into this issue.

The foundations created leeway both for experts and young colleagues in these areas of medicine to work on setting up national programs for cervical cancer screening.

Necessary collaboration among complementary specialties, consulting with more experienced colleagues and regular publication of results will improve women s gynecologic health care. Due to Consensus[18] we also point out the following recommendations:

1. Colposcopy allows identification, localization and delineation of premalignat lesions of the cervix, vagina and vulva and directs the biopsy site.
2. In some countries, colposcopy is used as a screening tool but because of its low specificity, it should not be used in primary screening but reserved for those women who have been shown to have abnormal cervical cytology.
3. Colposcopy must be preformed prior to treatment of cervical intraepithelial neoplasia.
4. Colposcopy should be preformed only by trained and experienced colposcopist. Colposcopists should audit their work to confirm that the outcome of their colposcopic assessment and colposcopically-directed treatment is keeping up with internationally agreed standards.
5. The colposcopic findings should be recorded in patient's charts.

We hope that above mentioned statements will enable a better insight and therapeutic outcome of this group of gynecologic patients.

REFERENCES

1. CROATIAN NATIONAL CANCER REGISTRY, Cancer Incidence in Croatia, Bulletin No 24–28. (Croatian National Institute of Public Health, Zagreb, 2001–2005). — 2. FERLAY J, BRAY F, PISANI P, PARKIN DM, GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide, IARC Cancer Base No. 5. Version 2.0. (IARC Press, Lyon, 2004). — 3. HACKER NF, Cervical cancer. In: BEREK JS, HACKER NF (Eds) Practical gynecologic oncology (Lippincott, Williams & Wilkins, Philadelphia, 2000). — 4. ZNAOR A, STRNAD M, Coll Antropol, 31 Suppl. 2 (2007) 37. — 5. PRETORIUS R, SEMRAD N, WATRING W, FOTHERONGHAM N, Gynecol Oncol, 42 (1991) 48. — 6. PAJTLER M, AUDY-JURKOVIĆ S, KARDUM-SKELIN I, MAHOVLIĆ V, MOZETIČ-VRDOLJAK D, OVANIN-RAKIĆ A, Coll Antropol, 31 Suppl. 2 (2007) 47. — 7. CUZIK J, ARBYN M, SANKARANARAYANAN R, TSU V, RONCO G, MAYRAND MH, DILLNER J, MEIJER CJ, Vaccine, 26 Suppl. 10 (2008). — 8. WRIGHT TC, KURMAN RJ, FERENCZY A, Precancerous Lesions of the Cervix. In: BLAUSTEIN'S Textbook of Pathology (Springer-Verlag, New York, 2002). — 9. LJUBOJEVIĆ N, BABIĆ S, AUDY-JURKOVIĆ S, OVANIN-RAKIĆ A, GRUBIŠIĆ G, JUKIĆ S, DRAŽANČIĆ A, LJUBOJEVIĆ-GRGEC D, Gynaecol Perinatol, 10 (2001) 85. — 10. LJUBOJEVIĆ N, BABIĆ S, AUDY-JURKOVIĆ S, OVANIN RAKIĆ A, JUKIĆ S, BABIĆ D, GRUBIŠIĆ G, RADAKOVIĆ G, LJUBOJEVBIĆ-GRGEC D, Coll Antropol, 25 (2001) 467. — 11. STAFL A, Obstet Gynecol, 48 (1976) 123. — 12. STAFL A, WILBANKS GD, Obstet Gynecol, 77 (1991) 313. — 13. WALKER P, DEXEUS S, DE PALO G, BARRASSO R, CAMPION M, GIRARDI F, JAKOB C, ROY M, Obstet Gynecol, 101 (2003) 175. — 14. OVANIN RAKIĆ A, PAJTLER M, STANKOVIĆ T, AUDY-JURKOVIĆ S, LJUBOJEVIĆ N, GRUBIŠIĆ G, KUVAČIĆ I, Gynaecol Perinatol, 12 (2003) 148. — 15. BENDET JL, PECORELLI S, Internat J Gynecol & Obstetrics, 70 (2000) 221. — 16. HACKER NF, Cervical cancer- Algorythm for the management of patients with an abnormal Pap smear and inadequate qolposcopy or microinvasive squamos cervical carcinoma on punch biopsy. In: BEREK JS, HACKER NF (Eds) Practical Gynecologic Oncology, 3rd Edition (Lippincot Williams & Wilkins, Philadelphia, Baltimore, New York, 2000). — 17. REDMAN C, JORDAN J, Coll Antropol, 31 Suppl. 2 (2007) 131. — 18. GRCE M, GRUBIŠIĆ G, KARDUM-SKELIN I, MAHOVLIĆ V, PAJTLER M, BABIĆ D, ĆORUŠIĆ A, ZNAOR A, Medix, 72 (2007) 93.

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DIJAGNOSTIČKI PRISTUP PREKANCEROZAMA I RANOM INVAZIVNOM RAKU VRATA MATERNICE

SAŽETAK

Invazivni rak vrata maternice je jedan od najčešćih uzroka smrti od malignih ginekoloških bolesti, sa oko 493 000 novootkrivenih slučajeva u svijetu godišnje. Rak vrata maternice napreduje sporo, od preinvazivne intraepitelne neoplazije (CIN) do invazivne faze, što znači da se može na vrijeme spriječiti sa redovitim testovima probira (PAPA test). U ovome članku iznosimo pregled novijih dostignuća u ranoj detekciji raka vrata maternice s posebnim naglaskom na mjesto i ulogu kolposkopije i njenih dosega, ali i ograničenja. Predlažemo da u svim dostupnim stanjima mikroinvazije i rane invazije neoplastičnog procesa vrata maternice kolposkopski pregledamo i vrat maternice i svodove rodnice, a u svrhu mogućeg određivanja koju širinu vaginalne manžete uključiti kod radikalne histerektomije i tako prevenirati mogući recidiv.