Original article

Surgical Treatment Outcomes in Patients with Stage pT1a and pT1b1 Cervical Cancer

Satoru Takeuchi

Kochi Health Sciences Center, Kochi City, Kochi, Japan

Abstract

Objective : The object of this study was to assess the outcomes of surgical treatment of stage pT1a and pT1b1 cervical cancer.

Method : The medical records of 59 patients at our institution with pT1a and pT1b1 cervical cancer who underwent an operation as their primary treatment between January 1996 and September 2006 were analyzed retrospectively.

Results : Ten patients underwent an operation which was less aggressive than the current operative modality at our institution. Three patients had recurrence. No patients had recurrence resulting from insufficient operations. No patients had any histologic subtype of adnexal metastasis in the resected specimens. Two of the five patients with squamous cell carcinoma and lymph node metastases at the initial operation had recurrence. Only one patient had a histologic subtype of adenosquamous carcinoma. The patient with adenosquamous carcinoma had recurrence.

Conclusion : The results suggest that the surgical procedure did not affect prognosis in the cases we analyzed by surgical modalities. The current evidence suggests that a patient in an early stage can undergo less aggressive surgery than the current operative modality requires.

Key words : early invasive cervical cancer, operative modality, recurrence

Introduction

In nearly all cases of cervical cancer, human papillomavirus (HPV) infection is present¹⁻⁴⁾. About 30-40 types of HPV are typically transmitted through sexual contact and infect the anogenital region. A woman of sexually active age can develop the disease. Fertility-sparing operations such as conization and trachelectomy have been performed in many early stage invasive cases. Radical hysterectomy has good results in terms of survival, although it is accompanied by negative side effects including loss of fertility, bladder dysfunction, colorectal motility disorders, lymph edema and sexual dysfunction⁵⁻⁷⁾. Patients with stage I b2 and II b are not candidates for fertility-sparing operations. Patients with stage I a and I b1 cervical cancer have undergone operations and the prognosis has been good. Operative procedures have been changed to minimize both complications and recurrence.

Currently, it is unclear whether the procedure can be further minimized in patients with stage I a and I b1 cervical cancer. The final goal is to resect the affected organs with minimal aggression and to avoid recurrence. A possible relationship between recurrence and the surgical procedure should be explored. Doing so will suggest the optimal operational procedure for patients with stage I a and I b1 cervical cancer.

Correspondence to : Satoru Takeuchi
Kochi Health Sciences Center,
151-21 Sasaki-Cho, Kochi City, Kochi 780-0954, Japan
E-mail : satoru_takeuchi@khsc.or.jp

Patients and Methods

The database was analyzed for the period January 1996 to September 2006. Fifty-nine patients with pT1a and pT1b1 cervical cancer underwent primary treatment for cervical cancer at our institution (Table 1, Table 2, Table 3). Clinical stage was determined by the criteria for clinical and pathological management of uterine cervical cancer edited by the Japan Society of Obstetrics and Gynecology in 1997. Forty-two

patients had squamous cell carcinoma (SCC) and 17 patients were classified with adenocarcinoma or adenosquamous carcinoma. The median age of the patients was 47 years (range, 23-79 years). The median length of the follow-up period was 38 months. Three patients had recurrence, and two of these three patients died from the disease.

Results

Table 2 and Table 3 show the treatment

Table 1 Patients' Characteristics (n=59)

		Number of Patients
Histologic Subtype	Squamous cell carcinoma	42
	Adenocarcinoma	16
	Adenosquamous carcinoma	1
Stage	pT1a	30
	pT1b1	29
Operative Modality	Conization	8
	Simple hysterectomy	10
	Type II radical hysterectomy	15
	Type III radical hysterectomy	26
Adjuvant Therapy	Radiation or Chemoradiation	9
	Chemotherapy	6

Table 2 Squamous Cell Carcinoma (n=42)

	Conization	Simple H	Type II	Type II +PLD	Type III +PLD	Total
● Stage pT1a1 without LVSI or CI	7	8	7	0	3	25
● Stage pT1a1 with LVS or CI	0	0	0	0	0	0
●○ Stage pT1a2 without LVSI or CI	0	0	1	1	0	2
○ Depth of invasion ≤ 3 mm, width of invasion > 7 mm and < 10 mm and without LVSI or CI	0	0	0	0	0	0
●○ Stage pT1a2 with LVSI or CI	0	1	0	0	0	1
○ Stage pT1b1 (other than the above)	0	0	0	4 (1)	10 (1)	14 (2)
	7	9	8	5	13	42

Figures in bold italics : Number of patients who underwent the operation prescribed by the current operative modality

() : number of patients with recurrence

LVSI : lymph-vascular space involvement

CI : confluent involvement

Simple H : simple total hysterectomy±BSO (bilateral salpingo-oophorectomy)

Type II : type II radical hysterectomy±BSO

Type II+PLD : type II radical hysterectomy+pelvic lymph node dissection±BSO

Type III+PLD : type III radical hysterectomy+pelvic lymph node dissection±BSO

Table 3 Adenocarcinoma and Adenosquamous Carcinoma (n = 17)

Classified by the general rules for clinical and pathological management of uterine cervical cancer as edited by the Japan Society of Obstetrics and Gynecology in 1997.

	Conization	Simple H +BSO	Type II	Type II +BSO	Type II +PLD	Type II +PLD+BSO	Type III +PLD	Type III +PLD+BSO	Total
●Stage pT1a (budding)	1	0	0	1	0	0	0	0	2
●Depth of invasion ≤ 3 mm, width of invasion ≤ 7 mm and without LVSI	0	0	0	0	0	0	0	1	1
●Stage pT1b1 (except the above)	0	1	0	0	0	1	2	10 (1)	14 (1)
	1	1	0	1	0	1	2	11	17

Figures in bold italics : number of patients who underwent the operation prescribed by the current operative modality,

() : number of patients with recurrence

Simple H+BSO : simple total hysterectomy+bilateral salpingo-oophorectomy

Type II : type II radical hysterectomy

Type III+PLD : type III radical hysterectomy+pelvic lymph node dissection

Type III+PLD+BSO : type III radical hysterectomy+pelvic lymph node dissection+bilateral salpingo-oophorectomy±para-aortic lymph node dissection

Table 4 Patients with Recurrence

Patient	pT	T	Age	Histologic Subtype	Lymph N meta	LVSI	Operation Procedure	Adjuvant Therapy after Operation	Radiation Field	Region of Recurrence
1	1b1	1b1	31	SCC	+	–	type II+PLD	Chemoradiation	Pelvis	Para-aorta
2	1b1	2b	42	SCC	+	++	type III+BSO +PLD	Chemoradiation	Pelvis, Para-aorta	Left pelvis
3	1b1	1b1	56	ASC	–	–	type III+BSO +PLD	Radiation	Pelvis	Left kidney

Lymph N meta : lymph node metastasis

SCC : squamous cell carcinoma

ASC : adenosquamous carcinoma

Type II : type II radical hysterectomy

Type III : type III radical hysterectomy

BSO : bilateral salpingo-oophorectomy

PLD : pelvic lymph node dissection

modality according to stage and other factors. Ten patients underwent operations which were less aggressive than the current operative modality. As shown in Table 4, three patients had recurrence. Of these three patients, two patients had a histologic subtype of SCC and were in stage pT1b1. One underwent a type II radical hysterectomy (type II radical H), and the other underwent a type III radical hysterectomy (type III radical H). One patient with a histologic subtype of adenosquamous carcinoma in stage pT1b1 underwent a type III radical H. Fourteen of the

seventeen patients with adenocarcinoma or adenosquamous carcinoma and twenty of the forty-two patients with SCC underwent adnexectomy. No patients had any histologic subtype of adnexal metastasis in the resected specimens. Two of the five patients with SCC and lymph node metastasis at the initial operation had recurrence. All three patients with recurrence underwent post-operative adjuvant radiation therapy as the initial treatment. One patient had recurrence in an intra-pelvic radiation treatment field. The other two patients had recurrence out of the radiation treatment field.

Only one of the fifty-nine patients had a histologic subtype of adenosquamous carcinoma. The patient with adenosquamous carcinoma had recurrence.

Discussion

If recurrence is rare, it is evident that a less aggressive surgery is preferable in respect to the patient's quality of life. The prognosis for patients with early lesions of cervical malignant tumors is generally favorable^{8,9}. In 1995, the International Federation of Gynecology and Obstetrics (FIGO) defined stage I A cancers, further dividing the stage into I A1 and I A2¹⁰. These substages were created to allow doctors to better select the appropriate procedures and treatment. The criteria for clinical and pathological management of uterine cervical cancer edited by the Japan Society of Obstetrics and Gynecology in 1997 did not divide stage I A adenocarcinoma into substages because of the diagnostic difficulty. The criteria indicates that a type I hysterectomy and conization would be acceptable if stromal invasion was up to 3 mm and no lymph vascular space involvement (LVSI) was present¹¹⁻¹⁵. For depth of invasion of ≤ 3 mm, LVSI has been reported in 4.5-29% of patients, but increasing to 11.1-46.7% for depth of invasion of 3.1-5.0 mm¹⁶. The incidence of positive nodes in patients with stage I A1 disease has been reported to be 0.5-0.8%^{17,18}. The overall incidence of lymph node metastases in patients with depth of invasion of 3-5 mm has been reported as 7.1%, although this varies from 0% to 13.8%^{15,19-23}. Patients with 3-5 mm of invasion present at conization and with no invasion in the hysterectomy specimen are at very low risk for lymph node metastases, recurrence, or death that is caused by the cancer¹⁵. Six hundred fifty-five patients with 0-5 mm of invasion were treated with conization only, and only 12 (1.8%) cases of recurrence and 1 (0.1%) death were reported¹⁵.

In our institution, the current operative modality is conization or simple total hysterectomy (simple H) in stage I a1 without LVSI and confluent involvement (CI), and simple

H in stage I a1 with LVSI or CI. The current operative modality is type II radical H and pelvic lymph node dissection (PLD) in stage I a2 without LVSI and CI, or in stage I b1 with depth of invasion ≤ 3 mm, width of invasion > 7 mm and < 10 mm, and without LVSI and CI. The modality is type III radical H and PLD in stage I a2 with LVSI or CI, or in stage I b1 with exception of the above mentioned. Bilateral salpingo-oophorectomy (BSO) is required in stage I b1 patients with adenocarcinoma or adenosquamous carcinoma²⁴⁻²⁷.

Ten patients underwent an operation which was less aggressive than the current operative modality (Table 2, Table 3). One patient with SCC in stage pT1a2 without LVSI and CI underwent a type II radical H without PLD. One patient with SCC in stage pT1a2 with LVSI underwent a simple H without PLD. Four patients with SCC in stage pT1 b1 underwent a type II radical H with PLD. One patient with adenocarcinoma in stage pT1b1 underwent a simple H with BSO and without PLD. One patient with adenocarcinoma in stage pT1b1 underwent a type II radical H with BSO and PLD. Two patients with adenocarcinoma in stage pT1b1 underwent a type III radical H and PLD without BSO. Recurrence was not the result of insufficient operations (Table 4). There was no adnexal metastasis in any patient with adenocarcinoma or adenosquamous carcinoma who underwent BSO. It would seem reasonable to retain normal-appearing ovaries in young women undergoing type III radical H for treatment of cervical adenocarcinoma and adenosquamous carcinoma, providing that no other cervical spread is present if the patients understand the small risk of undetected ovarian spread²⁶. Table 4 shows that the selected operative procedures for the three patients with recurrence were adequate in respect to the region of recurrence. The patient with stage pT1b1 underwent a type II radical H and recurrence occurred in the para-aortic region. It would have been impossible to prevent recurrence by performing a type III radical H without para-aortic lymph node dissection.

Conclusion

Based on the current evidence, these results suggest that a patient in an early stage can undergo less aggressive surgery than the current operative modality requires. As the number of the patients was few, the status necessary to minimize radicality of the operation cannot be proposed. In the future, in order to avoid unnecessary aggression, operative modality will be determined not only with stage but also with other risk factors such as gene abnormalities.

Reference

1. Laikangball P, Sengupta S, Bhattacharya P, *et al.* A comparative profile of the prevalence and age distribution of human papillomavirus type 16/18 infections among three states of India with focus on northeast India. *Int J Gynecol Cancer* 2007 ; 17 : 107–117.
2. Bosch FX, Manos MM, Munoz N, *et al.* Prevalence of human papillomavirus in cervical cancer : a worldwide perspective. *J Natl Cancer Inst* 1995 ; 87 : 798–802.
3. Walboomers JMM, Jacobs MV, Manos MM, *et al.* Human papillomavirus is a necessary cause of invasive cancer worldwide. *J Pathol* 1999 ; 189 : 12–19.
4. Munoz N. Human papillomavirus and cancer : the epidemiological evidence. *J Clin Virol* 2000 ; 19 : 1–5.
5. Samlal PAK, Ketting BWI, Velden J. Disease-free interval and recurrence pattern after the Okabayashi variant of Wertheim's radical hysterectomy for stage I B and II A cervical carcinoma. *Int J Gynecol Cancer* 1996 ; 6 : 120–127.
6. Bergmark K, Avall-Lundqvist E, Dickman PW, *et al.* Vaginal changes and sexuality in women with a history of cervical cancer. *N Engl J Med* 1999 ; 340 : 1383–1389.
7. Schultz WCMW, Bouma J, Van de Weil HBM. Psychosexual functioning after treatment for cancer of the cervix : a comparative and longitudinal study. *Int J Gynecol Cancer* 1991 ; 1 : 37–46.
8. Andras EJ, Fletcher GH, Rutledge F. Radiotherapy of carcinoma of the cervix following simple hysterectomy. *Am J Obstet Gynecol* 1973 ; 115 : 645–655.
9. Orr JW Jr, Ball GC, Soong SJ, *et al.* Surgical treatment of women found to have invasive cervix cancer at the time of total hysterectomy. *Obstet Gynecol* 1986 ; 68 : 353–356.
10. Creasman WT. New gynecologic cancer staging. *Gynecol Oncol* 1995 ; 58 : 157–158.
11. Ostor AG, Rome RM. Micro-invasive squamous cell carcinoma of the cervix : a clinico-pathologic study of 200 cases with long-term follow-up. *Int J Gynecol Cancer* 1994 ; 4 : 257–264.
12. Morris M, Mitchell MF, Silva EG, *et al.* Cervical conization as definitive therapy for early invasive squamous carcinoma of the cervix. *Gynecol Oncol* 1993 ; 51 : 193–196.
13. Keighley E. Carcinoma of the cervix among prostitutes in a women's prison. *Br J Vener Dis* 1968 ; 44 : 254–255.
14. Kolstad P. Follow-up study of 232 patients with stage I a1 and 411 patients with stage I a 2 squamous cell carcinoma of the cervix (microinvasive carcinoma), *Gynecol Oncol* 1989 ; 33 : 265–272.
15. Creasman WT, Zaino RJ, Major FJ, *et al.* Early invasive carcinoma of the cervix (3 to 5 mm invasion) : Risk factors and prognosis. A Gynecologic Oncology Group study. *Am J Obstet Gynecol* 1998 ; 178 : 62–65.
16. Sevin BU, Nadji M, Averette HE, *et al.* Microinvasive carcinoma of the cervix. *Cancer* 1992 ; 70 : 2121–2128.
17. Elliott P, Copplson M, Russell P, *et al.* Early invasive (FIGO stage I A) carcinoma of the cervix : a clinico-pathologic study of 476 cases. *Int J Gynecol Cancer* 2000 ; 10 : 42–52.
18. Oster AG. Pandora's box or Ariadne's thread? Definition and prognostic significance of microinvasion in the uterine cervix. *Squamous*

- lesions. *Pathol Annu* 1995 ; 30 : 103–136.
19. van Nagell JR Jr, Greenwell N, Powel DF, *et al.* Microinvasive carcinoma of the cervix. *Am J Obstet Gynecol* 1983 ; 145 : 981–991.
 20. Hasumi K, Sakamoto A, Sugano H. Microinvasive carcinoma of the uterine cervix. *Cancer* 1980 ; 45 : 928–931.
 21. Maiman MA, Fruchter RG, DiMaio TM, *et al.* Superficially invasive squamous cell carcinoma of the cervix. *Obstet Gynecol* 1988 ; 72 : 399–403.
 22. Buckley SL, Tritz DM, Van Le L, *et al.* Lymph node metastases and prognosis in patients with stage I A2 cervical cancer. *Gynecol Oncol* 1996 ; 63 : 4–9.
 23. Takeshima N, Yanoh K, Tabata T, *et al.* Assessment of the revised International Federation of Gynecology and Obstetrics staging for early invasive squamous cervical cancer. *Gynecol Oncol* 1999 ; 74 : 165–169.
 24. Tabata M, Ichinoe K, Sakuragi N, *et al.* Incidence of ovarian metastasis in patients with cancer of the uterine cervix. *Gynecol Oncol* 1987 ; 28 : 255–261.
 25. Toki N, Tsukamoto N, Kaku T, *et al.* Microscopic ovarian metastasis of the uterine cervical cancer. *Gynecol Oncol* 1991 ; 41 : 46–51.
 26. Sutton GP, Bundy BN, Delgado G, *et al.* Ovarian metastases in stage I B carcinoma of the cervix : a gynecologic oncology group study. *Am J Obstet Gynecol* 1992 ; 166 : 50–53.
 27. Shimada M, Kigawa J, Nishimura R, *et al.* Ovarian metastasis in carcinoma of the uterine cervix. *Gynecol Oncol* 2006 ; 101 : 234–237.