Correlation Between Reid's Colposcopic Index and Histologic Results from Colposcopically Directed Biopsy in Differentiating High-Grade from Low-Grade Squamous Intraepithelial Lesion at Rajavithi Hospital

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Objective: *To analyze the correlation and accuracy between Reid's colposcopic index (RCI) and histologic results from colposcopically directed biopsy (CDB) in differentiating high-grade squamous intraepithelial lesion (HSIL) from low-grade squamous intraepithelial lesion (LSIL).*

Materials and method: *A retrospective analysis of medical records of women who had abnormal Pap smear and underwent colposcopy, RCI scoring and CDB from January 1st, 2003 to December 31st, 2006 at Rajavithi Hospital was conducted.*

Results: *One hundred women were included in the present study. Compared with histological diagnosis from CDB, accuracy for four colposcopic criteria: margin pattern, color, vascular pattern and iodine staining were 73.0%, 79.0%, 75.0% and 69.2%, respectively. Combining these variables into RCI showed 89.0% overall accuracy. Color and vascular pattern showed a good agreement with histologic results from CDB (Kendall's tau C = 0.68 and 0.63; $p < 0.05$). Overall, RCI yielded a good agreement (Kendall's tau C = 0.66; $p < 0.05$).*

Conclusion: *RCI yields a good correlation with histology from CDB and it has high accuracy in differentiating HSIL from LSIL.*

Keywords: *Reid's colposcopic index, Colposcopically directed biopsy, CDB, RCI, Rajavithi*

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Modern colposcopy is more than a simple intermediate link between cytologic screening and histologic diagnosis[1]. Management algorithms of cervical intraepithelial neoplasia (CIN) are based on the colposcopic findings and the histology from colposcopically directed biopsies (CDB). Apart from excluding invasive carcinoma in the women who have an abnormal Pap smear, the other important role of colposcopy is to differentiate low-grade from high-grade CIN. It is also important that a colposcopist is able to differentiate among normal, minimally abnormal, and significantly abnormal colposcopic patterns, and to identify the most severe lesion on the cervix for taking CDB[1-5]. The benefit of colposcopy and CDB is to avoid over treatment of low-grade lesion, and under treatment of high-grade lesion. In has been accepted that "just forming an overall colposcopic impression" is not helpful in differentiating grading of CIN. The most reliable method of ensuring the accuracy of targeted biopsy is to grade lesions by a colposcopic score[1,3,6]. Many colposcopic grading systems have been developed to provide an objective, accurate, reproducible and clinically meaningful prediction of severity of CIN lesions based on discriminatory analysis of specific colposcopic sign. In modern colposcopy, the Reid's colposcopic index (RCI) represents the most reproducible and clinically valid means of standardizing the evaluation of cervical lesions[3,7,8]. The RCI uses four colposcopic features of premalignant cervical lesions to achieve this predictive accuracy. The four colposcopic criteria used are: (1) the margin of the lesion, (2) the colour of the acetowhitening, (3) the type of vascular pattern, and

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(4) the iodine staining reaction. Each criterion is assigned as score between 0 and 2 reflecting variation in colposcopic findings. Scores of 0 represent humanpapilloma virus (HPV) induced changes or CIN 1. A score of 1 suggests intermediate grade lesion (CIN 1 to CIN 2), with scores of 2 represent features suggestive of high-grade lesion (CIN 2, 3). The predictive value of individual criteria can be maximized by combination into a weighted colposcopic index. When the 4 criteria are summed, total scores ranging from 0 to 2 indicate immature metaplasia or CIN 1, scores of 3 to 5 indicate CIN 1 to CIN 2, and scores of 6 to 8 represent CIN 3[1-3,6-9]. This colposcopic index permits a more accurate colposcopic-histologic agreement compared with subjective judgment. The overall predictive accuracy of the index exceeds 90%[3,8,10]. In 2003, the RCI was introduced in Rajavithi hospital, Thailand. After several years of using it, the author has subsequently found that this index would help to enhance the accuracy of the colposcopic impression and to improve colposcopy training. However, there has been no study of accuracy of RCI in our institute and in this country so far.

The purpose of this study is to examine the correlation and accuracy between RCI and histologic results from CDB in differentiating high-grade squamous intraepithelial lesion (HSIL) from low-grade squamous intraepithelial lesion (LSIL).

Material and Method

The study was approved by the Research Ethics Committee of the Rajavithi hospital. Retrospective analysis of data was carried out on medical records of women who underwent colposcopy in Rajavithi hospital from 1st January 2003 to 31st December 2006. In our institute, all women with cytologic abnormalities (ASC-US or worse) were counseled and underwent colposcopy, the findings were documented, grades were assigned in each case by attending physicians and a punch biopsy was taken from the worst affected area via colposcopic guidance using 3% acetic acid (CDB). Cases were eligible in the present study if they met the author's inclusion criteria included the women underwent colposcopy with RCI scoring. The scoring system for deriving the RCI is detailed extensively in the literature[1-3,5-9] (Table 1). Report of histology from CDB taken at the scored area must be available. Pregnant women, women with unavailable histology from CDB and women with history of pelvic radiotherapy were excluded from the study. In the present study, all cases were colposcopically scored for 3 criteria included the margin of the lesion, the color of the acetowhitening, the type of vascular pattern. The colposcopic criteria were scored in the 0 point, 1 point, and 2 points (Table 1). Then, total scoring detecting for any lesion were as follows: 0-2, low- grade lesions; 3, intermediate grade lesion

Table 1. Reid's Colposcopic Index

Sign	Score		
	Zero points	One points	Two points
Margin	Exophytic condylomas; areas showing a micropapillary contour Lesions with distinct edges Feathered, scalloped edges Lesions with an angular, jagged shape "Satellite" areas and acetowhitening distal to the original squamocolumnar junction	Lesions with a regular (circular or semicircular) shape, showing smooth, straight edges	Rolled, peeling edges Any internal demarcation between areas of differing colposcopic appearance
Color	Shiny, snow-white color Areas of faint (semitransparent) whitening	Intermediate shade (shiny, but gray-white)	Dull reflectance with oyster-white color
Vessels	Fine-caliber vessels, poorly formed pattern	No surface vessels	Definite, coarse punctation or mosaic
Iodine	Any lesion staining mahogany brown; mustard-yellow staining by a minor lesions (by first three criteria)	Partial iodine staining (mottled pattern)	Mustard-yellow staining of a significant lesion (an acetowhite area scoring 3 or more points by the first three criteria)

(CIN 2); 4-6, high-grade lesion. Therefore, total "3-criterion RCI or abbreviated RCI" would range from 0-6. Lugol's iodine staining was not routinely applied and only some patients were scored by this criterion. Most of them were scored by the first three criteria. Therefore, in the present study, combined result of traditional RCI or "4-criterion RCI" were calculated by adding 0 point in the scores when the lesions scored less than 3 points by the first three criteria and adding 2 points in the scores when the lesions scored 3 or more points by the first three criteria[11]. The findings were documented, and also CDB were taken from the highest colposcopic score lesions. In some cases, when lesions were large and multiple CDB were done on the same cervix, only one result from the highest colposcopic score location of lesion was analyzed. The histologic results from CDB were compared with RCI. The data were analyzed using the statistical package for the social science (SPSS) version 17.0 significance was set at the level of $p < 0.05$. Since colposcopic grade and histologic diagnosis are categorical variables, association between categorical variable were assessed using the x^2 statistical analyses. Strengths of association were compared by means of Kendall's tau-C [tau-C = 0.93-1.00 means excellent agreement, tau-C = 0.81-0.92 means very good agreement, tau-C = 0.61-0.80 means good agreement, tau-C = 0.41-0.60 means agreement, tau-C = 0.21-0.40 means slight agreement, tau-C = 0.01-0.20 means poor agreement, tau-C $\leq$ 0.00 means no agreement][12].

Results

During the study period, 100 patients were eligible. All patients were Asian. The average age was 30 $\pm$ 12 years (range 16-80 years). Eighty-nine women (89.0%) aged less than 50 years. Twenty women (20.0%) were nulliparous. The rate of LSIL, HSIL and positive for malignancy cytology were 40.0%, 41.0% and 3.0%, respectively. In colposcopy, the iodine staining was done in 26 of 100 women. Of the 100 histology samples, 46.0% were low-grade lesion, 54.0% were high-grade lesion. Table 2 illustrates cross-tabulation of each colposcopic criterion against histologic diagnosis. Numbers within the gray boxes reflect accurate histologic predictions. Those to the right of the gray boxes are colposcopic underestimation of histologic findings, and those to the left are colposcopic overestimation. The predictive accuracy of the peripheral margin was 73.0%, the predictive accuracy of the color of acetowhitening was 79.0% (highest predictive accuracy), the predictive accuracy of the vascular pattern was 75.0%, and the predictive accuracy of the iodine staining was 69.2%. Table 3 illustrates the comparison between abbreviated (3-critrion) RCI and CDB histology in each woman. In this table, RCI was a

Table 2. Cross-tabulation of each colposcopic criterion against histologic diagnosis

Table 2.1 The peripheral margin criterion against colposcopic biopsy histology

Margin score	Colposcopic biopsy histology				Total
	HPV	CIN1	CIN2	CIN3	
0	25	14	5	12	56
1	3	3	3	6	15
2	0	1	2	26	29
Total	28	18	10	44	100

$X^2 = 41.1$, $p < 0.05$,

$$\text{Accuracy} = \frac{25 + 14 + 3 + 3 + 2 + 26}{100} \times 100 = 73\%$$

Table 2.2 The color of acetowhitening criterion against colposcopic biopsy histology

Color of acetowhite score	Colposcopic biopsy histology				Total
	HPV	CIN1	CIN2	CIN3	
0	26	14	1	4	45
1	1	4	7	14	26
2	1	0	2	26	29
Total	28	18	10	44	100

$X^2 = 72.9$, $p < 0.05$,

$$\text{Accuracy} = \frac{26 + 14 + 4 + 7 + 2 + 26}{100} \times 100 = 79\%$$

Table 2.3 The vascular pattern criterion against colposcopic biopsy histology

Vascular pattern score	Colposcopic biopsy histology				Total
	HPV	CIN1	CIN2	CIN3	
0	24	12	3	3	42
1	4	3	3	12	22
2	0	3	4	29	36
Total	28	18	10	44	100

$X^2 = 53.4$, $p < 0.05$,

$$\text{Accuracy} = \frac{24 + 12 + 3 + 3 + 4 + 29}{100} \times 100 = 75\%$$

combination of the first 3 criteria: the margin of the lesion, the colour of the acetowhitening, the type of vascular pattern. Total score was 6 points, excluding score from iodine staining. Forty-four of 54 patients scoring 2 points or less was either human papilloma viral infection (HPV) or CIN 1. Three of 4 cases scoring 3 points were CIN 2. Forty-one of 42 patients scoring four to six points were CIN 2-3. In Table 3, numbers within the gray boxes reflect accurate histologic predictions. Those to the right of the gray boxes are colposcopic underestimation of histologic findings, and those to the left are colposcopic overestimation. RCI underestimated and overestimated in 10 (10.0%) and 2 cases (2.0%), respectively. As expected, combination of 3 criteria yielded a substantial increase in accuracy of the colposcopy in predicting histologic diagnosis. Overall predictive accuracy rose to 88%. Table 4 illustrates the comparison between traditional (4-crition) RCI and CDB histology in each patient. In the present study, iodine staining was not routinely performed, 4-criterion RCI was calculated by adding the iodine staining score to the 3-citerion RCI as mentioned earlier. Forty-four of 54 patients scoring two points or less was either HPV infections or CIN 1. Three patients scoring 3-5 points were CIN 1-2, and 41 of 42 patients scoring 6-8 points were CIN 2-3. Accurate histologic prediction was shown in the grey boxes. Colposcopy underestimation and overestimation were shown in right and left of the grey boxes, respectively. Overall predictive accuracy was 89.0%. The data of the Table 5 show predictive accuracy of each criterion. The accuracy of pattern of the peripheral margin, color of acetowhitening , vascular pattern ,iodine staining was 73.0%, 79.0%, 75.0% and 69.0%, respectively. Combining the four criteria increases the predictive power ($x^2 = 83.8$; $p < 0.05$) and accuracy (89.0%). RCI had good correlation with colposcopic biopsy histology (Kendall's tau-C = 0.66; $p < 0.05$).

Disscusion

The purpose of a colposcopy is to assist the colposcopist in selecting the most abnormal lesions to biopsy and rule out the presence of invasive cancer. In practice, when complex lesions occupying the majority of the transformation zone are present, the task of selecting the biopsy sites that best represent the most abnormal lesion can be challenging. Many colposcopic assessment systems have been developed to serve this matter such as Stafl's schema, Coppleson's schema, Rubin and Barbo system, Burghardt's system and RCI[1,6,9]. One of the most common uses at the present time is RCI. In 1984, Reid and colleagues used a score based on five colposcopic criteria[7]. One year later, an

Table 2.4 The iodine staining criterion against colposcopic biopsy histology

Iodine staining score	Colposcopic biopsy histology				Total
	HPV	CIN1	CIN2	CIN3	
0	4	3	0	1	8
1	4	2	1	1	8
2	0	2	1	7	10
Total	8	7	2	9	*26

$X^2 = 12.3$, $p < 0.05$,

Accuracy = $\frac{4 + 3 + 2 + 1 + 1 + 7}{26} \times 100 = 69.2\%$

*The iodine staining was done in 26 of 100 patients

Table 3. Comparison of abbreviated Reid's colposcopic index* and colposcopic biopsy histology

Reid' s colposcopic index*	Colposcopic biopsy histology				Total
	HPV	CIN1	CIN2	CIN3	
RCI = 0-2	28	16	3	7	54
RCI = 3	0	1	3	0	4
RCI = 4-6	0	1	4	37	42
Total	28	18	10	44	100

*Combination of the first 3 criteria: margin, color and vascular. Total score was 6 points, excluding score from iodine staining

Table 4. Comparison of traditional Reid's colposcopic index* and colposcopic biopsy histology

Reid's colposcopic index*	Colposcopic biopsy histology				Total
	HPV	CIN1	CIN2	CIN3	
RCI = 0-2	28	16	3	7	54
RCI = 3-5	0	1	3	0	4
RCI = 6-8	0	1	4	37	42
Total	28	18	10	44	100

*Total score was 8 point. Iodine staining was not done; therefore, traditional RCI was calculated by adding 0 or 2 points to the abbreviated RCI depending on the score after the first 3 criteria, If the score after the first three criteria is $\geq$ 3, add 2. If the score after the first three criteria is < 3, add 0[11].

Table 5. A comparison of statistical significance (x^2), strength of association (Kendall's tau-C), and predictive accuracy for four colposcopic criteria

Colposcopic signs	x^2*	Kendall's tau C*	Predictive accuracy (%)
Peripheral margin	41.1	0.51	73
Color	72.9	0.68	79
Vascular atypia	53.4	0.63	75
Iodine staining	12.3	0.54	69
Combined index	83.8	0.66	89

*Significant at $p < 0.05$

improved colposcopic index based on four colposcopic criteria was proposed for more accuracy[8]. This scoring system provides a less subjective measurement of lesion severity based on colposcopic signs and provides the clinician with direction for the targeted biopsy. It can also simplify the difficult task of learning coloscopy because formulation of RCI is based on critical analysis rather than pattern recall[5,9]. Using RCI in colposcopy produce more accuracy, higher agreement and strength of the correlation than "nonRCI" colposcopy impression[13,14]. The present study described the use and accuracy of RCI for the first time in this country. The accuracy of pattern of the peripheral margin, color of acetowhitening, vascular pattern, iodine staining was 73.0%, 79.0%, 75.0% and 69.2%, respectively. Combining the four criteria increased the predictive power. Overall predictive accuracy was 89.0% and had good correlation with histology from CDB. The result appears to be consistent with the literature[8,13,14]. In original study by Reid et al[8], the figure was 79.0%, 72.0%, 81.0%, 72.0% for each criterion with 97.0% overall accuracy. Roughly, the author's result is similar to the original study. However, when focusing on detail, it is apparent that there are concordance and difference in many points. First, the highest predictive accuracy of colposcopic criterion in Reid's study was vascular pattern while the highest predictive accuracy in the present study was color of acetowhitening. Secondly, the iodine staining criterion yielded lowest predictive accuracy similar to the original study. In fact, this criterion is quite non-specific. Because of glycogen depletion, either low-grade or high-grade lesions will stain mustard yellow with Lugol's iodine. Therefore, iodine staining of both low-grade and high-grade lesions is characterized by the same yellow discoloration. Differentiation of score 0 point and 2 points in this criterion actually depends upon the application of other 3 colposcopic criteria, not upon the shade of the iodine stain itself[5,6,9]. Apart from that, Lugol's iodine sometimes causes vaginal mucosal irritation. Use of the RCI in outpatient clinics is therefore somewhat inconvenient because of cumbersome iodine staining. In the author's institute, not all colposcopists use iodine staining. This criterion has been used only in some cases especially in training program. In fact, most colposcopy teaching depends on projection of static colposcopic images and only the first 3 criteria of RCI can be scored. There were many studies using abbreviated RCI that omitted iodine staining in colposcopic assessment of the cervix[15-18]. Recently, Hong et al[19] examined the rates of diagnosis of LSIL and HSIL using a modified RCI that omitted the iodine staining procedure and replaced it with the location of the lesion in the transformation zone. The result of the colposcopic impression using this modified RCI was superior to HPV testing. The sensitivity, specificity, positive predictive value, and negative predictive value of the colposcopic impression for detecting HSIL were 91.3%, 92.9%, 93.6%, and 90.3%, respectively. These results strongly indicate that the modified RCI that omits the iodine staining can accurately predict the histologic grade of CIN and can be applied easily in clinical practice without affecting the diagnostic accuracy of the traditional RCI.

Although the accuracy and correlation of RCI have been reported to be high in some investigations[8,13,14], at the present time, the accuracy of colposcopy has been increasingly questioned. Some studies suggest that its accuracy and correlation are imperfect[15,17]. As recently reviewed, colposcopic impression, RCI each criterion and total RCI score can not discriminate between lesions that harbor CIN 2 + and those do not. The sensitivity for detecting CIN 2/ 3 or worse of a high grade diagnosis by RCI is very low[15,17]. RCI agreement is poor[15]. Simple identification of an acetowhite lesion is a highly sensitive indicator for the identification of CIN 2+ and biopsy of all acetowhite lesions will yield the greatest sensitivity for detecting high-grade lesion[17]. Those recent studies raise concerns about current colposcopic practice based on the RCI. The role of colposcopy in the prevention of cervical cancer is continues to evolve.

Certainly, limitations of the present study do exist. First, its retrospective nature precludes standardization of protocol. Secondly, the lack of central review of all CDB may be considered a limitation of the

present study as some pathologists may not have a special interest or expertise in cervical histopathology. In addition, the author did not assess the fourth RCI criteria, Lugol's iodine staining in all cases. Although this criterion has limitation, as previously described, its use still provides benefit for some reasons. A variegated iodine pattern (mixed brown and yellow, score = 1) tends to represent less severe neoplasia while epithelium that turns brown suggests normal epithelium. In some cases, iodine may provide more distinct margin discrimination as compared with acetic acid. It can improves sensitivity by reducing the number of false-negative exams caused by overlooking thin, high-grade lesions that are still in the process of emerging within an actively metaplasing transformation zone[5]. Finally, the colposcopists were not blinded for the result of the referral smear, which can appear as a limitation. The study's aim, however, is to evaluate this scoring system in the real situation where the clinician knows a referral smear in advance.

In conclusion, this study demonstrates high accuracy and correlation between colposcopy and histology from CDB when using RCI. This scoring system appears to be helpful in residency and gynecologic oncology fellow training. However some recent studies raised concerns regarding colposcopic practice based on the RCI. Further study is still required to search for the ways for improving the correlation and accuracy. Until a better system is available, a sytstematic colpscopic assessment like the RCI is still valuable and beneficial.

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Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่าง Reid's colposcopic index และผลตรวจทางพยาธิวิทยาจาก colposcopically directed biopsy ในการจำแนก high-grade จาก low-grade squamous intraepithelial lesion ที่โรงพยาบาลราชวิถี

สธน บุญลิขิต

วัตถุประสงค์*: เพื่อวิเคราะห์หาความสัมพันธ์ระหว่าง Reid's colposcopic index (RCI) กับผลพยาธิวิทยาจากการตัดชิ้นเนื้อที่ปากมดลูกผ่านการตรวจด้วยกล้องคอลโปสโคป (colposcopically directed biopsy, CDB) และความแม่นยำในการจำแนก high-grade จาก low-grade squamous intraepithelial lesion ของปากมดลูก*

วัสดุและวิธีการ*: ได้ศึกษาสตรีที่มีผลเซลล์วิทยาผิดปกติและได้รับการส่งตัวมาที่คลินิกคอลโปสโคป ตั้งแต่ วันที่ 1 มกราคม พ.ศ. 2546 ถึง 31 ธันวาคม พ.ศ. 2549 โดยเก็บข้อมูลจากสตรีที่ได้รับการตรวจด้วยกล้องคอลโปสโคปและประเมินความรุนแรงของรอยโรคโดยการให้คะแนนแบบ RCI ร่วมกับ CDB เพื่อส่งตรวจทางพยาธิวิทยา นำข้อมูลที่ได้มาวิเคราะห์และสรุปผล*

ผลการศึกษา*: มีสตรีที่เข้าเกณฑ์ในการศึกษาจำนวน 100 คน ความแม่นยำของเกณฑ์ 4 ข้อของ RCI ได้แก่ ขอบของรอยโรค การติดสี acetowhite ลักษณะของหลอดเลือด การติดสีไอโอดีนเท่ากับ ร้อยละ 73, 79, 75 และ 69 ตามลำดับ การใช้เกณฑ์ทั้ง 4 ร่วมกันเป็น RCI พบว่าเพิ่มความแม่นยำโดยสามารถวินิจฉัยได้ตรงกับผลทางพยาธิวิทยาร้อยละ 89 พบว่าเกณฑ์การติดสี acetowhite และลักษณะของหลอดเลือด มีความสัมพันธ์ในระดับดีกับผลพยาธิวิทยาจาก CDB (Kendall's tau C = 0.68 และ 0.63; $p < 0.05$) โดยรวม RCI มีความสัมพันธ์ในระดับดีกับผลพยาธิวิทยาจาก CDB อย่างมีนัยสำคัญทางสถิติ (Kendall's tau C = 0.66; $p < 0.05$)*

สรุป*: การใช้ Reid's colposcopic index ในการวินิจฉัยรอยโรคที่ปากมดลูกมีความสัมพันธ์กับผลทางพยาธิวิทยาจากการตัดชิ้นเนื้อที่ปากมดลูกผ่านการตรวจด้วยกล้องคอลโปสโคปในระดับดี และมีความแม่นยำตรงกับผลทางพยาธิวิทยาสูงสามารถใช้แยก high-grade จาก low-grade squamous intraepithelial lesion ได้*