Comparison of liquid-based cytology cervical smears with histopathological findings

Comparison of cervical cytology with histopathology

Seyhan Özakkoyunlu Hasçiçek[1], Tuba Oğuzsoy[2], Kamile Gülçin Eken[1], Fevziye Kabukçuoğlu[1],
1Department of Pathology, University of Health Sciences Sisli Hamidiye Etfal Training and Research Hospital,
[2]Department of Pathology, Faculty of Medicine, Marmara University, İstanbul, Turkey

Abstract

Aim: Cervical cancer is still a health problem in countries where cervical cancer screening is not routinely performed. A significant decrease in the rate of mortality from cervical cancer has been observed since the Pap test was introduced. Within the last decade liquid-based cytology (LBC) has replaced the Pap test. Our aim is to compare cervical smears prepared with the liquid-based cytology method with histopathological findings. Material and Method: Cervical smears and corresponding cervical biopsy reports of 300 patients diagnosed with epithelial cell abnormality between 2014-2016 were reevaluated retrospectively. Smears were prepared with the LBC test SurePath. Biopsy materials were stained with hematoxylin eosin. Slides were reported according to Bethesda 2014 classification. Biopsy materials were classified into 4 categories according to the WHO 2014 classification. Results: Cytology results of 273 patients (91%) were abnormal. Biopsy results showed lesions such as low grade cervical intraepithelial lesion, high grade cervical intraepithelial lesion, and squamous cell carcinoma in 178 patients (59.3%). The calculated sensitivity and specificity for LBC were 89.89% and 7.38% respectively, indicating low accuracy of specificity for LBC. Discussion: The management of treatment in diagnosis of epithelial cell abnormality in cervical cytology should be according to the sets of specified protocols. Because we may encounter high grade squamous intraepithelial lesions in biopsy with the diagnosis of atypical squamous cells of undetermined significance (ASCUS) in cytology, the necessity of colposcopy can be disputed for the management of this group of lesions.

Keywords

2014 Bethesda System; Cervical Cancer; Liquid-Based Cytology

DOI: 10.4328/JCAM.5763 Received: 22.02.2018 Accepted: 28.03.2018 Published Online: 04.04.2018 Printed: 01.09.2018 J Clin Anal Med 2018;9(5): 359-62
Corresponding Author: Seyhan Özakkoyunlu Hasçiçek, Department of Pathology, University of Health Sciences Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey. GSM: +905370223868 E-Mail address: Shascicek@gmail.com
ORCID ID: 0000-0002-3243-8811

Introduction

Cervical cancer is still a health problem in countries where cervical cancer scanning is not routinely performed; despite this, cervical cancer is one of the human malignancies that can be successfully reduced by medical intervention [1,2]. Premalignant lesions are characterized by abnormal cellular or epithelial architecture in the areas surrounding the junction between the squamous and columnar epithelium [3]. The American Society for Colposcopy and Cervical Pathology (ASCCP) recommends initial cervical sampling for women 21 years old, Pap test every three years for women 21-29 years old; it prefers co-testing (Pap test and HPV testing) every five years for women over 30 years old. In 1940 the Pap test was developed by George Papanicolau [4]. An important decrease in the rate of mortality from cervical cancer has been observed following introduction of the Pap test [4]. In the Pap test technique, because of the coverage of abnormal cells with blood, mucus, or inflammation, there can be increase in the false negative rates [5,6,7]. The liquid-based cytology (LBC) test was developed in 1960s and 1970s to decrease the rates of false negatives [8]. The 2001 Bethesda system, the most widely accepted classification to report cervical cancer, was updated in 2014 with no significant changes. In the Bethesda system, squamous epithelial cell abnormality is divided into five categories: Atypical squamous cells of undetermined significance (ASCUS), atypical squamous cells cannot exclude HSIL (ASC-H), low grade squamous intraepithelial lesion (LSIL), high grade squamous intraepithelial lesion (HSIL), and squamous cell carcinoma (SCC). According to the WHO classification 2014, squamous cell tumors and precursor lesions are divided into 3 categories: Low grade squamous intraepithelial lesion, high grade squamous intraepithelial lesion, and squamous cell carcinoma, NOS [9]. In this study we compared our cytology results of 'squamous epithelial cell abnormality' with histopathologic results and aimed to evaluate the accuracy of cytology in detecting precancerous lesions and squamous cell carcinoma.

Material and Method

The Pap test reports of 300 patients who had both cervical smears and cervical biopsies diagnosed with epithelial cell abnormality between 2014-2016 were reevaluated retrospectively. Cervical cytology materials were taken by a "broom-like" device with detachable head and this head was placed in ethanol-based preservative fluid. The LBC test SurePath was used. Slides that contained more than 5000 epithelial cells were evaluated according to the Bethesda 2001 classification. Biopsy materials were routinely stained with the hematoxylin eosin method. After histopathological examination we classified the results into 4 categories according to the WHO classification 2014. For statistical analyses SSPS statistics 24 (IBM SPSS, Turkey) was used. We determined the sensitivity, specificity, and positive and negative predictive values of each method—SurePath LBC and histopathology.

Results

All Pap test reports between 2014-2016 were documented with a retrospective database search. 20452 cervical cytology reports were analyzed; ASCUS, ASC-H, LSIL, HSIL, and SCC rates were 3.93%, 0.1%, 1.11%, 0.51%, and 0.01% respectively. The mean age of the patients was 40.08 (range: 16-85 years). Cytology results of 273 patients (91%) were abnormal, while 27 patients (9%) had normal results. Of the 273 patients, 140 (46.7%) were ASCUS, 25 (8.3%) were ASC-H, 78 (26 %) were LSIL, 28 (9.3 %) were HSIL, and 2 (0.7 %) were SCC (Table 1). Among the 300 patients, 122 patients (40.7%) had normal biopsy results, 114 patients (38%) were LSIL, 61 patients (20.3%) were HSIL, and 3 patients (1.0%) were SCC (Table 2). Comparison of LBC with histopathology showed that of the 273 patients with abnormal cytology, 160 (58.6%) had abnormal biopsy results. 18 patients had abnormal biyopsy results while cytology was normal and 9 patients had normal biopsy results while cytology was abnormal (Table 3,4). The calculated sensitivity and specificity for LBC were 89.89% and 7.38%, indicating low accuracy. The sensitivity, specificity, and positive-negative predictive values of cervical cytology for ASCUS, ASC-H, LSIL, HSIL, and SCC diagnoses are given in Table 5.

Table 1. Liquid-based cytology results of all patients

Cytology	Number of patients	%
Normal	27	9.0
ASCUS	140	46.7
ASC – H	25	8.3
LSIL	78	26
HSIL	28	9.3
SCC	2	0.7
Total	300	100

Table 2. Biopsy results of all patients

Biopsy results of patients	Number	%
Normal	122	40.7
LSIL	114	38
HSIL	61	20.3
SCC	3	1
Total	300	100

Table 3. Correlation of cytology and biopsy results

LBC	Biopsy			
	Abnormal	Normal	Kappa	P-value
Abnormal	160 (58.6%)	113 (41.4%)	0.10	p›0.05
Normal	18 (66.6%)	9 (33.3%)		

Table 4. Detailed correlation of cytology and biopsy results

Cytology / Biopsy	Normal	LSIL	HSIL	SCC
N	9	12	6	0
ASCUS	80	47	13	0
ASC-H	12	7	6	0
LSIL	19	45	14	0
HSIL	2	3	20	3
SCC	0	0	2	0

Table 5. Cytology accuracy for ASCUS, ASC-H, LSIL, HSIL

	Sensitivity	Specificity	PPV	NPV
ASCUS	34%	34%	43%	26%
ASC-H	7%	90%	52%	40%
LSIL	33%	84%	76%	46%
HSIL	15%	98%	93%	44%

Discussion

Cervical cancer is a preventable disease if we are successful in early diagnosis. Since the introduction of cytology into clinical practice by Papanicolaou and Traut in 1944, we have been able to detect preinvasive stages, thereby reducing the morbidity and mortality of this disease. By 2001, revised Bethesda system terminology had created the need for a standard approach to manage abnormal cervical cytology cases for managing minor cervical cytological abnormalities [10]. In 2014 the Bethesda system was updated with no significant changes. Then, the American Society for Colposcopy and Cervical Pathology (ASCCP) initiated a process for developing evidence-based consensus guidelines to aid clinicians in managing abnormal cytology results [11,12].

Over the years, knowledge has advanced and standard scanning programs have changed. In 2012, national organizations published guidelines such as the Lower Anogenital Squamous Terminology (LATS) and the American Society for Colposcopy and Cervical Pathology (ASCCP) consensus, which recommend longer scanning intervals and a later age to start scanning [13,14]. The 5-year risk of CIN 3 is only 8/10000 in women aged 30-64 years with negative co-test [15]. Today, co-testing with cytology and HPV testing at 5-year intervals is preferred for women aged 30-64 years for cervical cancer scanning [16,17].

In our study, the squamous cell abnormalities were present in 91% of the cytology materials. ASCUS was present in 46.7% , ASC-H in 8.3%, LSIL in 26%, HSIL in 9.3%, and SCC in 0.7% of the cases. In the ASCUS diagnosed group, 57.1% had healthy cervical biopsy, 33.6% were LSIL, and 9.3% were HSIL. ASCUS is the most common cytological abnormality. It carries the lowest risk of HSIL and one-third to two-thirds are not human papilloma virus (HPV) associated [13]. LATS and ASCCP guidelines are recommended to manage ASCUS cases with HPV-negative co-testing results with routine follow-up at 3 years. For women with HPV positive ASCUS, colposcopy is recommended. If we can't identify cervical intraepitelial lesion in HPV positive ASCUS by colposcopy, co-testing at 12 months is recommended. For women with ASCUS cytology and no HPV result, repeating cytology at 1 year is acceptable [13]. Overtreatment should be avoided as the routine use of diagnostic excisional procedures such as loop electrosurgical excision for women with an initial ASCUS in the absence of HSIL is not appropriate [13].

Biopsy of LSIL patients with cytology showed LSIL in 57.7% and HSIL in 17.9%. LSIL is highly associated with HPV infection. According to ASCCP consensus guidelines, colposcopy is recommended for women with LSIL cytology and no HPV test or positive HPV test. For LSIL cases with negative HPV test, repeating co-testing at 1 year is preferred; colposcopy is also acceptable. According to analysis of the Kaiser Permanente Northern California Medical Care plan (KPNC), women with LSIL at ages of 21-24 years carry a lower risk of HSIL than older women [14]. Following up these women with cytology at 12 month intervals is recommended [13]. In the KPNC database, risk of HSIL in HPV-negative LSIL cases is low, similar to ASCUS alone [14].

Fallani et al. compared biopsy results of patients with ASCUS and SIL cytological diagnosis; biopsy of ASCUS patients showed LSIL in 36.3% and HSIL in 15.7% [15]. The researchers found LSIL in 67.7% and HSIL in 20.8% of the SIL patients [18]. In our outcomes, abnormal biopsy findings were 42.9% in the ASCUS group, 52% in the ASC-H group, 75.6% in the LSIL group, 92.8 in the HSIL group and 100% in the SCC group. Atılgan et al. reported biopsy positivity 56% in the ASCUS group, 50% in the ASC-H group, 66% in the LSIL, and 100% in the HSIL group [19]. The ASCUS/SIL ratio is useful for assessment of intralaboratory and interlaboratory comparison. The prevalance rates for both ASCUS and SIL depend on the risk factors of the patient population and ASCUS / SIL ratio provides some degree of correction [20]. In a study by Geisinger et al., the ASCUS / SIL ratio changed from 0.58 to 1.02 [21]. The Turkish Cervical Cancer and Cervical Cytology Research Group indicated a value of 2.0 for ASCUS /SIL ratio [22]. Our ASCUS / SIL ratio is nearly 1.4.

The management of treatment in diagnosis of epithelial cell abnormality in cervical cytology should be according to the sets of specified protocols. Our study suggests that we may encounter HSIL with the diagnosis of ASCUS. Clinicians should keep in mind that results of microscopic evaluation depend on factors such as appropriate sampling, adequacy of the material, preparation of the slide, and the attention and experience of the pathologist. Our proposal for clinicians is to evaluate cytological diagnosis with other diagnostic methods and select the best treatment method for patients according to the guidelines.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Syrjänen K, Di Bonito L, Gonçalves L, Murjal L, Santamaria M, Mahovlic V et al. Cervical cancer screening in Mediterranean countries: Implications for the future. Cytopathology 2010;21:359-67.
2. Cobucci R, Maisonnette M, Macedo E, Santos Filho F C, Rodovalho P, Nobrega M M et al. A PAP test accuracy and severity of squamous intraepitelial lesion. Indian J Cancer 2016;53:74-6.
3. Alphs HH, Wu TC, Roden RBS. Prevention and treatment of cervical cancer by vaccination. Moleculer pathology of gynecology cancer. Humana Press 2007:125-54.
4. Papanicolaou GN, Traut HF. The diagnostic value of vaginal smears in the carcinoma of the uterus. Am J Obstet Gynecol 1941;42:193-206.
5. Lee KR, Ashfaq R, Birdsong GG, Corkill ME, McIntosh KM, Inhorn SL. Comparison of conventional Papanicolaou smears and fluid-based thin-layer system for cervical cancer screening. Obstet Gynecol 1997; 90 (2):278-84.
6. Budak Ş, Şentürk MB, Kaya C, Akgöl S. A comparative study of conventional and liquid- based cervical cytology. Ginekol Pol 2016;87:190-3.
7. Rozemeijer K, Penning C, Siebers AG, Naber SK, Matthijsse SM, van Ballegooi-

jen M et al. Comparing SurePath, ThinPrep, and conventional cytology as primary test method: SurePath is associated with increased CIN II+ detection rates. Cancer Causes & Control 2016;27(1):15-25.
8. Meijer CJ, Walboomers JM. Cervical cytology after 2000: where to go? J Clin Pathol 2000;53:41-43.
9. Kurman RJ, Carcangiu ML, Herrington CS, Young RH. WHO classification of tumours of female repruductive organs. 4th ed.Lyon;2014. p.169-182
10. ASC-US - LSIL Triage Study (ALTS) Group. A randomized trial on the management of low grade squamous intraepithelial lesion cytology interpretations. Am J Obstet Gynecol 2003;188:1393-400.
11. Wright TC, Cox JT, Massad LS, Twiggs LB, Wilkinston EJ. 2001 Consensus guidelines for the management of women with cervical cytological abnormalities and cervical cancer precursors: Part1: Cytological abnormalities. JAMA 2002;287:2120-9.
12. Wright TC Jr, Cox JT, Massad LS, Carlson J, Twiggs LB, Wilkinson EJ. 2001 ASCCP-sponsored Consensus Workshop.2001 consensus guidelines for the management of women with cervical intraepithelial neoplasia. J Low Genit Tract Dis 2003;7(3):154-67.
13. Katki HA, Schiffman M, Castle PE, Fetterman B, Poitras NE, Lorey T, et al. Five-Year Risk of CIN 3+ and cervical cancer among women with HPV testing of ASC-US Pap Results. J Low Genit Tract Dis 2013;17:36-42.
14. Massad LS, Einstein MH, Huh WK, Katki HA, Kinney WK, Schiffman M et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. Obstetrics & Gynecology 2013; 121(4):829-46.
15. Fallani MG, Pena C, Fambrini M, Marchionni M. Cervical cytologic reports of ASCUS and LSIL. Cyto-histological correlation and implication for manegement. Minerva Ginecol 2002;54(3):263-9.
16. Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam SL, Cain J et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin 2012;62:147-72.
17. Moyer VA, LeFevre ML, Siu AL, Bibbins-Domingo K,Curry SJ, Flores G et al. For the U.S. Preventive Services Task Force. Screening for cervical cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2012;156:880-91.
18. Barut MU, Kale A, Kuyumcuoğlu U, Bozkurt M, Ağaçayak E, Özekinci S et al. Analysis of sensitivity, specificity and positive and negative predictive values of smear and colposcopy in diagnosis of premalignant and malignant cervical lesions. Med Sci Monit 2015;21:3860-7
19. Atılgan R, Artaş G, Kaplan S, Özkan ZS, Kavak SB, Can B et al.Comparison of histopathological results of thinprep and conventional cervicovaginal smears. Fırat Med J 2015;20(1):19-24
20. Ozer A, Albayrak M, Kanat-Pektas M. Pap Smear Abnormalities in Women Admitted to a Tertiary Health Center in Southeast Turkey. J Clin Anal Med. 2016;7(2):210-3.
21. Geisinger KR, Vrbin C, Grzybicki DM, Wagner P, Garvin AJ, Raab SS. Interobserver variability in human papillomavirus test results in cervicovaginal cytologic specimens interpreted as atypical squamous cells. Am J Clin Pathol 2007;128(6):1010-4.
22. Turkish Cervical Cancer and Cervical Cytology Research Group. Prevalance of cervical cytological abnormalities in Turkey. Int J Gynaecol Obstet 2009;106(3):206-9.

How to cite this article:
Hasçiçek SÖ, Oğuzsoy T, Eken KG, Kabukçuoğlu F. Comparison of liquid-based cytology cervical smears with histopathological findings. J Clin Anal Med 2018;9(5): 359-62.