ความไวและความจำเพาะของการตรวจวินิจฉัยรอยโรคขั้นสูงก่อนการเป็นมะเร็งปากมดลูกด้วยการตัดชิ้นเนื้อภายใต้กล้องคอลโปสโคป ศึกษาย้อนหลัง ในโรงพยาบาลวชิระภูเก็ต

จินตนา สิงหวรรณกุล
ตำแหน่งนายแพทย์ชำนาญการ
สังกัดหน่วยงานสูติ-นรีเวชกรรม โรงพยาบาลวชิระภูเก็ต

บทคัดย่อ

ที่มา: การตรวจปากมดลูกด้วยกล้องคอลโปสโคป เพื่อค้นหารอยโรคก่อนมะเร็ง มีข้อมูลการศึกษายืนยันว่าช่วยให้ได้รักษาอย่างรวดเร็ว[1] ความแม่นยำของการวินิจฉัยด้วยกล้องคอลโปสโคปขึ้นกับประสบการณ์ของผู้ตรวจ มีการศึกษา meta-analysis พบว่าความไวในการตรวจคอลโปสโคปร้อยละ 68 ความจำเพาะร้อยละ 93[2]

วัตถุประสงค์: ศึกษาความไวและความจำเพาะการตรวจวินิจฉัยรอยโรคขั้นสูงด้วยกล้องคอลโปสโคป (colposcopy impression) และการตัดชิ้นเนื้อภายใต้กล้องคอลโปสโคป (colposcopy directed biopsy) เปรียบเทียบกับการวินิจฉัยชิ้นเนื้อขั้นสุดท้ายได้จากการตัดปากมดลูกรูปกรวยด้วยห่วงไฟฟ้า (loop electric excision procedure, LEEP) หรือผลทางพยาธิวิทยาของมดลูก

วิธีการศึกษา: เก็บข้อมูลย้อนหลังการตรวจปากมดลูกด้วยกล้องคอลโปสโคปและตัดชิ้นเนื้อ ระหว่างวันที่ 1 มกราคม 2562 ถึง 31 กรกฎาคม 2564 ผลวินิจฉัยด้วยคอลโปสโคป (colposcopy impression) และผลการตัดชิ้นเนื้อภายใต้กล้องคอลโปสโคป(colposcopy directed biopsy) เปรียบเทียบกับวินิจฉัยสุดท้ายจากผลชิ้นเนื้อตัดปากมดลูกด้วยห่วงไฟฟ้า(LEEP)หรือผลพยาธิมดลูก ประเมินความสอดคล้องของผล วิเคราะห์ความไว ความจำเพาะของการตรวจ

ผลการศึกษา: สตรีที่ได้รับการตรวจปากมดลูกด้วยคอลโปสโคป จำนวน 264 ราย ได้รับการตัดปากมดลูกด้วยห่วงไฟฟ้า 90 ราย และมีสตรีที่ตรวจด้วยคอลโปสโคปเห็นปากมดลูกได้เหมาะสม (adequate) 66 ราย นำมาศึกษาพบว่าการวินิจฉัยรอยโรคขั้นสูงด้วยการตัดชิ้นเนื้อภายใต้กล้องคอลโปสโคปมีความไวร้อยละ 83.3 ความจำเพาะร้อยละ 91.6 และการตรวจวินิจฉัยด้วยกล้องคอลโปสโคป ความไวร้อยละ 74 ความจำเพาะร้อยละ 75

สรุป: การวินิจฉัยรอยโรคขั้นสูงด้วยการตัดชิ้นเนื้อภายใต้การกล้องคอลโปสโคป มีความไว ความ- จำเพาะและความแม่นยำสูง การตัดชิ้นเนื้อหลายตำแหน่งช่วยเพิ่มความแม่นยำ

คำสำคัญ: การตัดชิ้นเนื้อภายใต้กล้องคอลโปสโคป, ความจำเพาะ, ความไว, รอยโรคขั้นสูงก่อนเป็นมะเร็งปากมดลูก

Sensitivity and Specificity of Colposcopy Directed Biopsy for the Diagnosis of High-Grade Lesions Retrospective Study at Vachira Phuket Hospital

Chintana Singhawannakul

Abstract

Background: Colposcopy is a standard for the early diagnosis of cervical intraepithelial neoplasia (CIN) and to plan treatment.[1] The accuracy of colposcopy varies in different reports depending on experience. A 2023 meta-analysis study reported sensitivity of 68 percent and specificity of 93 percent.[2]

Objectives: To produce descriptive statistics for sensitivity and specificity of colposcopy directed biopsy (CDB) and colposcopy impression (CI) compared with final pathological diagnosis.

Method: Data was retrospectively collected from January 2019 to July 2021. CI reports and pathological reports of CDB were compared with a final pathological diagnosis from either the loop electric excision procedure (LEEP) or hysterectomy.

Results: 264 patients underwent a colposcopy procedure during this study. 90 patients underwent LEEP only 66 patients who reported adequate colposcopy were included in the study. CDB for detected high-grade lesions (HGL) had 83.3 percent sensitivity and 91.6 percent specificity. Colposcope impression had 75 percent sensitivity and 74 percent specificity.

Conclusion: CDB for the diagnosis of HGL has high sensitivity and specificity. Multiple biopsy procedures should be undertaken to improve accuracy.

Keywords: Colposcopy directed biopsy, high-grade lesion,
sensitivity, specificity

Introduction

As of 2020, there were approximately 604,17 new cases of cervical cancer worldwide. The global incidence rate is around 13.3 cases per 100,000 women and a mortality rate of 7.2 deaths per 100,000 women-years[3]. Thailand's incidence rate is around 13 cases per 100,000 women and 11 cases per 100,000 women in Phuket[4].

There has been a shift in global cervical cancer prevention policy towards primary prevention screening and early treatment of precancerous lesions which has successfully reduced the incidence and mortality. Colposcopy is a basic and cost-effective form of examination for the diagnosis of high-grade lesions (HGL), but wide ranges of sensitivity and specificity rates have been reported for the detection of HGL, at 30–90% and 44–97%, respectively.[5-7] The accuracy of colposcopy is limited by the variability of premalignant lesions to detection. Colposcopy is more sensitive for detecting HGL than low-grade lesions (LGL), but its accuracy remains limited. The present study therefore aimed to evaluate the diagnosis performance of colposcopy directed biopsy for HGL as measured by sensitivity and specificity.

Objective

To determine the sensitivity and specificity of CDB and CI for detecting HGL.

Material and methods

This study employs a cross-sectional retrospective design for diagnostic testing. Data were collected from the electronic medical record system and pathology reports, all gathered by a single gynecologist. The data collection followed standardized record forms from the Thai Society of Colposcopy and Pathology.

The final histopathological diagnosis was defined as all specimen's most severe grade of disease (CDB, LEEP, or hysterectomy). A pathological report of CDB and a final diagnosis of CIN 2 or worse were labeled as positive disease, while a report of CIN 1 or less was labeled as negative disease. Colposcope impression refers to a clinician's visual assessment when examining the cervix. The diagnostic accuracy of CI and CDB was determined by comparing the diagnosis from CI and CDB with the final pathological diagnosis from LEEP or hysterectomy. If the CI and CDB result is less than or equal to CIN1 but the final diagnosis is CIN2 or worse, this indicates a discrepancy.

Study population and target population

Data was collected from women who had abnormal cytology or HPV high-risk infection and underwent CDB at Vachira Phuket Hospital colposcopy clinic from January 2019 to July 2021 and after that were indicated for LEEP according to standard protocol. There were 1) diagnosis of

microinvasive (MIC) or adenocarcinoma *in situ* (AIS), 2) results in discrepancy between cytology and subsequent CDB, and 3) therapeutic procedure of HGL. Patients were excluded from the study if they had inadequate colposcopy.

Study tool

Record forms from the Thai Society of Colposcope and Pathology was used for the collected data. The recorded data included patient characteristics, colposcope findings, number of biopsy tissues, and pathological diagnosis from CDB. Patients who were pregnant, had inadequate colposcope, had no tissue for diagnosis, had current or previous cervical cancer, had post-radiation and loss follow-up, or had incomplete data records were excluded.

Data analysis

Descriptive statistics were analyzed using SPSS version 22.0 and a 2x2 table was used for descriptive statistics, sensitivity, and specificity.

Protection of the rights of research participants

No personally identifiable information was recorded to ensure the anonymity of the research participants. This study was approved by the Vachira Phuket Hospital Research Ethics Committee (VPHREC) (VRH REC 008/2023)

Results

During the study period, 264 patients who had abnormal cytology results were included in the colposcopy examination. A total of 239 patients underwent CDB. Subsequently, 90 patients were indicated for LEEP, and only 66 patients with adequate colposcope were eligible for the study. The mean age was 44.2 years, with 38% in the 41–50-year-old age group.

Table 1 presents the agreement of pathological diagnosis from CDB and LEEP or hysterectomy. Of the 66 patients, CDB identified 4 (6.06%) with no squamous intraepithelial lesion, 16 (24.24%) with LGL, 45 (68.19%) with HGL, and 1(1.51%) with MIC.

Table 1. Pathological diagnosis of CDB and LEEP or hysterectomy (n=66).

CDB	LEEP or hysterectomy				Total
	No SIL	LGL	HGL	MIC	
No SIL	1	0	3	0	4
LGL	4	6	6	0	16
HGL	0	1	39	5	45
MIC	0	0	0	1	1

CDB (colposcopy directed biopsy); LEEP (loop electric excision); SIL (squamous intraepithelial lesion); LGL (low-grade lesion); HGL (high-grade lesion); MIC (microinvasive).

Table 2. Comparison data between CDB and final diagnosis for detected high-grade lesion.

CDB	Final Diagnosis		Total
	Positive	Negative	
Positive	45	1	46
Negative	9	11	20
Total	54	12	66

CDB (colposcopic-directed biopsy).

Table 2 shows that the accuracy of CDB for HGL detection was 84.8%, with sensitivity and specificity of 83.3% and 91.6%, respectively. The accuracy rate was higher among women with MIC (100%).

Table 3. Comparison data between colposcopy impression (CI) and final diagnosis for detected high-grade lesion.

CI	Final Diagnosis		Total
	Positive	Negative	
Positive	40	3	43
Negative	14	9	23
Total	54	12	66

CI (colposcopy impression).

Table 3 shows the comparison data between CI and final diagnosis for detected high-grade lesions, which shows that sensitivity and specificity were 74% and 75%. 14 patients were underdiagnosed for HGL from CI.

Discussion

This study identified an adequate colposcopy rate of 72.7% (192 out of 264), with most women in the over 50-year-old age group significantly more likely to have inadequate examinations (42%). This finding contrasts with a 2018 Korean study[8] that reported 91.2% adequacy, likely due to the previous study's younger patient population. It is important to note that 149 patients were excluded due to having cytology consistent with CDB (low-grade lesion). The colposcopy procedures in the present study were performed by a team of five experienced colposcopists with 5-10 years of training.

This study identified a lower rate of underestimation in CDB compared to LEEP, with 13.6% of CDB cases underestimated

compared to 23.1% in Jung et al.'s study (Group CDB, pathological normal/LGL vs. LEEP pathology, HGL).[8] Notably, most underestimated cases in this study had only one biopsy point. Several studies have demonstrated a positive correlation between the number of colposcopic biopsies and the detection rate of HGL.[9] In 2018, Vallapapan et al.[10] found that performing three cervical biopsies during colposcopy maximizes sensitivity for HGL detection (100%) compared to two biopsies (97%). The present study showed increased sensitivity with more biopsies (93% with two or more biopsies), we also suggest that three biopsies might be optimal. Underdiagnosis of CIN by colposcopy impressions is likely to be associated with thin HGL, particularly CIN2. Thin HGL usually presents as small to minute lesions and lacks the classic HGL characteristic of colposcope findings, which may explain why this type of lesion is underdiagnosed by colposcopy. To prevent the underdiagnosis of thin HGL, it is necessary to highlight the need for biopsy in regions with acetowhite, even if the colposcopy impression might be metaplasia or LGL. In agreement with the findings of Li et al[11]. demonstrates the improved detection of HGL when combining endocervical curettage (ECC) with colposcopy biopsy. The overall agreement for HGL diagnosis was significantly higher with this combined approach (72.43%) compared to colposcopy biopsy alone (67.54%). The evidence for identifying women most likely to benefit from endocervical sampling based on transitional zone (TZ) type is also inconclusive. Research indicates that even when the TZ is completely visible under colposcopy, 5% of patients still have positive ECC findings.[13] TZ type was not an independent predictor of ECC positivity. Incomplete visualization of the TZ is likely more linked to the colposcopist's experience and may not entirely raise concern for missed endocervical lesions.[14] Phianpiset's study[15] suggested a strategy involving no biopsy with a follow-up strategy in the lowest-risk group, which is inconsistent with ASCCP recommendations but is in alignment with a strategy of multiple targeted biopsies in the intermediate-risk and highest-risk groups.

The present study found that CDB sensitivity and specificity for detected HGL were higher than CI by 83.3 percent and 91.6 percent respectively. No serious aspect is underdiagnosis of microinvasive or invasive carcinoma. Similar to the same study at Srinagarind Hospital, CDB sensitivity and specificity (84 percent and 100 percent, respectively) were high for detecting HGL.[16]

Conclusion

In this study, CDB was found to have high sensitivity and
specificity for the detection of HGL at Vachira Phuket Hospital.

Limitation

Due to its retrospective nature, this study faced limitations with potential data

loss and selection bias. Specifically, data was missing for patients diagnosed solely via colposcopy who did not undergo either CDB or LEEP.

Recommendations

Recommendations for the application of research results

This study demonstrates improved detection of HGL when combining multiple colposcopy biopsies.

Recommendations for future research

Future research should be a prospective study.

Research grant

This study was supported by a research grant from Vachira Phuket Medical Center (VMEC).

Reference

1.Pierce JG Jr, Bright S. Performance of a colposcopic examination, a loop electrosurgical procedure, and cryotherapy of the cervix. Obstet Gynecol Clin North Am [serial online] 2013 [cited 2024 Aug 25]; 40(4):731-57. Available from: URL: https://pubmed.ncbi.nlm.nih.gov

2. Qin D, Bai A, Xue P, Seery S, Wang J, Mendez MJG, Li Q, Jiang Y, Qiao Y. Colposcopic accuracy in diagnosing squamous intraepithelial lesions: a systematic review and meta-analysis of the International Federation of Cervical Pathology and Colposcopy 2011 terminology. BMC Cancer [serial online] 2023 [cited 2024 Aug 25];23(1):187. Available from: URL: https://pubmed.ncbi.nlm.nih.gov

3. Singh D, Vignat J, Lorenzoni V, Eslahi M, Ginsburg O, Lauby-Secretan B, et al. Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the WHO Global Cervical Cancer Elimination Initiative. Lancet Glob Health [serial online] 2023 [cited 2024 Aug 25];11(2):197-206. Available from: URL: https://pubmed.ncbi.nlm.nih.gov

4. Ministry of Public Health. Health Data Center: Chronic Disease Surveillance System. Thailand: Ministry of Public Health. [online] 2024 [cited 2024 Sep 6]. Available from: URL: https://hdcservice.moph.go.th/hdc/reports/report.php

5. Petousis S, Christidis P, Margioula-Siarkou C. Discrepancy between colposcopy, punch biopsy and final histology of cone specimen: a prospective study. Arch Gynecol Obstet [serial online] 2018 [cited 2024 Aug 25]; 297:1271-5. Available from: URL: https://pubmed.ncbi.nlm.nih.gov

6. Karimi-Zarchi M, Peighmbari F, Karimi N, Rohi M, Chiti Z. A comparison of 3 ways of conventional Pap smear, liquid-based cytology and colposcopy vs cervical biopsy for early diagnosis of premalignant lesions or cervical cancer in women with abnormal conventional Pap test. Int J Biomed Sci [serial online] 2013 [cited 2024 Aug 25];9(4):205-10.

Available from: URL: https://pubmed.ncbi.nlm.nih.gov
7. Nam K. Colposcopy at a turning point. Obstet Gynecol Sci [serial online] 2018[cited 2024 Aug 25];61:1-6. Available from: URL:https://pubmed.ncbi.nlm.nih.gov
8. Jung Y, Lee AR, Lee SJ, Lee YS, Park DC, Park EK. Clinical factors that affect diagnostic discrepancy between colposcopically directed biopsies and loop electrosurgical excision procedure conization of the uterine cervix. Obstet Gynecol Sci [serial online] 2018 [cited 2024 Aug 25];61(4):477-88. Available from: URL: https://pubmed.ncbi.nlm.nih.gov
9. Stoler MH, Vichnin MD, Ferenczy A, Ferris DG, Perez G, Paavonen J. The accuracy of colposcopic biopsy: analyses from the placebo arm of the Gardasil clinical trials. Int J Cancer [serial online] 2011[cited 2024 Aug 25];128:1354-62. Available from: URL:https://pubmed.ncbi.nlm.nih.gov
10. Vallapapan A, Chandeying N, Srijaipracharoen S, Uthagethaworn K. The role of random cervical biopsies in addition to colposcopy-directed biopsies in detection of CIN2+. J Obstet Gynaecol [serial online] 2019 [cited 2024 Aug 25];39(2):184-9. Available from: URL: https://pubmed.ncbi.nlm.nih.gov
11. Li M, Zhang X, Zhang Q, Zhao Y, Zhao C, Li J, Wei L. Underdiagnosis of cervical intraepithelial neoplasia by colposcopy and its association with thin high-grade squamous intraepithelial lesions. Oncol Lett [serial online] 2023 [cited 2024 Aug 25];26:287. Available from: URL: https://pubmed.ncbi.nlm.nih.gov
12. Sijing L, Ying J, Jing W, Xiaoge L, Ming L, Zhaoning D. Additional role of ECC in the detection and treatment of cervical HSIL. Front Med [serial online] 2023 [cited 2024 Aug 25];10:1-7. Available from: URL: https://pubmed.ncbi.nlm.nih.gov
13. Mi L, Zhuan J, Zhang D, Hui B. Role of ECC in detection of HSIL+ under comprehensive colposcopy and multi-site biopsy. Chin J Clin Obstet Gynecol [serial online] 2019 [cited 2024 Aug 25] ;20(2):128-31. Available from: URL:https://pubmed.ncbi.nlm.nih.gov
14. Li Y, Luo H, Zhang X, Chang J, Zhao Y, Li J, Li D, Wang W. Development and validation of a clinical prediction model for endocervical curettage decision-making in cervical lesions. BMC Cancer [serial online] 2021[cited 2024 Aug 25] ;21(1):804. Available from: URL: https://pubmed.ncbi.nlm.nih.gov
15. Phianpiset R, Ruengkhachorn I, Jareemit N, Ittiamornlert P, Chaopotong P, Hanamornroongruang S, et al. ASCCP risk-based colposcopy recommendations applied in Thai women with atypical squamous cells of undetermined significance or low-grade squamous intraepithelial lesion cytology. Obstet Gynecol [serial online] 2020 [cited 2024 Aug 25];136(3):510-7. Available from: URL: https://pubmed.ncbi.nlm.nih.gov
16. Ouitrakul S, Udomthavornsuk B, Chumworathayi B, Luanratanakorn S, Supoken A. Accuracy of colposcopically directed

biopsy in diagnosis of cervical pathology at Srinagarind Hospital. Asian Pac J Cancer Prev [serial online] 2011[cited 2024 Aug 25] ;12(9):2451-3. Available from: URL: https://pubmed.ncbi.nlm.nih.gov