Factors affecting pain during outpatient clinic based surgical procedures in gynecologic oncology

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Abstract
Colposcopy-directed punch biopsy (punch biopsy) and endocervical curettage (ECC) are accompanied by considerable pain. However, many physicians perform these procedures without adequate pain management. Therefore, identification of factors affecting pain experienced during the procedures may encourage physician effort in selective pain management. This study investigated factors affecting the severity of pain experienced during punch biopsy and ECC in an outpatient clinic of gynecologic oncology department.

In this retrospective, exploratory study, a total of 101 Korean patients with abnormal cervical cytology underwent punch biopsy and ECC under a paracervical block performed for pain relief. Residents under training performed these procedures and recorded patient-reporting maximum Numeric Rating Scale (NRS) scores experienced during the procedures. Residents were classified into four outpatient clinic training groups (1st–4th); the group designators correspond to the resident’s experience in performing these procedures. A linear mixed model adjusted for physician factors such as either residents or outpatient clinic training groups was used to analyze the association between each variable and maximum NRS score.

Among the outpatient clinic training groups, maximum NRS scores significantly decreased in the 4th group, compared with those in the 1st group although those were not different among groups when adjusted for residents. Some of cervical cytology findings and discrepancies between the severity of cervical cytology results and those of punch biopsy or ECC showed significant associations with maximum NRS scores. However, when adjusted for either residents or outpatient clinic training groups, maximum NRS scores were not different by age, body mass index, presence of menopause, cervical cytology findings, discrepancies between the severity of cervical cytology results and those of punch biopsy or ECC, and tissue volume.

There are no significant factors affecting the severity of pain experienced during punch biopsy and ECC.

Abbreviations: ASC-H = atypical squamous cells, cannot rule out high-grade squamous intra-epithelial lesion, ASCUS = atypical squamous cells of undetermined significance, BMI = body mass index, ECC = endocervical curettage, HSIL = high-grade squamous intraepithelial lesion, LSIL = low-grade squamous intraepithelial lesion, NRS = numeric rating scale.

Keywords: biopsy, curettage, outpatient clinic hospital, pain, papanicolaou test

1. Introduction

A large number of patients with abnormal cervical cytology undergo subsequent colposcopy-directed punch biopsy (punch biopsy) and endocervical curettage (ECC). These procedures are painful, which may cause uncomfortable after effects and evoke fear of follow-up care if not adequately managed. In the TOMBOLA trial (Trial Of Management of Borderline and Other Low-grade Abnormal smears), a United Kingdom multicenter randomized, controlled trial, the frequencies of moderate or more severe pain, and the duration of pain were similar in punch biopsy and large loop excision of the transformation zone groups.[1] In addition, in women referred for colposcopy, anxiety, and fear of the diagnosis or procedure, often associated with the fear of physical pain, were the most common barriers to the follow-up of an abnormal pap smear.[2]

Several studies have investigated the efficacy of various methods to relieve pain during cervical punch biopsy. Cervical injection of lidocaine and forced coughing have been reported to be effective in relieving pain during cervical biopsies and/or ECC.[3,4] However, topical anesthetic sprays and gels were ineffective in providing pain relief.[5–7]

Although many patients experience significant pain during punch biopsy and ECC and express concern about it, many physicians perform these procedures without pain management. Therefore, we speculate that prediction of the severity of pain experienced during punch biopsy and ECC will encourage physicians to use adequate methods for pain relief, depending on the patient, resulting in better pain management. To our knowledge, there have been no studies investigating the factors associated with pain experienced during punch biopsy and/or ECC. In this study, we aimed to evaluate the factors affecting the pain experienced during

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severity of pain experienced during punch biopsy and ECC in an outpatient clinic of the gynecologic oncology department.

2. Methods

Our retrospective, exploratory study included patients who underwent cervical cytology, punch biopsy, and ECC at the Seoul National University Bundang Hospital between July 1, 2014, and July 31, 2015. This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (No. B-1508/312–118) on August 31, 2015. Informed consent was waived.

The inclusion criteria were as follows: patients who had an abnormal cervical cytology, those with both punch biopsy and ECC results, and those who underwent paracervical block (PCB) for pain relief. We excluded patients who were not screened using liquid-based cytology and those who did not undergo punch biopsy and ECC performed by residents under training. At our hospital, punch biopsy and ECC are considered outpatient clinic-based surgical procedures. Residents under training mainly perform these procedures in the outpatient clinic of the gynecologic oncology department. The medical records of 101 eligible patients with abnormal cervical cytology were reviewed.

At our hospital, routine recommendations for cervical cancer screening include the following methods: Liquid-based cytology is usually performed using the BD SurePath test (BD Diagnostics-TriPath, Burlington, NC), based on the manufacturer’s recommended protocol. Cytological results of each sample are interpreted by cytopathologists, based on the 2001 Bethesda system.13 If punch biopsy and ECC should be performed because of abnormal cervical cytology, PCB is performed if pain management is needed. PCB is placed by injecting a 10 mL total dose of 1% lidocaine about 10 mm into the cervical stroma at the 4- and 8-o’clock positions of the cervicovaginal junction (5 mL at each position). Patients underwent punch biopsy and ECC 7 minutes after lidocaine injection. For punch biopsy, 4 samples of cervical tissue (<5 mm) are obtained from the 3-, 6-, 9-, and 12-o’clock positions of the cervix when abnormal lesions are not detected by colposcopy; when abnormal lesions are detected, samples from the suspicious lesions are obtained. Subsequent ECC is performed using the smallest curette. Residents under training perform these procedures and record the severity of patient-reporting pain that they experienced during the procedures using the Numeric Rating Scale (NRS). The specimens are sent to pathologists with expertise in gynecological oncology.

In this study, resident’s experience and patient-associated factors such as age, body mass index (BMI), menopause, results of cervical cytology, discrepancy between cervical cytology and punch biopsy or ECC results, and tissue volume were evaluated as factors affecting the severity of pain experienced during procedures. For evaluation of resident’s experience, residents were classified into 1st, 2nd, 3rd, and 4th groups, depending on the experience in performing punch biopsy and ECC in an outpatient clinic. The residents in the 1st, 2nd, 3rd, and 4th outpatient clinic training groups had an experience of performing punch biopsy and ECC of 1, 2, 3, and 4 months, respectively, and for the 1st, 2nd, 3rd, and 4th time, respectively, because residents worked in an outpatient clinic for a month at a time. A total of 22 residents of grades 1 to 3, two males and 20 females, performed punch biopsy and ECC under PCB and recorded patient-reporting maximum NRS scores experienced during procedures (Fig. 1). Results of cervical cytology were categorized as atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cells, cannot rule out high-grade squamous intra-epithelial lesion (ASC-H), high-grade squamous intraepithelial lesion (HSIL), and

| Maximum NRS score (mean value) | 19 patients | 40 patients | 24 patients | 18 patients |
|--------------------------------|-------------|-------------|-------------|-------------|
| R1 (1, 2)                        |             |             |             |             |
| R2 (3)                            |             |             |             |             |
| R3 (4)                            |             |             |             |             |
| R4 (5)                            |             |             |             |             |
| R5 (6)                            |             |             |             |             |
| R6 (7)                            |             |             |             |             |
| R7 (8)                            |             |             |             |             |
| R8 (9)                            |             |             |             |             |
| R9 (10)                           |             |             |             |             |
| R10 (11)                          |             |             |             |             |
| R11 (12)                          |             |             |             |             |
| R12 (13)                          |             |             |             |             |
| R13 (14)                          |             |             |             |             |
| R14 (15)                          |             |             |             |             |
| R15 (16)                          |             |             |             |             |
| R16 (17)                          |             |             |             |             |
| R17 (18)                          |             |             |             |             |
| R18 (19)                          |             |             |             |             |
| R19 (20)                          |             |             |             |             |
| R20 (21)                          |             |             |             |             |
| R21 (22)                          |             |             |             |             |
| R22 (23)                          |             |             |             |             |
| R23 (24)                          |             |             |             |             |
| R24 (25)                          |             |             |             |             |
| R25 (26)                          |             |             |             |             |
| R26 (27)                          |             |             |             |             |
| R27 (28)                          |             |             |             |             |
| R28 (29)                          |             |             |             |             |
| R29 (30)                          |             |             |             |             |
| R30 (31)                          |             |             |             |             |
| R31 (32)                          |             |             |             |             |
| R32 (33)                          |             |             |             |             |
| R33 (34)                          |             |             |             |             |
| R34 (35)                          |             |             |             |             |
| R35 (36)                          |             |             |             |             |
| R36 (37)                          |             |             |             |             |
| R37 (38)                          |             |             |             |             |
| R38 (39)                          |             |             |             |             |
| R39 (40)                          |             |             |             |             |
| R40 (41)                          |             |             |             |             |
| R41 (42)                          |             |             |             |             |
| R42 (43)                          |             |             |             |             |
| R43 (44)                          |             |             |             |             |
| R44 (45)                          |             |             |             |             |
| R45 (46)                          |             |             |             |             |
| R46 (47)                          |             |             |             |             |
| R47 (48)                          |             |             |             |             |
| R48 (49)                          |             |             |             |             |
| R49 (50)                          |             |             |             |             |
| R50 (51)                          |             |             |             |             |
| R51 (52)                          |             |             |             |             |
| R52 (53)                          |             |             |             |             |
| R53 (54)                          |             |             |             |             |
| R54 (55)                          |             |             |             |             |
| R55 (56)                          |             |             |             |             |
| R56 (57)                          |             |             |             |             |
| R57 (58)                          |             |             |             |             |
| R58 (59)                          |             |             |             |             |
| R59 (60)                          |             |             |             |             |
| R60 (61)                          |             |             |             |             |
| R61 (62)                          |             |             |             |             |
| R62 (63)                          |             |             |             |             |
| R63 (64)                          |             |             |             |             |
| R64 (65)                          |             |             |             |             |
| R65 (66)                          |             |             |             |             |
| R66 (67)                          |             |             |             |             |
| R67 (68)                          |             |             |             |             |
| R68 (69)                          |             |             |             |             |
| R69 (70)                          |             |             |             |             |
| R70 (71)                          |             |             |             |             |
| R71 (72)                          |             |             |             |             |
| R72 (73)                          |             |             |             |             |
| R73 (74)                          |             |             |             |             |
| R74 (75)                          |             |             |             |             |
| R75 (76)                          |             |             |             |             |
| R76 (77)                          |             |             |             |             |
| R77 (78)                          |             |             |             |             |
| R78 (79)                          |             |             |             |             |
| R79 (80)                          |             |             |             |             |
| R80 (81)                          |             |             |             |             |
| R81 (82)                          |             |             |             |             |
| R82 (83)                          |             |             |             |             |
| R83 (84)                          |             |             |             |             |
| R84 (85)                          |             |             |             |             |
| R85 (86)                          |             |             |             |             |
| R86 (87)                          |             |             |             |             |
| R87 (88)                          |             |             |             |             |
| R88 (89)                          |             |             |             |             |
| R89 (90)                          |             |             |             |             |
| R90 (91)                          |             |             |             |             |
| R91 (92)                          |             |             |             |             |
| R92 (93)                          |             |             |             |             |
| R93 (94)                          |             |             |             |             |
| R94 (95)                          |             |             |             |             |
| R95 (96)                          |             |             |             |             |
| R96 (97)                          |             |             |             |             |
| R97 (98)                          |             |             |             |             |
| R98 (99)                          |             |             |             |             |
| R99 (100)                         |             |             |             |             |
| R100 (101)                        |             |             |             |             |

Figure 1. Distribution of patient-reporting mean maximum NRS scores experienced during punch biopsy and ECC according to physician factors (residents and outpatient clinic training groups). In 1st, 2nd, 3rd, and 4th outpatient clinic training groups, 6, 9, 3, and 4 residents performed punch biopsy and ECC on 19, 40, 24, and 18 patients, respectively. ECC = endocervical curettage, NRS = Numeric Rating Scale.
squamous cell carcinoma. Adenocarcinoma in situ was not detected in these patients. Discrepancy between cervical cytology and punch biopsy or ECC results was categorized as “no change in severity,” “decrease in severity,” or “increase in severity.” To evaluate the discrepancy between severity as assessed by punch biopsy or ECC results and cervical cytology, ASCUS and LSIL groups were considered as a single group corresponding to cervical intraepithelial neoplasia grade (CIN) 1, and ASC-H and HSIL groups were considered as a single group corresponding to CIN2 or CIN3.

2.1. Statistics
Mean value of maximum NRS scores measured for each patient during the period that each resident performed the procedures was calculated. Mean value of mean maximum NRS scores acquired by each resident in each outpatient clinic training group was analyzed to evaluate differences among the groups. Statistical analyses were performed using Stata/SE 14 (StataCorp LP., College Station, TX). Data are expressed as either the mean ± standard deviation for continuous variables with a normal distribution or median and interquartile range for variables with non-normal distributions. For analysis of the differences in continuous variables among the groups, data were analyzed using the independent t-test or one-way analysis of variance followed by the Bonferroni method for parametric data and the Wilcoxon rank-sum test or the Kruskal–Wallis test followed by the Wilcoxon rank-sum test for nonparametric data. A linear mixed model adjusted for physician factors such as either residents or outpatient clinic training groups was used to analyze the association between each variable and the maximum NRS score. P < .05 was considered statistically significant.

3. Results
Among the outpatient clinic training groups, maximum NRS scores significantly decreased in the 4th group compared with those in the 1st group. However, when adjusted for residents, maximum NRS scores were not significantly different among outpatient clinic training groups (Table 1).

Maximum NRS scores were not dependent on age, BMI, presence of menopause, and tissue volume. Maximum NRS scores did not differ even after adjustment for either residents (Table 1) or outpatient clinic training groups (data not shown).

For patients with cervical cytology results categorized as LSIL, maximum NRS scores significantly decreased compared with those categorized as ASC-H. However, maximum NRS scores were not different among patients with other cervical cytology results. When adjusted for either residents (Table 1) or outpatient clinic training groups (data not shown), maximum NRS scores showed no difference according to cervical cytology results.

When severity as per cervical cytology results was compared with that as per punch biopsy results, maximum NRS scores significantly decreased when discrepancy was categorized as increase in severity compared to when categorized as no change in severity. When severity as per cervical cytology results was compared with that as per ECC results, maximum NRS scores also significantly decreased when the discrepancy was categorized as decrease in severity than when categorized as no change in severity. In addition, with regard to ECC results, maximum NRS scores tended to decrease (P = .018) with increase in severity than with no change in severity, suggesting that with very small sample sizes, even samples with very different medians may not produce a significant Wilcoxon rank-sum test statistic.[9]

However, when adjusted for either residents (Table 1) or outpatient clinic training groups (data not shown), maximum NRS scores showed no difference according to discrepancies in severity assessed by cervical cytology results and punch biopsy or ECC results.

Sensitivities at cut-offs CIN2 or worse for detecting CIN2 or worse from subsequent loop electrosurgical excision procedure (LEEP) or hysterectomy were 60%, 91.7%, 81.8%, and 60% for punch biopsy and 20%, 58.3%, 18.2%, and 60% for ECC in the 1st, 2nd, 3rd, and 4th outpatient clinic training groups which included 7, 13, 13, and 5 patients, respectively.

Complications related to punch biopsy and/or ECC and pain were not identified.

4. Discussion
In this exploratory study, residents under training performed punch biopsy and ECC with PCB for pain relief and recorded the severity of patient-reporting pain experienced during the procedures in Korean patients with abnormal cervical cytology results. When resident’s experience and patient-associated factors were evaluated some factors showed significant associations with maximum NRS scores. However, when adjusted for either residents or outpatient clinic training groups, maximum NRS scores were not dependent on the factors thought to affect the severity of pain experienced during these procedures.

Punch biopsy and ECC are commonly performed as outpatient clinic-based procedures. Surgical proficiency is expected to be achieved within a short time. Although PCB in our study was performed for pain relief, resulting in pain control with an efficacy similar to that of cervical injection of lidocaine (Visual Analog Scale, 3.15–4.91).[13] maximum NRS scores varied according to outpatient clinic training groups. In our study, pain experienced during these procedures significantly reduced when residents with an experience of 4 months performed them compared to when those with an experience of 1 month performed the procedures. However, when adjusted for residents the severity of pain was not significantly different among these groups suggesting pain experienced by patients during these procedures is not dependent on physician’s experience for them. Previous studies reported that sensitivity at cut-offs CIN2 or worse for detecting CIN2 or worse from an excisional cervical biopsy including LEEP or hysterectomy was 80.1% (95% confidence interval, CL 73.2–85.6%) for punch biopsy and 12.2% (95% CI 8.9–16.2%) for ECC.[10,11] Although very small number of patients were included for calculation of sensitivity of an excisional cervical biopsy in each outpatient clinic training group, our findings demonstrate supporting previous studies[10,11] that acceptable accuracy for these procedures might be achieved after exposure to these procedures over a few months. These findings suggest that physician proficiency might not reduce pain experienced during punch biopsy and ECC.

We initially supposed that old patients, especially postmenopausal women, would experience more severe pain during punch biopsy and ECC because of vaginal atrophy compared to young patients. We also supposed that exposure of the cervix would be more difficult resulting in more severe pain in patients with a higher BMI than in those with a lower BMI. In our study, patients with a higher BMI (≥25 kg/m²) had a tendency to experience more severe pain compared to those with a lower BMI (<25 kg/m²). However, our data also showed that these variables are not significantly associated with pain experienced during
Variables associated with patient-reporting maximum NRS score experienced during punch biopsy and ECC.

| N | Maximum NRS score | P | P in multiple comparisons | Adjusted P |
|---|-------------------|---|---------------------------|------------|
| Outpatient clinic training group, mean ± SD | | | | |
| The 1st group | 19 | 5 (3–7) | .016 * | .004 † † | .389 |
| The 2nd group | 40 | 4 (2–5) | | | |
| The 3rd group | 24 | 3 (1.5–6) | | | |
| The 4th group | 18 | 1.5 (1–5) | | | |
| Age, median (IQR), y | | | | |
| 20–29 | 30 | 4 (3–5) | .4 * | | |
| 40–49 | 61 | 4 (2–5) | | | |
| 60–79 | 10 | 2 (1–5) | | | |
| BMI, median (IQR), kg/m² | | | | |
| <25 | 51 | 3 (2–5) | .076 † | | |
| ≥25 | 10 | 5 (4–6) | | | |
| Menopause, mean ± SD | | | | |
| (+) | 67 | 3.69 ± 1.92 | .701 † | | |
| (−) | 34 | 3.82 ± 2.25 | | | |
| Cervical cytology results, mean ± SD | | | | |
| ASC-US | 30 | 3.67 ± 1.94 | .020 † † | | |
| LSIL | 34 | 3.09 ± 1.93 | | | |
| ASC-H | 14 | 5.07 ± 2.13 | | | |
| HSIL | 17 | 3.35 ± 1.90 | | | |
| Squamous cell carcinoma | 6 | 4.67 ± 1.96 | | | |
| Discrepancy between cervical cytology and punch biopsy, median (IQR) | | | | |
| Decrease of severity | 25 | 3 (1–5) | .001 * | | |
| No change of severity | 64 | 4 (3–5) | | | |
| Increase of severity | 12 | 1 (1–3.5) | | | |
| Discrepancy between cervical cytology and ECC, median (IQR) | | | | |
| Decrease of severity | 75 | 3 (2–5) | .013 * | | |
| No change of severity | 19 | 5 (3–7) | | | |
| Increase of severity | 7 | 2 (1–4) | | | |
| Tissue volume (ECC), mean ± SD | | | | |
| Scanty amounts | 64 | 3.78 ± 2.13 | 2.42 † | | |
| Adequate amounts | 37 | 3.49 ± 1.67 | | | |

* P value for the differences among the groups using the Kruskal-Wallis test.
† P value using the Wilcoxon rank-sum test.
‡ P value using independent t test.
§ P value using one-way ANOVA.
¶ P value for the difference between the 1st versus the 4th outpatient clinic training group by multiple comparisons using the Kruskal-Wallis test, followed by the Wilcoxon rank-sum test.
‖ P value for the difference between LSIL versus ASC-H by multiple comparisons using one-way ANOVA, followed by the Bonferroni method.
\* no change versus increase of severity.
\* no change versus decrease of severity.
\* Data were adjusted for residents using the linear mixed model. P value for the difference between the groups by multiple comparisons using the Kruskal-Wallis test, followed by the Wilcoxon rank-sum test. Differences are reported between:
ASC-H = atypical squamous cells, cannot rule out high-grade squamous intra-epithelial lesion; ASC-US = atypical squamous cells of undetermined significance; BMI = body mass index; ECC = endocervical curettage; HSIL = high grade squamous intraepithelial lesion; IQR = interquartile range; LSIL = low-grade squamous intraepithelial lesion; NRS = numeric rating scale.

A previous study using human cervical tissues reported that hemoglobin levels were significantly increased in tissues with CIN 2 or worse compared to those in normal tissues or tissues with CIN 1. Therefore, it is possible that patients with worse cervical cytology results might experience more severe bleeding during punch biopsy and ECC, resulting in additional pain associated with performing the procedures for a longer time. Moreover, severe pain induced by the procedures might disturb adequate tissue collection. In our study, patients with ASC-H experienced more severe pain during the procedures compared with those with LSIL, supporting our claim. However, when adjusted for physician factors, cervical cytology results and tissue volume obtained during the procedures did not show an association with the severity of pain experienced during the procedures, suggesting that punch biopsy and ECC can be properly completed within a short time without severe complications.

Severe pain during the procedures may result in inaccurate and less significant pathologic results, as the patients might disturb the procedure. Therefore, we presumed that when severity assessed by punch biopsy results decreased (increased) in comparison with that assessed by cervical cytology results, pain severity would increase (decrease). Supporting this speculation, our data showed that when severity as per punch biopsy results increased in comparison with that per cervical cytology results, pain decreased. However, with regard to ECC results, maximum NRS scores did not show a consistent trend. Moreover, when adjusted for physician factors, discrepancy between the severity
per cervical cytology results and that per punch biopsy or ECC results did not affect maximum NRS scores, suggesting that pain induced by the procedures was not as severe, as adequate procedures could not be performed.

In our hospital, NRS scores have been routinely recorded in medical records in the cases that PCB has been performed. Therefore, our study included only patients who underwent PCB. Punch biopsy and ECC with PCB have been performed by residents under training who were scheduled to work in an outpatient clinic for a month at a time. Moreover, these procedures were performed in patients without any specific medical problems. As a result, our data may not have the potential of selection bias. However, it is possible some of patients had baseline pain that specific treatments were not needed. What the residents performing the procedures collected patient-reporting pain may be the limitation of our retrospective study. However, we supposed that its influence on outcomes would be not significant because residents did not have any secondary gain such as obtaining good score in evaluation of training with reference to NRS scores collected. It is possible NRS scores might not reflect adequately pain experienced by patients during the procedures which has subjective nature. Although small sample size limits significance of our results, this exploratory study may improve understanding of these common procedures.

5. Conclusion

The current study demonstrated that no factors including physician’s experience had significant affects on the severity of pain experienced during punch biopsy and ECC. Large-scale randomized trials are needed to further clarify factors affecting these procedures and encourage better pain management.

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