J Gynecol Oncol. 2018 Jul;29(4):e52
https://doi.org/10.3802/jgo.2018.29.e52
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Original Article

Quality of tissue from punch biopsy forceps vs. round loop electrode in colposcopically directed biopsy: a randomized controlled trial

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Received: Sep 4, 2017
Revised: Nov 1, 2017
Accepted: Mar 3, 2018

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Funding
This research received a full grant from the Faculty of Medicine, Prince of Songkla University.

ABSTRACT

Objective: To compare the quality of tissue from punch biopsy forceps (PB group) with round loop electrode (LE group) in colposcopically directed biopsy along with the evaluation of pain associated with each procedure.
Methods: Patients with abnormal cervical cytologic results and abnormal colposcopic findings were enrolled into a randomized trial into either a PB group or LE group. The quality of tissue was evaluated in regards to the size of tissue, site of tissue, and tissue damage. Each quality had 1 to 3 points and the sum of each quality contributed to the total tissue score that ranged from 3 to 9. Pain associated with each procedure was assessed by a visual analog scale (VAS). This was a clinical trial study and was registered at www.clinicaltrials.in.th (Identifier: TCTR20160404001).
Results: Ninety-six women who met all eligibility requirements were enrolled in the study. Forty-eight patients were randomly assigned to the PB group and 48 patients were randomized into the LE group. The characteristics of the patients were similar between the 2 groups with the exception of the median age. The median total tissue score was 8 points in the LE group which was more than the median of 7 points in the PB group with a statistically significant difference (p=0.014). However, the median VAS pain score in both groups was 3.4 (p=0.82).
Conclusion: The quality of cervical tissues obtained from biopsy with a round loop electrode was better than the punch biopsy forceps with no difference in the level of pain.

Keywords: Colposcopy; Cervix Uteri; Biopsy; Diagnostic Equipment; Histology; Pain

INTRODUCTION

A colposcopically directed biopsy (CDB) should be undertaken to confirm tissue diagnosis from histology in suspicious cervical lesions even by an experienced colposcopist [1]. Moreover, CDB is a confirmation that is necessary in young nulliparous women which avoids any unnecessary conization [2-5]. The accuracy of a CDB in the diagnosis of cervical pathology is 87.8% and the sensitivity and specificity are 84.9% and 100%, respectively [6]. However, the accuracy of the histopathological diagnosis of tissue specimens depends on obtaining adequate samples by CDB [7]. In general, we use punch biopsy forceps in CDB. Two tools are available to conduct a biopsy under colposcopy in Songklanagarind Hospital:

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: R.A.; Data curation: W.T., R.A.; Formal analysis: W.T., K.K.; Funding acquisition: R.A.; Investigation: W.T., R.A., K.K.; Methodology: R.A.; Project administration: R.A.; Resources: R.A.; Software: W.T.; Supervision: R.A.; Validation: W.T., R.A., K.K.; Visualization: W.T.; Writing - original draft: W.T.; Writing - review & editing: W.T., R.A.

the round loop electrode and punch biopsy forceps. The round loop electrode can control the extent of tissue in comprehensive lesions. The disadvantages include the need of experienced hands because the patients may otherwise receive electrical and thermal effects at the tissue margin which may disturb the final pathology evaluation.

To our knowledge, there is no study on the efficacy of the round loop electrode. The complications of a loop electrode, that include bleeding and infection, were found in 5.4% [8,9]. The advantages of punch biopsy forceps are ease of use and less time consumption. For experienced clinicians, the average time to biopsy is 2–3 minutes [9,10]. Punch biopsy forceps are used widely as well as being less expensive than the loop electrode. However, a disadvantage of punch biopsy forceps is the tissue may slide which results in tissue fragments being sent to the pathologist. In general, no topical anesthesia is used during a CDB because ibuprofen or topical lidocaine were not shown to reduce pain [11,12]. Pain scores during punch biopsy forceps were 2.31±1.60 [12] but currently there is no study to compare pain scores of each biopsy procedure. A study to compare the quality of tissue from punch biopsy forceps with round loop electrodes in CDB has not been reported. Experienced colposcopists usually use different tools depending on each situation but a new study may be beneficial in making a decision on the appropriate tool in CDB. Hence, the objective of this study was to compare the quality of tissue from punch biopsy forceps with round loop electrode in CDB as well as to evaluate pain associated with each procedure.

MATERIALS AND METHODS

After approval from the ethics committee at Prince of Songkla University, we conducted a randomized controlled trial between July 2016 and February 2017 in the colposcopic clinic of Songklanagarind Hospital at Prince of Songkla University in Thailand. We recruited women who were not pregnant and had an abnormal Pap smear defined as atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells cannot rule out high-grade squamous intraepithelial lesion (ASC-H), low-grade squamous intraepithelial lesion (LSIL) or high-grade squamous intraepithelial lesion (HSIL) with or without human papillomavirus (HPV) DNA positive that indicated colposcopy. Excluded women were those who had a previous conization, hysterectomy, radiation or recent infection, or were immunocompromised hosts, had a pacemaker, abnormal bleeding or hematologic disease. After signing the informed consent, we collected the characteristic data of the patients that included age, reproductive status, parity, history of pills taken, history of chronic pelvic pain/dysmenorrhea, previous sexually transmitted diseases, smoker or nonsmoker, cytology report, and HPV status. Patients were placed in the lithotomy position and a grounding pad was attached to the patient's thigh. The cervix was visualized using a bivalve speculum. The operator applied normal saline, 3%–5% acetic acid, and Lugol's iodine solution to the cervix to determine any abnormal colposcopic findings. This was diagnosed by the Reid colposcopic index [13]. Women who had a Reid colposcopic index of low grade disease, high grade disease or invasive disease who needed a biopsy were randomly assigned to either the punch biopsy forceps group (PB group) or the round loop electrode group (LE group). This was assigned by sealed envelopes. Block randomization was done by a computer generated, random number of each procedure with allocation concealment. In the PB group, the most suspicious lesion was biopsied by punch biopsy forceps using Kevorkian biopsy forceps (Integra™ Miltex®, model MH30-1482; Integra LifeSciences Corporation, Plainsboro, NJ, USA) (**Fig. 1**). We used the same model of forceps in all patients in the PB group. The section

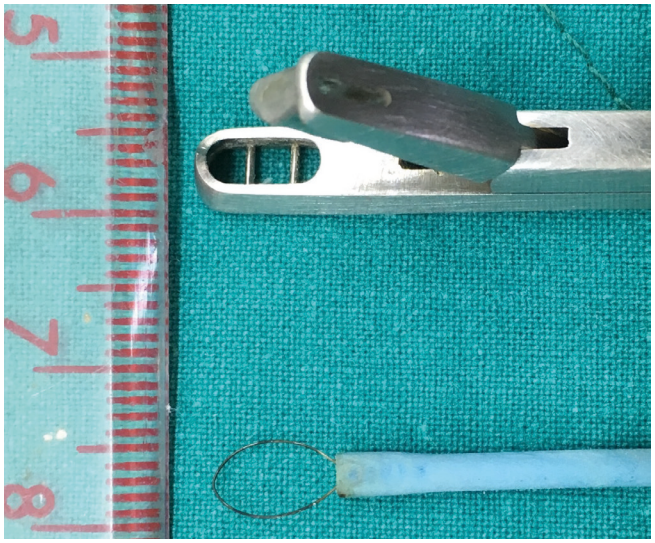

Fig. 1. Diagnostic equipment for cervical biopsy: Kevorkian biopsy forceps (upper) and the round loop electrode (lower).

was rectangular in shape designed to facilitate a clean cut and help reduce crush artifact during the biopsies [14]. The operator used the teeth on the lower jaw fixed to the endocervix while the upper jaw was fixed to the biopsy specimens at the squamocolumnar junction with a perpendicular pattern. In the LE group, the operator used the round loop electrode B1D made from stainless steel and connected to a 35–55 watt electrical generator (**Fig. 1**). The loop diameter was ¼ inch. The round loop electrode was also perpendicular to the lesion starting with the loop 3 mm away from the tissue. The biopsy was performed by the cutting mode to a depth of 7 mm equal to the diameter of the loop electrode.

All operators had at least 50 cases per year of experience in colposcopic biopsy. Before the study was started, all operators were instructed to use the same surgical technique for biopsy in both groups. The specimens were placed in 100% formalin and sent for histopathology. After biopsies, bleeding was estimated, observed and pressured with gauze for approximately 1 minute. If further bleeding occurred, hemostasis was generally achieved by electrocoagulation with a ball-head electrode or the application of Monsel's solution. Patients were observed for about 10 minutes after the procedure in case of any immediate complications. A bleeding complication was defined as severe bleeding that required surgical intervention to stop the bleeding. Procedure-associated pain was evaluated within 1 minute after the CDB by a 10-cm visual analog scale (VAS) while the operator observed for bleeding.

All specimens were evaluated and reviewed by an experienced pathologist. Tissue quality was evaluated based on data in European guidelines for quality assurance in cervical histology [15] including the size of tissue (area equal to width multiplied by length), site of tissue, and tissue damage. The quality was simplified into scores for comparison (**Table 1**). The score

Table 1. Quality of tissue scores

Quality of tissue	Scores (points)		
	1	2	3
1. Size of tissue	Tissue area is less than 5 mm^2.	Tissue area is between 5–10 mm^2.	Tissue area is more than 10 mm^2.
2. Site of tissue	There is neither epithelial nor stromal tissue.	There is either epithelial or stromal tissue.	There are both epithelial and stromal tissue.
3. Tissue damage	There is either distortion or electrocautery effect that cannot evaluate pathologic result.	There is either distortion or electrocautery effect but can evaluate pathologic result.	There is neither distortion nor electrocautery effect.

https://doi.org/10.3802/jgo.2018.29.e52

of each quality ranged from 1 to 3 and the total tissue score ranged from 3 to 9. All patients came for follow-up in the gynecologic outpatient clinic to evaluate any complications such as bleeding or infection. They were also informed of the pathological report and further management requirements.

Sample size calculation was based on detecting a difference between the mean scores of the methods. The range of scoring was 6 units and we treated this as a continuous variation. Standard deviation (SD) was the normal variation and the expected SD was 1.5. The minimal difference in tissue score to be detected was 1.5. The alpha value was set at 0.05 and the power was set at 80%. The sample size was calculated to be 48 patients for each group. The total tissue scores as well as the VAS pain scores of each group were compared.

Statistical analysis was performed using the Student's t-test, χ^2 test, Fisher's exact test, and Wilcoxon rank sum test. Probability values less than 0.05 were considered statistically significant. Statistical analysis was performed with the SPSS 17.0 package program (Statistical Package Social Science; SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 96 patients were included in the study. Forty-eight patients were in the PB group and 48 patients were in the LE group with no patients lost to follow-up (**Fig. 2**). The characteristics of both groups were similar with the exception of median age (**Table 2**). The median age in the LE group was older than the PB group (44.8 vs. 38.9 years old) (p=0.011). Almost all of the patients in the 2 groups were premenopausal women. ASC-US and LSIL were common abnormal cytology reports in both groups. An adequate colposcopic assessment found 81.2% in the PB group and 68.8% in the LE group (p=0.240). Low grade diseases were the most common of the colposcopic diagnosis and histology reports in both groups. **Table 3** shows a comparison of the tissue scores. The total tissue score is the sum of each quality score (size of tissue, site of tissue, and tissue damage). The median tissue score in the LE group was significantly higher than in the PB group (8 vs.7) (p=0.014). In the LE group, 54.2% of the

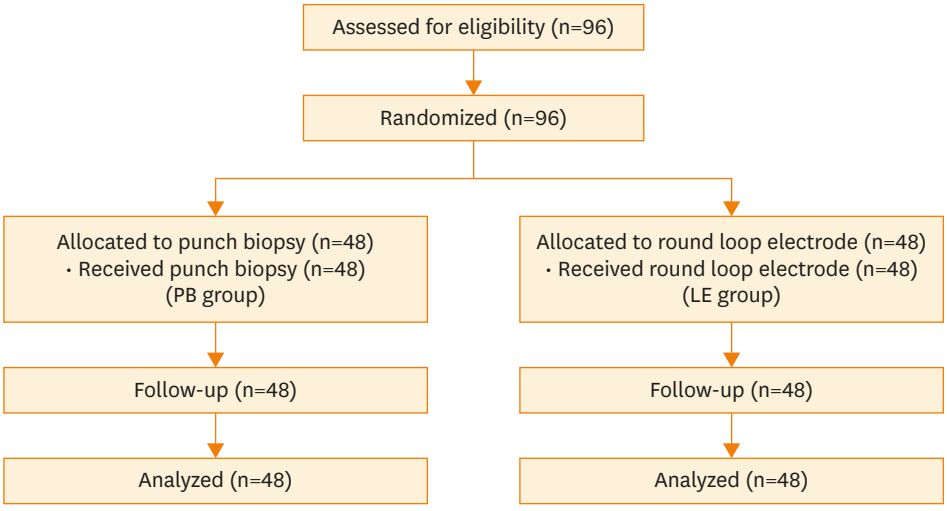

Fig. 2. Flow of patients through the study.
LE group, round loop electrode group; PB group, punch biopsy forceps group.

https://doi.org/10.3802/jgo.2018.29.e52

Table 2. Patient characteristics

Characteristics	PB group (n=48)	LE group (n=48)	p-value
Age (yr)	38.9 (10.2)	44.8 (12.2)	0.011*
Reproductive status			0.190†
Premenopause	42 (87.5)	36 (75)	
Menopause	6 (12.5)	12 (25)	
Parity			0.350†
Nulliparous	15 (31.2)	10 (20.8)	
Multiparous	33 (68.8)	38 (79.2)	
History of pills used			0.520†
Yes	15 (31.2)	19 (39.6)	
No	33 (68.8)	29 (60.4)	
History of chronic pelvic pain/dysmenorrhea			1.000†
Yes	21 (43.8)	21 (43.8)	
No	27 (56.2)	27 (56.2)	
Previous sexually transmitted disease			0.490‡
Yes	3 (6.2)	6 (12.5)	
No	45 (93.8)	42 (87.5)	
Smoking			1.000‡
Yes	1 (2.1)	0 (0)	
No	47 (97.9)	48 (100)	
Cytology report			0.720†
ASC-US	17 (35.4)	15 (31.2)	
ASC-H	9 (18.8)	8 (16.7)	
LSIL	17 (35.4)	16 (33.3)	
HSIL	5 (10.4)	9 (18.8)	
HPV status			0.740†
Unknown	26 (54.2)	27 (56.2)	
HPV 16 or 18 positive	14 (29.2)	11 (22.9)	
HPV 16 and 18 negative	8 (16.7)	10 (20.8)	
Colposcopic assessment			0.240†
Adequate	39 (81.2)	33 (68.8)	
Inadequate	9 (18.8)	15 (31.2)	
Reid colposcopic index score			0.790†
0–2	6 (12.5)	8 (16.7)	
3–5	33 (68.8)	30 (62.5)	
6–8	9 (18.8)	10 (20.8)	
Histological report			0.730‡
No dysplasia, koilocytosis	30 (62.5)	28 (58.3)	
CIN1	6 (12.5)	4 (8.3)	
CIN2	1 (2.1)	3 (6.2)	
CIN3/CIS	11 (22.9)	13 (27.1)	
Post-operative complication			1.000‡
Yes	1 (2.1)	1 (2.1)	
No	47 (97.9)	47 (97.9)	
Further management			0.250†
Yes	12 (25)	16 (33.3)	
No	36 (75)	32 (66.7)	

Values are presented as mean (SD) or number (%).
ASC-H, atypical squamous cells cannot rule out high-grade squamous intraepithelial lesion; ASC-US, atypical squamous cells of undetermined significance; CIN, cervical intraepithelial neoplasia; CIS, carcinoma in situ; HPV, human papillomavirus; HSIL, high-grade-squamous intraepithelial lesion; LE group, round loop electrode group; LSIL, low-grade squamous intraepithelial lesion; PB group, punch biopsy forceps group; SD, standard deviation.
*Student's t-test; †χ^2 test; ‡Fisher's exact test.

patients had a score of 3 points for the size of tissue, while only 25% in the PB group had 3 points with a statistical significance (p<0.001). There were no differences in the tissue sites in the biopsy procedures. All patients in the LE group had 3 points for site of tissue which meant there were both epithelial and stromal tissues in all specimens and almost all specimens (93.8%) in the PB group had 3 points with no statistical significance between the 2 groups. On the other hand, 3 points for damage of tissue meant neither distortion nor electrocautery

https://doi.org/10.3802/jgo.2018.29.e52

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Table 3. Comparison of tissue scores

Characteristics	PB group (n=48)	LE group (n=48)	p-value
Total tissue scores (median)	7	8	0.014*
Size of tissue			<0.001†
1	20 (41.7)	5 (10.4)	
2	16 (33.3)	17 (35.4)	
3	12 (25)	26 (54.2)	
Site of tissue			0.240‡
1	0 (0)	0 (0)	
2	3 (6.2)	0 (0)	
3	45 (93.8)	48 (100)	
Tissue damage			0.003†
1	0 (0)	0 (0)	
2	36 (75)	47 (97.9)	
3	12 (25)	1 (2.1)	

Values are presented as number (%).
LE group, round loop electrode group; PB group, punch biopsy forceps group.
*Wilcoxon rank sum test; †χ^2 test; ‡Fisher's exact test.

Table 4. Comparison of VAS pain scores

Comparisons	PB group (n=48)	LE group (n=48)	p-value*
VAS pain score (median)	3.4	3.4	0.820

LE group, round loop electrode group; PB group, punch biopsy forceps group; VAS, visual analog scale.
*Wilcoxon rank sum test.

effect. Three points for damage of tissue in the PB group was in 25% but in the LE group it was only 2.1%. Two points for damage of tissue meant either distortion or electrocautery effect which was evaluated by pathologic results. Most patients in the LE group (97.9%) had 2 points for tissue damage which was a significant difference compared to 75% of the patients in the PB group (p=0.003). Pain associated with the procedure was evaluated in all patients of both groups (**Table 4**). In both groups, the median VAS pain score was 3.4 (p=0.820).

DISCUSSION

To the best of our knowledge, this is the first trial that compared the quality of cervical tissue obtained from CDB with punch biopsy forceps and round loop electrode. The tissue quality in the LE group was significantly better than the tissue in the PB group based on the total tissue scores. Size of tissue scores in the LE group were also higher than in the PB group with statistical significance. Although no previous studies have compared the quality of tissue from these tools, we can explain the results. The tissue sizes in the LE group were large because the round loop electrode is an electrical cut that can be precisely controlled to penetrate every suspicious area especially in tissue of hard consistency or in a stenotic cervical os. The use of a round loop electrode can achieve adequate biopsies without slipping as opposed to punch biopsy with forceps. Concerning the site of tissue which is determined by both epithelial and stromal tissue content, both biopsy procedures reached both sites of tissue with no significant difference. Surprisingly, we found 6.2% in the PB group had 2 points for site of tissue which meant the tissue contained only cervical epithelium or stroma. This finding may lead to a misdiagnosis or reoperation of the diagnosis procedure. In contrast, all patients in the LE group had 3 points for site of tissue. The damage of tissue was evaluated by the distortion or by the electrocautery effect. The round loop electrode has electrocautery effects that are unavoidable. Srisomboon et al. [16] noted that non-evaluable pathological margins on cervical conization specimens were in 4.4%. On the contrary, no

https://doi.org/10.3802/jgo.2018.29.e52

patients in our study had non-evaluable histology. However, only 2.1% of those in the LE group had no distortion or electrocautery effect. We think this effect may be improved by adjusting the electrical power. The use of punch biopsy forceps caused some distortion or fragments of tissue when we pulled the tissue biopsy, particularly in cervical tissue of hard consistency. However, all tissues could still be evaluated by pathologic results. The VAS pain score associated in each procedure was 3.4 in both groups which was similar to another study that reported pain scores during the punch biopsy forceps procedure as 2.31±1.60 [12].

The strength of this study is the randomized, controlled trial methodology to compare the quality of cervical tissues obtained from biopsy in 2 procedures including the assessment of pain. We proposed tissue scores for simplification of the comparison and an objective interpretation of the cervical histology by quality of tissue in 3 categories. However, this study had some limitations. First, the quality of tissue was evaluated by a single pathologist. Interobserver reliability should have been evaluated. Second, the population of patients was too small to demonstrate different complications between the 2 groups. If there is a difference in complications, it is an important thing to consider when choosing the procedures. Hence, further studies should evaluate the cost effectiveness of each procedure to decide which tool is best suited for each situation. Since the quality of tissue from the round loop electrode was better than the punch biopsy forceps with no difference in the pain score, we suggest using the round loop electrode in CDB for good tissue quality to evaluate the histology. However, no single tool is appropriate for every situation. Experienced colposcopists usually choose different tools for each situation according to their own preferences. In conclusion, the quality of cervical tissues obtained from biopsy with round loop electrode was better than the punch biopsy forceps and there was no difference in the levels of pain associated with each procedure.

ACKNOWLEDGMENTS

We would like to thank the Epidemiology Unit, Faculty of Medicine, Prince of Songkla University for assistance with the statistical analysis.

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