

Original

The Evaluation of Cervical Cancer Screening by Combining Speculoscopy with Papanicolaou Smear Examination in Taiwan

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Key Words

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Background. Cervical cancer is the most common malignancy in women in Taiwan. In order to improve the detection of cervical lesions using the Papanicolaou (Pap) smear in screening, a number of adjunctive tests have been developed. The purpose of this study is to evaluate the utility of a magnified chemiluminescent screening examination (speculoscopy) combined with the Pap smear (PapSure) in detecting cervical cancer.

Methods. A total number of 572 women underwent routine cervical cancer screening by receiving a Pap smear and speculoscopy examination. When either the Pap smear or speculoscopy result was positive, colposcopy was performed. Targeted biopsies were taken from any suspicious lesions that were found by positive colposcopies and the data analyzed using McNemar's test.

Results. Eighty-two women had a positive on either screening test. Of the 62 biopsy specimens obtained, 3 women showed high-grade squamous intraepithelial lesions (HGSIL), and 13 women showed low-grade squamous intraepithelial lesions (LGSIL). The histopathological findings were correlated at different levels with the results of the Pap smear alone and speculoscopy alone and both combined. The Pap smear alone detected 1.0% (6 of 572) of significant pathology, while speculoscopy alone detected 2.3% (13 of 572) of significant pathology. The use of the PapSure showed enhanced detection (16 of 572) compared with either the Pap smear alone or speculoscopy alone.

Conclusions. Speculoscopy can be combined with the Pap smear (PapSure) as a cervical cancer screening test to yield a higher detection rate of biopsy-confirmed cervical pathology in women than the use of the Pap smear or speculoscopy alone. [*Chin Med J (Taipei) 2002;65:430-434*]

Cervical cancer is the most common malignancy in women in Taiwan. The early detection and treatment of precancer, either low-grade squamous intraepithelial lesions (LGSIL) or high-grade squamous intraepithelial lesion (HGSIL), can prevent the majority of cervical squamous cell carcinomas. The primary screening used to detect precancerous abnormalities

and cervical cancer is the Papanicolaou (Pap) smear, which is 1 of the most effective known cancer screens and has succeeded in promoting women's health worldwide.¹ Nevertheless, the sensitivity and specificity of Pap smears vary widely,²⁻⁵ from 11% to 99% and 14% to 97%, respectively. According to a previous study,⁶ the mean sensitivity of the Pap smear in detect-

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ing cervical abnormalities was 58% in screening populations and 66% in follow-up populations. In order to improve the screening detection of cervical lesions by the Pap smear, a number of adjunctive tests have been developed.⁷⁻¹⁰ For instance, speculoscopy, which has been approved by the Food and Drug Administration in the United States, is a magnified visual examination of both the cervix and vaginal canal by a physician or a qualified technician. It uses chemiluminescent light to detect abnormalities. Studies have found that the combination of Pap smear plus speculoscopy (PapSure) identified pathological findings in a greater percentage of women than screening with the Pap smear alone.^{11,12} The purpose of this study is to evaluate the relative detection rate of the Pap smear and/or speculoscopy for the screening of cervical cancer in Taiwanese women.

Methods

A total of 572 women were studied in the outpatient department at Kaohsiung Municipal Ta-Tung Hospital from October to December 2000. All of them had not received the Pap smear examination for more than three years or had received regular Pap smear examinations whereby results had more than twice shown an inflammatory change. They were enrolled and received a Pap smear and speculoscopy. The sampling of Pap smears was obtained according to standard procedures.¹³ Pap smear examinations were performed at the Department of Pathology, Kaohsiung Municipal Min-Sheng Hospital. Cellular morphological abnormalities more severe than inflammatory atypia were recorded as a positive result in cytological screening. Interpretation and classification of cytological abnormalities were based on the diagnostic criteria as described by Coleman & Kurman.^{14,15} Once Pap smear results were obtained, speculoscopy was performed as described previously.^{11,16} In brief, the cervix and the vagina were then washed with 5% acetic acid, and the room lights either dimmed or extinguished. Following a 30 to 40 second delay, the cervix was examined using an activated blue-white Speculite chemiluminescent light (Trylon Corporation, Torrance,

CA) attached to the upper dilator blade of the vaginal speculum and inserted into the vagina. Under low-power magnification (6X), the cervix was then observed using binocular glasses to detect acetowhite lesions.

A Pap smear was considered to be positive if it showed either a LGSIL or HGSIL, or atypical squamous cells of undetermined significance (ASCUS). Pap smears were considered negative if read as normal, displaying inflammatory changes or metaplasia. Speculoscopy was considered to be positive when a distinct acetowhite area was observed. If either the Pap smear or the speculoscopy result was positive, the result of PapSure was also considered positive, and then colposcopy was performed. Targeted biopsies for histopathologic evaluation were taken from any suspicious lesions that were found by colposcopy. Biopsy specimens were examined and reported by pathologists at the Cancer Society of Kaohsiung City, Department of Pathology. Tissue slices were stained with haematoxylin-eosin using standard procedures. The histopathologic diagnoses were classified by CIN (Cervical Intraepithelial Neoplasia) grading, described as CIN 1, CIN 2, CIN 3, and invasive cancer.¹⁷ Flat condyloma (FC) and CIN 1 were regarded as LGSIL, while CIN 2 and CIN 3, were considered to be HGSIL.¹⁸

True positive results were chosen from one of the following pathological conditions: FC, CIN 1, CIN 2, CIN 3, or invasive cancer. True and false negative results could not be exactly identified since biopsies could not be performed on the women with negative cytological and colposcopic screening. Therefore, pathological references were not available for the negative screening results. However, four parameters were used to compare the respective efficiencies of the Pap smear, speculoscopy and PapSure as screening methods,¹⁹ which were:

1. The detection rate (DR): the number of true positive pathologic reports divided by the total number of women screened.
2. The ratio of sensitivities (Rse): the detection rate of one screening method divided by the detection rate of the other screening method.
3. The approximated specificity: being uncertain about

true or false negatives, we could approximate the specificity by the number of negative screening results divided by the total number of women screened subtracted from the number of women with pathological lesions.

4. The positive predictive value: the number of women with pathological lesions divided by the number of women with positive screening results.

Data were analyzed using McNemar's test. A p value < 0.05 was considered statistically significant.

Results

A total of 572 women who fulfilled the criteria of screening were studied. Of them 362 (63.3%) were menopausal, 199 (34.8%) were postmenopausal, and 11 (1.9%) had had a surgical operation of total abdominal hysterectomy that was not due to a cervical malignant condition. As shown in Table 1, 7 (1.2%) women had positive Pap smears and 79 (13.8%) had positive speculscopy examinations. Using the PapSure method, 82 (14.3%) women were positive and underwent colposcopy. Overall, 85.7% of the women (490 of 572) were negative for both the Pap smear and speculscopy, while less than 1% (4 of 572) were positive for both screens.

Of the 82 women who underwent colposcopy, 62 (75.6%) had a positive colposcopic examination. Of the 62 women who underwent a cervical biopsy, 7 had

a positive Pap smear, 59 had a positive speculscopy and 4 had positives for both tests. Biopsies were not obtained from women with a negative colposcopy, since the women were assumed to exhibit no cervical pathological process. The pathology and corresponding findings on either colposcopy or speculscopy are shown in Table 1. A total of 16 women were proved cervical pathology by histology and the remaining 46 women showed negative findings. The distribution of the histopathologic findings indicates that 13 women were LGSIL (FC or CIN 1) and 3 women were HGSIL (CIN 2 or 3). Of the 3 women with documented HGSIL, 2 had positive Pap smears, while 2 had positive speculscopy. Of the 13 women with LGSIL, 2 women showed positive Pap smears, and negative speculscopy, 2 women showed positive on both screens, and 9 women showed negative Pap smears, and positive speculscopy.

Table 2 displays the results of histopathologic findings correlated with the results of the Pap smear and speculscopy alone as well as combined. Pap smears alone detected 1.0% (6 of 572) of significant pathology, and speculscopy alone detected 2.3% (13 of 572) of significant pathology. However, the detection rate of PapSure was 2.8% (16 of 572), which shows an enhanced detection rate compared with either the Pap smear alone or speculscopy alone.

Further analysis of the findings, presented in Table 3, reveals the comparison of sensitivities between the Pap smear and speculscopy in the detection of all

Table 1. Relationship between the results of combined examination and histopathology findings in 572 women screened

Screening results	No. of patients	Biopsy done	Histopathology				
			NP	FC	CIN 1	CIN 2	CIN 3
Speculscopy (+) Pap smear (+)	4	4	1	2	0	0	1
Speculscopy (+) Pap smear (-)	75	55	45	4	5	0	1
Speculscopy (-) Pap smear (+)	3	3	0	0	2	0	1
Speculscopy (-) Pap smear (-)	490	0	0	0	0	0	0
Total	572	62	46	6	7	0	3

NP = negative pathology; FC = flat condyloma; CIN = cervical intraepithelial neoplasia; (+) = positive screening results; (-) = negative screening results.

Table 2. The detection rates of speculoscopy and Pap smear

Screening methods	Histopathology			Total
	CIN 2/CIN 3	FC/CIN 1	Normal	
Speculoscopy				
Positive	2	11	66	79
Negative	1	2	490	493
Pap smear				
Positive	2	4	1	7
Negative	1	9	555	565
Total	3	13	556	572

CIN = cervical intraepithelial neoplasia; FC = flat condyloma.

Table 3. Contingency tables for comparing results from speculoscopy, Pap smear and PapSure in screening groups (n = 572)

Pap smear	Pathologic lesions		Normal	
	Positive	Negative	Positive	Negative
Speculoscopy				
Positive	3	10	1	65
Negative	3	0	0	490
PapSure				
Positive	6	10	1	65
Negative	0	0	0	490

pathologic lesions. According to the data in Table 3, the ratio of sensitivity of speculoscopy to Pap smear was calculated at 2.2 (13 vs 6), while the ratio for PapSure to Pap smear alone was approximately 2.7 (16 vs 6). The results in Table 4 indicate that the speculoscopy compared to the Pap smear greatly enhances test sensitivity. However, the specificity value decreases significantly, from 99.8% for the Pap smear alone to 88.1% for the speculoscopy alone (McNemar's test, $\chi^2 = 63.0, p < 0.05$). The findings indicate that

PapSure tends to increase Pap smear sensitivity but decrease Pap smear specificity.

Discussion

In an official report of Pap smears²⁰ taken from January to December 1999, the positive detection rate in Taiwan was only 1.01%, far lower than that reported in the United States. The present study indicates that a lower detection rate of cervical cancer is also found using the Pap smear alone. In the PapSure test, the combination of the Pap smear with speculoscopy, the ratio of sensitivities increased significantly, to 2.7, as compared to the Pap smear alone. In previous studies,^{11,12,21-23} similar results were found whereby the combination of speculoscopy with the Pap smear could improve the detection of both high-grade and low-grade cervical lesions. The 2 screening tests, which use different methods of detection, should be considered as independent and complementary screening tools. The Pap smear procedure involves a microscopic examination of a slide prepared from brushing or scraping cell exfoliated from the surface epithelium. Speculoscopy is a visual examination of the cervix using low-energy chemiluminescent light to detect the abnormal epithelium.²³ However, the final diagnosis rests on a histopathologic examination.

In addition to higher sensitivity of the PapSure, the most important finding was that of the 16 women who were documented with cervical pathology, 13 had LGSIL. Of those 13 women with LGSIL, 9 (69.2%) had negative Pap smears but were positive on speculoscopy (Table 1). With the combination of the Pap smear and speculoscopy, all lesions would have

Table 4. Comparison of the efficacy of speculoscopy, Pap smear and PapSure in detection of all pathologic lesions

	Speculoscopy	Pap smear	PapSure
Detection rate (%)	2.3	1.0	2.8
Ratio of sensitivities	2.2 (13/6) ^a	1.0	2.7 (16/6) ^b
McNemar's test for sensitivity	$\chi^2 = 2.77, p > 0.05^a$		
Specificity (%)	88.1	99.8	88.1
McNemar's test for specificity	$\chi^2 = 63.0, p < 0.05^a$		
Positive predictive value (%)	16.5	85.7	19.5

^aspeculoscopy vs Pap smear; ^bPapSure vs Pap smear.

been detected. Of the 2 examinations, speculoscopy is more sensitive than the Pap smear in detecting low-grade lesions. Early detection of LGSIL is important in that the type of lesion has a high risk of developing into more severe lesions. On the other hand, speculoscopy findings are less specific than those taken from the Pap smear test (88.1% vs 99.8%). For screening purposes, the early diagnosis and treatment is worthwhile to prevent the development of severe disease. Although the utilization of speculoscopy method alone shows a high false positive rate (83.5%), the combination with the Pap smear appears to have the higher detection rate in asymptomatic population. The discrepancy between the findings of speculoscopy and the Pap smear test may be attributed to the fact that the Pap smear is insufficient in identifying lesions and may be incapable of detecting lesions on the cervix. Thus, the combination of the Pap smear and speculoscopy is essential for more accurate detection of cervical disease.

References

1. Celentano DD, de Lissovoy G. Cervical cancer screening. *Public Health Rev* 1989/1990;17:172-240.
2. Fletcher A, Matyas N, Grubb C, Camberlain J. Four and a half year follow up of women with dyskaryotic cervical smears. *Brit Med J* 1990;301:641-4.
3. Upadhyay SN, Jha RS, Sinha TK, Mishra NK. Accuracy of cytology in screening for cervical cancer. *Indian J Med Res* 1984;80:457-62.
4. Jones DE, Creasman WT, Dombroski RA, Lentz SS, Waeltz JL. Evaluation of the atypical Pap smear. *Am J Obstet Gynecol* 1987;157:544-9.
5. Singh P, Pang M, Ratnam SS. Selective cervical conization following colposcopy: a critical evaluation of 107 cases. *Singapore Med J* 1985;26:289-94.
6. Fahey MT, Irwig L, Macaskill P. Meta-analysis of Pap test accuracy. *Am J Epidemiol* 1995;141:680-9.
7. Benedet JL, Anderson GH, Matisic JP. A comprehensive program for cervical cancer detection and management. *Am J Obstet Gynecol* 1992;166:1254-9.
8. Lonky NM, Edwards G. Comparison of chemiluminescent light versus incandescent light in the visualization of acetowhitened epithelium. *Am J Gynecol Health* 1992;6:11-5.
9. Lonky NM, Mann WJ, Massad LS, Mutch DG, Blanco JS, Vasilev SA, et al. Ability of visual tests to predict underlying cervical neoplasia: colposcopy and speculoscopy. *Obstet Gynecol Surv* 1996;51:102-4.
10. Taylor LA, Sorensen SV, Ray NF, Halpern MT, Harper DM. Cost-effectiveness of the conventional Papanicolaou test with a new adjunct to cytologic screening for squamous cell carcinoma of the uterine cervix and its precursors. *Arch Fam Med* 2000;9:713-21.
11. Mann W, Lonky N, Massad S, Scotti R, Blanco J, Vasilev S. Papanicolaou smear screening augmented by a magnified chemiluminescent exam. *Int J Gynaecol Obstet* 1993;43:289-96.
12. Wertlake PT, Francus K, Newkirk GR, Parham GP. Effectiveness of the Papanicolaou smear and speculoscopy as compared with the Papanicolaou smear alone: a community-based clinical trial. *Obstet Gynecol* 1997;90:421-7.
13. Berek JS, Adashi EY, Hillard PA. *Novak's Gynecology*. 12th edition. Baltimore: Williams & Wilkins, 1996:454-5.
14. Coleman DV, Evans DMD. *Biopsy Pathology and Cytology of the Cervix*. London: Chapman and Hall Medical, 1988:197-205.
15. Kurman RJ, Malkasian GD Jr, Sedlis A, Solomon D. From Papanicolaou to Bethesda: the rationale for a new cervical cytologic classification. *Obstet Gynecol* 1991;77:779-82.
16. Loiudice L, Abbiati R, Boselli F, Gecchini G, Costa S, Grossi E, et al. Improvement of Pap smear sensitivity using a visual adjunctive procedure: a co-operative Italian study on speculoscopy (GISPE). *Eur J Cancer Prev* 1998;7:295-304.
17. Fu YS, Reagan JW. Pathology of the uterine cervix, vagina, and vulva. In: Bennington JL, ed. *Major Problems in Pathology*, Vol 21. Philadelphia: W.B. Saunders, 1989:225-35.
18. Richart RM. A modified terminology for cervical intraepithelial neoplasia. *Obstet Gynecol* 1990;75:131-3.
19. Shatzkin A, Connor RJ, Taylor PR, Bunnag B. Comparing new and old screening tests when a reference procedure cannot be performed on all screenees. *Am J Epidemiol* 1987;125:672-8.
20. Department of Health, the Executive Yuan, R.O.C. *Pap smear screening registry system annual report* 2000;9:26.
21. Edwards G, Rutkowski C, Palmer C. Cervical cancer screening with Papanicolaou smear plus speculoscopy by nurse practitioners in a health maintenance organization. *J Lower Genit Tract Dis* 1997;1:141-7.
22. Massad LS. The role of speculoscopy in the diagnosis of cervical dysplasia. *J Lower Genit Tract Dis* 1997;1:154-8.
23. Massad LS, Lonky NM, Mutch DG, Mann WJ, Blanco JS, Vasilev SA, et al. Use of speculoscopy in the evaluation of women with atypical Papanicolaou smears: improved cost effectiveness by selective colposcopy. *J Reprod Med* 1993;38:163-9.