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OPEN PEER REVIEW

The Recurrence Rate of Cervical Intraepithelial Neoplasia After Loop Electrosurgical Excision Versus Cold Knife Conization: A Cross-Sectional Study

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

0 comments

No public comments in this round.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Associate Editor and Reviewers

Thank you for your valuable comments.

1. In the method section: With what diagnosis were they candidates for surgery?

Indications for cone biopsy include CIN III, have been proven by biopsy sampling, the discrepancy between cytology and biopsy and colposcopy results, suspected cancer lesions with microscopic invasion, positive ECC, unsatisfactory colposcopy, or related persistent symptoms despite normal colposcopy.

What was their pop name?

Pap smears of the patients included NILM, LSIL, ASCH, ASCUS, and HSIL.

2. Results: The second line of the second paragraph: What was the difference?

The cases with high-risk HPV were 281 (95.6%) in the LEEP group and 32 (91.4%) in the CKC group, with no significant differences between the groups (p=0.394) regarding the prevalence of **high-risk HPV.**

3. The English editing needs to be revised

Was done.

4. What cases had recurrence with what pathology and CIN? Were the margins free in the previous pathology?

Recurrence with CINII were reported in 7 women (25.9) in the LEEP group and 2 cases (33.3%) in the CKC group. While CINIII detection were in 20 women (74.1%) in the LEEP group and 4 cases (66.7) in the group CKC. In the cases with lesion recurrence marginal involvement in the previous pathology were not reported.

5. Results and method need to be revised and rewrite again. The text is ambiguous

Was rewrite.

6. The comparison in the discussion section is done incompletely, the type of pathologies is not specified in the text, and it is not known with what pathology the recurrence of the patients happened.

In the present study, the mean recurrence rate of high-grade cervical lesions had no significant differences in the two applied conization methods. Recurrence with CINII were reported in 7

women (25.9) in the LEEP group and 2 cases (33.3%) in the CKC group. While CINIII detection were in 20 women (74.1%) in the LEEP group and 4 cases (66.7) in the group CKC.

2 Revision 1

1 comment · 2 Aug 2024

Associate Editor

MINOR REVISION 2 Aug 2024

Thank you for submitting your valuable manuscript to the journal. We would like to inform you that the peer review of your manuscript is now complete and that, despite several useful points, it needs "Minor Revision". Below you may find the peer review comments. Please reply to them one by one and resubmit the manuscript.
1. As suggested earlier, the discussion section is incomplete and insufficient. It needs a serious revision; it is recommended to compare recurrence in different studies with that in the current study. Also, the types of pathologies in the previous studies should be compared with those in the present study, and similarities and contradictions should be mentioned.
2. Some parts of table one are unnecessary and have nothing to do with the subject of the study unless those risk factors are mentioned in the introduction.

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor
Thank you for your valuable comments.

1. As suggested earlier, the discussion section is incomplete and insufficient. It needs a serious revision, it is recommended to compare the recurrence in different studies with the current study. Also, the types of pathologies in the previous studies should be compared with the present study and similarities and contradictions should be mentioned.

It was edited.

In line with our study, the recurrence rate of high-grade cervical lesions is reported at 6.6%, although it can vary as low as 2.1% in CKC and equal to 14% in LEEP (21). In some previous studies, the risk of CIN2+ recurrence at one next year is detected about twice-fold in women who underwent LEEP rather than in CKC (22, 23), this fact is also represented in our study.
One study from multiple hospitals in China which includes 5050 women and another cohort study from the national population of Sweden which consists of 153632 women with CIN or carcinoma in situ who underwent CKC or LEEP conization, indicated that women who underwent CKC treatment had a significant lower risk of recurrent cervical lesions compared to those who underwent LEEP treatment, which confirms our findings (24).
In contrast to our findings, in a retrospective study by Galli et al. reported that the recurrence rate was 8.3% vs 11.1% in women undergoing LEEP vs. CKC group (25). Furthermore, four trials, including 1035 women with CIN, reported that women who received LEEP for CIN had a significantly lower persistence at a 6-month follow-up biopsy and significantly lower recurrence at a 12-month follow-up biopsy than those who received cryotherapy without a higher complication rate (26).
In some others studies, there was no significant difference between CKC or LEEP groups regards overall proportion of positive surgical margins (27). In a study by Wang et al., 447 cases (259 with LEEP and 188 with CKC) were evaluated. The mean recurrence rate of high-grade cervical lesions had no significant differences in the two applied conization methods. Recurrence with CINII was reported in 7 women (25.9) in the LEEP group and 2 cases (33.3%) in the CKC group. While CIN3 detection was in 20 women (74.1%) in the LEEP group and 4 cases (66.7) in the CKC group (28).
Similar to our findings, some former studies (29, 30) showed that post-LEEP or cryotherapy surgery complications seem rare and the same. In contrast, in some studies, CKC was associated with higher complications such as preterm labor, premature rupture of membranes,

and adverse neonatal outcomes. Higher biopsy specimen and risk of post-conization bleeding and stenosis (31, 32).

In addition, they concluded that women who received CKC are associated with a lower risk of HPV persistence and recurrent cervical lesions as compared to women who received LEEP (25); otherwise, HPV persistence rate was not evaluated in our study. Close follow-up is necessary for prompt detection and treatment of persistent or recurrent disease (30).

2. Some parts of table one are unnecessary and have nothing to do with the subject of the study unless those risk factors are mentioned in the introduction.

Was revised as below.

Table 1. The baseline information of the patients

P-value	CKC Group Mean ± SD or Number (%)	LEEP Group Mean ± SD or Number (%)	Variable
0.089	34.5±8.7	37.2±8.4	**Mean women age** (years)
			Gravida (times)
0.057	(37.1) 13	(23.1) 68	0
	(62.9) 22	(76.9) 226	1 ≤
0.508	22.6±4.2	22.1±4.2	**Mean age of first intercourse** (years)
			Number of sexual partners
0.459	(77.1) 27	(79.2) 233	**1**
	(22.9) 8	(20.8) 61	1 ≤
			Smoking
0.574	(11.4) 4	(14.3) 42	Yes
	(88.6) 31	(85.7) 252	No
			Underlying disease
	(88.6) 31	(86.1) 253	No
	(0.0) 0	(2.7) 8	Diabetes mellitus
	(2.8) 1	(1.1) 3	Hypertension
	(0.0) 0	(2.4) 7	HIV
0.555	(0.0) 0	(2.7) 8	Multiple sclerosis
	(0.0) 0	(1.1) 3	SLE
	(8.6) 3	(4.1) 12	Others
			High-risk HPV
0.394	(91.4) 32	(95.6) 281	Positive
	(8.6) 3	(4.4) 13	Negative

3 Revision 2

0 comments

No public comments in this round.