

Laparoscopic ovarian transposition in young women with cervical squamous cell carcinoma treated by primary pelvic irradiation

H. Shou, Y. Chen, Z. Chen, T. Zhu, J. Ni

Department of Gynecology Oncology, Zhejiang Provincial Cancer Hospital, Hangzhou (China)

Summary

Objective: To report the authors' experience with laparoscopic ovarian transposition and ovarian function preservation in young women with cervical squamous cell carcinoma treated by primary pelvic irradiation. **Materials and Methods:** Twenty-seven premenopausal patients were treated with radiotherapy for a cervical squamous cell carcinoma. Laparoscopic ovarian transposition to paracolic gutters with uterine conservation with pelvic common iliac lymph node and para-aortic lymph node sampling were performed in ten patients at the same time of laparoscopic ovarian transposition. Preservation of ovarian function was assessed by patients' symptoms and serum follicle-stimulating hormone level. **Results:** Bilateral or unilateral laparoscopic ovarian transposition was performed in 27 patients: 22 cases Stage IIB, one case Stage IIIA, and four cases Stage IIIB. No immediate intraoperative or postoperative complications were observed. Two of the ten patients were confirmed by lymph node metastases. One patient was lost to follow-up. Ovarian preservation was achieved in 18 (69.2%) of 26 patients. No patient was detected with ovarian metastasis at follow-up. **Conclusions:** Laparoscopic ovarian transposition is a safe and effective procedure for preserving ovarian function. This procedure may be considered in premenopausal women who need to undergo pelvic irradiation for cervical squamous cell carcinoma, especially for those less than 40 years of age. Otherwise, para-aortic lymph node or common iliac lymph nodes sampling at the same time of laparoscopic ovarian transposition may preferably guide radiation therapy.

Key words: Ovarian transposition; Squamous cell carcinoma; Pelvic irradiation; Laparoscopy.

Introduction

Recent studies on the treatment of cancer have focused on the quality of life (QOL) of patients. The total number of patients with cervical carcinoma includes an increasingly large percentage of young women [1], and preservation of ovarian function is thought to be particularly important to the physiologic and psychosexual well-being of these patients. The loss of ovarian function in such young women is one of the usual consequences of chemotherapy and radiotherapy, causing climacteric symptoms, which often seriously impair their QOL [2]. The conventional method of treatment has been radiological for middle and advanced stage cervical cancer. When the ovaries are preserved in a normal position, ovarian function can easily be lost due to radiation. A review of published studies indicated that the ovarian metastasis rate from uterine cervical cancer is very low, especially in cervical squamous cell carcinoma. Therefore the authors performed a transposition of the ovaries through laparoscopy in patients with cervical squamous cell carcinoma, so that they would be outside of the field of radiation during postoperative radiotherapy.

Materials and Methods

Using a retrospective review of the medical records, the authors identified all women who underwent laparoscopic ovarian transposition at Zhejiang Cancer Hospital between August 2008 and August 2011. Patients and tumor characteristics as well as treatment plan and follow-up data were collected (Tables 1 and 2). Thirteen women younger than 45 years were included. The mean age of the patient population was 34.6 years (range, 25-44); 22 patients were younger than 40 years. Twenty-two cervical cancers were Stage IIB, One was Stage IIIA and another four were Stage IIIB (FIGO staging system). All the histological types are squamous cell carcinoma. All had received pelvic radiotherapy and concurrent cisplatin-containing chemotherapy and brachytherapy. Laparoscopic ovarian transposition was completed before pelvic irradiation. All had a history of regular menstrual cycle and no vasomotor symptoms before the ovarian transposition. Ten patients, who had probable positive lymph node with preoperative radiologic imaging and in which lymph node puncture biopsy was difficult to perform, underwent pelvic common iliac lymph node and para-aortic lymph node sampling at the same time of laparoscopic ovarian transposition. A random follicle-stimulating hormone (FSH) level was obtained before the procedure. The surgery was not performed if the patient had (1) evidence of carcinomatous, ovarian, or tubal metastasis on imaging study and (2) amenorrhea and/or vasomotor symptoms and serum FSH level greater than 40 IU/L. The patients were informed of the risks and benefits, with a description of the procedure, and informed con-

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Table 1. — Patient characteristics.

Variable (n. = 27)	Findings
Mean age at operation (range)	34.6 years (25–44)
> 40 years	5
< 40 years	22
Cancer Stage ^a (n. of cases)	27
IIB	22
IIIA	1
IIIB	4

^a All the histological types were squamous cell carcinoma and Stage for cervical cancer according to International Federation of Gynecology and Obstetrics (FIGO) classification.

sents were obtained. After therapy completion, all patients were evaluated by a radiation oncologist and gynecologic oncologist after one month, followed by evaluations at three-month intervals for two years and then every six months thereafter. On follow-up, ovarian function was evaluated by the presence or absence of postmenopausal symptoms and by the measurement of FSH. Transient ovarian failure may last for a long time, and the authors defined ovarian failure as FSH levels elevated (> 40 U/L) twice apart (in three- to six-month interval) two years after complete treatment of cancer. The local ethics committee at Zhejiang cancer Hospital approved the study.

Surgical procedure

The operation was performed under general anesthesia. A total of three trocars were used. First, a ten-mm trocar was inserted through an umbilical incision, and the endoscopic camera was then introduced. Two extra five-mm trocars were placed in each lumbar quadrant. All pelvic and abdominal structures were inspected in a clockwise fashion before proceeding with the procedure. If adhesions were noted around the uterus, ovaries, pelvic cavity, and thought to interfere with the procedure, then adhesiolysis was performed. The utero-ovarian ligaments were divided. The ovaries were then mobilized on the infundibulopelvic ligaments. The peritoneum under and lateral to the infundibulopelvic ligaments were incised enough to reach the level of iliac crest, under direct vision of the ureter. The ovaries were fixed in the paracolic gutters at the level of pelvic brim with a sufficient angle to maintain good blood supply. The upper and lower poles of the ovaries were marked with metal clips. Pelvic common iliac lymph node and para-aortic lymph node sampling was performed in patients with probable positive lymph node at the same time of laparoscopic ovarian transposition.

Results

The mean operative time was 125 minutes (range, 70–170) and average blood loss was 59 ml (range, 10–100) (Table 3). Twenty-one patients were thought to be appropriate for bilateral ovarian transposition; in the re-

Table 2. — Summary of patients characteristics, treatment, and outcome.

Case No.	Age, yrs	Diagnosis Stage	Surgical procedure	Lymph node metastasis	Elevated FSH	Ovarian benign lesion	Ovarian metastasis	Survival	F/U
1	38	IIB	BOT+PLNS+PALNS	NO	NO	NO	NO	YES	30
2	43	IIB	BOT	-	YES	NO	NO	YES	32
3	36	IIB	BOT	-	NO	Ovarian cyst	NO	YES	31
4	39	IIB	BOT	-	NO	NO	NO	YES	26
5	38	IIB	BOT	-	NO	NO	NO	YES	30
6	32	IIB	UOT	-	NO	NO	NO	YES	44
7	36	IIB	UOT	-	NO	NO	NO	YES	35
8	29	IIB	UOT+PLNS+PALNS	YES	YES	NO	NO	YES	36
9	26	IIB	BOT	-	NA	NO	NO	NO	25
10	41	IIIA	BOT+PLNS+PALNS	NO	YES	NO	NO	YES	36
11	30	IIIB	BOT	-	YES	NO	NO	YES	59
12	44	IIIB	BOT+PLNS+PALNS	YES	YES	NO	NO	YES	30
13	38	IIB	UOT+PLNS+PALNS	NO	YES	NO	NO	YES	40
14	30	IIB	UOT+PLNS+PALNS	NO	NO	Ovarian cyst	NO	YES	55
15	28	IIB	BOT+PLNS+PALNS	NO	NO	NO	NO	YES	41
16	36	IIB	BOT	NO	NO	NO	NO	YES	38
17	41	IIB	BOT+PLNS+PALNS	NO	YES	NO	NO	YES	25
18	39	IIB	BOT	-	NO	NO	NO	YES	39
19	29	IIB	BOT	-	NO	NO	NO	YES	25
20	35	IIB	UOT	-	NO	NO	NO	YES	28
21	42	IIIB	BOT	-	NO	NO	NO	YES	25
22	32	IIB	BOT	-	NO	NO	NO	YES	37
23	34	IIB	BOT	-	NO	NO	NO	YES	26
24	29	IIB	BOT	-	NO	NO	NO	YES	35
25	33	IIB	BOT+PLNS+PALNS	NO	YES	NO	NO	YES	31
26	30	IIIB	BOT	-	NO	NO	NO	YES	44
27	25	IIB	BOT+PLNS+PALNS	NO	NO	NO	NO	YES	26

BOT: bilateral ovarian transposition; UOT: unilateral ovarian transposition; PLNS: pelvic common iliac lymph node sampling; PALNS: para-aortic lymph node sampling; NA: not available; F/U: follow-up in months.

Table 3. — Results.

Operation time, mean (range)	125 min (70–170)
Estimated blood loss, mean (range)	59 ml (10–100)
Hospital stay, mean (range)	4.9 days (3–8)
Complications	0
Lymph node Metastasis, n. of cases (%)	2 (20%)
Ovarian function after treatment	
Menopausal, n. of cases (%)	8 (30.8%)
Bilateral ovarian transposition	6
Unilateral ovarian transposition	2
> 40 years	4
< 40 years	4
Functional, n. of cases (%)	18 (69.2%)
Bilateral ovarian transposition	14
Unilateral ovarian transposition	4
> 40 years	1
< 40 years	17

maining six patients unilateral ovarian transposition was performed. Ten patients had undergone pelvic common iliac lymph node and para-aortic lymph node sampling at the same time. Two patients were finally proved to have common iliac lymph node metastasis. The procedure was completed by laparoscopic approach in all 27 women as planned without conversion to laparotomy. There were no immediate intraoperative or postoperative complications reported in the first 30 days after surgery. The mean duration of hospitalization was 4.9 days (range three to eight). Pelvic radiotherapy were planned to be carried out immediately in all patients after surgery. Conventional whole pelvic radiation therapy was performed in all cases. Twenty-six cases had undergone pelvic radiotherapy, concurrent cisplatin-containing chemotherapy, and brachytherapy. Extended-field irradiation of para-aortic lymph nodes was carried out in the two patients with lymph node metastasis. One case (patient 9) discontinued pelvic radiotherapy halfway because of intestinal fistula due to tumor necrosis. The patient did not adhere to the study protocol, and no timed postoperative FSH level was assessed in this patient.

In addition to the evaluation and surveillance for their cancer, women were asked about their menopausal symptoms. Serum FSH levels were checked in the three- and six-month intervals after completion of planned treatment. The mean follow-up was 34.4 months ranging from 25 to 59 months. Eighteen patients (69.2%) had FSH levels less than 40 IU/L, four of these patients underwent unilateral ovarian transposition and 17 of them were less than 39 years of age. None of the patients described reported menopausal symptoms. Of the eight patients who had elevated FSH level after completion of their cancer treatments, four patients were over 40 years of age.

There was no radiological or clinical evidence of isolated ovarian metastasis in the transposed ovaries. Nevertheless,

there were two patients (patient 3 and 14) who had an ovarian cyst. Therapy was not given because these patients were asymptomatic. All the patients survived at follow-up and recurrence did not occur, except for patient 9. This patient who did not complete radiotherapy and had undergone chemotherapy and brachytherapy, eventually went into renal failure.

Discussion

Preservation of ovarian hormonal function in women undergoing treatment for cancer is receiving increasing attention. Improved long-term survival will mandate that strategies be developed to minimize or avoid this important morbidity.

Although concurrent chemoradiotherapy results in a good outcome for patients with middle and advanced stage cervical cancer [3], exposure to radiation can lead to early ovarian failure. In the literature, radiation doses of less than three Gy to the ovary led to ovarian failure in 11% of women, more than three Gy in 60% of women, and over five Gy were sufficient to sterilize the ovary [4]. Typically, within four to six weeks after radiation, serum E2 levels decline, whereas FSH levels progressively increase and menopausal symptoms become evident. Women with ovarian failure experience vasomotor hot flushes, urogenital dysfunction, and emotional disturbances, and risk of osteoporosis at long term. Since the publication of the Women Health Initiative (WHI) study [5], there has been a major shift to minimize the use of hormone replacement therapy (HRT) because of the associated increased risk of thromboembolic phenomena, cerebrovascular accidents, and breast cancer. Ovarian transposition outside the pelvic irradiation field has been shown to reduce the ovarian irradiation dose by 90% to 95% compared with the untransposed ovary [6].

Laparoscopic surgery has been one of the important innovations in modern-day surgery, allowing the patient to have a rapid recovery. The published laparoscopic experience with ovarian transposition has been limited to few small series [7-9]. The transposed ovary can induce complications such as torsion of ovarian pedicle, bleeding, and symptomatic ovarian cyst [10]. Although the risk of ovarian metastasis has been thought to be rare and negligible, ovarian metastasis on transposed ovary in patients treated for the cervix carcinoma has been reported [11-13].

A review of published studies indicated that the incidence of ovarian metastasis from uterine cervical cancer is less than 0.5% of squamous cell carcinoma and 1.4% of adenocarcinoma [13]. Shimada *et al.* [11] demonstrated that ovarian metastasis occurred more frequently among patients with adenocarcinoma than among those with squamous cell carcinoma (5.31% vs. 0.79%). Outcome for patients with ovarian metastasis was very poor and not related to FIGO Stage and histological type. Yamamoto *et al.* [12] analyzed the risk

factors of ovarian metastases in Stage IB–IIIB cervical carcinoma. Ovarian metastasis was identified in two of 485 (0.4%) patients with squamous cell carcinoma and in 12 of 146 (8.2%) patients with non-squamous tumors of the cervix; however histologic type and blood vessel invasion were significant independent risk factors for ovarian metastases, as revealed by multivariate logistic regression analysis.

The present authors aimed to evaluate the feasibility, the complication rates, and the functional outcome after laparoscopic ovarian transposition before pelvic irradiation in their patients younger than 45 years of age. Because ovarian metastasis occurred more frequently among patients with adenocarcinoma than among those with squamous cell carcinoma, the authors collected 27 women younger than 45 years with squamous cell carcinoma. They have found laparoscopic ovarian transposition to be a feasible procedure in their patient population with a short operative time and with minimal complications. Metal clips are easily identified to locate the ovaries. In this study, patient 3 and 14 developed an ovarian cyst. Therapy was not made in one of these patients that was asymptomatic. There was also no case of ovarian metastasis or recurrence in 26 patients who underwent ovarian transposition during follow-up.

The success of ovarian function preservation after transposition is variable in the literature. Successful preservation of ovarian function after ovarian transposition is dependent on two factors: the dose of radiation received by the ovary and the age of the patient [9, 14, 15]. Pahisa *et al.* [16] reported a 72.7% success rate in 11 patients after a mean follow-up of 44 months. Al-Badawi *et al.* [7] reported an ovarian preservation rate of 65% at a mean follow-up of 33 months. The reported age of ovarian transposition was usually less than 45 years, Han *et al.* [17] suggested that the rate of ovarian preservation is low after 40 years, Ovarian transposition should be performed only in patients less than 40 years of age. Hwang *et al.* [18] reported that the rate of normal ovarian function after lateral ovarian transposition after adjuvant radiation was 65.5% in < 40 years of age, and 35.5% in > 40 years of age.

In the present series, 69.2% of the patients maintained normal FSH levels at a mean follow-up period of 34.4 months; 80% of the five patients over 40 years of age experienced ovarian failure. Otherwise, the authors noted that four patients had normal ovarian function after irradiation in six unilateral ovarian transposition's patients. Therefore, unilateral ovarian transposition perhaps is an effective procedure and can cut down the risk of ovarian transposition. This finding was nearly identical by Clough *et al.* [14].

For patients with known metastases to the para-aortic lymph nodes or common iliac lymph nodes, para-aortic radiation is probably necessary [19]. In this study, the authors performed pelvic lymph node or para-aortic lymph node sampling in ten patients at the same time of laparoscopic

ovarian transposition. Two of the patients had confirmed metastases, therefore extended-field irradiation of para-aortic lymph nodes was necessary.

In conclusion, laparoscopic transposition of ovaries outside the irradiation field is a safe and effective procedure for the preservation of ovarian function. The result of the present study shows that ovarian metastasis in patients with cervical and vaginal squamous cell carcinoma is extremely rare. Therefore, radiotherapy without transposition of the ovaries for cervical squamous cell carcinoma is not recommended as a treatment for young patients, especially for those less than 40 years of age. Unilateral ovarian transposition perhaps is an alternative method. Para-aortic lymph node or common iliac lymph node sampling at the same time of laparoscopic ovarian transposition may preferably guide radiation therapy. More studies are needed to determine the long-term health and QOL benefits of ovarian preservation in young cancer patients.

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Address reprint requests to:

Y. CHEN, M.D.

Department of Gynecology Oncology,

Zhejiang Provincial Cancer Hospital,

38 Guangji Road, Hangzhou,

310022 (China)

e-mail: hfshou@126.com