

Retrospective analysis of surgery for cervical stump carcinoma at early stage

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Abstract. Cervical stump cancer is a rare type of disease as total hysterectomies are performed infrequently. The purpose of this retrospective study was to assess the diagnosis, treatment, follow-up methods and complications of 10 patients with cervical stump carcinoma treated with surgery in Anhui Provincial Hospital affiliated to Anhui Medical University (Hefei, China). From January 2006 to October 2016 a total of 10 patients underwent surgery for carcinoma of the cervical stump. The pathological reports revealed 80% of cases were squamous cell carcinoma and 20% of cases were adenocarcinoma. The FIGO stage distribution was as follows: Carcinoma *in situ* (10%); IB₁ (70%); IIA (20%). The patients received a transvaginal trachelectomy or a radical trachelectomy and pelvic lymphadenectomy (either laparoscopic or laparotomic abdominal); four of the patients were treated with adjuvant chemotherapy, and two with concurrent chemoradiotherapy. The parametrial and resection margin infiltration, lymph node metastasis and lymph vascular space invasion (LVSI) were negative in all patients, and the deep stromal invasion rate was 66.7% (6/9). No incidences of recurrence or mortality were recorded during the follow-up interval of 6-120 months. Compared with the four patients who received laparotomic abdominal surgery, significantly less blood loss was recorded for the five patients who underwent laparoscopic surgery ($P<0.01$). There was no significant difference observed in the surgery time ($P>0.01$) or in the hospital stay duration ($P>0.01$) for the patients treated with laparotomic abdominal surgery and laparoscopic surgery. One patient experienced bladder fistula due to bladder over-dilation, but recovered quickly after the catheter was reinserted. Surgery for cervical stump cancer

at an early-stage is a viable and safer procedure, particularly the laparoscopic approach.

Introduction

Carcinoma of the cervical stump rarely occurs in patients who have previously received a subtotal hysterectomy, and accounts for 2-5% of all cervical cancer cases worldwide from 1970 (1-3). Barillot *et al* (1) analyzed 213 cases of cervical stump carcinoma and they observed that the locoregional control at equal time points between radiotherapy alone and surgery were very similar, however the lethal complications of radiotherapy were lower. Hellström *et al* (2) concluded that there was no difference in the longterm prognosis for radio-logically treated squamous cell carcinoma cervical stump cancer and other cervical carcinomas, however the prognosis for adenocarcinoma stump cancers was worse than those in an intact uterus. For the treatment of early cervical stump cancer, Diaz-Feijoo *et al* (3) reported that total laparoscopic radical trachelectomy and intraoperative sentinel node identification was effective and safe. To date, there has been no standardized treatment of this type of cervical neoplasm. The majority of gynecological tumor experts conform to existing strategies of radiotherapy or laparotomic abdominal (or laparoscopic) radical surgery. Presentation ≥ 2 -years following a subtotal hysterectomy is considered to indicate true cervical stump cancer, whereas an interval of < 2 -years interval following subtotal hysterectomy is considered to denote a 'coincidental' carcinoma that may have been present at the time of the subtotal hysterectomy (4-7). In the present study, 10 cases of patients with cervical stump cancer were retrospectively analyzed with regard to the clinical characteristics (including age, clinical stage and histopathology), treatment and follow-up data. The results suggested that surgery for cervical stump cancer at an early-stage is a viable and safe procedure, particularly the laparoscopic approach as this type of surgery has fewer associated complications, including reduced blood loss and a shorter recovery time.

Patients and methods

Ethics statement. All the patients were recruited following the receipt of written consent between January 2006 and October 2016 at the Anhui Provincial Hospital affiliated to Anhui

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Medical University (Hefei, China). The study was reviewed and approved by the ethics review board of Anhui Provincial Hospital. All procedures performed in the study were in accordance with the ethical standards of the institutional research committee and with the 7th revised edition of the declaration of Helsinki.

Patient characteristics. A total of 10 patients were evaluated with respect to their medical history, a physical examination (including a pelvic examination), routine lab work and a chest X-ray; the diagnosis was determined according to the system of the International Federation of Gynecology and Obstetrics (FIGO) by two or more gynecological tumor experts who were blinded to the patient data. Each patient had a histological diagnosis determined via biopsy prior to treatment.

The median patient age was 52.4 ± 4.8 years (range 46–61 years). All patients had previously undergone a subtotal hysterectomy for benign disease such as fibromyoma and menometrorrhagia. The mean time interval between the subtotal hysterectomy and diagnosis of cervical stump cancer was 11.4 ± 5.6 years (range, 5–21 years; all patients had an interval of ≥ 5 years). The clinical data, including tumor stage and histology, are presented in Table I.

All the patients were followed up twice a year by gynecologic oncologists for ten years. A complete physical exam, including a pelvic examination, was performed on each visit. Vaginal smears and a colposcopy were conducted annually, as were routine chest X-rays and squamous cell carcinoma antigen studies. The median time of observation for patients alive at the last follow-up visit was 33.20 ± 37.78 months (range, 6–120 months).

Treatment. Patients with a cervical cancerous stump diagnosed as *carcinoma in situ* were administered a transvaginal trachelectomy. Patients with a cervical cancer stump diagnosed at stage IB₁/IIA were treated with a radical trachelectomy and pelvic lymphadenectomy (8). A total of 5 cases were treated using a laparoscopic procedure: the laparoscope was placed into position 3 cm above the umbilicus through an 11-mm umbilical trocar with a direct-puncture, and three other trocars were introduced in the Trendelenburg position. Two accessory 12- and 5-mm trocars were then placed under direct visualization in the iliac fossae, and one 5-mm accessory trocar at the midline between the umbilicus and the left subcostal margin. The number and position of trocars were then used to perform a distal radical trachelectomy and a pelvic lymphadenectomy.

Following inspection of the abdominal cavity, the retroperitoneal spaces were opened and a systematic bilateral pelvic lymphadenectomy from the common iliac artery to the inferior boundary of the circumflex iliac vein was performed. Then, the paravesical, pararectal, rectovaginal, and vesicovaginal spaces were fully expanded, thereby delineating the uterosacral ligaments and the parametria. Uterine vessels were cut and coagulated at their origin from the hypogastric vessels; the parametrial tissue and the uterosacral ligaments were also transected by coagulation and cutting.

Dissection of tissue adhesion, the ureteral tunnel, urinary bladder and ureteral separation was performed with the aid of an Ultracision® Harmonic Scalpel (Ethicon, Inc., Cincinnati, OH, USA). The uterus-lifting cup was placed into the cervical

Table I. The clinical characteristics of the cervical stump cancer cases.

Variable	No. patients
Age (years)	
≤50	4
>50	6
Clinical stage	
<i>Carcinoma in situ</i>	1
IB ₁	7
IIA	2
Histology	
Squamous carcinoma	7
Keratin	1
Non-Keratin	6
Adenocarcinoma	2
High	1
Middle	1
Low	0

cavity to facilitate tissue dissection and the development of parametria and paracolpia. The proximal paracervical tissue and the vagina were transected and removed vaginally. The vaginal cuff was then closed laparoscopically by continuous suture. In total, four cases were treated with laparotomic abdominal radical trachelectomy and pelvic lymphadenectomy. A suprapubic catheter was inserted. Two of the patients subsequently received postoperative concurrent chemoradiotherapy due to deep stromal invasion. Four patients were treated with adjuvant chemotherapy (Paclitaxol and platinum).

Results

Histology. Squamous cell carcinoma was identified in 80% of cases, with the remaining 20% determined to be adenocarcinoma. This histological type distribution is similar that reported worldwide in the NCCN Guidelines® 2015 in which squamous cell carcinoma accounted for ~80% of all cervical cancer cases and adenocarcinoma accounted for ~20% of all cases (8–12).

Age. The median age of patients with cervical stump carcinoma was 52.4 years, similar to the median age of 58 years reported by Miller *et al* (4), compared with 49 years in patients with cervical carcinoma of the intact uterus.

Clinical presentation. The clinical symptoms included vaginal bleeding (90%) and abnormal cytology (10%). No other symptoms were observed. All patients presented with hemoglobin levels of >11 g/dl. The median interval between the onset of symptoms and a diagnosis was 5.45 months (Table II). In 10% of cases, the symptoms were present for ~2 years prior to the establishment of a diagnosis. The mean operative time was 214.6 min; the mean estimated blood loss was 180.0 ml for laparoscopic surgery, and 687.5 ml for laparotomic abdominal surgery (Fig. 1); the mean length of the hospital stay was

Table II. The pathology patterns and the adjuvant treatment of patients with cervical stump cancer.

Case	Diagnosis interval (months)	Differentiation (Squamous or adenocarcinoma)	Deep stromal invasion	Parametrium and the resection margin of the vaginal involvement	LN Metastasis	LVSI	CT	RT	Follow-up (months)
1	1	Keratin	<1/2	Neg.	Neg.	Neg.	No	No	12
2	2	Non-Keratin	>2/3	Neg.	Neg.	Neg.	Yes	No	60
3	4	Non-Keratin	>1/2	Neg.	Neg.	Neg.	Yes	Yes	12
4	24	Non-Keratin	>1/2	Neg.	Neg.	Neg.	Yes	No	8
5	6	High	>1/2	Neg.	Neg.	Neg.	Yes	Yes	6
6	3	Non-Keratin	<1/2	Neg.	Neg.	Neg.	Yes	No	13
7	0.5	Middle	>2/3	Neg.	Neg.	Neg.	Yes	No	28
8	2	Non-Keratin	<1/2	Neg.	Neg.	Neg.	No	No	6
9	6	L	L	L	L	L	L	L	67
10	6	Non-Keratin	>2/3	Neg.	Neg.	Neg.	No	No	120

LN, lymph node; LVSI, lymph vascular space invasion; CT, chemotherapy; RT, radiotherapy; L, data that was lost and cannot be collected; Neg, negative.

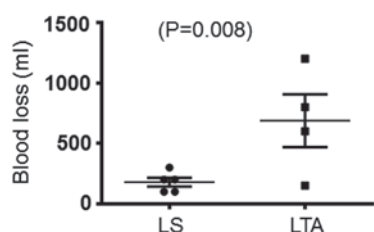


Figure 1. Scatter diagram of blood loss associated with LS and LTA ($P<0.01$). The mean estimated blood loss was 180.0 ml for LS and 687.5 ml for LTA. LS, laparoscopic surgery; LTA, laparotomic abdominal surgery.

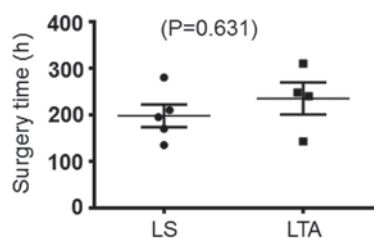


Figure 2. Scatter diagram of duration of the LS and the LTA ($P>0.05$). LS, laparoscopic surgery; LTA, laparotomic abdominal surgery.

14.8 days. The catheters of all patients were removed on the 21st postoperative day after residual urine volumes of 80 ml. There was no significant difference in the surgery time and the duration of hospital stay between the laparoscopic surgery and the laparotomic abdominal surgery (Figs. 2 and 3). The pathological characteristics of the patients are presented in Table II. Overall, six patients were received adjuvant chemotherapy, two of whom also received combined radiotherapy (Table II).

Follow-up and complications. All the patients were followed-up and no cases of recurrence were observed; the mean follow-up time was 33.20 ± 37.78 months (range, 6-120 months). No intra-operative or postoperative complications occurred, with the exception of one patient who experience bladder fistula that

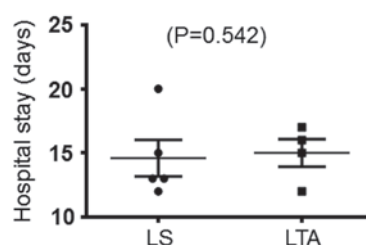


Figure 3. Scatter diagram of duration of hospital stay following LS and LTA ($P>0.05$). LS, laparoscopic surgery; LTA, laparotomic abdominal surgery.

occurred the day following the removal of the catheter due to bladder over-dilation; the patient recovered quickly after reinserting the catheter.

Discussion

Carcinoma of cervical stump accounts for 3-9% of all cases of cervical cancer (2,13). Miller *et al* (4) reported that the symptomatology, stage distribution and histology of cervical stump cancer were not significantly different to those of cervical carcinoma of the intact uterus. The individualization of therapy depends on the tumor stage, volume and depth of invasion. Although the 5-year survival rates of patients with cervical stump cancer compare favorably with patients with intact uteri, the complication rate appears to be enhanced by previous surgery and palliative care. Surgery is recommended for patients with pre-invasive disease and small volume (2 cm) invasive lesions limited to the cervix (stage IA and IB). In the present study, patients with stage IIA cervical stump cancer were surgically treated and no complications were identified.

A review of PubMed revealed that the majority of current reports are associated with the cornerstone management of radiation therapy; comparatively few reports are associated with radio-surgical combination methods. However, severe complications such as cystitis and rectum fistula have been reported, this is due to the absence of the uterus which acts as

a shield. Of the present 9 cases treated with radical trachelectomy and pelvic lymphadenectomy (5 with laparoscopic; 4 with laparotomic abdominal surgery), only one patient experienced the complication of bladder fistula, and the patient recovered soon after reinserting the catheter.

Compared with patients with cervical cancer and intact uteri, the patients with cervical stump cancer were generally older and typically had concurrent complicating conditions such as hypertension or diabetes (14-19). The benefits of preserving the cervix may be associated with the patient's desire to preserve sexual, bladder and bowel function as previously reported, an approach that remains controversial among gynecologists (20-22). It must be noted that regular cervical screening following a subtotal hysterectomy is essential. Vaginal bleeding is a severe symptom in non-menstruating female.

As amputation of the radical cervical stump is considered to be challenging following a supravaginal hysterectomy, the majority of patients were subjected to concurrent chemoradiotherapy. Severe rectal, bladder and sigmoid complications following radiation have been reported due to the loss of protection offered by the intact uterus. Currently, surgery is the recommended approach for this type of tumor. With the development and proficiency of the laparoscopic surgical technique, ever more complicated laparoscopic surgical techniques have been made clinically available. This type of surgery has fewer associated complications, particularly with regard to reduced blood loss and a shorter recovery time.

In China, patients with malignant tumors often stay longer in hospital for reasons, including patient requests, age and physical weakness, compared with patients in developed countries. Oncologists must be vigilant to the appearance of complications. As the laparoscopic surgery approach has a number of inherent advantages, including easier identification of the ureter using laparoscopic enlargement and less injuries, laparoscopic surgery is recommended for the treatment of patients with early-stage cervical stump cancer.

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