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ORIGINAL ARTICLE

Diagnostic accuracy of cytology and colposcopy in cervical squamous intraepithelial lesions

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Objective. To evaluate the diagnostic accuracy of cytology and colposcopy in women with an abnormal cervical smear using histology as the 'gold standard'.
Design. Survey of consecutively referred women with abnormal smear.
Setting. The out-patient colposcopical clinic of Herning Hospital, Denmark.
Patients. 813 women with a median age of 29.0 years (range 15–71 years) with their first abnormal smear.
Results. For detecting cervical high-grade lesions (HGL) the sensitivity of cytology was 41% (36–47%), of colposcopy 67% (62–72%) and in combination 75% (70–80%), so at least 25% of HGL were underestimated. Colposcopy underestimated more CIN-2 than CIN-3 lesions and more small lesions and lesions in smaller transformation zones. Cytology underestimated more CIN-2 lesions but equal numbers of small and large lesions and transformation zones.
Conclusions. Colposcopy was a better tool for diagnosing HGL than cytology, but even in combination too many HGL were missed. All women with abnormal cytology should therefore have colposcopical and histological investigation and prospective studies of the natural history of cervical squamous lesions should include histological evidence.

Key words: cervix; colposcopy; cytology; dysplasia

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The management strategy for women with abnormal cervical smears varies widely. It has been recommended that women presenting with mild dyskaryosis should be referred for definitive diagnosis by histology of a colposcopically directed biopsy, although recently a more conservative strategy for cytological surveillance of mild dyskaryosis has been suggested (1).

In conducting prospective long term follow-up studies of the natural history of cervical abnormalities the strategy of surveillance also varies, because the diagnoses are based on either cytology alone, colposcopy and cytology or biopsies.

We have conducted a study to evaluate the diagnostic accuracy of cytology and colposcopy in women with abnormal cervical smear, using histology as the 'gold standard'.

Material and methods

During the period 1985 to 1988 a total of 814 women consecutively attended the outpatient clinic of the Department of Obstetrics and Gynecology

Abbreviations:
TZ: transformation zone; CI: confidence interval; HGL: high grade lesion; LGL: low grade lesion.

of Herning Hospital, Denmark, because of their first abnormal cervical smear.

A gynecological history was taken, together with a gynecological examination, and colposcopy was performed by one of two experienced colposcopists (KHF, KCH) before and after application of 4 per cent acetic acid. The size of the lesion and the transformation zone (TZ) were described as small, medium and large when less than 26%, 26–50% and more than 50% of the cervix was engaged, respectively and the colposcopic diagnosis high-grade or low-grade lesion, inflammation or normal cervix was noted.

Directed biopsies were taken from any area with abnormal colposcopic characteristics or if the cervix appeared normal at 6 and 12 o'clock positions on the cervix supplied with an endo-cervical curettage from the non-visible part of the TZ. Twenty-eight patients (3%) were not evaluable by colposcopy because the TZ was completely invisible, all others had either a fully visible or a partly visible TZ. The cytological and histological diagnoses were according to established criteria (2).

No special setting was made for our study. Smears for screening were taken by general practitioners and were screened by pathology laboratory technicians and only the suspicious ones were seen by the pathologist. Women with abnormal smears were then referred for colposcopy and the smear was not repeated.

The histological diagnosis was used as the 'gold standard' to which cytology and colposcopy were compared. The results of all three diagnostic methods were divided into the following categories, partly according to the Bethesda system (3):

- high-grade lesion (HGL): high-grade cervical intraepithelial neoplasia (CIN-2 and CIN-3)
- low-grade lesion (LGL): cellular changes associated with human papillomavirus (HPV), low-grade cervical intraepithelial neoplasia (CIN-1)
- inflammation
- normal (except on cytology)

One woman with no histological diagnosis was excluded.

The results were evaluated by Fisher's exact test and Mann-Whitney rank sum test. Level of significance was 5 per cent and the confidence intervals (CI) are 95 per cent intervals.

Results

The median age among the 813 included women was 29.0 years (range 15–71 years). HGL were found in 42% (340/813) of the included women. No-one had invasive cancer. Women with HGL were older ($p<0.001$) and had larger lesions than the women with LGL (Table I). The relationship between histology and cytology/colposcopy are shown in Table II, III and IV. HGL was compared to non-HGL, i.e. LGL, inflammation or normal. From these figures the sensitivity (high-grade cytology/colposcopy given high-grade histology), the specificity (non-high-grade cytology/colpo-scopy given non-high-grade histology) and the predictive value of high-grade result (high-grade histology given high-grade cytology/colposcopy) and predictive value of low-grade result (non-high-grade histology given non-high-grade cytology/colpo-scopy) using cytology alone, colposcopy alone or

Table I. Age of women and size of lesion

	All	Normal	Inflammation	LGL	HGL
Numbers (%)	813 (100)	61 (7)	6 (1)	406 (50)	340 (42)
Age median	29.0	37.8	20.5	27.0	29.9
Range (years)	15–71	19–63	16–39	15–66	19–71
Size of the lesion					
Small	274 (34)	17 (6)	2 (1)	208 (76)	47 (17)
Medium	245 (30)	6 (2)	1 (0)	105 (43)	133 (55)
Large	207 (25)	1 (0)	0 (0)	58 (28)	148 (72)
No data	87 (11)	37 (43)	3 (3)	35 (40)	12 (14)

Women with high-grade lesions had larger lesions than women with non-high-grade lesions (low-grade lesions, inflammation or normal cervix; $p<0.001$)
Small: < 26 % of the cervix; Medium: 26–50 % of the cervix; Large: > 50 % of the cervix.

Table II. Comparison of cytology and histology

		Histology				
		Normal	Inflam-mation	LGL	HGL	Total
Cytology	inflammation	0	0	2	2	4
	LGL	49	6	345	191	591
	HGL	12	0	55	136	203
Total		61	6	402	329	798

Cytology not available in 15 patients.
LGL: low-grade lesions; HGL: high-grade lesions.

Table III. Comparison of colposcopy and histology

		Histology				
		Normal	Inflam-mation	LGL	HGL	Total
Colposcopy	Normal	27	1	11	1	40
	Inflammation	0	2	14	3	19
	LGL	21	3	316	105	445
	HGL	3	0	54	222	279
	TZ not visible	10	0	10	8	28
Total		61	6	405	339	811

None colposcopic results in two patients.
LGL: low-grade lesions; HGL: high-grade lesions; TZ: transformation zone.

using cytology and colposcopy in combination as diagnostic tools are calculated (Table V).

Cytology alone only diagnosed 41% (36–47%) of HGL and 32% (29–36%) of the LGL or inflammation on cytology were actually HGL on histology (Table II). Colposcopy diagnosed 67% (62–72%) of HGL (Table III) and the combination cytology/colposcopy was best diagnosing 75% (70–80%), but still 25% were underestimated (Table IV). By colposcopy 22% (18–25%) of non-HGL were HGL and combined 18% (15–22%) of non-HGL were HGL on histology.

Colposcopy diagnosed 106 HGL (33 CIN-2 and 73 CIN-3) not found by cytology. In contrast cytology diagnosed 21 HGL (16 CIN-2 and 5 CIN-3) not found by colposcopy.

The size of the TZ had no influence on the numbers underestimated by cytology (Table VI). Cytology underestimated fewer CIN-3 lesions than CIN-2 lesions. Colposcopy diagnosed relatively more of the CIN-3 lesions than the CIN-2 lesions and also more large lesions and lesions in larger TZ.

Table VI. Characteristics of the high-grade lesions, which were underestimated. In numbers (%)

	All High-grade	Underestimated by Cytology	Colposcopy	Both
CIN-2*	119 (100)	80 (67)	58 (49)	47 (39)
CIN-3	201 (100)	109 (54)	47 (23)	36 (18)
Size of transformation zone				
** small	33 (100)	19 (58)	19 (58)	14 (42)
medium	141 (100)	88 (62)	56 (40)	43 (30)
large	146 (100)	82 (56)	30 (21)	26 (18)
Size of lesion				
*** small	44 (100)	27 (61)	29 (66)	21 (48)
medium	130 (100)	79 (61)	48 (37)	40 (31)
large	143 (100)	83 (58)	26 (18)	22 (15)
no data	3 (100)	–	2 (67)	-
Total	320 (100)	189 (59)	103 (32)	83 (26)

* cytology underestimated more CIN-2 than CIN-3 ($p < 0.05$); colposcopy underestimated more CIN-2 than CIN-3 ($p < 0.001$); ** colposcopy underestimated more small TZ ($p < 0.001$). *** colposcopy underestimated more small lesions ($p < 0.001$).
Small: <26% of the cervix. Medium: 26–50% and large: more than 50% of the cervix.

Discussion

In our selected group of women with any degree of abnormal cervical smear admitted to colposcopy, we found that colposcopy was superior to cytology in detecting high grade abnormalities.The sensitivity of cytology was 41% (36–47%) for separating HGL from LGL and this was comparable to others. Reid et al. (4) found a sensitivity of 52% (31–73%) for detecting HGL and Soutter et al. (5) 46% (32–59%). Tabbara et al. (6) found by two different investigators 66% to 79%, but the predictive value of a negative result was as low as 18% and the overall agreement was very poor (*kappa* = 0.18).

We found that colposcopy was a useful tool separating LGL from HGL although this is not agreed by others (7,8). Some have also successfully used colposcopy in detecting human papilloma-virus infection (9, 10).

We underestimated 25% of HGL, especially the CIN-2 lesions and women with smaller lesions and smaller transformation zones. Like others (11, 12) we showed that patients with HGL had larger lesions than others but in contrast to Barton et al. (13) we did not find more false-negative smears in smaller lesions.

It has been stated that mild dyskaryosis should be an indication for immediate referral for colposcopy and biopsy (5, 13–17), as should atypical smears (5, 17, 18). Others suggest a more conservative approach with cytological surveillance and only referral if the dyskaryosis persists (1, 19–24). The numbers of patients recalled for colposcopy might be reduced when a smear is combined with cervicograph and HPV-DNA testing (4). Furthermore quantifying the HPV-16 DNA level in smears by polymerase chain reaction might predict underlying CIN (25).

We found that 42% had histologically HGL after their first abnormal smear and that it was impossible

Table IV. Comparison of cytology and colposcopy with histology

		Histology Non-HGL	HGL	Total
Cytology and colposcopy	non-HGL	349	79	428
	HGL*	100	241	341
Total		449	320	769

* Cytology and/or colposcopy showing HGL.
No colposcopy: 2, Transformation zone not visible: 28, no cytology: 14. HGL: high-grade lesions.
non-HGL: low-grade lesions, inflammation or normal cervix.

Table V. Diagnostic accuracy of cytology, colposcopy and both combined. In per cent (95% confidence intervals)

	Cytology	Colposcopy	Both
Sensitivity	41 (36–47)	67 (62–72)	75 (70–80)
Specificity	86 (82–89)	87 (84–90)	78 (74–80)
Predictive value of HGL	67 (60–73)	80 (74–84)	71 (66–75)
Predictive value of non-HGL	68 (64–71)	78 (75–82)	82 (78–85)
Accuracy	67 (64–71)	80 (77–82)	77 (74–80)

HGL: high-grade lesions; Non-HGL: low-grade lesions, inflammation or normal.

to differentiate between HGL and LGL on the smears. The false negative rate for cytology was more than 50%, even in CIN-3 lesions and in large lesions, although others found no negative rate for these lesions (26). Until we have more answers from randomised controlled trials, our policy is that women with any degree of abnormal smear should be referred immediately for colposcopy and biopsy.

As many as 25% of HGL were underestimated if the diagnosis was not confirmed by biopsy, so there is a potential risk of overlooking HGL if follow-up studies are based only on cytology with or without colposcopy.

In conclusion, we found that cytology had a low sensitivity for detecting HGL, but the sensitivity could be improved by adding colposcopy. Even combined, too many HGL were missed. All women with abnormal cytology should, therefore, have colposcopical and histological investigation, and prospective studies of the natural history of cervical squamous lesions should include histological evidence.

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