RESEARCH ARTICLE

Agreement between Colposcopic Diagnosis and Cervical Pathology: Siriraj Hospital Experience

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Abstract

Aim: To evaluate the agreement between colposcopic diagnosis and cervical pathology a retrospective chart review was performed. Materials and Methods: This study included 437 patients who underwent colposcopy and cervical biopsy or conization at Siriraj Hospital from October 2010 - December 2012. The patient clinical characteristics, cervical cytology results, colposcopic diagnoses, cervical pathology results were recorded and correlations between variables were analyzed. Results: Agreement of colposcopic diagnosis and cervical pathology was matched in 253 patients (57.9%). The strength of agreement with weighted Kappa statistic was 0.494 (p<0.001). Colposcopic diagnoses more often overestimated (31.1%) than underestimated (11%) the cervical pathology. Agreement of colposcopic diagnosis and cervical pathology within 1 grade was found in 411 patients (94.1%). Positive predictive value (PPV) of high grade colposcopy or more was 75.5%, whereas the negative predictive value (NPV) of insignificant and low grade colposcopy was 83.8%. False positives of high grade colposcopy or more were 21%. False negatives of insignificant or low grade colposcopy were 19.1%. Conclusions: Strength of agreement between colposcopic diagnosis and cervical pathology was found to be only moderate. A biopsy at colposcopy should be performed at a gold standard level to detect high grade lesions.

Keywords: Colposcopic diagnosis - cervical pathology - agreement - biopsy

Asian Pac J Cancer Prev, **15 (1)**, 423-426

Introduction

Cervical cancer is the second most common malignancy in women worldwide after breast cancer (Ferlay et al.). In Thailand, its incidence was 17.7/100,000 of Thai female population during 2004-2006 (Khunhaprema et al., 2012). Cervical cancer incidences and deaths have decreased since the implementation of widespread cervical cancer screening with cervical cytology and/or human papilloma virus (HPV) (Saslow et al., 2012). The knowledge of HPV has been advanced. However, the cervical cytology is still the mainstay of cervical cancer screening. Colposcopy is the next investigation step for abnormal cervical screening patients after the followings; a) two consecutive unsatisfactory cytology results; b) most cases of positive HPV testing; c) repeated atypical squamous cell of undetermined significance (ASC-US) cytology; d) low grade squamous intraepithelial lesion (LSIL) cytology; e) atypical squamous cell, cannot exclude high grade squamous intraepithelial lesion (ASC-H) cytology; f) high grade squamous intraepithelial lesion (HSIL) cytology; g) some types of glandular abnormality (Massad et al., 2013). The accuracy of colposcopy depends on the experience of the examiner. There is only fair correlation between colposcopic impression and histology diagnosis. The perfect agreement between the colposcopic impression and histology was seen in 32-37% of subjects. The agreement within one-step between the colposcopic impression and histology was found in 75-77% (Massad and Collins, 2003; Baum et al., 2006). The colposcopy alone is known to under diagnose approximately one-third of HSIL (Underwood et al., 2012).

The primary objective of this study is to evaluate the agreement between colposcopic diagnosis and cervical biopsy pathology in Siriraj Hospital. This result will indicate the important of colposcopic directed biopsy. The secondary objectives are to evaluate the positive predictive value (PPV) of the high grade colposcopic diagnosis and the negative predictive value (NPV) of low grade colposcopic diagnosis.

Materials and Methods

The medical records of all patients who underwent colposcopic examination at Siriraj Hospital between October 2010 and December 2012 were retrospectively

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reviewed after received an Institutional Review Board approval. Sample size was calculated from 52% agreement of colposcopic diagnosis and cervical pathology within our pilot study. We accepted type I error at 5%; the sample size was calculated to be at least 423 patients. The patients' clinical characteristics, cervical cytology results, colposcopic diagnoses, cervical pathology results were recorded. The correlation between colposcopic diagnosis and cervical biopsy pathology were analyzed. Subgroup analysis according to examiner experience was also performed.

All colposcopies were performed by 11 attending physicians or by obstetrics and gynecology resident/ gynecologic oncology fellows under supervision of those attending physicians. Six of the attending physicians had worked in this field for more than 15 years. The others graduated with fellowship of gynecologic oncology from high volume medical schools. Colposcopy was performed with a routine pattern with 5% acetic acid. Colposcopic diagnosis was graded as normal, benign, low grade lesion, high grade lesion, microinvasive cancer (MIC) and invasive cancer. The most suspicious area was biopsied. The biopsy specimens were examined by the gynecologic pathologist of our institute. Pathology reports were collected from the institutional database. Pathology slide review was not performed. All data were gathered in a spreadsheet (Excel, Microsoft, Redmond, WA). The significance of agreement between colposcopic diagnosis and cervical pathology was determined using weighted $\varkappa$ statistics(Viera and Garrett, 2005). Sensitivity, specificity, PPV, NPV, false positive and false negative were used to compare colposcopic diagnosis and cervical pathology.

Results

This study included 1,251 patients who underwent colposcopy during the study period. The patients who did not undergo cervical biopsy (617 patients), had history of hysterectomy (90 patients), had type III transformation zone (27 patients), had colposcopy because of vagina and vulvar lesion (26 patients), had prior history of radiation to the pelvic area (25 patients) and had incomplete data (29 patients) were excluded. Therefore, 437 patients were remained for analysis. Mean age of study group was 40.8 years. Nine patients previously received HPV vaccine.

The cervical cytology results were available in 393 patients including negative cytology in 17 patients, ASC-US in 71 patients, ASC-H in 85 patients, LSIL including HPV change and cervical intraepithelial neoplasia 1 (CIN1) in 97 patients, HSIL including CIN2 and CIN3 in 89 patients, AGC in 23 patients, AIS in 2 patients and invasive cancer in 9 patients. There were 17 patients with normal cervical cytology who underwent colposcopy because of history of abnormal cervical cytology in 5, suspected cervical lesion in 11, and in one patient who had positive high risk HPV test. The colposcopic diagnosis and cervical pathology was available in 437 patients. Colposcopy was diagnosed as benign in 43 patients (these consisted of cervicitis in 3, squamous metaplasia in 5, insignificant change in 8 and polyp in 27), low grade lesion in 186 patients (these consisted of CIN1 in 163, HPV lesion in 17 and condyloma in 6), high grade lesion in 169 patients, MIC in 8 patients, invasive cancer in 31 patients. The cervical pathology was reported as benign in 125 patients (these consisted of benign/unremarkable in 49, polyp in 21, squamous metaplasia in 24, chronic cervicitis in 18, reactive change in 13), LSIL in 118 patients (these consisted of HPV change in 60, CIN1 in 56, condyloma in 2), HSIL (including CIN2, CIN3 and AIS) in 171 patients, MIC in 1 patient and invasive cancer in 22 patients

The agreement of colposcopic diagnosis and cervical pathology was matched in 253 patients (57.9%) as shown in Table 1. The strength of agreement with weighted Kappa statistic was 0.494 ($p<0.001$, 95%CI=0.435-0.552). The colposcopic diagnosis was overestimated in 136 patients (31.1%) and underestimated in 48 patients (11%). The agreement of colposcopic diagnosis and cervical pathology within 1 grade was founded in 411 patients (94.1%).

We also subgroup analyzed according to the level of examiner experiences into two groups: those with more than 15 years and those with less than 15 years of experience. The agreements of colposcopic diagnosis and cervical pathology were matched in 96/183 (52.5%) and 157/254 (61.8%), respectively. The strength of agreements with Kappa statistic were 0.450 ($p<0.001$, 95%CI=0.357-0.544) and 0.527 ($p<0.001$, 95%CI=0.451-0.602), respectively.

PPV of high grade colposcopic diagnosis or more was 75.5% (157/208). NPV of low grade colposcopic diagnosis or less was 83.8% (192/229). Sensitivity of colposcopic diagnosis to detect high grade cervical pathology or more was 80.9% (157/194). Specificity of colposcopy (when negative was defined as low grade lesion or less) was 79% (192/243). False positive of high grade colposcopy or more was 21% (51/243). False negative of low grade colposcopy or less was 19.1% (37/194). These data are demonstrated in Table 2.

Table 1. The Agreement between Colposcopic Diagnosis and Cervical Pathology

Colposcopic diagnosis	Cervical biopsy pathology				
	Normal/ Benign	LSIL	HSIL	MIC/ Invasive cancer	Total
Benign	37*	4**	2	0	43
Low grade lesion	64**	87*	35**	0	186
High grade lesion	22	27**	113*	7**	169
MIC/Invasive cancer	2	0	21**	16*	42
Total	125	118	171	23	437

*Agreement: HSIL=253/437, MIC/Invasive cancer=57.9%,**Agreement with in 1 grade:HSIL=411/437, MIC/Invasive cancer=94.1%

Table 2. The Colposcopic Diagnosis and Cervical Pathology in Low Grade and High Grade Lesion

Colposcopic diagnosis	Cervical pathology		
	Normal/L Benign/LSI	HSIL/MIC/ Invasive cancer	Total
Benign/Low grade lesion	192	37	229
High grade lesion/MIC/Invasive cancer	51	157	208
Total	243	194	437

We analyzed the agreement among cervical cytology, colposcopic diagnosis and cervical cytology with pathology. The agreement of cervical cytology was matched with colposcopic diagnosis in 63.1% (135/214). The strength of agreement with weighted Kappa statistic was 0.478 (p<0.001, 95%CI=0.391-0.564). When compared with colposcopic diagnosis, the cervical cytology was overestimated in 29 of 214 patients (13.5%) and underestimated in 50 of 214 patients (23.4%). The agreement of cervical cytology was matched with cervical pathology in 64% (137/214). The strength of agreement with weighted Kappa statistic was 0.516 (p<0.001, 95%CI=0.436-0.596). When compared with cervical pathology, the cervical cytology was overestimated in 52 of 214 patients (24.3%) and underestimated in 25 of 214 patients (11.7%). The ASC-US, ASC-H and AGC cytology were excluded from these analyses.

Discussion

Colposcopy is still important as the next step of abnormal cervical cytology. The agreements of colposcopic diagnosis and cervical pathology were varied. No standard criteria and scoring system was recommended. Our study is the largest series comparing colposcopic diagnosis and cervical pathology in Thailand. The strength agreement between colposcopic diagnosis and cervical pathology in our study was moderate (κ=0.494, p<0.001, 95%CI=0.435-0.552). If colposcopic diagnosis is high grade lesion or more, the cervical pathology will be HSIL, MIC or invasive cancer in 75.5%. Conversely, if colposcopic diagnosis is low grade lesion or less, the cervical pathology will be normal, benign or LSIL in 83.8%.

The agreement of colposcopic diagnosis and cervical pathology was better than other studies. Baum et al. and Massad et al. reported the perfect agreement of 32-37% and agreement within one grade of 75-77%(Massad and Collins, 2003; Baum et al., 2006). The strength of agreement with weighted Kappa statistic was better than the study of Brotzman GL, et al (κ=0.26), Baum et al. (κ=0.2) and Massad et al. (κ=0.2)(Massad and Collins, 2003; Brotzman and Schellhase, 2004; Baum et al., 2006). Nevertheless, Benedet et al. reported a higher of agreement (51.9%) and a substantial level of correlation (κ=0.61) in a study of 84,244 patients (Benedet et al., 2004). However, their data were collected since 1986 and did not identify the atypical cervical cytology (ASC-US, ASC-H) which indicates more patients may need colposcopy.

In our study, the colposcopic diagnoses were more often overestimated (31.1%) than underestimated (11%) the cervical pathology. These findings were also reported in the other study and by meta-analysis (Mitchell et al., 1998; Massad and Collins, 2003). The overestimated colposcopic diagnosis led to unnecessary cervical biopsy. However, benefits of early treatment in suspected high grade lesion patient may overcome the risk of the biopsy process. From Table 1, the disagreement of colposcopic diagnosis and cervical pathology (beyond 1 grade) was in 26 patients (2 underestimated, 24 overestimated). Two underestimated patients had benign colposcopy with HSIL cervical pathology. One patient had cervical polyp that might have obscured the abnormal lesion and the HSIL was on that polyp. Conization showed only squamous metaplasia. The other patient had normal colposcopic finding, however the conization in this case showed CIN3. For 24 overestimated patients, two patients had invasive cancer on colposcopy with benign cervical pathology for unknown reason. The remaining 22 overestimated patients had HSIL on colposcopy with benign cervical pathology. Some cervical pathology results may cause these overestimations (9 patients-squamous metaplasia, 4 patients-chronic cervicitis, 9 patients-unknown reasons). Six patients from this group underwent conization. The others were followed closely.

There is no difference of agreement between colposcopic diagnosis and cervical pathology according to the level of performance experience. Baum ME, et al. and Homesley HD, et al. also reported a non-significant difference in agreement and correlation in each year of residency training(Homesley et al., 1985; Baum et al., 2006). Bekkers, et al. also concluded in their study that level of experience did not improve colposcopic performance(Bekkers et al., 2008). However, we agreed that a more structured colposcopic training program and re-evaluation system may be more beneficial for the resident and all colposcopists.

The sensitivity and specificity of colposcopy to diagnose high grade lesion, MIC or invasive cancer was 80.9% and 19%, which is comparable to previous studies (56-85% and 69-80%, respectively) (Mitchell et al., 1998; Massad and Collins, 2003; Baum et al., 2006). PPV of high grade colposcopy was 75.5%, which is comparable to previous studies (38.9-57%)(Mitchell et al., 1998; Massad and Collins, 2003; Baum et al., 2006). NPV of low grade colposcopy or less was 83.8%, which is comparable with previous studies (85-89.1%)(Mitchell et al., 1998; Massad and Collins, 2003; Baum et al., 2006). If we performed cervical biopsy in every abnormal colposcopic abnormality, 21% of these patients would be exposed to the unnecessary risk of cervical biopsy. However, 19.1% of patients will benefit from early treatment of high grade lesion or invasive cervical cancer.

Benedet et al reported 3 sets of paired comparisons including; colposcopic diagnosis with cervical pathology, cervical cytology with colposcopic diagnosis, and cervical cytology with cervical pathology (Benedet et al., 2004). They found the agreement in 51.9% (κ=0.61), 42.2% (κ=0.56) and 34.7% κ=0.42, respectively. Our study showed similar levels of agreement. The common causes of disagreement are interpretation or sampling errors. The recommendation is based on the most severe result. If cervical cytology showed HSIL with normal or low grade colposcopic diagnosis, cervical biopsy should be performed. If the colposcopic diagnosis was high grade with normal or low grade cervical biopsy pathology, conization should be performed. In our study, the level of agreement between cervical cytology and cervical pathology was high. However, the colposcopy is still necessary in the process of cervical biopsy. Diagnostic conization without prior biopsy in every abnormal cytology patient will be overtreatment.

This study has several limitations. Firstly, the clinical information from a retrospective chart review is relatively limited. This can affect the accuracy of the analysis of clinical outcomes. Secondly, the colposcopic diagnosis may be biased by a known cervical cytology result. Thirdly, colposcopy has no standard criteria or scoring system, therefore the colposcopic interpretations are relatively subjective. Lastly, we excluded the colposcopy without biopsy result which may change our results. Further prospective study with taking more than one biopsy may increase the sensitivity of detection of high grade lesion(Gage et al., 2006). The follow up study for the patients who undergo cervical conization or hysterectomy will confirm the accuracy of cervical biopsy. Also, the cost effectiveness between unnecessary cervical biopsy and delays in the diagnosis of high grade lesion should be compared. Utilizing high quality cytology laboratories, quality assurance colposcopists and pathologists will increase accuracy of colposcopy(Benedet et al., 2004). Evidence for new techniques of spectroscopy and other diagnostic devices is limited(Louwers et al., 2009). Most are in the developing process and not available worldwide. The level of sensitivity and specificity in detection of HSIL of these new techniques are not much better than conventional colposcopy(Louwers et al., 2009). In this HPV vaccinated era, the ratio of high grade cervical cytology will decrease. These new techniques may be beneficial for adding to routine colposcopy to improve the detection rate of cervical neoplasia. Web-based learning introduced by the International Federation of Cervical Pathology and Colposcopy (IFCPC) will help to improve colposcopy worldwide.

In conclusion, strength of agreement between colposcopic diagnosis and cervical pathology was moderate, without significant difference by the levels of experience. The biopsy at colposcopy should be used as a gold standard to detect high grade lesion.

Acknowledgements

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