タイトル	Retrospective Study of Colposcopy for Precancerous Cervical Lesions and Correlation between Diagnosis and Number of Biopsy Specimens
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公開者	The Medical Society of Toho University
発行日	2020.09.01
ISSN	21891990
掲載情報	Toho Journal of Medicine. 6(3). p.99-103.
資料種別	学術雑誌論文
内容記述	Original Article
著者版フラグ	publisher
JaLCDOI	info:doi/10.14994/tohojmed.2019-025
メタデータのＵＲＬ	https://mylibrary.toho-u.ac.jp/webopac/TD37886057

Original Article

Retrospective Study of Colposcopy for Precancerous Cervical Lesions and Correlation between Diagnosis and Number of Biopsy Specimens

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ABSTRACT

Introduction: Histological diagnosis is performed in patients with abnormal findings on cervical cytology and macroscopic abnormalities of the cervix. In general, targeted histological diagnosis is performed to extract the specimens from lesions with abnormal findings under a colposcope. In this study, we aim to retrospectively verify the number of specimens from different cervical lesions that are most effective for diagnosis.

Methods: We included women with abnormal findings on cervical cytology who underwent targeted biopsy under a colposcope in our hospital from August 2013 to March 2016. The number of specimens extracted and the number of biopsies required to achieve diagnosis were examined in patients with cervical histopathology showing cervical intraepithelial neoplasia (CIN)1, CIN2, and CIN3. Furthermore, when cervical histology showed indications for conization and total hysterectomy, these procedures were performed to confirm the ultimate histopathological diagnosis.

Results: The definite diagnosis of CIN was made from one, one and two, and one, two, and three biopsies in 81.6%, 96.1%, and 100% patients, respectively.

Conclusions: All patients with CIN1 to CIN3 were diagnosed with three biopsies. In particular, higher number of biopsies was associated with higher rates of definite diagnosis. However, in no cases, definite CIN diagnosis was made at the four biopsies, suggesting that four or more cervical histological biopsies are generally unnecessary. Furthermore, given that 100% patients were diagnosed by their three biopsies, and at most, only three biopsies should be performed.

Toho J Med 6 (3): 99–103, 2020

KEYWORDS: colposcopy, cervical intraepithelial neoplasia, biopsy, cervical cancer

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DOI: 10.14994/tohojmed.2019-025

Received Oct. 31, 2019: Accepted Dec. 19, 2019
Toho Journal of Medicine 6 (3), Sept. 1, 2020.
ISSN 2189–1990, CODEN: TJMOA2

Introduction

Cervical cancer is the fourth most common cancer in women with an estimated 570,000 new cases in 2018 representing 7.5% of all female cancer death.[1] Cervical cancer is the easiest gynecologic cancer to prevent with regular screening tests and follow-up; it is highly curable when found and treated early.[2]

The detection of cytological abnormalities through screening has resulted in a fall in the incidence of cervical cancer because of the treatment of these pre-invasive lesions.[3]

Colposcopic examination of the cervix allows assessment of the abnormality before it is treated, either by excision or ablation.[4–6] Colposcopy is a subjective test; its purpose is to identify disease, obtain representative specimens for histology, and direct patient management.[7, 8]

In 2013, the American Society for Colposcopy and Cervical Pathology updated its guidelines to suggest that a histological diagnosis should be done for patients with abnormalities on cervical cytology or those with macroscopic abnormalities of the cervix.[9] The punch biopsy also plays a role in the management of women undergoing ablative treatment for CIN because pretreatment biopsies are required to exclude invasive disease.[10, 11] Generally, targeted histological biopsy is performed to directly extract specimens from the lesions with abnormal findings under a colposcope. However, colposcopy is a subjective test, and its accuracy has been recently questioned.[12, 13] According to Nakamura et al., CIN2 and more severe lesions are diagnosed by one-lesion biopsy in 78.1% patients and by two-lesion biopsies in ≥90%, regardless of the tester.[14] Stoler MH et al. reported that one, two, and three or more biopsies led to 47%, 65%, and 77% of definite diagnoses, respectively. Collecting specimens from more lesions is historically recommended to improve the accuracy of cervical tissue biopsy.[15] However, cervical histological diagnosis, an invasive test, causes bleeding, and it is ideal to establish a certain diagnosis with a less-invasive one.

Therefore, we investigated the number of biopsies required for accurate histological diagnosis in 350 patients who underwent colposcopy and histological biopsy. In those requiring conization, histological diagnoses before and after conization were also compared.

Methods

We included women with abnormal findings on cervical cytology who underwent colposcopy and histological biopsy from August 2013 to March 2016 at our hospital. Nine testers were involved. We investigated the number of biopsies and their lesions required for the cervical histopathological diagnoses of CIN1, CIN2, and CIN3. Furthermore, the preoperative histological and histopathological diagnoses of the conization specimens in patients who underwent conization or total hysterectomy were analyzed. The order of biopsy was decided as per the tester's discretion. Hematoxylin and eosin staining and the World Health Organization classifications were used for histopathological diagnosis. Moreover, when cervical histology showed indications for conization and total hysterectomy, these procedures were performed to confirm the ultimate histopathological diagnosis.

This study was approved by the relevant ethics committee of Toho University Ohashi Medical Center (No. H 17018).

Results

A total of 350 female patients were histologically diagnosed with chronic cervicitis, CIN, and adenocarcinoma in situ (AIS). Their characteristics are shown in Table 1. In terms of age, 71 (20.3%), 137(39.1%), 86 (24.6%), and 56 (16.0%) were in their 20s, 30s, 40s, and 50s, respectively. The median age was 36 (20-79) years. In addition, the results of cervical cytology indicated ASC-US, LSIL, HSIL, AGC, ASC-H, CIS, and SCC in 24 (6.9%), 133 (46.6%), 177 (50.6%), 5 (1.4%), 3 (0.86%), 3 (0.86%), and 5 (1.4%) patients, respectively.

Targeted histological diagnosis under a colposcope revealed chronic cervicitis, CIN1, CIN2, CIN3, and AIS in 65 (18.6%), 107 (30.6%), 89 (25.4%), 87 (24.9%), and 2 (0.57%) patients, respectively. Furthermore, 43 (12.3%), 153 (43.7%), 132 (37.7%), and 22 (6.3%) patients underwent one, two, three, and four biopsies, respectively. As shown in Table 2, 231 (81.6%), 272 (96.1%), and 283 (100%) of them were diagnosed at their one, one and two, and one, two, and three biopsies, respectively.

Furthermore, we investigated the number of biopsies by each CIN grade and the number of biopsies required for diagnosis. In CIN1, one, two, three, and four biopsies were taken in 14 (13.1%), 58 (54.2%), 32 (29.9%), and 3 (2.8%) patients, respectively. Furthermore, 89 (83.2%), 105 (98.1%), and 107 (100%) patients were diagnosed with CIN1 at their one, one and two, and one, two, and three biopsies, respectively (Fig. 1). In CIN2, one, two, three, and four biopsies

Table 1 Characteristics of the study participants

Characteristics	N	%
Age (years)		
20-29	71	20.3
30-39	137	39.1
40-49	86	24.6
≥ 50	56	16.0
Cytology		
ASC-US	24	6.9
LSIL	133	46.6
ASC-H	3	0.86
HSIL	177	50.6
AGC	5	1.4
CIS	3	0.86
SCC	5	1.4
Histology		
Total	350	100
Chronic cervicitis	65	18.6
CIN1	107	30.6
CIN2	89	25.4
CIN3	87	24.9
AIS	2	0.57
Number of cervical specimens (CIN1, CIN2, CIN3)		
Total	283	100
One	29	10.2
Two	117	41.3
Three	120	42.4
Four	17	6.0
Number of biopsies to diagnosis (CIN1, CIN2, CIN3)		
Total	283	100
One	231	81.6
One and two	272	96.1
One, two, and three	283	100

Table 2 Number of cervical specimens and number of biopsies to diagnose (CIN)

Number of cervical specimens and number of biopsies to diagnose (CIN1, CIN2, and CIN3)	N	%
Number of cervical specimens (CIN1)		
Total	107	100
One	14	13.1
Two	58	54.2
Three	32	29.9
Four	3	2.8
Number of biopsies to diagnose (CIN1)		
Total	107	100
One	89	83.2
One and two	105	98.1
One, two, and three	107	100
Number of cervical specimens (CIN2)		
Total	89	100
One	9	10.1
Two	36	40.4
Three	41	46.1
Four	3	3.4
Number of biopsies to diagnose (CIN2)		
Total	89	100
One	75	84.3
One and two	87	97.8
One, two, and three	89	100
Number of cervical specimens (CIN3)		
Total	87	100
One	6	6.9
Two	23	26.4
Three	47	54.0
Four	11	12.6
Number of biopsies to diagnose (CIN3)		
Total	87	100
One	67	77.0
One and two	80	92.0
One, two, and three	87	100

were taken in 9 (10.1%), 36 (40.4%), 41 (46.1%), and 3 (3.4%) patients, respectively. Furthermore, CIN2 diagnoses were reached at the one, one and two, and one, two, and three biopsies in 75 (84.3%), 87 (97.8%), 89 (100%) patients, respectively (Fig. 2). In CIN3, one, two, three, and four biopsies were performed in 6 (6.9%), 23 (26.4%), 47 (54.0%), and 11 (12.6%) patients, respectively. Furthermore, 67 (77.0%), 80 (83.8%), and 87 (100%) patients were diagnosed with CIN3 at their one, one and two, and one, two, and three biopsies, respectively (Fig. 3). Thus, CIN diagnosis was established at the one, one and two, and one, two, and three biopsies in 81.6%, 96.1%, and 100% patients, respectively.

A total of 81 CIN3 patients underwent cervical conization or total hysterectomy, of which 59, 8, and 14 patients were diagnosed with CIN3, CIN2, and chronic cervicitis by histopathology, respectively. Furthermore, of the five CIN 2 patients who underwent this procedure, four patients were diagnosed with CIN3, and one patient was diagnosed with CIN2, histopathologically.

Discussion

We studied 350 patients with abnormal findings in cervical cytology. All were diagnosed with CIN1-CIN3 by the three biopsies. Furthermore, with more number of biopsies, definite diagnoses were made at a higher probability. However, no patient was definitely diagnosed at the four biopsies. Therefore, four or more biopsies are generally considered unnecessary for cervical histology. In addition, given that 100% patients were diagnosed by their three bi-

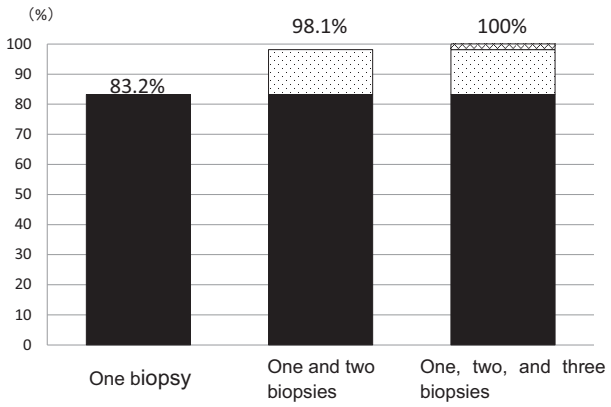

Fig. 1
Number of biopsies and detection rates of CIN1 diagnosis
Overall 83.2% patients were diagnosed at one biopsy, 98.1% were diagnosed at one and two biopsies, and 100% were diagnosed at one, two, and three biopsies.

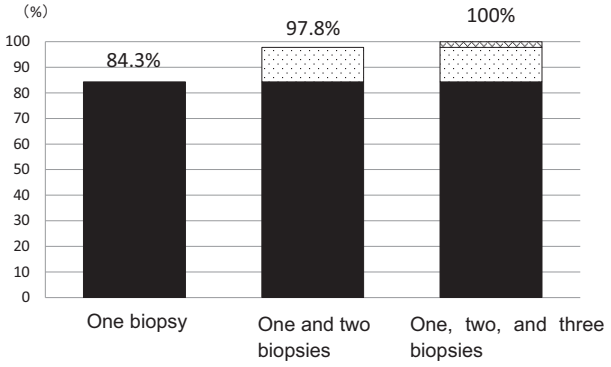

Fig. 2
Number of biopsies and detection rates of CIN2 diagnosis
Overall 84.3% patients were diagnosed at one biopsy, 97.8% were diagnosed at one and two biopsies, and 100% were diagnosed at one, two, and three biopsies.

opsies, and at most, only three biopsies should be performed.

Furthermore, the results of cervical histology after conization or total hysterectomy were investigated. The most severe abnormality found in the present study was CIN3.

In addition to the detection rate of CIN3 is seem lower than CIN1 and CIN2, there is no significant difference (Table 3).

However, future studies should investigate more number of cases to cognize the reason.

There are inconsistent results regarding the detection rates of colposcopic diagnosis.

Nicolas et al. reported that HSIL was detected in biopsies of the specimens extracted from one, two, and three

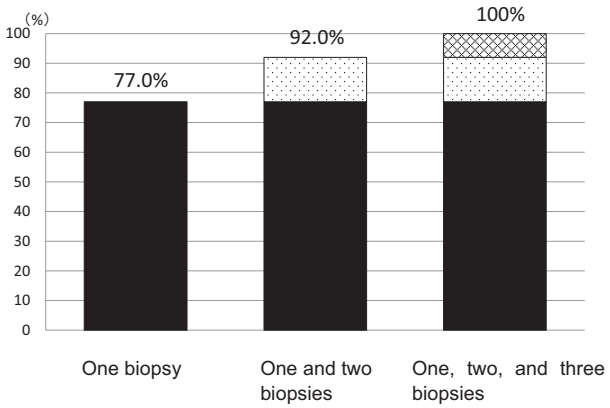

Fig. 3
Number of biopsies and detection rates of CIN3 diagnosis
Overall 77.0% patients were diagnosed at one biopsy, 92.0% were diagnosed at one and two biopsies, and 100% were diagnosed at one, two, and three biopsies.

Table 3 Association between CIN and the sensitivity of colposcopic procedure, Chi-square test

	one	two	three	
CIN1	89	16	2	107
CIN2	75	12	2	89
CIN3	67	13	7	87
	231	41	11	283

P-value = 0.1967

lesions in 60.6%, 85.6%, and 95.6% patients, respectively.[16]

According to Nakamura et al., 78.1% CIN2 or severe lesions were detected at the first biopsy, but at least two biopsies should be taken.[14] In contrast, Robert et al. showed that CIN2 and severe lesions were colposcopically diagnosed in only 57.1% patients.[17] Because the detection rates differ between these reports, there is no consensus on the number of biopsies required for cervical histological diagnosis.

We considered that the difference of detection rates occurs from difference from exerminers of each hospital. In this study, nine exerminers were involved, but some of them were enrolled in a short period of time and nine exerminers aren't corresponded to six authors listed. The order of biopsy is different depending on the exerminers; therefore, to obtain more accurate data, a number of exerminers should be limited or should unify the order of biopsy when there are more than one exerminer.

There are several limitations of the study. First, given that the order of specimen extractions varied as per the

tester who performed the cervical histology, the accurate number of biopsies required for definite diagnosis has not been necessarily clarified. For example, in performing a biopsy of the upper and lower lesions of the cervix, in some cases, even if the upper lesion was stronger, the specimen is extracted first from the lower lesion to prevent the invasion of blood flowing from the biopsy site of the upper lesion. However, biopsies from four sites are considered unnecessary.

To obtain more accurate data, future studies should standardize the order of cervical biopsies between testers from the most severe lesions to the less severe ones.

Conflicts of interest: None declared.

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