Original Article

Prospective Evaluation of Correlation between Modified Reid's Colposcopic Index (RCI) and Histopathology Result from Colposcopic Directed Biopsy

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Objective: To evaluate correlation between Modified Reid Colposcopic Index and histopathology from colposcopic directed biopsy.

Materials and Methods: At least atypical squamous cell of undetermined significance (ASC-US) according to the Bethesda classification 2001 was diagnosed in 60 eligible women. At the time of colposcopic examination, the four colposcopic criteria used are: 1) margin of cervical lesion, 2) color of acetowhite, 3) appearance of vessels on cervical lesion, and 4) location of the lesion. Each criterion was assigned in score between 0 to 2 and the summation of all four criteria made a total score ranging from 0 to 8. A score of less than or equal to 2 was classified as low grade lesion indicating of human papillomavirus (HPV) infection or cervical intraepithelial neoplasia (CIN)1. Intermediate grade was 3 to 5 indicating of CIN2 while, high grade lesion as a reflection of at least CIN3 is 6 to 8. Colposcopic directed biopsy on all lesions were performed for histopathologic examination.

***Results*:** The strength of agreement with Spearman rank correlation was 0.69. Sensitivity, specificity, positive and negative predictive value for differentiate high from low grade lesion were 91.7%, 66.7%, 64.7% and 92.3%, respectively. The overall accuracy of modified RCI after adjusted was 76.7%. Accuracy in a subgroup of low and high grade lesion were 92.3% and 64.7%, respectively.

Conclusion: Modified Reid's colposcopic index had a good positive correlation to cervical histopathology and also had high accuracy to differentiate low from high grade lesion.

Keywords: Modified Reid's Colposcopic Index; Colposcopic directed biopsy; Colposcopy; Intraepithelial cervical neoplasia

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Colposcopy is currently used as an adjunct intervention to enhance diagnostic capability in women with an abnormal cervical cytology test in order to select the most abnormal area and perform biopsy to evaluate histopathology[1-4]. Colposcopy is not used as cervical cancer screening technique[1,4]. To perform the colposcopic directed biopsy, it depends on the experience of colposcopist in which the reported accuracy has been varied in the literature[2,3,5,6]. The sensitivity and specificity in colposcopic directed biopsy to detect high grade CIN were ranged between 64% to 99% and 30% to 93%, respectively[7]. The method to reduce error in colposcopic directed biopsy is colposcopic grading[2,3,8,9].

Colposcopic grading had many techniques[1,10] including Hisselmann colposcopic grading system, Coppleson grading system, Stafl grading system, Burke grading system, Swede score, Reid colposcopic index. Reid Colposcopic Index (RCI) was a systematic colposcopic evaluation that consists of various evaluating criteria. It has been more comparatively used than other methods because it is considered to be highly accurate (97% accuracy)[1,9,11].

At HRH Princess Maha Chakri Sirindhorn Medical Center (MSMC), Lugol's iodine solution application has not been used in the colposcopic exam because many patients reported a symptom of vaginal irritation. In addition, either low grade or high grade lesion was not stained by iodine appearing in similar yellow discoloration appearance which was difficult to differentiate for limited experience colposcopic practitioners[12]. Hong DG et al[12] reported the sensitivity of modified RCI to detecting high grade lesion was 94.4% and specificity was 65%. However, they have not been reported for its correlation. The objective of this study was to evaluate the correlation between modified RCI and histopathology from colposcopic directed biopsy in MSMC.

Materials and Methods

This study was prospective correlation study. Subjects were the patients who had abnormal cervical cytology and underwent colposcopic examination at the colposcopic clinic of the MSMC. The period of study was between June 2013 and May 2014. The inclusion criteria were: 1) At least

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ASC-US according to the Bethesda classification 2001 was diagnosed in these patients, 2) satisfactory colposcopic exam, 3) visible lesion under colposcopy. The exclusion criteria were: 1) pregnant women, 2) colposcopic exam for following previous cervical abnormality. The study received approval from the Institutional Ethics Committee (MEDSWUEC-9/2556).

Modified RCI was shown in Table 1. At the time of colposcopic examination, a cervical lesion was scored after applying 3% acetic acid for 2 minutes. The four colposcopic criteria used were: 1) margin of cervical lesion, 2) color of acetowhite lesion, 3) appearance of vessels on cervical lesion, and 4) location of the lesion. Each criterion was assigned in score between 0 to 2 and the summation of all four criteria made a total score ranging from 0 to 8. A score of less than or equal to 2 was classified as low grade lesion indicating an assumption of HPV infection or CIN1. Intermediate (3 to 5) and high grade (6 to 8) indicated a possibility of CIN2 and at least CIN3, respectively. Colposcopic directed biopsy on all lesion was performed for histopathologic examination.

All procedure mentioned above was done by either of the two gynecologic oncologist and one gynecologic resident under supervision of gynecologic oncologist. All colposcopists were standardized to use modified RCI.

Sample size estimation was calculated with an expectation of the primary objective, correlation between RCI and histopathology result equal to 0.42 which calculated from Hong DG's study[12]. By assigning α value equal to 0.05, the power of 90% ($\beta = 0.1$) and significant p-value less than 0.05 at least 55 patients was needed. We add 10% of calculated sample size to overcome an anticipation of missing data, therefore, it is required a total sample size of at least 60 patients.

Statistical analysis was performed using SPSS software (version 19.0, SPSS Incorporated). Spearman rank correlation between modified RCI and histopathology was evaluated. Performance of the modified RCI includes accuracy, Chi-square test, sensitivity, specificity, positive and negative predictive value were also examined.

Results

Sixty three eligible patients with abnormal cervical cytology were included in the study. Of these, two patients were excluded due to cervical cancer after being followed-up and one patient was abnormal cervical cytology in pregnant women as shown in Figure 1.

Demographic data are presented in Table 2. The mean age was 39.5±10.5 years old with the minimum and maximum was 16 and 70 years old, respectively. Most patients had been diagnosed LSIL (n=17 case, 28.3%) from the cervical cytology followed by HSIL (15 case, 25%), ASC-US (13 case, 21.6%), respectively. Squamous cell carcinoma, AGC-NOS, AGC-FN, AIS, and adenocarcinoma were found only in 1 case (1.7%) each.

Only 6 patients (10%) were nulliparous while 8

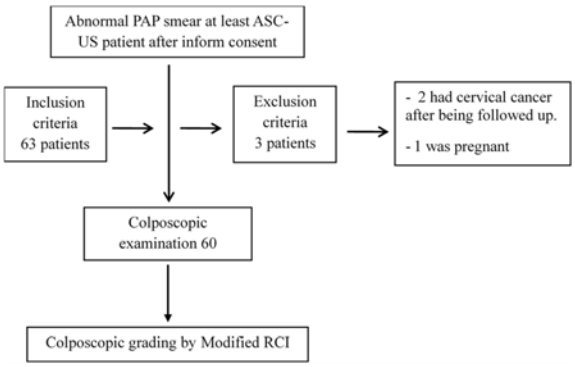

Figure 1. Flow of study.

Table 1. Modified Reid Colposcopic Index (modified RCI)[12]

Sign	Score		
	0 points	1 points	2 points
Margin	- Exophytic condylomas; area showing a micropapillary contour - Lesions with distinct edges - Feathered, scalloped edges - Lesions with angular, jagged shape - Satellite areas and acetowhitening distal to original squamocolumnar junction	Regular shape, smooth, straight edges	- Rolled, peeling edges - Any internal demarcation between areas of differing colposcopic appearance
Color	- Shiny, snow-white color - Areas of faint (semi-transparent) whitening	Intermediate shade (shiny, but gray-white)	Dull reflectance with oyster-white color
Vessel	- Fine-caliber - Poorly formed pattern	No surface vessels	Definite, coarse punctuation or mosaic
Location	Outer one-half of the transformation zone	Inner one half of transformation zone	Invade endocervical canal

(13.4%) participants had more than 3 children. Contraceptive methods were divided into no contraceptive used (23 cases, 38.3%), hormonal contraceptive used (20 cases, 33.4%), male condom (2 cases, 3.3%), female sterilization (8 cases, 13.4%), and other such as lactation or calendar method (7 cases, 11.6%). Abnormal cervical cytology was found in 4 patients (6.6%) during their routine post-partum check-up and 6 cases (10%) were menopausal patients as shown in Table 2.

Table 2. Characteristic of patients

Parameter	Case (%)
PAP smear	
ASC-US	13 (21.6)
ASC-H	10 (16.6)
LSIL	17 (28.3)
HSIL	15 (25)
AGC-NOS	1 (1.7)
AGC-FN	1 (1.7)
AIS	1 (1.7)
Adenocarcinoma	1 (1.7)
Parity	
0	6 (10)
1	22 (36.6)
2	24 (40)
≥3	8 (13.4)
Contraception method	
No	23 (38.3)
Hormonal	20 (33.4)
Male condom	2 (3.3)
Female sterilization	8 (13.4)
Other	7 (11.6)

ASC-US = Atypical squamous cell of undetermined significance; ASC-H = Atypical squamous cells – cannot exclude HSIL; LSIL = Low-grade squamous intraepithelial lesion; HSIL = High grade squamous intraepithelial lesion; AGC-NOS = Atypical glandular cells not otherwise specified; AGC-FN = Atypical glandular cells favor neoplasia; AIS = Adenocarcinoma in situ

Distribution of cervical histopathology diagnosis in correlation with the modified RCI is demonstrated in Table 3. Modified RCI had a good strength of correlation with the histopathology report (r = 0.69 using Spearman's rank correlation method, p-value less than 0.001) with an overall accuracy of 68.4%.

To calculate the test performance for clinical practice, we adjusted low and intermediate/high grade group from modified RCI to low and high grade lesion, respectively. In addition, CIN1 and equal or more CIN2 diagnosed from histopathology were classified as low and high grade histopathology, respectively. After group adjustment, low and high grade lesion from modified RCI reflected low and high grade histopathology, respectively. The agreement was matched as shown in Table 4. Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy for differentiate high grade lesion from low grade lesion were 91.7, 66.7, 64.7, 92.3 and 76.7 percent, respectively with statistical significant.

The accuracy of modified RCI in subgroup of CIN1, CIN2 and at least CIN3 were 92.3, 30 and 78.6, respectively as shown in Table 5. In subgroup of low and high grade lesion, accuracy were 92.3 and 64.7 percent, respectively.

Discussion

Colposcopy requires extensive training experience and the appropriate number of patients in order to maintain the skills[15]. Sensitivity and specificity for differentiating high grade CIN and cancer from low grade CIN, without using colposcopic grading, ranged from 85 to 89% and 52 to 69%, respectively[7,16].

Tatiyachonwiphut et al[17] reported the strength of correlation of colposcopic diagnosis, without using colposcopic grading with kappa value was 0.494. Therefore, when using modified RCI, the strength of correlation, sensitivity and specificity was higher than colposcopic diagnosis without using colposcopic grading.

Reid R and Scalzi P[9] reported Reid's Colposcopic Index (RCI) that accuracy was 97%, but did not study the sensitivity, specificity, and correlation. Mousavi et al[18] studied the correlation between RCI and histopathology. The

Table 3. Modified Reid's Colposcopic Index and Histopathology

Modified RCI	Histopathology			Total
	CIN1 (%)	CIN2 (%)	At least CIN3 (%)	
Low grade	24 (92.3)	2 (7.7)	0 (0)	26
Intermediate grade	10 (50)	6 (30)	4 (20)	20
High grade	2 (14.3)	1 (7.1)	11 (78.6)	14
Total	36 (60)	9 (15)	15 (25)	60

CIN = cervical intraepithelial neoplasia

Table 4. Validity and Efficacy of Modified Reid's Colposcopic Index

Modified RCI	Histopathology		Total
	Low grade (CIN1)	High grade (CIN2, at least CIN3)	
Low grade	24	2	26
High grade	12	22	34
Total	36	24	60

CIN = cervical intraepithelial neoplasia
For prediction of high grade, sensitivity: 91.7% (22/24), specificity: 66.7% (24/36), positive predictive value: 64.7% (22/36) and negative predictive value: 92.3% (24/26), accuracy: 76.7% (46/60)

Table 5. Accuracy of Modified Reid's Colposcopic Index

Modified RCI	Accuracy
CIN1	92.3%
CIN2	30%
At least CIN3	78.6%
Low grade lesion (CIN1)	92.3%
High grade lesion (CIN2 & at least CIN3)	64.7%
Overall modified RCI (after adjusted)	76.7%

CIN = cervical intraepithelial neoplasia; RCI = Reid's colposcopic index

results were good strength of correlation with kappa value was 0.74. In our study, the accuracy of modified RCI was not as high as in overall accuracy in RCI, but it also was a high sensitivity for detect high grade lesion and the same strength of correlation as Mousavi study. Therefore, we can use modified RCI in the colposcopic examination.

Ferris and Listaker[19] studied the prediction of cervical histologic result by use abbreviated Reid's colposcopic index, which did not use iodine and use only three criteria (margin of lesion, color of acetowhite and appearance of vessel). The results showed that poor strength of correlation with kappa value was 0.17, and the sensitivity, specificity, positive predictive value and negative predictive value to detection of CIN3 were 37.3%, 89.7%, 30.8% and 92.1%. Therefore, we replace the position of the lesion instead of iodine criteria.

Hong et al[12] studied the use of Modified Reid Colposcopic Index that uses position of the lesion instead of iodine criteria, like our study, to expected high grade squamous intraepithelial lesions and the results seem to higher performance (sensitivity, specificity, positive and negative predictive value) than our study. However, we were found good strength of correlation (Spearman rank correlation = 0.75 to 1.0: very good to excellent relationship, 0.5 to 0.75: moderate to good relationship, 0.25 to 0.5: fair degree of relationship, 0 to 0.25: little or no relationship)[20]. The result was inconsistent with Hong DG study because our study may have had a small sample size in high grade lesion. Nevertheless, if the result from modified RCI was low grade lesion that was a believable result.

In our study found that the modified RCI had high accuracy in low grade lesion, especially in CIN1 higher than CIN3. In Farley et al study[3] found that colposcopy was more accurate when lesions are more severe, but decrease accuracy in microinvasive and frankly invasive cancer. The reason why the results were not correlated with Farley study, because the use of modified RCI has not a colposcopist's bias to diagnosis.

Our study result can support using a modified Reid's colposcopic index in a colposcopic clinic with omit iodin use and had a more advantage for a beginner colposcopist to gain an experience. Limitations of our study were: 1) the colposcopist knows a severity of abnormal Pap smear that patients who were examined, 2) if the colposcopy diagnosis could not find the lesion, we could not offer a score of modified RCI.

Conclusion

Modified Reid's Colposcopic Index had a good positive correlation to cervical histopathology and also had high accuracy to differentiate low grade lesion from high grade lesion.

What is already known on this topic?

The efficacy of colposcopy depends on the experience of colposcopist. The method to reduce error in colposcopic directed biopsy is colposcopic grading.

What this study adds?

Modified Reid's colposcopic index by removing iodine staining and replacing with location of lesion had a good positive correlation to cervical histopathology.

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Potential conflicts of interest

The authors declare no conflict of interest.

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