ACTA MEDICA LITUANICA. 2006. VOLUME 13 No. 2. P. 88–91

Histological evaluation of cervical oncocytology and cone biopsy value in the treatment of cervical pathology

Sigitas Petraitis,

Konstantinas Povilas Valuckas,

Vilius Rudaitis, Nidal Ghaoui

Institute of Oncology,
Vilnius University (IOVU),
Santariskiu 1,
LT-08661 Vilnius, Lithuania
E-mail: petraitis@loc.lt

Objective. To evaluate and analyse the correlation between cervical cytology and postconization histology.

Materials and Methods. 473 female patients operated on (diathermo-conization) at IOVU were retrospectively analysed. All patients had at least one preoperative cervical cytology evaluated according to the Bethesda system, and all postoperative specimens were histologically evaluated.

Results. 53 (11.2%, 95% PI 8.4–14.0) patients had invasive cancer on histology, 289 (61.1%, 95% PI 56.7–65.5) patients had Ca *in situ*, CIN2 was found in 78 (16.5%, 95% PI 13.1–19.8) patients, CIN1 in 21 (4.4%, 95% PI 2.6–6.3) patients and 32 (6.8%, 95% PI 4.5–9.6) patients with chronic cervicitis. From the 473 patients, 418 (88.6%) had HSIL on cytology, after conization, invasive cancer was verified in 49 (11.7%, 95% PI 8.6–14.8) patients, Ca *in situ* was found in 259 (62.0%, 95% PI 57.3–66.6) patients, CIN2 in 73 (17.5%, 95% PI 13.8–21.1) patients, CIN1 in 19 (4.5%, 95% PI 2.5–6.5) patients and chronic cervicitis in 18 (4.35%, 95% PI 2.4–6.3) patients. From the 473 cytology specimens when compared to histology, 53 (11.2%) patients were diagnosed with invasive cancer, mostly microinvasive cancer. Ca *in situ* was found in 289 (61.1%), CIN2 was found in 78 (16.5%), CIN1 was found in 21 (4.4%) and chronic cervicitis was found in 32 (6.8%) cases.

Conclusion. These data show that in cases of HSIL cytology it is imperative to pursue a proactive treatment protocol (screen and treat), especially in countries with a high incidence of cervical cancer.

Key words: cervical oncocytology, dia-thermoconization, histological examination

INTRODUCTION

Active surgical intervention is a realistic method of treatment and diagnosis for early cervical pathology in Lithuania. That's why it is important to evaluate the value of cervical cone biopsy in the treatment and diagnosis of cervical pathology. The effectiveness of cervical pap screening for cervical pathology is unquestionable. Countries applying active pap screening are leading the way regarding the control of cervical cancer rates (1). Finland started its screening program in 1964, and in 2003 the incidence of cervical cancer was 4.3/1000,000 (2). In Lithuania 2004, 569 new cases were registered with 31.1/100,000-incidence rate and a mortality rate of 13.6/100,000, which is one of the highest in Europe (3). The Lithuanian cervical screening program has been initiated in 2004 and the main goal of this program is to decrease the incidence and mortality rate of this disease (4). **Objective**. To evaluate and analyze the correlation between cervical cytology and post-conization histology. **Materials and methods.** In the years 2004–2005, 473 patients were treated in the OIVU Oncogynecology Department. All patients had at least one cervical cytology evaluated according to the Bethesda system. The mean age of the group was 42 years, the oldest patient being 76 and the youngest 19 years old. 430 (90.9%) had at least one delivery and 43 (9.1%) had no previous deliveries. All patients were operated on (diather-moconization) and a postoperative histology report was obtained.

According to the cytology of the 473 patients, 418 (88.6%) patients had HSIL (high-grade squamous intraepithelial lesions). Cancer cells were found in 23 (4.9%), LSIL (low-grade squamous intraepithelial lesions) in 11 (2.3%), AGC (Atypical glandular cells) 1 (0.2%),

ASC-US (atypical squamous cells of undetermined significance) 6 (1.3%) and ASC-H in 14 (3.0%). In cases of AGC and ASC-US, conization was preformed for macroscopic changes including erosions and postpartum cervical rupture. **Results.** From 473 patients, 418 (88.6%) had HSIL on cytology. The respective results of histology are given in Table 1.

Table 1. **Histology results for patients with HSIL cytology**

Histology	n	%	95% PI
Invasive cervical cancer	49	11.7	8.4–14.0
Ca *in situ*	259	62.0	57.3–66.6
CIN 2	73	17.5	13.8–21.1
CIN 1	19	4.5	2.5–6.5
Chronic cervicitis	18	4.3	2.4–6.3
Total	418	100.0	

Squamous cancer cells were found in 23 (4.9%) patients on cytology, after conization invasive squamous carcinoma was found in 3 (13.0%) patients, Ca *in situ* was found in 17 (74.0%) patients and chronic cervicitis in 3 (13.0%).

On cytology, LSIL was found in 11 (2.3%) patients. On histology, 1 (9.1%) patient had squamous cell carcinoma T1A1, Ca *in situ* 3 (27.3%), CIN-2 in 2 (18.2%), and 5 (45.4%) patients had chronic cervicitis.

We had one patient with AGC cytology and Ca *in situ* on histology.

ASC-H cytology was found in 14 (3.0%) patients. After conization, 7 (50.0%) patients had Ca *in situ* on histology, 5 (35.7%) patients had CIN-2 and chronic cervicitis in 2 (14.3%) patients. A summary of the final histology results are given in Table 2.

Table 2. **Final histology results**

Histology	n	%	95% PI
Invasive cervical cancer	53	11.2	8.4–14.0
Ca *in situ*	289	61.1	56.7–65.5
CIN 2	78	16.5	13.1–19.8
CIN 1	21	4.4	2.6–6.3
Chronic cervicitis	32	6.8	4.5–9.0
Total	473	100.0	

Fifty-three patients had invasive cancer on histology. From the 53 patients, 31 (58.%) had stage T1A1, 8 (15.1%) patients had stage T1A2 and 14 (26.4%) had T1B1.

All 289 (61%) with Ca *in situ* histology stage had a follow-up oncocytology after 3 months and a second cytology after 6 months; 17 (5.9%) had recurrence on cytology. In 113 (39.1%) from 289 patients with Ca *in situ*, the histology report showed a nonclear resection margin, yet after repeating PAP smear only 3 (2.7%) patients had HSIL on cytology. This was attributed to the fact that in addition to conization we applied electrocoagulation to the zone to the excision margin.

DISCUSSION

Our results show that in cases of HSIL cytology 49 (11.7%) patients had invasive cancer, 259 (62.%) patients had Ca *in situ*, and 73 (17.5%) patients had CIN-2 histology. Overall, from 473 patients 367 (77.6%) had Ca *in situ* or CIN-2, in both cases surgical intervention was indicated. Ostor (5) and Kenneth (6) showed that CIN-2 could progress to Ca *in situ* in 20% of cases and Ca *in situ* progresses to invasive cancer in 30% of cases. For this reason, in countries with a high incidence of cervical cancer like Lithuania, cases of HSIL cytology should be treated surgically upon the diagnosis to perform cone biopsy. The width is a matter for discussion, yet it is imperative to treat HSIL cytology and obtain a histology report. In 1996, Bishop et al. developed the PATH program. The main goal of this program was to reduce cervical cancer morbidity in developing countries.

It was suggested to apply a more aggressive treatment algorithm in cases of abnormal PAP smear – to perform a leep-excision of the transformation zone. The method is inexpensive, highly efficient in cases of preinvasive cervical lesions, complications are rare and easy to manage (7). In 2005, Numnum et al. published the results of a prospective study that included 54 patients. They concluded that in cases of HSIL cytology after coloposcopy, conization and histological verification should be considered (8). In 2004, Charoenkwan et al. published a very similar trial in which electro-excision was performed in cases of HSIL. Ca *in situ* was found in 96% cases and they suggested to perform a conization in HSIL cases in low-income countries where morbidity from cervical carcinoma is high (9). In a randomised controlled trial conducted among 3521 women, Brewster et al. tested the feasibility and acceptability of immediate treating of women with a severely abnormal pap smear and compared the treatment rates and 12–month follow-up rates with those for women who received usual care. Women randomised to usual care (n = 1805) were discharged immediately after pap examination. The other group (n = 1716) remained in the clinic until the results of their pap test were available. Large loop electrosurgical excision procedure was preformed in single–visit patients with either a diagnosis of HSIL/AGC or suspicion of cancer. The rate of abnormal pap test was 4.1%. Six months after randomization, 88% of the single visit and 53% of the usual care patients with HSIL/AGC had completed the treatment. One year later, 63% of the single–visit program presented for the follow–up versus only 21% in the usual care group. They concluded that the single–visit program was feasible and the degree of acceptability was high; furthermore, the single visit

program provides an opportunity to increase the rate of immediate treatment and follow-up. (10)

Of course, there is another opinion that LEEP in HSIL may be too aggressive. Some authors (11–13) think that early confiscation is not justified in cases of young, nulliparous women because of iatrogenic cervical insufficiency. In our study, only 9.1% of subjects were nulliparous. We think that performing a shallow circular excision of transformation zone could be very useful in cases of preinvasive cervical lesions eliminating the error of missing microinvasive carcinoma.

The protocol for the management of preinvasive lesions suggested by us is slightly different from the WHO recommendations (14). The difference is that we suggest to pass over colposcopy and cervical biopsy, especially that biopsy by itself cannot determine the exact stage in cases of early invasive carcinoma. In performing a cone biopsy we get an adequate specimen for histology and save the treatment cost. In our country, where the incidence of cervical cancer is high, the screen-and-treat approach is an effective treatment protocol in cases of HSIL cytology.

CONCLUSIONS

1. From 418 cases with HSIL cytology, 62% of patients had Ca *in situ* and 11.7% had invasive cervical cancer on histology.
2. From all patients with invasive cancer on histology, 73.6% had T1a1 and T1a2 stage.
3. These data show that in countries with a high incidence of cervical cancer, women diagnosed with HSIL cytology should be treated actively by applying cervical cone biopsy and histological verification (according to Screen-and-Treat Protocol).

Received 11 January 2006
Accepted 13 April 2006

References

1. Papanicolaou develops PAP test, January 1928. Discovering U.S. history. Gale research, 1997. Reproduced in Student Resourse Center. Farmington Hills, Mich.: Gale group. December 2000. http://galenet.galegroup.com/servlet/SRC/
2. Anttila A, Nieminen P. Cervical cancer screening program in Finland. Eur J Cancer 2000 Nov; 36(17): 2209–14.
3. Pagrindiniai onkologines pagalbos rezultatai Lietuvoje. VUOI vezio registras, 2004; 8.
4. Kurtinaitis J. Onkologinių ligų kitimo tendencijos ir onkologinių ligonių išgyvenamumas Lietuvoje. Habilitacinio darbo santrauka. 2003; 39–40.
5. Östör AG. Natural history of cervical intraepithelial neoplasia – a critical review. Int J Gynecol Pathol 1993 12; 186–92.
6. Kenneth DH, Berek JS. Intraepithelial disease of the crevix, vagina, and vulva. Novaks Gynecology 2002; 16: 486.
7. Bishop A, Sherris J, Tsu VD, Kilbourne-Brook M. Cervical dysplasia treatment: key issues for developing countries. Bull Pan Am Health Organ 1996 Dec; 30(4): 378–86.
8. Numnum TM, Kirby TO, Leath CA, Huh WK, Alvarez LD, et al. Prospective evaluation of "see and treat" in women with HSIL Pap smear results: is this an appropriate strategy? J Low Genit Tract Dis 2005 Jan; 9(1): 2–6.
9. Charoenkwan K, Srisomboon J, Siriaunkgul S, Khunamornpong S, Suprasert P, Phongnarisorn C, Siriaree S, Cheewakriangkrai CA. "See and Treat" approach for high grade squamous intraepithelial lesion on cervical cytology. J Med Assoc Thai 2004 Aug; 87(8): 865–8.
10. Brewster WR, Hubbel FA, MD, Largent J et al. Feasiblity of management of high–grade cervical lesions in a single visit. JAMA 2005; 294: 2182–2187.
11. Luesley DM, Cullimore J, Redman CWE et al. Loop diathermy excision of the cervical transformation zone in patients with abnormal cervical smears. BMJ 1990; 300: 1690–93.
12. Murdoch JB, Grimshaw RN, Monaghan JM. Loop diathermy excision of the abnormal cervical transformation zone. Int J Gyneco Cancer 1991; 1: 105–111.
13. Chappatte OA, Bryne DL, Raju KS et al. Histological differences between colposcopic-directed biopsy and loop excision of the transformation zone: a cause for concern. Gyneco Oncol 1991; 43: 46–50.
14. Comprehensive Cervical Cancer Control. WHO, 2005: 73–74; Annex 3–4.

Sigitas Petraitis, Konstantinas Povilas Valuckas, Vilius Rudaitis, Nidal Ghaoui

CITOLOGINĖ GIMDOS KAKLELIO PATIKRA: HISTOLOGINIS ĮVERTINIMAS IR KONIZACIJOS REIKŠMĖ GYDYMO TAKTIKAI

Santrauka

Darbo tikslas. Gimdos kaklelio ankstyvos patologijos diagnostika ir aktyvus chirurginis gydymas yra aktualus mūsų šalyje, todėl įvertinome gimdos kaklelio konizacijos reikšmę ir vietą nustatant gimdos kaklelio patologiją. Atlikome retrospektyvią citologiškai tirtų ir gydytų pacienčių analizę, nustatėme, kaip įvairūs citologiniai gimdos kaklelio gleivinės pakitimai, vertinti pagal Bethesda sistemą, susiję su histologinio tyrimo rezultatais.

Metodika. Citologiškai ištirtos 473 ligonės, rezultatai vertinti pagal Bethesta sistemą. Daugumai (418 (88,6%)) ligonių nustatyti HSIL būdingi pakitimai: 23 (4,9%) ligonėms – plokščialąstelinės karcinomos ląstelės, 11 (2,3%) atvejų rasti LSIL pokyčiai. Citologiškai AGC nustatyta vienai (0,2%) pacientei, ASC-US – 6 (1,3%) ir rasta 14 (3,0%) ASC-H atvejų.

Visoms ligonėms atlikta gimdos kaklelio konizacija, medžiaga ištirta histologiškai.

Rezultatai. Nustatėme, kad esant HSIL citologinio tyrimo rezultatui net 11,7% ligonių histologiškai įrodytas invazinis plokščialąstelinis gimdos kaklelio vėžys, o iš visų 473 citologiškai tirtų moterų invazinio vėžio atvejai – 53. Praktiškai kiekvienoje citologinio tyrimo grupėje nustatyta Ca *in situ* patologija: iš viso 289 (61,1%) atvejai. Citologiškai ištyrus visas ligones, 367 (arba 77,6%) nustatyta CIS ir CIN2 patologija,

kurią reikia gydyti chirurgiškai. Gimdos kaklelio konizacija leido patikslinti mikroinvazinio vėžio stadijas ir pakoreguoti ligonės gydymo taktiką. Taigi T1A1 stadijos vėžį nustatėme 31 (58,5%) pacientei, T1A2 – 8 (15,1%) atvejais. Invazinis T1B1 stadijos vėžys nustatytas 14 (26,4%) pacienčių.

Mūsų gydymo taktika skiriasi nuo šiuo metu PSO rekomenduojamų gimdos kaklelio patologijos kontrolės standartų. Jų siūlomas ilgesnis tyrimo kelias, įterpiant kolposkopiją ir tikslinę biopsiją, ir tik po jos rekomenduojama atlikti gimdos kaklelio konizaciją. Mūsų nuomone, taip prarandamas brangus laikas. Po tikslinės biopsijos vis tiek nėra aiški tolimesnė gydymo taktika, ypač invazinio vėžio atveju, padidinami ligonės tyrimo ir gydymo kaštai, blogėja tiriamos pacientės psichologinė būklė ir gyvenimo kokybė. Mūsų tyrimo atveju nuo patologinio citologinio tepinėlio rezultato iki galutinės histologinės diagnozės praėjo apie 12 dienų. Ši metodika buvo priimtina tiek pacientei, tiek gydytojui. Pacientė nebuvo prarasta tarp kelių vizitų pas bendrosios praktikos gydytoją ir ginekologą, efektyviai ir greitai, be komplikacijų buvo išgydytas ikivėžinis susirgimas arba nustatytas invazinis vėžys.

Išvados. Esant HSIL onkocitologinio tyrimo rezultatui dažnai (62,0%) histologiškai nustatoma CIS ir net 11,7% atvejų – invazinis plokščialąstelinis gimdos kaklelio vėžys. Iš visų invazinio vėžio atvejų T1A1 ir T1A2 gimdos kaklelio karcinoma histologiškai įrodyta 73,6% ligonei. Šie duomenys mums leidžia teigti, kad šalyse, kur sergamumas gimdos kaklelio vėžiu yra didelis, būtina, citologiškai nustačius HSIL pakitimus gimdos kaklelyje, nedelsiant aktyviai gydyti, tai yra atlikti gimdos kaklelio konusinę biopsiją ir histologiškai verifikuoti esamą patologiją.

Raktažodžiai: citologinė gimdos kaklelio patikra, histologinis tyrimas, konizacija