Screening for cancer of the cervix with simultaneous Pap smear and colposcopy. – The efficacy of Pap smear and colposcopy –

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Summary

Objective: Some Japanese institutes have been performing a population screening program for cervix cancer involving the simultaneous use of Pap smear and colposcopy. This program may be a good model for evaluating the efficacy of Pap smears and colposcopy. *Methods & Materials:* The subjects included 2,000 women who underwent primary screening at the Kanagawa Health Service Association. *Results:* 1) The incidence of ACF (atypical colposcopic findings) was 3.6%, whereas that of abnormal Pap smears (ASC-US and above) was 1.1%; 2) Of 88 women who showed abnormal findings on Pap smear and/or colposcopy, only three cases appeared abnormal in both methods, i.e., the two methods were complementary; 3) Colposcopy was more useful for detecting mild dysplasia than the Pap smear. However, colposcopy may possibly detect benign reparatory lesions; 4) The incidence of unsatisfactory colposcopic findings (UCF) was high (24.2%), whereas no unsatisfactory cases were found by Pap smear. *Conclusions:* The sensitivity of the Pap smear for detecting mild dysplasia is low, whereas that of colposcopy is high. However, colposcopy may not be suitable for primary screening due to its high UCF. The low sensitivity of Pap smears may be improved by repetition or adding ancillary HPV testing.

Key words: Pap smear; Colposcopy; Cervical cancer; Screening.

Introduction

It has been clarified that cancer of the cervix originates from human papillomavirus (HPV) infection [1]. Accordingly, the introduction of HPV testing has been suggested as the useful strategy for screening of this cancer [2, 3].

The standard screening method for this type of cancer is use of the Pap smear as the primary screening method, and colposcopy for the detailed exam. The Kanagawa Health Service Association, however, has a long history of using Pap smears and colposcopy simultaneously for primary screening. This program may be a good model for evaluating the two methods.

The present study evaluated the role and efficacy of the Pap smear and colposcopy in primary screening for cancer of the cervix.

Materials and Methods

Materials

The subjects included 2,000 consecutive women who underwent screening at the Central Clinic of the Kanagawa Health Service Association between February 10 and September 15, 2009. The screening programs are based on governmental or company regulations or individual application. The cytology sampling and colposcopy were performed by the first author.

Methods

– Pap smear

The cell samples were obtained using a cotton tip (Osaki applicator, Osaki Medical Co. Ltd, Nagoya, Japan) and cytobrush plus (Medscand Medical and CooperSurgical Co., Trumbull, USA) rinsed with physiological saline for the vaginal portio and the cervical canal, respectively, and the cells from the two samples were separately placed onto each half of a slide, and the tips of the instruments were rotated without making the cell-free area on the slide. The slide samples were immediately placed into 95% ethyl alcohol for fixation. Then, the samples were sent to the Cytology Center of our Institution and processed using routine Papanicolaou staining and diagnostic procedures.

The cytologic diagnosis was based on the Bethesda System for reporting cervical cytology [4, 5].

– Colposcopy

The colposcopic diagnosis was based on the Barcelona 2002 colposcopic classification [6]. Additionally, normal colposcopic findings (NCF) were divided into two subcategories, NCF I and NCF II. Abnormal colposcopic findings (ACF) were divided into four groups, according to their subgroupings for white epithelium (W), punctation (P) and mosaic (M), which were divided into three categories, as listed below.

NCF

1) NCF I: NCF with a squamocolumnar junction (SCJ) localized outside of the external os.

2) NCF II: NCF with a SCJ localized within the cervical canal that was confirmed by opening the canal with a forceps.

ACF

3) ACF1: W1, M1, P1, in which squamous metaplasia was suspected.

4) ACF2: W2, M2, P2, in which mild or moderate dysplasia was suspected.

5) ACF3: W3, M3, P3, in which severe dysplasia or carcinoma in situ was suspected.

6) ACF4: atypical vessels (aV) associated with W, M, P, in which microinvasive cancer was suspected.

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Fig. 1

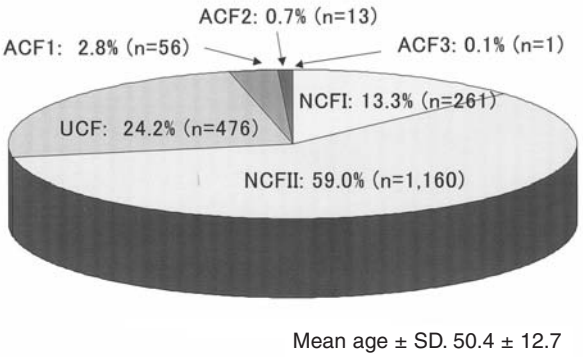

Fig. 2

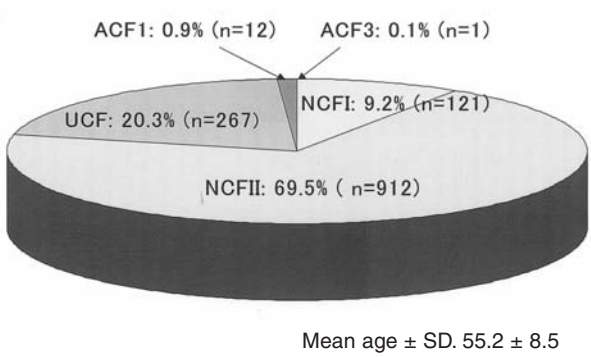

Fig. 3

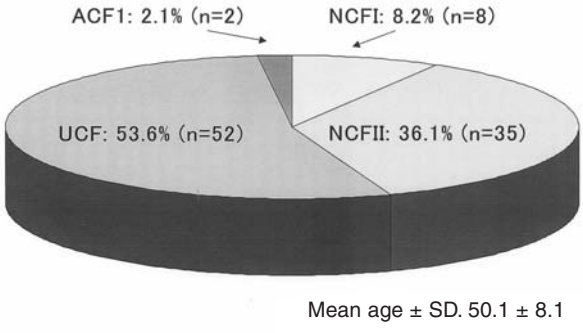

Fig. 4

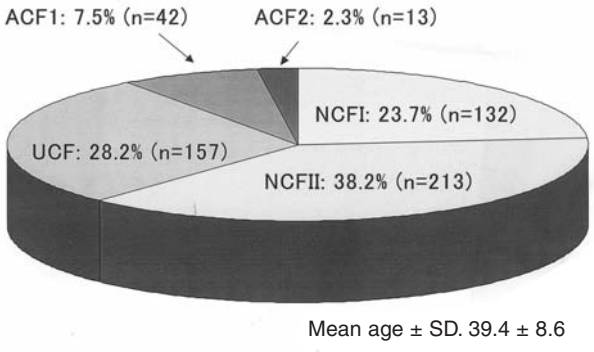

Figure 1. — Distribution of colposcopic findings in all women screened (n = 1,967).
Figure 2. — Distribution of colposcopic findings in women who had undergone vaginal delivery (n = 1,313).
Figure 3. — Distribution of colposcopic findings in women who had undergone cesarean section (n = 97).
Figure 4. — Distribution of colposcopic findings in women who had never undergone a delivery (n = 557).

W was quantitatively subgrouped based on thickness, i.e., color (bluish, pure, or ivory white) and surface texture (smooth or coarse). M was based on the presence of a regular or irregular vessel network and vessel diameter. P was based on the distance between Ps and P shape.

Suggestions for women who demonstrated abnormal Pap smear or colposcopy findings.

Women with ASC-US were advised to undergo a second cytology examination within six months, and those with ACF1 were instructed to undergo a second colposcopy within one year. Those with LSIL or ACF2 or worse findings were advised to undergo a detailed examination involving cytology, colposcopy, and colposcopy-guided biopsy.

Results

Thirty-three women had undergone hysterectomy (calculated from the 335th subject, and the incidence of hysterectomy was 2.0%). Therefore, 1,967 women underwent the "pure" screening for cervical cancer.

Incidence of unsatisfactory Pap smear and colposcopy findings

Incidence of unsatisfactory colposcopic findings (UCF), NCF I, and NCF II in the 1,967 women who underwent colposcopy was 24.2%, 13.3%, and 59.0%, respectively (Figure 1, mean age ± SD: 50.4 ± 12.7).

When subgrouped according to delivery history and delivery modality, the incidence of women who had undergone vaginal delivery including cesarean section (CS) in one of multiple deliveries, those who had only undergone CS and those who had no history of delivery was 67.0% (n = 1,340, mean age ± SD; 55.2 ± 8.5), 5.0% (n = 99, 50.1 ± 8.1), and 28.1% (n = 561, 39.4 ± 8.6), respectively. Incidence of UCF in these three subgroups was 20.3% (Figure 2), 53.6% (Figure 3), and 38.2% (Figure 4), respectively.

In Pap smears, no unsatisfactory cases were encountered in this series.

Abnormal findings

– Colposcopy

Incidence of ACF1, ACF2, and ACF3 in colposcopy was 2.8% (n = 56), 0.7% (n = 13) and 0.1% (n = 1), respectively, and the overall incidence was 3.6% (Figure 1). No ACF4 or worse findings were found. Among the subgroups of delivery modality, the incidence of ACF in the women who underwent vaginal delivery, CS, and those with no delivery history was 1.0% (ACF1: 0.9% and ACF3: 0.1%) (Figure 2), 2.1% (only ACF1) (Figure 3), and 9.8% (ACF1: 7.5% and ACF2: 2.3%) (Figure 4), respectively.

– Pap smear

The incidence of an abnormal Pap smear was 1.1%, including incidences of 0.7% (n = 14) for ASC-US, 0.1% (n = 1) for AGC, and 0.3% (n = 6) for LSIL. There were no cases with HSIL or worse findings in this series.

Of the colposcopy findings of 14 cases with ASC-US and one with AGC, 11 were classified as NCF, two as UCF, and two as ACF1. In six LSIL cases the colposcopy findings were classified as NCF in 4, UCF in one, and ACF1 in one case.

– Cases with both abnormal Pap smear and colposcopy findings

Only three cases presented abnormal findings for both cytology and colposcopy, although 88 cases presented abnormal findings in one of the two methods. All three cases were classified as ACF1 on colposcopy, and two were found to be ASC-US, and one was found to be LSIL on Pap smear. The latter case was confirmed to be moderate dysplasia after a detailed exam. The other two cases are being followed-up.

– Diagnosis at the detailed examination

Cases that were classified as ACF1 on colposcopy were subjected to the standard follow-up procedure without a detailed examination. However, one case that was also classified as LSIL on Pap smear, was subjected to a detailed exam, and moderate dysplasia was diagnosed, as mentioned above. In 13 cases classified as ACF2 and one classified as ACF3, eight cases of mild dysplasia were diagnosed, and the other six are currently being examined. All of these cases were found to be negative by cytology.

No lesion was found in 15 cases that were classified as either ASC-US or AGC excluding five that are currently being investigated, and in six cases classified as LSIL, one case of moderate dysplasia and two of mild dysplasia were found, and the other three are currently being examined. The two cases of mild dysplasia were grouped in NCF by colposcopy at the primary screening. However, a tiny ACF1 lesion was found on the external os during a second colposcopy performed as part of the detailed examination, and colposcopy-guided biopsy confirmed mild dysplasia.

Discussion

Cancer of the cervix originates at the squamocolumnar junction (SCJ), where layers of squamous cells and columnar cells come into contact with each other. Therefore, the SCJ should be visualized on colposcopy, and cellular samples should be correctly obtained on Pap smear when screening is performed. The result of colposcopy is categorized as unsatisfactory colposcopic findings (UCF), if the SCJ is not visible. The incidence of UCF was 24.2% in total and 20.3% in women with a history of vaginal delivery, whereas in women with a history of CS and those who had not undergone a previous delivery it was 63.6% and 28.2%, respectively. In other words, at least one out of every four women show unsatisfactory findings on colposcopy. The incidence of UCF was high in the present series, although it is generally considered to range from 10-15%. This may be due to the increasing size of the older age group in the Japanese population. The mean age of the present series was 50.4 ± 12.7. The colposcopy results suggest that colposcopy is not suitable for primary screening for cervical cancer. In contrast, there were no unsatisfactory Pap smear results in this series. The incidence of ASC-US, which is described to be 5% or less in the Bethesda system4), was 0.7%.

The incidence of abnormal findings on colposcopy was 3.6%, and those in women who had undergone vaginal delivery and CS were 1.0% and 2.3%, respectively, whereas that in those who had no history of delivery was 9.8%. Therefore, the screening procedure for women who had no history of delivery should be performed carefully. In contrast, the incidence of abnormal cytology was 1.1%, which is reasonable for primary screening in Japan. However, abnormal colposcopy findings occurred more frequently than abnormal Pap smear findings. The detailed examination revealed that eight cases of mild dysplasia were found through colposcopy, whereas only two cases were found through Pap smear. One case of moderate dysplasia was detected with both methods, although only three cases were found to be abnormal by both methods. In the two cases of mild dysplasia detected by cytology tiny lesions were found on the external os at the secondary colposcopy performed during the detailed examination. Therefore, the two methods act complementarily in the detection of cervical lesions, although it is possible that colposcopy is more able to detect mild dysplasia than the Pap smear. Similar results have been reported by Kuramoto *et al*. [7]. They screened 12,138 women at the Tumor Clinic of Kitasato University Hospital and found abnormal findings with cytology and/or colposcopy in 1,918 women excluding those with cancer. Sensitivity (class III a and above) for mild and moderate dysplasia of the Pap smear was 28% (n = 228) and 61% (n = 100), whereas that for severe dysplasia and carcinoma in situ (CIS) was 92.6% (n = 68) and 96.3% (n = 98), respectively. In contrast, sensitivity of colposcopy was all above 85% regardless of the severity of the lesion. We should realize that the ability of the Pap smear to detect less severe lesions like mild or moderate dysplasia is low, whereas its ability to detect more serious lesions such as severe dysplasia and CIS is high. It has also been found that 74.9% (n = 646) of 862 cases with positive colposcopy and negative cytology findings were diagnosed with reserve cell proliferation or squamous metaplasia [7]. Consequently, we should understand that ACF in colposcopy is not always related to neoplastic lesions with the ability to progress to cervical cancer. Our procedure for an ACF1 lesion is follow-up without biopsy; otherwise, the incidence of the detailed examination would be elevated by a further 2.8%, although more mild dysplasias may also be detected.

Primary screening for cervical cancer using both Pap

smears and colposcopy has been performed in some institutes in Japan as well as Central and Eastern Europe including Hungary [8], whereas that using cytology has only been performed in the USA and Western Europe. Recently, the high sensitivity of HPV testing for detecting cervical lesions has been reported, and it is recommended that the HPV test should be added as an ancillary test when cytology results present findings of ASC-US [2, 5]. In addition, other reports have recommended simultaneous cytology and HPV testing [2] or HPV testing followed by cytology for positive HPV [3]. In other words, the use of colposcopy tends to be firmly restricted. This may be due to the high cost of colposcopy in Western countries compared with that in Japan.

Colposcopy produces a high incidence of unsatisfactory cases, whereas it is better at detecting milder dysplasia than the Pap smear. Therefore, we should be prepared to accept a low incidence of mild lesions in exchange for being able to detect severe lesions if screening is performed using only cytology. Repeating the Pap smear test may compensate for this unfavorable characteristic. Wright [9] reports that the sensitivity of the Pap smear for detecting CIN2 (moderate dysplasia) or worse lesions was 56.4% when ASC-US or worse findings appeared to be positive and 42.2% when those of LSIL or worse were positive, although these results are much lower than those of our series [7]. Conversely, he noted that using HPV testing in addition to cytology elevated the detection sensitivity to 97.4% [9]. HPV testing is a promising ancillary method that could be used to compensate for the low-detection sensitivity of cytology as a replacement for colposcopy.

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