Original Article

Real-world study of 191 cases with cervical cancer who were diagnosed by loop electrosurgical excision procedure

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Background: To investigate the appropriate treatment plan and postoperative outcomes of patients with cervical cancer who were diagnosed by loop electrosurgical excision procedure (LEEP) in the real world.

Methods: A total of 191 patients were divided into two groups according to whether they received chemotherapy before surgery: one group received chemotherapy treatment before radical surgery (CT + RS group, n=44), and the other group received radical surgery directly (DS group, n=147). In this Cohort study, we analyzed the clinicopathological characteristics, treatment process, operative duration, blood loss and duration of antibiotic use after surgery of these two groups patients admitted to the West China Second University Hospital of Sichuan University between January 2013 and December 2020.

Results: The age, stage, histological type and the lymph node metastases of patients were balanced among the groups. In the laparotomy group, the postoperative antibiotic use time of the CT + RS group was longer than that of the DS group (4.62±1.37 *vs.* 3.53±1.05 days). In the laparoscopy group, the CT + RS group has longer operation time (4.48±0.59 *vs.* 3.08±1.27 hours), and longer antibiotic use time (4.00±0.00 *vs.* 3.32±1.06 days). Blood loss in group B was less than that in group A and C (91.29±10.74 *vs.* 166.15±46.84 *vs.* and 137.08±17.16 mL).

Conclusions: Preoperative chemotherapy may has no effect on reducing blood loss and shortening operation time, but may increases toxic and side effects of chemotherapy and postoperative antibiotic use time. The time interval between hysterectomy and LEEP can be considered as 1–2 months to reduce surgical bleeding.

Keywords: Cervical cancer; loop electrosurgical excision procedure (LEEP); preoperative chemotherapy; time interval

Received: 14 February 2021; Accepted: 11 November 2021; Published: 25 March 2022.

doi: 10.21037/gpm-21-13

View this article at: https://dx.doi.org/10.21037/gpm-21-13

Introduction

With the extensive application of loop electrosurgical excision procedure (LEEP) in China, most of the cervical precancerous lesions can be diagnosed early and treated in a timely manner, but at the same time, there is also widespread non-indicative abuse of LEEP, which makes a large number of patients diagnosed with cervical cancer by LEEP in the real world. Some existing studies have shown that changes in cervical morphology and periuterine inflammatory infiltration after LEEP increase the difficulty

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for follow-up surgery (1,2). The different study's result shows the time interval between LEEP and subsequent hysterectomy is different. Sullivan *et al.* (3) suggested that this surgery should be performed more than 6 weeks later. Jia *et al.* (4) stated that the safest time for hysterectomy is within 24 h or later than 6 weeks. On the other hand, Tae Kim *et al.* (5) and Samlal *et al.* (6) reported that clinical features do not correlate with this time interval, and that therefore, a hysterectomy can be performed at any time. And for that, there are no studies on the follow-up treatment of cervical cancer diagnosed after LEEP. Therefore, it is of great significance to choose the right time and plan for the follow-up operation and reduce postoperative complications.

We present the following article in accordance with the STROBE reporting checklist (available at https://gpm.amegroups.com/article/view/10.21037/gpm-21-13/rc).

Methods

Patient data

This retrospective study was carried out in the Department of Obstetrics and Gynecology, West China Second University Hospital of Sichuan University. The study included 191 patients histologically diagnosed with IA1/IIA2 cervical cancer after LEEP who subsequently underwent the radical hysterectomy between January 2013 and August 2017. Inclusion criteria were as follows: (I) cervical cancer was diagnosed pathologically after LEEP; (II) follow-up treatment was completed in our hospital and the clinicopathological data were complete; (III) no other serious complications before treatment and no concomitant malignancy or prior invasive malignancy; (IV) FIGO stages determined by two gynecologic oncologists. Clinical staging was performed according to the International Federation of Gynecology and Obstetrics staging criteria (FIGO2009).

Patient information was taken from the hospital's case recording system. Patients were divided into two groups according to whether they received chemotherapy before surgery. Analyzing the clinicopathological characteristics, treatment process, operative duration, blood loss and duration of antibiotic use after surgery of these two groups patients.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The ethical approval was not required because patient's records/information were anonymized and de-identified prior to analysis.

Treatments

One hundred and eighty three patients underwent radical hysterectomy and 8 patients with cervical cancer staging IA1 who asked for preserving fertility underwent cervical conization. Seventy three patients received laparoscopy, 110 received laparotomy. One hundred and forty seven patients received surgery directly (8 patients received cervical conization and 139 patients received radical hysterectomy) and 44 patients received 1–3 cycles of platinum-based chemotherapy before surgery.

Statistical analysis

SPSS version 26.0 was used for statistical analysis. Data were analyzed with Student's *t*-test for quantitative variables and Chi-square test for qualitative variables. Chi-square test was used when the number of cases was more than 5. If the number of cases was less than 5, the Fisher exact probability method was used for bilateral test. Statistical significance was represented by $P<0.05$.

Results

Patient characteristics

From January 2013 to August 2017, a total of 191 patients diagnosed with stage IA1/IIA2 cervical cancer were eligible for this study. Forty-four patients were in the CT + RS group and 147 patients were in the DS group. In the DS group (excluded 8 patients underwent cervical conization), the included patients were divided into three subgroups according to the time from LEEP to hysterectomy: Group A (within 1 month, n=28), group B (between 1 and 2 months, n=55), and group C (>2 months, n=64). The patient characteristics are displayed in *Table 1*. The mean age was 42.4±7.6 years (range, 23–71 years). There were 147 patients received surgery directly (8 patients received cervical conization and 139 patients received radical hysterectomy) and 44 patients received chemotherapy before surgery. No patients had lymph node metastasis. Eighteen patients had vessel invasive: 4 patients in the CT + RS group, 14 patients in the DS group. Seventy one patients had stromal invasion: 16 patients in the CT + RS group, 55 patients in the DS group.

Effects of chemotherapy on subsequent radical surgery

One hundred and ten patients underwent laparotomy

Table 1 Patients characteristics

Item	CT + RS (N=44) (%)	DS (N=147) (%)	P
Age (years)			
<45	29	82	
≥45	15	57	0.481
Stage			
IA1-IB2	40 (20.9)	135 (70.7)	
IIA1-IIA2	4 (2.1)	12 (6.3)	0.765
Histological type			
Well-differentiated squamous carcinoma	28 (56.8)	105 (71.4)	
Low-differentiated squamous carcinoma	7 (22.7)	21 (14.3)	
Adenocarcinoma	8 (18.2)	19 (12.9)	
Adenosquamous carcinoma	1 (2.3)	2 (1.4)	0.648
Vessel invasive			
Positive	4 (9.1)	14 (9.5)	
Negative	40 (90.9)	133 (90.5)	0.931
Stromal invasion			
Positive	16 (36.4)	55 (37.4)	
Negative	28 (63.6)	92 (62.6)	0.899
Lymph node metastasis			
Positive	0	0	
Negative	44 (100.0)	147 (100.0)	–

CT + RS, chemotherapy treatment before radical surgery; DS, direct surgery.

(57.6%): 39 patients in the CT + RS group (20.4%), 71 patients in the DS group (37.2%). There was no statistically significant difference between the CT + RS group and the DS group in the operation time and blood loss amount (3.77±0.8 *vs.* 3.59±1.38 hours, P=0.395; 516.67±294.31 *vs.* 464.23±361.11 mL, P=0.440). However, the postoperative antibiotic use time in the CT + RS group was significantly higher than that in the DS group (4.62±1.37 *vs.* 3.53±1.05 days, P<0.05) (*Table 2*).

Seventy three patients underwent laparoscopy (38.2%): 5 patients in the CT + RS group (2.6%), 68 patients in the DS group (35.6%). There was no statistically significant difference between the CT + RS group and the DS group in the blood loss amount (200±122.47 *vs.* 121.76±100.16 mL, P=0.101). However, the operation time and postoperative antibiotic use time in the CT + RS group was significantly higher than that in the DS group (4.48±0.59 *vs.* 3.08±1.27 days, P=0.003; 4.00±00 *vs.* 3.32±1.06 hours, P<0.05) (*Table 2*).

Table 2 Comparison of perioperative variables among study groups

Parameters	Group		P
	CT + RS (N=44)	DS (N=139)	
Operation time (h)			
Laparotomy	3.77±0.80	3.59±1.38	0.395
Laparoscopy	4.48±0.59	3.08±1.27	0.003
Blood loss (mL)			
Laparotomy	516.67±294.31	464.23±361.11	0.440
Laparoscopy	200±122.47	121.76±100.16	0.101
Postoperative antibiotic use time (day)			
Laparotomy	4.62±1.37	3.53±1.05	0.000
Laparoscopy	4.00±0.00	3.32±1.06	0.000

CT + RS, chemotherapy treatment before radical surgery; DS, direct surgery.

The influence of time intervals between LEEP and subsequent hysterectomy

One hundred and forty seven patients underwent hysterectomy without chemotherapy, including 71 patients underwent laparotomy and 68 patients underwent laparoscopy. In the laparoscopy group, mean blood loss was 166.15±46.84 mL in group A, 91.29±10.74 mL in group B, and 137.08±17.16 mL in group C, respectively, with statistically significant (P=0.048). There was no statistically significant difference between the group A, group B and group C in the operation time and postoperative antibiotic use time (3.11±1.10 h, 2.73±1.14 h, 3.53±1.42 h, P=0.069; 3.62±1.19 days, 3.16±1.18 days, 3.32±1.05 days, P=0.417). However, in the laparotomy group, there was no statistically significant difference between the group A, group B and group C in the operation time, blood loss and postoperative antibiotic use time (*Table 3*).

Complications

As for complications, postoperative complications occurred in 3 patients, including 1 patient had postoperative urinary

Table 3 Comparison of perioperative variables among different time interval groups

Parameters	Group			P
	A (N=28)	B (N=55)	C (N=64)	
Operation time (h)				
Laparotomy	3.74±1.93	3.19±1.13	3.78±1.24	0.269
Laparoscopy	3.11±1.10	2.73±1.14	3.53±1.42	0.069
Blood loss (mL)				
Laparotomy	317.85±54.87	485±85.27	509.71±63.77	0.234
Laparoscopy	166.15±46.84	91.29±10.74	137.08±17.16	0.048
Postoperative antibiotic use time (day)				
Laparotomy	3.64±0.93	3.45±0.96	3.54±1.17	0.874
Laparoscopy	3.62±1.19	3.16±1.18	3.32±1.05	0.417

system injury in the DS group, 1 had postoperative hypostatic pneumonia, and 1 had postoperative lymphocyst in the CT + RS group. Among the 44 patients undergoing surgery after chemotherapy, 16 patients had CTCAE I–III toxic and side effects (36.4%), including 9 (20.5%) gastrointestinal reactions, 4 (9.1%) alopecia, 2 (4.5%) bone marrow suppression, and 1 (2.3%) abnormal liver function.

Discussion

Treatment for cervical cancer is to adopt surgery or concurrent chemoradiotherapy after comprehensive consideration of individualized treatment plan according to clinical stage, pathological type, comprehensive patient situation and medical technical level (7). Recently, with the continuous innovation of chemotherapy drugs and the rapid development of clinical trials, preoperative chemotherapy has achieved positive effects in the treatment of cervical cancer, and has been gradually paid attention to (8,9). However, there is no uniform standard of treatment and it is unclear how preoperative chemotherapy affects subsequent surgery and survival (10-13). In this retrospective analysis, all patients were diagnosed with cervical cancer after LEEP, requiring further treatment. When patients who underwent cervical conization require subsequent hysterectomy, there are several inconsistent suggested criteria to determine the time for the safest hysterectomy (3,5,14,15). There is no standard time interval between LEEP and hysterectomy and it is not known whether patients will benefit from chemotherapy while waiting for a hysterectomy. Through Medline search, we could find very few articles describing the relationship of postoperative clinical aspects to the chemotherapy before hysterectomy and various time intervals between the LEEP and the hysterectomy. This study analyzed the treatment regimens and clinical efficacy of these patients, with a view to accumulating the diagnosis and treatment experience of such patients and exploring the optimization of treatment regimens.

Preoperative chemotherapy, as one of the adjuvant treatments for cervical cancer, can kill subclinical lesions and eliminate micrometastases, which has attracted wide attention. However, not all patients with cervical cancer are suitable for preoperative chemotherapy. Those patients who are ineffective or insensitive to chemotherapy may delay the best treatment opportunity due to chemotherapy and increase the economic burden of patients (16,17). There have been no studies on patients who diagnosed with cervical cancer after LEEP underwent hysterectomy after chemotherapy. This study analyzed the results in the real world for the first time, and the results showed that chemotherapy before hysterectomy after LEEP had no effect on reducing blood loss and shortening the operation time, but increased the toxic and side effects of chemotherapy and increased the postoperative antibiotic use time. It might because that chemotherapy-induced tissue organization, edema, and congestion may increase the difficulty of subsequent surgery. In addition, the use of chemotherapy drugs may cause leukopenia and reduce human immunity, so the use of antibiotics after surgery may be prolonged.

The appropriate time interval between LEEP and

subsequent hysterectomy has no uniform standard. Sullivan *et al.* (3) reported that performing definitive minimally invasive surgery for cervical cancer within 6 weeks after cervical excision is associated with increased risk for 30-day complications, thus suggesting that this surgery should be performed more than 6 weeks later. Jia *et al.* (4) stated that the safest time for hysterectomy is within 24 h or later than 6 weeks. Yin *et al.* (14) reported that hysterectomy should be performed at least 4 weeks after conization. On the other hand, Tae Kim *et al.* (5) and Samlal *et al.* (6) reported that clinical features do not correlate with this time interval, and that therefore, a hysterectomy can be performed at any time.

In this Cohort study we found no statistically significant differences between the group A, group B and group C with respect to mean operation times, blood loss and postoperative antibiotic use time in the laparotomy group. However, in the laparoscopy group, mean blood loss was 166.15±46.84 mL in group A, 91.29±10.74 mL in group B, and 137.08±17.16 mL in group C, respectively, with statistically significant (P=0.048). This result suggested that the time interval between hysterectomy and LEEP of 1 to 2 months can reduce surgical bleeding. Malinak *et al.* (18) conducted a histopathological study on hysterectomy specimens according to the interval between LEEP and hysterectomy. They found that stroma blood vessels and capillary vessels were dilated to accumulate erythrocytes, polymorphs, and other inflammatory cells, and that these phenomena became more severe with the passage of time, and that they generally continued until 3 weeks postoperatively. In this study, we also experienced more hemorrhage in group A and C, compared with the finding of group B. This result is concordant with that of Malinak *et al.* (18).

Wisborg *et al.* (19) only reported a few cases of postoperative complications such as rectal fistula and peritonitis. In the present study, 3 patients experienced postoperative complications: one case of urinary system injury in the DS group, one case of hypostatic pneumonia and one case of postoperative lymphocyst in the CT + RS group. Therefore, the occurrence of complications was found not to be significantly affected by the time interval between LEEP and hysterectomy. However, 36.4% (16/44) of the patients receiving preoperative chemotherapy developed chemotherapy-related toxic and side effects. In addition, preoperative chemotherapy increases postoperative antibiotic use time. Therefore, it is worth further study whether patients after LEEP need chemotherapy while waiting for hysterectomy.

This study has some limitations. We only included a small number of patients, and the retrospective analysis is not sufficiently rigorous to settle the question of the effects of preoperative chemotherapy in cervical cancer patients diagnosed by LEEP and the option of appropriate time interval between LEEP and subsequent hysterectomy. Studies with larger sample sizes and multicenter prospective randomized studies are needed to further research. However, due to the real-world research data collection limitations and the development of medical level, we cannot choose samples that are too old for research. Therefore, in the future research, we can consider to include the data of other medical institutions at the same level for research.

Conclusions

Preoperative chemotherapy may has no effect on reducing blood loss and shortening operation time, but may increases toxic and side effects of chemotherapy and postoperative antibiotic use time. The time interval between hysterectomy and LEEP can be considered as 1–2 months to reduce surgical bleeding.

Acknowledgments

We are grateful to Prof. Cong XIE and Lisa for copy editing the manuscript.
Funding: The Key Project of Sichuan Provincial Department of Science and Technology: "Study on the key factors affecting the diagnosis and treatment of major diseases in obstetrics and gynecology (19ZDYF)".

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gpm.amegroups.com/article/view/10.21037/gpm-21-13/rc

Data Sharing Statement: Available at https://gpm.amegroups.com/article/view/10.21037/gpm-21-13/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gpm.amegroups.com/article/view/10.21037/gpm-21-13/coif). All authors report that they received consulting fees from funding: The Key Project of Sichuan Provincial Department of Science and Technology: "Study on the key factors affecting the diagnosis and treatment of major

diseases in obstetrics and gynecology (19ZDYF)".

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The ethical approval was not required because patient's records/information were anonymized and de-identified prior to analysis.

References

1. Wong AS, Li WH, Cheung TH. Predictive factors for residual disease in hysterectomy specimens after conization in early-stage cervical cancer. Eur J Obstet Gynecol Reprod Biol 2016;199:21-6.
2. Song Y, Wang Q, Sui L, et al. Clinical significance of loop electrosurgical excisional procedure in diagnosis and treatment of cervical adenocarcinoma in situ and invasive cervical adenocarcinoma. Zhonghua Fu Chan Ke Za Zhi 2018;53:178-82.
3. Sullivan SA, Clark LH, Staley AS, et al. Association between timing of cervical excision procedure to minimally invasive hysterectomy and surgical complications. Gynecol Oncol 2017;144:294-8.
4. Jia H, Ye J, Guo H, et al. Timing selection and experience summary of the subsequent laparoscopic total hysterectomy. China Family Planning and Obstetrics and Gynecology 2018;10:74-7.
5. Tae Kim Y, Sung Yoon B, Hoon Kim S, et al. The influence of time intervals between loop electrosurgical excision and subsequent hysterectomy on the morbidity of patients with cervical neoplasia. Gynecol Oncol 2005;96:500-3.
6. Samlal RA, van der Velden J, Schilthuis MS, et al. Influence of diagnostic conization on surgical morbidity and survival in patients undergoing radical hysterectomy for stage IB and IIA cervical carcinoma. Eur J Gynaecol Oncol 1997;18:478-81.
7. Feng Y, Cao T, Wang Y, et al. Neoadjuvant chemotherapy followed by conization to spare fertility in cases of locally advanced cervical cancer: A case report and review of the literature. Mol Clin Oncol 2016;5:411-6.
8. Gupta S, Maheshwari A, Parab P, et al. Neoadjuvant Chemotherapy Followed by Radical Surgery Versus Concomitant Chemotherapy and Radiotherapy in Patients With Stage IB2, IIA, or IIB Squamous Cervical Cancer: A Randomized Controlled Trial. J Clin Oncol 2018;36:1548-55.
9. Zhao H, He Y, Zhu LR, et al. Effect of neoadjuvant chemotherapy followed by radical surgery for FIGO stage IB2/IIA2 cervical cancer: A multi-center retrospective clinical study. Medicine (Baltimore) 2019;98:e15604.
10. Matsuzaki S, Klar M, Mikami M, et al. Management of Stage IIB Cervical Cancer: an Overview of the Current Evidence. Curr Oncol Rep 2020;22:28.
11. Benson R, Pathy S, Kumar L, et al. Locally advanced cervical cancer - neoadjuvant chemotherapy followed by concurrent chemoradiation and targeted therapy as maintenance: A phase II study. J Cancer Res Ther 2019;15:1359-64.
12. van Kol KGG, Vergeldt TFM, Bekkers RLM. Abdominal radical trachelectomy versus chemotherapy followed by vaginal radical trachelectomy in stage 1B2 (FIGO 2018) cervical cancer. A systematic review on fertility and recurrence rates. Gynecol Oncol 2019;155:515-21.
13. Zou W, Han Y, Zhang Y, et al. Neoadjuvant chemotherapy plus surgery versus concurrent chemoradiotherapy in stage IB2-IIB cervical cancer: A systematic review and meta-analysis. PLoS One 2019;14:e0225264.
14. Yin X, Zhu L, Tan W, et al. Time Intervals Between Prior Cervical Conization and Posterior Hysterectomy Influence Postoperative Infection in Patients with Cervical Intraepithelial Neoplasia or Cancer. Med Sci Monit 2018;24:9063-72.
15. Hou X, Lei P, Ding Y, et al. Effect of time interval between circumferential electrocervical resection and hysterectomy on surgical outcome. Advances in Modern Obstetrics and Gynecology 2019;28:784-7.
16. Zhao H, He Y, Yang SL, et al. Neoadjuvant chemotherapy with radical surgery vs radical surgery alone for cervical cancer: a systematic review and meta-analysis. Onco Targets Ther 2019;12:1881-91.
17. Tesfai FM, Kroep JR, Gaarenstroom K, et al. Fertility-sparing surgery of cervical cancer >2 cm (International

Federation of Gynecology and Obstetrics 2009 stage IB1-IIA) after neoadjuvant chemotherapy. Int J Gynecol Cancer 2020;30:115-21.
18. Malinak LR, Jeffrey RA Jr, Dunn WJ. The conization-hysterectomy time interval: a clinical and pathologic study. Obstet Gynecol 1964;23:317-29.
19. Wisborg T. The cone biopsy--hysterectomy time interval related to wound infection. Acta Obstet Gynecol Scand 1972;51:1-4.

doi: 10.21037/gpm-21-13
Cite this article as: Zhang M, Chen J, Li K, Luo Y, Yin R. Real-world study of 191 cases with cervical cancer who were diagnosed by loop electrosurgical excision procedure. Gynecol Pelvic Med 2022;5:6.