

# Comparison of the efficacy and complications of different surgical methods for cervical intraepithelial neoplasia

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## Summary

**Objective:** The aim of this study was to offer some reference for the treatment of cervical intraepithelial neoplasia (CIN) by comparing complication rates and treatment failure rates of different surgical methods of CIN. **Methods:** 1,256 cases of CIN diagnosed by punch biopsy and pathological confirmation of postoperative specimens between January 2002 and June 2007 were reviewed and analyzed, in which 74 cases underwent the loop electrosurgical excision procedure (LEEP), 869 patients adopted cold knife conization (CKC), 49 patients received vaginal enlarged amputation of cervix, and 264 patients accepted extrafascial hysterectomy. The chi-square test was used to compare the rate of complication and treatment failure of different surgical methods. **Results:** The rates of surgical complications for LEEP, CKC, vaginal enlarged amputation of the cervix and extrafascial hysterectomy were, respectively, 8.1% (6/74), 6.2% (54/869), 6.1% (3/49) and 2.3% (8/264), but this difference was not statistically significant. The treatment failure incidences for LEEP, CKC, vaginal enlarged amputation of cervix and external fascia hysterectomy were, respectively, 4.1% (3/74), 0.2% (2/869), 0.0% (0/49) and 0.4% (1/264). When comparing among the groups, the treatment failure incidence was higher in LEEP than that in CKC ( $p = 0.004$ ) and extrafascial hysterectomy ( $p = 0.034$ ); there was no statistically significant difference between CKC and extrafascial hysterectomy, and no significant difference was revealed between vaginal enlarged amputation of cervix and any other group. **Conclusion:** LEEP, CKC, vaginal enlarged amputation of cervix and extrafascial hysterectomy are all secure and effective procedures for patients with CIN, and patients can make their own individual choice depending on different conditions.

**Key words:** Cervical intraepithelial neoplasia, Gynecologic surgical procedures; Treatment outcome.

## Introduction

In the past decades, great changes have taken place in the therapy of cervical intraepithelial neoplasia (CIN) from radical hysterectomy or radiotherapy at the beginning to trachelectomy. And in the past ten years cryotherapy or laser ablation and even pharmacotherapy have been put forward by some scholars to offer conservative management [1]. There are many types of management for CIN; however, the literature is inconsistent as to the efficacy and complications of different therapies, and the best treatment remains controversial [2, 3]. To offer some reference for the treatment of CIN, 1,256 inpatients with CIN diagnosed between January 2002 and June 2007 at the Maternal and Child Health Hospital of Jiang Xi were enlisted. These cases were classified by therapies to compare the rate of complications and treatment failure of different surgical methods.

## Material and Method

### Patients

Patients (average age 36.8, range 18-69) with CIN diagnosed between January 2002 and June 2007 in the Maternal and Child Health Hospital of Jiang Xi were enlisted in the study; 602 cases had CIN and 654 cases had cervical carcinoma in situ.

### Screening standard

In order to exclude vulvar intraepithelial neoplasia (VIN), vaginal intraepithelial neoplasia (VAIN), glandular intraepithelial neoplasia, invasive cancer of the uterine cervix and other invasive carcinomas, all the patients with CIN were required to undergo physical examination, cytology, colposcopy, punch biopsy and endocervical curettage before the operation. All patients were confirmed both by punch biopsy under colposcopy and postoperative pathology, and the most serious result was considered as the diagnosis.

### Evaluation standard

Surgical complications can occur at any time during surgery or afterwards. Intraoperative hemorrhage means blood loss more than 500 ml during the operation, and postoperative hemorrhage means that gauze and even sutures or hysterectomy are required to ensure homeostasis. Menstrual abnormalities include mild menses, menostaxis and menstrual irregularity. Any persistent lesion or recurrence or any unsuspected invasive carcinoma confirmed by histology are treatment failures. A persistent lesion of CIN is any grade of CIN detected within the first year after the operation [4]; while the recurrence of CIN is any grade of CIN or invasive carcinoma detected one year or later after the operation [5]. A persistent lesion or recurrence after extrafascial hysterectomy is VAIN or when invasive carcinoma occurs on the vaginal stump.

### Surgical methods

Young patients with CIN who want to preserve the uterus and/or reproductive function receive the loop electrosurgical excision procedure (LEEP) or cold knife conization (CKC).

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Vaginal enlarged amputation can be adopted when the lesion size observed under colposcope is more than 3/4 of the cervix or the lesion involves the glandular structure. When patients with positive surgical margins after CKC desire uterine and reproductive function preservation, vaginal enlarged amputation is also an option. Extrafascial hysterectomy is chosen when patients with CIN also have ovarian cysts or myoma or prolapse of the uterus and other diseases while reproductive function has been completed. Extrafascial hysterectomy can also be a complementary treatment for patients with positive surgical margins after CKC, for which there are two surgical methods - transabdominal or transvaginal. All our patients were classified into four groups: LEEP, CKC, vaginal enlarged amputation of cervix and extrafascial hysterectomy.

#### Clinical and pathological data

Seventy-four (5.9%) patients with CIN adopted LEEP, in which one patient had a positive margin after operation and four patients with excisional margins were cauterized unduly; 869 (69.2%) patients received CKC, and two patients had positive margins after surgery; 49 (3.9%) patients accepted vaginal enlarged amputation of cervix, and 264 patients underwent extrafascial hysterectomy. Clinical and pathological data of the four groups are summarized in Table 1.

#### Follow-up method

All patients were followed up at 3-month intervals during the first year after surgery. During the first year pelvic examination and cytology were done at each follow-up visit, while colposcopy was performed every six months, and human papilloma

virus (HPV)-DNA was screened 8-12 months after the operation. From the second year after surgery cytology and colposcopy were done once a year. Follow-up was continued as long as a persistent lesion or recurrence was detected. If no persistent lesion or recurrence was detected, the terminal time for follow-up was June 2008. During the follow-up, 82 (6.5%) patients were lost.

#### Statistical analysis

Continuous data are shown as average  $\pm$  standard deviation ( $\bar{x} \pm s$ ). The difference of numeration datas was performed using Pearson  $\chi^2$  or Fisher probabilities in a 2 x 2 table; a value of  $p < 0.05$  was considered statistically significant.

## Results

#### Comparison of surgical complications

The total incidence of surgical complications was 5.5% (69/1256). Rates of surgical complications for LEEP, CKC, vaginal enlarged amputation of cervix and extrafascial hysterectomy were, respectively, 8.1% (6/74) 6.2% (54/869) 6.1% (3/49) and 2.3% (8/264), but this difference was not statistically significant ( $\chi^2 = 7.155$   $p = 0.067$ ). The surgical complications of all treatments are summarized in Table 2.

#### Comparison of treatment efficacy

The follow-up time for surviving patients ranged from 12 to 78 months, mean 29 months. Among these patients four had persistent lesions, two had recurrences and the overall rate of treatment failure was 0.5%. The treatment failure incidences for LEEP, CKC, vaginal enlarged amputation of cervix and extrafascial hysterectomy were 4.1% (3/74), 0.2% (2/869), 0.0% (0/49) and 0.4% (1/264). When comparing between the groups, the treatment failure incidence of LEEP was higher than that of CKC ( $\chi^2 = 18.906$ ,  $p = 0.004$ ) and extrafascial hysterectomy ( $\chi^2 = 6.676$ ,  $p = 0.034$ ), and there was no statistically significant difference between CKC and extrafascial hysterectomy. Also no statistically significant difference was revealed between vaginal enlarged amputation of the cervix and any of the other three groups. Cases with persistent lesions or recurrence after surgery are summarized in Table 3.

Table 1. — Clinical and pathological data of four groups.

Patient data	LEEP n=74	CKC n = 869	Vaginal enlarged amputation n = 49	External fascia hysterectomy n = 264	Total n = 1256
Age	33.7 $\pm$ 6.3	35.5 $\pm$ 6.6	34.8 $\pm$ 5.9	42.4 $\pm$ 7.5	36.8 $\pm$ 7.4
Gravidity					
0	3 (4.1)	25 (2.9)	1 (2.0)	5 (1.9)	34 (2.7)
1	10 (13.5)	79 (9.1)	0 (0)	11 (4.2)	100 (8.0)
$\geq 2$	61 (82.4)	765 (88.0)	48 (98.0)	248 (93.9)	1122 (89.3)
Parity					
0	7 (9.5)	72 (8.3)	2 (4.1)	7 (2.7)	88 (7.0)
1	40 (54.1)	411 (47.3)	25 (51.0)	105 (39.8)	581 (46.3)
$\geq 2$	27 (36.4)	386 (44.4)	22 (44.9)	152 (57.5)	587 (46.7)
Cervical size					
$\leq 3$	46 (62.2)	346 (39.8)	17 (34.7)	116 (43.9)	525 (41.8)
3.1 3.5	19 (25.7)	350 (40.3)	24 (49.0)	93 (35.2)	486 (38.7)
3.6 4.0	6 (8.1)	127 (14.6)	5 (10.2)	46 (17.4)	184 (14.6)
$> 4.0$	3 (4.1)	46 (5.3)	3 (6.1)	9 (3.4)	61 (4.9)
Lesion size					
Smooth	0 (0)	5 (0.6)	0 (0)	3 (1.1)	8 (0.6)
1/3	22 (29.7)	326 (37.5)	2 (4.1)	114 (43.2)	464 (36.9)
1/3 2/3	34 (45.9)	343 (39.5)	5 (10.2)	74 (28.0)	456 (36.3)
2/3	18 (24.3)	195 (22.4)	42 (85.7)	73 (27.7)	328 (26.1)
Vaginal extension					
yes	3 (4.1)	139 (16.0)	12 (24.5)	65 (24.6)	219 (17.4)
no	71 (95.9)	730 (84.0)	37 (75.5)	199 (75.4)	1037 (82.6)
Glandular extension					
yes	3 (4.1)	145 (16.7)	15 (30.6)	138 (52.3)	301 (24.0)
no	71 (95.9)	724 (83.3)	34 (69.4)	126 (47.7)	955 (76.0)

Continuous data are shown as average  $\pm$  standard deviation; enumeration data are shown in the form of n (%).

Table 2. — Surgical complications of all treatments.

Complications	LEEP n = 74	CKC n = 869	Vaginal enlarged amputation n = 49	External fascia hysterectomy n = 264
Intraoperative bleeding	0	0	0	1
Intraoperative bleeding	5	27	0	1
Abnormal menstruation	1	24	2	0
Spontaneous abortion	0	3	1	0
Abdominal incision infection	0	0	0	2
Abdominal incision				
consistent pain	0	0	0	1
Postoperative ankylenteron	0	0	0	1
Total	6 8.1%	54 (6.2%)	3 (6.1%)	6 (2.3%)

Table 3. — Six cases with persistent lesions or recurrence after surgery.

Case	Surgical method	Age	Preoperational Lesion size	Preoperational vagina extension	Postoperational surgical margin	Time to persistent lesion or recurrence	Diagnosis of persistent lesion or recurrence	Retreatment method
1	LEEP	42	< 1/3	Yes	Negative	8	CIN III	Hysterectomy
2	LEEP	37	> 2/3	No	Negative	9	CIN II	CKC
3	LEEP	49	< 1/3	Yes	Not clear	6	CIN III	Hysterectomy
4	CKC	40	> 2/3	No	Negative	52	CIN II	Hysterectomy
5	CKC	31	< 1/3	No	Negative	8	CIN I	LEEP
6	Extrafascial hysterectomy	42	< 1/3	No	Negative	17	Invasive carcinoma	Radiotherapy

## Discussion

With the increasing incidence of CIN and younger age of onset, the surgical resection extent and operative technique of CIN has come into focus. LEEP has been extensively applied in treating CIN because it will not destroy reproductive function; however, it is still controversial as to whether LEEP will become the alternative method of CKC in treating CIN [6].

It is reported that there is no obvious difference between the surgical efficacy of LEEP and CKC, but more than 50% of postoperative specimens of LEEP will be cauterized unduly. As a result, a definite pathological diagnosis can not be determined in approximately 7%-8.3% of specimens [4]. Meanwhile the postoperative specimen of LEEP is smaller than that of CKC, and the positive surgical margin rate is increased correspondingly; especially in treating cervical carcinoma in situ the recurrence rate for LEEP is 29%, while only 6% for CKC [7]. In our study 69.2% patients with CIN opted for CKC, and 5.9% patients with CIN received LEEP. There was no apparent difference in surgical complications between them, but the surgical failure rate of LEEP was higher than that of CKC. It was reported by Kietpeerakool *et al.* [8] that menopause and specimens with a size less than 10 mm are critical factors in predicting a positive surgical margin. Therefore we advocate that patients with a relatively larger lesion use CKC, and patients without endocervical canal extension who want to preserve reproductive function can choose LEEP.

Vaginal enlarged amputation of cervix was put forward by Maltez [9]. Its recurrence rate is relatively low as part of the vaginal wall attached to the cervix will be excised in this operation. In the literature Souen *et al.* [10], reported the recurrence rate of vaginal enlarged amputation of cervix to be the lowest among the different methods in treating 334 patients with cervical carcinoma in situ. Since 2002 we have recommended vaginal enlarged amputation of cervix to patients with squamous cervical carcinoma Staging IA1, CIN patients with large lesion size (when lesion size observed with the help of colposcopy is more than 3/4 of the cervix), patients with CIN and VAIN, recurring CIN II - patients, patients with residual lesions and positive surgical margins, and patients who want to preserve uterine and reproductive function.

The surgical efficacy was 100% during a recent follow-up and no surgical complication was observed [11]. The median follow-up in our study was 29 months. The results showed that the surgical complication rate was 6.1%, and that no patient had residual lesion or suffered recurrence. There was no statistically significant difference of surgical failure when compared to others; however, four patients in the group of vaginal enlarged amputation of cervix were those who were found to have CIN after LEEP (three of them were carcinoma in situ) and required additional surgery. The ratio of cases with a lesion size larger than two-thirds of the cervix was higher than that of other groups. Therefore, we advocate that patients with extensive lesion size, suffering recurrence after LEEP or CKC, or with residual lesions can choose vaginal enlarged amputation of cervix when reproductive function is desired. There was no statistically significant difference regarding surgical failure of vaginal enlarged amputation of cervix when compared to that of others. The small sample capacity of this group may account in part for that, and studies with a larger sample capacity and a longer follow-up time still need to be carried out.

From 2002 to 2007, the cases of extrafascial hysterectomy accounted for 21% of all cases, and the surgical complications were similar to LEEP, CKC and vaginal enlarged amputation of the cervix. The surgical failure rate was lower than that of LEEP, but there was no statistically significant difference when compared to CKC and vaginal enlarged amputation of cervix. Recently patients with CIN have become younger, the number of patients with a desire to save uterine and or reproductive function has increased, and some studies have shown that to some degree extrafascial hysterectomy is an over-treatment for CIN III. Therefore extrafascial hysterectomy is not the preferred therapy for CIN. However, when patients with CIN also have ovarian cysts, uterine myomas, uterine prolapse, or when patients with an atrophic cervix after menopause can not choose CKC and the patient also has a positive surgical margin after CKC, extrafascial hysterectomy can be chosen.

To sum up, LEEP, CKC, extrafascial hysterectomy, vaginal enlarged amputation of cervix can all be a safe and available treatment for CIN if surgical indications are strictly controlled. For patients who desire fertility, LEEP

can be used if the lesion is smaller than one-third of the cervix and there is no cervical canal extension, while when the lesion is larger than that CKC is the preferred treatment. Patients with extensive lesion size, with recurrence after LEEP or CKC, or with residual lesion can choose vaginal enlarged amputation of cervix when reproductive function is still desired. Extrafascial hysterectomy is a choice for patients without the desire to save reproductive function, when CKC is not suitable for the patients with an atrophic cervix after menopause and/or when patients also have a gynecologic benign cyst.

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