# Is "additional cut" effective for positive margin in cervical conization? It varies with doctors: a retrospective study

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**Abstract**

Objective: We aimed at discussing additional cuts, a common problem in cervical conization. Whether the doctor's choice of additional cuts in conization surgery could reduce the occurrence of positive cone margin. Design: A retrospective study. Setting: First Affiliated Hospital of Dalian Medical University (Dalian, China). Population: 965 patients underwent cervical conization. Methods: Statistical analysis of patients' pathological reports. Main outcome measures: The age, preoperative pathology, pathological results of conization, whether or not to make additional cuts, cone depth and cone volume were studied. Result: Of the 965 patients included, age, pathology result of conization, whether to make additional cuts, cone depth and cone volume, there were significant difference between positive and negative cone groups. Next, the Multivariable logistic regression analysis suggested that older age (OR,1.036; 95%CI, 1.017 to 1.054; $p<0.001$), the pathology result of conization was HSIL or cervical cancer (OR,13.203; 95%CI,6.024 to 28.936; $p<0.001$), additional cuts (OR, 2.480; 95%CI 1.608 to 3.826; $p=0.01$) and smaller cone depth (OR, 0.591; 95%CI, 0.362 to 0.965, $p=0.036$), these factors were the independent risk for the positive margin group. Conclusions: A certain proportion of additional cuts can be effectively excised the positive margin that cannot be cut in the initial conization. Moreover, choosing the appropriate cone size can maintain a low positive margin rate without additional cuts. Keywords: Additional cuts; Cone depth; Cone volume; Doctor's habit; High-grade squamous intraepithelial lesion; Cervical cancer

## 1 Introduction:

Cervical cancer is one of the most common cancers among women, meanwhile the mortality of cervical cancer is high, in 2020 there were estimated 604,000 newly cases and 342,000 cases of death worldwide. Research suggests that squamous intraepithelial lesion (SIL) caused by persistent infection of Human Papillomavirus (HPV) is closely related to the occurrence of cervical cancer, so effective screening measures for SIL can be a great way to prevent.[1,2] For women with histologically confirmed high-grade squamous intraepithelial lesion (HSIL), we have used cold knife conization (CKC), loop electrosurgical excision procedure (LEEP; including large loop excision of the transformation zone or cone biopsy with loop excision) and laser conization (LC) to do the conization with a diagnostic purpose, also as a principal treatment approach .[3]

In clinical work, it is common to have positive margins at the time of making cervical conizaiton, a meta-analysis showed that about 25% of cases occur incomplete excision, and some researchers considered the proportion of complete excision of lesions to be a quality criterion for clinical practice.[4] Several variables such as age more than 50 years, high parity, menopausal status have been reported to be associated with positive margin.[5,6] Furthermore, positive margin is one of the main causes of HSIL recurrence, for women with positive margin, there is a higher risk of residual or recurrent HSIL or worsening than women with clean margin, patients with positive cone margin had a nearly 2.7-fold recurrence rate than patients with negative cone margin.[5,7,8] Consequently, when doing conization surgery, some doctors may worry about positive margin shown on the pathology reports because their cut range was not enough, and they choose to make additional cuts when doing conization. However, whether the additional cuts can effectively avoid the appearance of positive margin is still unclear. Only a few articles mentioned the addition cuts, making it when necessary and additional cut does not appear to have a good preventive effect on cervical cancer.[9,10] Also, to the author's knowledge, there is little information in the literature about the association between the positive margin and the choice to make additional cuts.

In this study, we retrospectively analyzed pathology report data from patients, who underwent cervical conization, to find out whether making additional cuts could reduce the rate of positive margin in cervical conization. This study aims to provide a suitable choice for doctors to make additional cuts in cervical conization.

## 2 Methods:

We retrospectively reviewed the records of 1002 patients who underwent cervical conization (including CKC and LEEP) at the First Affiliated Hospital of Dalian Medical University (Dalian, China) from January 2018 to October 2019, including patients with HSIL, cervical squamous carcinoma, adenocarcinoma in situ (AIS), and few patients with low-grade squamous intraepithelial lesion (LSIL), on the preoperative diagnosis reports. Of the 1002 patients, 965 patients got clear margin results on their pathology reports and data information was complete, excluding 17 patients with the cut margins cannot be assessed and 20 patients with missing data **(Fig. 1)** . According to the pathological results of the conization, the patients were divided into two groups, positive cone margin group (n=174) and negative cone margin group (n=791). This study was approved by Ethics Committee of the First Hospital of Dalian Medical University.

In previous studies of conization, positive margin were defined as there are lesions (LSIL, HSIL, or cervical cancer) at or near ($\leq$1mm) the cut surface,[11,12] but in this study, the definition of positive margin used for this analysis included the distance between the lesion and the cut surface was $\leq$1mm, and (or) there are lesions at the site of additional cut. The expansion of the definition of positive margin allows unclean margin cases, like margin is negative but have lesions at the additional cut site, were included in the study. For patients who underwent additional cuts, we think that the additional cut is effective if there is a lesion (LSIL, HSIL, or cervical cancer) at the site of additional cut. In this study, we defined doctors, who have the habit of making additional cut, as additional cut rate greater than 20% and surgical involvement more than five.

IBM SPSS statistics version 25 was used for statistical analysis. Chi-square test ($\chi^2$ test) and Mann-Whitney U test were used to compare clinicopathological variables (age, preoperative pathology results, pathology results of conization tissue, whether to make additional cuts, the depth and volume of cone) between positive margin group and negative margin group. Multivariable logistic regression analyses were used to test the value of clinical parameters in predicting positive margin. A $p$ values of$<$0.05 was considered statistically significant.

## 3 Result

Patients' characteristics were presented in **Table1** . Of the 965 study patients, the median age was 41 years (range 35-50). In the pathology result of diagnosis before the conization, 2.5% had LSIL, 97.5% had HSIL or cervical cancer. Only a small fraction (3.7%) of the pathological results of the conization tissue were negative for intraepithelial lesions or malignancy (NILM), HSIL and cervical cancer account for the majority (74.2%). The median values of cone depth and volume were 1.80cm (range 1.30-2.30) and 1.81cm$^3$ (rang 1.18-2.94) respectively.

We evaluated the correlation between patient characteristics and cone margin status, we used Mann-Whitney U test and chi-square test to evaluate the association of factors and positive margins (**Table 2** ). Older age (p=0.007), the pathology result of conization tissue was HSIL or cervical cancer (p<0.001), choose to make additional cuts (p<0.001), smaller cone depth (p<0.001) and smaller cone volume (p=0.01) had significantly higher rate of positive margin in total subjects.

Multivariable logistic regression analysis revealed that making additional cuts (odds ratio [OR], 2.480; 95%CI 1.608 to 3.826; p=0.01), the pathology result of conization is HSIL or cervical cancer (OR,13.203; 95%CI,6.024 to 28.936; p<0.001), age (OR,1.036; 95%CI, 1.017 to 1.054; p<0.001) and smaller cone depth (OR, 0.591; 95%CI, 0.362 to 0.965, p=0.036) were independent risk factors of positive margin group **(Fig. 2)** .

Subsequently, we analyzed the additional cuts rate and the effective additional cuts rate of doctors, who had the habit of making additional cuts **(Table 3)** . In our study, a total of 64 doctors participated in the conization surgery, and six of them (9.4%) had the habit of making additional cuts, and four of the doctors had an additional cuts rate greater than 80%. Of these six doctors, expect for one doctor's additional cut was ineffective, the rest of the doctors had a relatively high effective additional cut rate.

Next, Table 4 shows that the cone volume in the additional cuts group was from 0.89cm$^3$ to 1.57cm$^3$ (median = 1.25cm$^3$), there was an extremely significant difference (p<0.001) in cone volume between the not making additional cuts group and the making additional cuts group. On whether the doctor had the habit of making the additional cuts group, doctors who had the habit of making additional cuts had significantly smaller cone volume than doctors who not had this habit (median=1.16 cm$^3$ and 2.20 cm$^3$, respectively; p<0.001).

## 4 Discussion

### 4.1 Main Findings

In this study, we observed that older age, shorter cone depth, making additional cuts, the pathology result of conizaiton tissue was HSIL or cervical cancer were independent risk factors for positive margin in conization. We thought the additional cuts was the independent risk factor of positive surgical margin, this was because in the included cases, most patients with positive margin underwent additional cuts. Among doctors, who have the habit of making additional cuts, their additional cuts were overwhelmingly effective. Additionally, the cone volume was significantly smaller, of the additional cuts cases and cases made by doctors who had habit of making additional cuts.

### 4.2 Strengths and limitations

A number of studies have analyzed the influencing factors associated with positive cone margin. However, to our knowledge, this study is the first study on the problem of making additional cuts in cervical conization.

There are limitations of this study. This analysis only refers to 965 pathology reports at the First Affiliated Hospital of Dalian Medical University (Dalian, China), and only 64 doctors involved in. Moreover, there are rare studies on the publications of additional cut in cervical conization, resulting in a lack of research in other hospitals or regions has not been investigated, the generalizability of the results is uncertain. We cannot definitively say that additional cut can reduce the occurrence of positive margin in conization to some extent. A retrospectively Korean study of 65 cases performed that conization type and cone volume were statistically significant for preterm delivery[13], but we unable to investigate whether additional cuts have an impact on preterm delivery due to a lack of follow-up of patients.

### 4.2 Interpretation

Through Chinese practices for cervical conization[14]recommended that the indication for surgery for cervical conization was cervical cytology as HSIL, AIS or cervical cancer, also in clinical practices, patients underwent conization surgery were mainly HSIL. However, in this experiment, 2.5% of patients had a pre-diagnosis of LSIL (Table 1), this was largely because doctors believe that those patients had the potential to develop the disease, different grades of lesions at the biopsy site, missed or misdiagnosed HSIL. This was similar to a Japanese report[15] on the pre-diagnosis of CIN (cervical intraepithelial neoplasia) 1 and 2 in patients with conization, the report states that approximately half of patients initially diagnosed with CIN 1 and 2 actually contain CIN3 or invasive cancer in the cervical tissue. Therefore, it is necessary to combine actual clinical observations to decide whether to make conization in patients with LSIL.

About the size of the cone, we found that optimal cone volume and cone depth can effectively avoid positive margin. Papoutsis et al.[16] reported that in large loop excision of transformation zone (LLETZ) treatment, cone volume$<2.1\text{cm}^3$ and cone depth $<10$mm, or the cone volume less than 8.6% of initial cervical volume, women were at risk of having positive margin. Different from cone depth, Kawano et al.[17] suggested that in women younger than 40 years, optimal cone length of 15mm and 20mm in single-quadrant and multi-quadrant diseases, respectively.

## 5 Conclusions

In conclusion, in patients who underwent cervical conization, the depth of conization, patient's age, pathology result of conization tissue, and make additional cuts influence positive cone margin with statistical significance. This retrospective review showed that a certain proportion of additional cuts can be effectively remove the positive margins, that have not been cut during conization; during conization, cutting the appropriate cone size, which can maintain a low positive margin rate without making additional cuts; and the behavior of making additional cuts is more of a doctors' personal habit.

### 5.1 Clinical recommendations

We found that although additional cuts were effective in removing the unclear portion of the initial cone, the choice of making the additional cuts often occurs in the population of doctors with a small cone size. So, as we hypothesize, a suitable cone size can simultaneously avoid the appearance of positive margins without selecting the additional cuts. We need to evaluate more patients and develop an appropriate cone option based on different age stages and preoperative pathological results.

### 5.2 Research recommendations

There is a lack of research on the problem of additional cuts in cervical conization. Therefore, we still do not know whether the choice of additional cuts has an effect on the patient's postoperative period. Unfortunately, this was not addressed in this study due to a lack of follow-up date.

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**Table**

| Characteristics | Values |
|---|---|
| **Age (yr)** | |
| Median | 41 |
| 25th-75th percentile | 35-50?>? |
| 40 | 467 (48.4) |
| >40 | 498 (51.6) |
| **Pathology result (pre-diagnosis)** | |

| Characteristics | Values |
| --- | --- |
| LSIL | 24 (2.5) |
| HSIL | 915 (94.8) |
| Cervical cancer | 26 (2.7) |
| **Pathology result of conization tissue** | |
| NILM | 36 (3.7) |
| LSIL | 213 (22.1) |
| HSIL | 665 (68.9) |
| Cervical cancer | 51 (5.3) |
| **Cone depth (cm)** | |
| Median | 1.80 |
| 25th-75th percentile | 1.30-2.30 |
| **Cone volume ($cm^3$)** | |
| Median | 1.81 |
| 25th-75th percentile | 1.18-2.94 |

| Variable | Positive margin cone group | Negative margin cone group | p-value |
| --- | --- | --- | --- |
| **Age (yr) *** | 44.5 (37-52.25) | 40 (34-49) | 0.007 |
| **Pathology result (pre-diagnosis) *** | | | 0.074 |
| LSIL | 1 (0.6) | 23 (2.9) | |
| HSIL and Cervical cancer | 173 (99.4) | 768 (97.1) | |
| **Pathology result of conization tissue*** | | | <0.001 |
| NILM and LSIL | 7 (4.0) | 242 (30.6) | |
| HSIL and Cervical cancer | 167 (96.0) | 549 (69.4) | |
| **Whether to do additional cuts**** | | | <0.001 |
| Cut | 65 (37.4) | 146 (18.5) | |
| Uncut | 109 (62.6) | 645 (81.5) | |
| **Cone depth (cm) *** | 1.50 (1.20-2.00) | 1.80 (1.40-2.40) | <0.001 |
| **Cone volume ($cm^3$) *** | 1.57 (1.17-2.26) | 1.88 (1.18-3.01) | 0.01 |

| Doctor | Amount of surgical involvement | Additional cuts rate (%) | Effective additional cuts rate (%) |
| --- | --- | --- | --- |
| A | 82 | 34.1 | 25.0 |
| B | 57 | 98.2 | 33.9 |
| C | 49 | 95.9 | 10.6 |
| D | 35 | 88.6 | 22.6 |
| E | 8 | 87.5 | 14.3 |
| F | 13 | 30.8 | 0.0 |

| Variable | Cone volume ($cm^3$) | p-value |
| --- | --- | --- |
| **Whether to do additional cuts** | | <0.001 |
| YES (n=211) | 1.25 (0.89-1.57) | |
| NO (n=754) | 2.09 (1.31-3.27) | |
| **Doctors' habit** | | <0.001 |
| Like making additional cuts (n=252) | 1.16 (0.87-1.47) | |
| Do not like making additional cuts (n=713) | 2.20 (1.43-3.27) | |

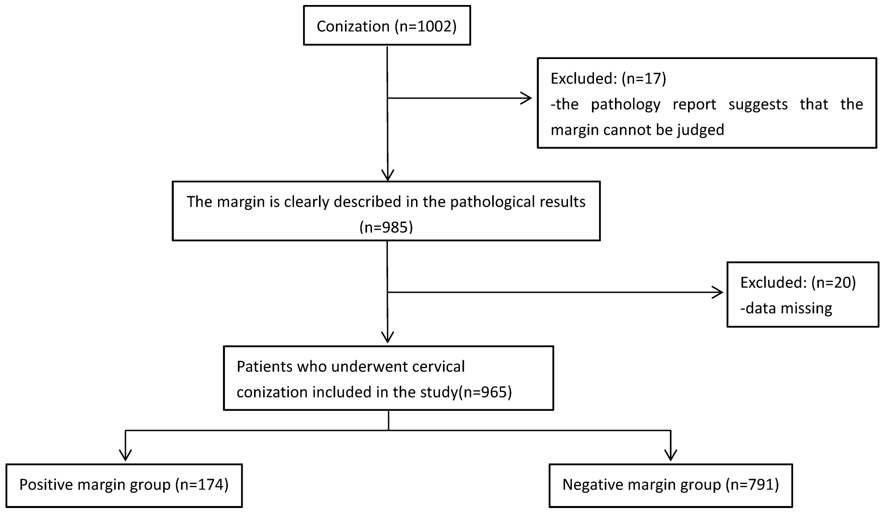


**Fig. 1** Patient selection flowchart.

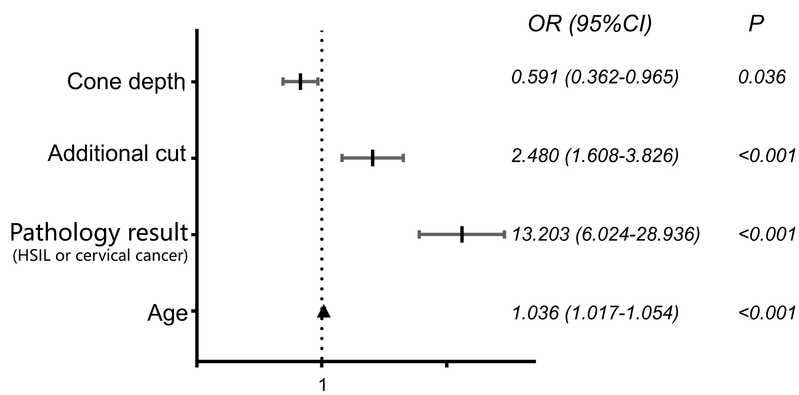


Fig. 2 Multivariable logistic regression analysis to the correlation between clinicopathology factors and positive margin OR, odds ratio; HSIL, high-grade squamous intraepithelial lesion.