RESEARCH ARTICLE

High Dose Rate Cobalt-60 After Loading Intracavitary Therapy of the Uterine Cervical Carcinoma in Srinagarind Hospital, Analysis of Residual Disease

Montien Pesee*, Srichai Krusun, Prawat Padoongcharoen

Abstract

Objectives: To evaluate residual disease in uterine cervical cancer patients treated with teletherapy using combined high dose rate Cobalt-60 brachytherapy. Materials and Methods: A retrospective study of uterine cervical cancer patients, FIGO stages IB-IVB (International Federation of Gynecologists and Obstetricians recommendations), treated by radiotherapy alone between April 1986 and December 1988 was conducted and the outcomes analysed. The patients were treated using teletherapy 50 Gy/25 fractions, five fractions per week to the whole pelvis together with HDR Cobalt -60 afterloading brachytherapy of 850 cGy/fraction, weekly to point A for 2 fractions. Results: The study covered 141 patients with uterine cervical cancer. The mean age was 50.0 years with a range of 30-78 years. The mean tumor size was 4.1 cm in diameter (range 1-8 cm). Mean follow - up time was 2.94 years (range 1 month-6.92 years). The overall incidence of residual locoregional disease was 3.5%. Residual disease, according to stage IIB, IIIB and IVA was present in 2.78%, 3.37% and 50.0%. It was noted that there was no evidence of residual disease in stage IB and IIA cases. Conclusion: Combined teletherapy along with high dose rate Cobalt -60 brachytherapy of 850 cGy/fraction, weekly to point A for 2 fractions resulted in overall 3.5% residual disease and a 96.5% complete response. The proposed recommendation for improving outcome is initiation of measurements for early detection of disease.

Keywords: Uterine cervical carcinoma - teletherapy - high dose rate Cobalt -60 brachytherapy - residual diseases

Asian Pacific J Cancer Prev, **13 (9)**, 4835-4837

Introduction

Carcinoma of the uterine cervix has been recognized to be the major problem of malignant diseases in developing countries particularly in Thai women (Sriamporn et al., 2004). The large tumor volumes in addition to the advanced staging of cases resulted in radioresistant tumors, which were contributing factors limiting the effectiveness of radiation therapy. In addition, the time gap between teletherapy and brachytherapy in most patients was reported to be more than 2 weeks due to limitation of hospital facilities (Pesee et al., 1995). The combination of these circumstances was an important factor influencing the selection of high dose rate Cobalt - 60 brachytherapy fractionation. Definitive radiotherapy alone is the standard treatment in uterine cervical cancer (Bermudez et al., 2010). There is no consensus on the best technique of brachytherapy (Visser et al., 2001; Symonds, 2003). Perez CA, et al report evidence of less than 10% pelvic failure for cervical cancer at stage IB and IIA with tumor sizes less than 2 cm in diameter and pelvic failure rates of 30-50% have been reported in extensive cervical cancer (Perez et al.,1998).

This retrospective study was therefore conducted on admissions between April 1986 and December 1988, to determine the extent of residual tumor of uterine cervical carcinoma after treatment using combined teletherapy 50Gy/25 fractions together with high dose rate Cobalt-60 brachytherapy of 850 cGy/fraction to point A weekly for 2 fractions, now designated as current combined treatment (CCT).

Objectives

The purpose of this retrospective study was to evaluate the extent of residual disease in uterine cervical cancer patients treated by using CCT.

Materials and Methods

This study was performed in the Radiotherapy Division, Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002.

Inclusion criteria were: (1) uterine cervical cancer FIGO stages IB-IVB treated with radiotherapy alone between April 1986 and December 1988 (2) treatment using CCT (3) completion of the treatment regimen (4) minimum

*Division of Radiotherapy, Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand *For correspondence: pmonti@kku.ac.th*

follow-up time 1 month. Exclusion criteria were: (1) uterine cervical carcinoma treated by another fractionation schedule. (2) failure to complete the treatment regimen. The staging of the original tumor disease was classified by the tumor clinic committee of gynecologists and radiation oncologists according to International Federation of Gynecologists and Obstetricians (FIGO) recommendations (International Federation of Gynecologists and Obstetricians, 1995).This project was approved by the Human Ethics Committee of Khon Kaen University (HE470104).

The residual disease was defined as the presence of persistent tumors that were noted 4-6 weeks after completion of treatment. Responses to treatment were assessed at 4-6 weeks after completion of treatment. In order to define a complete positive response, there could not be any residual tumor plus a negative papanicolaou smear and/or a negative biopsy in some suspicious cases. All patients were treated with Cobalt-60 teletherapy units. The prescribed dose of teletherapy was 50Gy/25 fractions, five fractions per week to the whole pelvis through AP and PA 15x15 cm^2 or 16x16 cm^2 port.The ports were extended to 15x18 cm^2 for the stage IIIA patients. In addition, the parametrial boosts of 200 cGy for 3-5 days after the completion of brachytherapy were provided to stage IIIB patients with massive tumor at the parametrium. Brachytherapy was performed by using high dose rate Cobalt-60 brachytherapy (RALSTRON -20B) about 2-4 weeks after completion of teletherapy with doses of 850cGy/fraction to point A for 2 fractions, once weekly fractionation. The point A doses were approximately 75.50 Gy for early stages, and approximately 81.50-85.50 Gy for advanced stages.

Table 1. Patient Characteristics

		Number of case (%)	
Gender (Female) (Total=141)			
Age groups (range):	30-39 years	24	(17)
	40-49 years	44	(31.2)
	50-59 years	48	(34)
	60-69 years	19	(13.5)
	70-79 years	6	(4.3)
Mean age (range)	30-78 years	49.98	
Stage of disease:	Stage IB	4	(2.8)
	Stage IIA	6	(4.3)
	Stage IIB	36	(25.5)
	Stage IIIA	2	(1.4)
	Stage IIIB	89	(63.1)
	Stage IVA	2	(1.4)
	Stage IVB	2	(1.4)
Mean tumor size (range) in cms.		4.1 (1-8)	
Gross appearance:	Exophytic	99	(70.2)
	Ulcerative	21	(14.9)
	Infiltrative	14	(9.9)
	others	7	(5.0)
Follow up time:	Mean (range)		
	(1 month-6.92 years)	2.94	
Pathology:	Squamous cell carcinomas	131	(92.9)
	Adenocarcinomas	9	(6.4)
	Adenosquamous cell carcinoma	1	(0.7)

Table 2. Outcome of Treatment

Pelvic control	Positive outcome:	Cases	(%)
Complete response (CR)		136/141	(96.5)
Residual diseases at cervix		4/141	(2.8)
Residual disease at cervix + parametrium		1/141	(0.7)

Table 3. Stage and Outcome

Stage of diseases	Complete response		Residual diseases	
	cases	(%)	cases	(%)
Stage IB	4/4	(100.00)	0/4	(0)
Stage IIA	6/6	(100.00)	0/6	(0)
Stage IIB	35/36	(97.22)	1/36	(2.78)
Stage IIIA	2/2	(100.00)	0/2	(0)
Stage IIIB	86/89	(96.63)	3/89	(3.37)
Stage IVA	1/2	(50.00)	1/2	(50.00)
Stage IVB	2/2	(100.00)	0/2	(0)

Results

Patient characteristics are summarized in Table 1 and the details of residual diseases in Tables 2-3. There were 3.5% of locoregional residual diseases. The residual diseases in stage IIB, IIIB and IVA were 2.78%, 3.37% and 50% , however, no evidence of residual diseases was found in stage IB and IIA .

Discussion

The control of tumors in the pelvis is crucial to the survival of the patients in all stages. Regarding intensity-modulated radiation therapy (IMRT), there was 14% of pelvic failure (Hasselle et al., 2011), however, the local control and overall survival were generally inconclusive (Veldeman et al., 2008). Recently, the report of pelvic failure of 3D-conformal radiotherapy using accelerated hyperfractionation without intracavitary brachytherapy was 14.3% (Matsuura et al., 2007). The pelvic tumor control of stages III-IVA cervical cancer patients treated with concurrent chemoradiation versus radiotherapy alone was 62% versus 59% (Perez, 1997). In reference to the radiotherapy and hyperthermia modality, the complete response rate for advanced cervix cancer was 77% (Franckena et al., 2009). Additionally, treatment failure in stage IIIB cervical cancer from the study of Mabuchi et al was between 35-66.7% (Mabuchi et al., 2010).

CCT resulted in 96.5% of complete response and overall 3.5% incidence of residual diseases. The incidences of residual diseases according to stages IIB, IIIB and IVA were 2.78%, 3.37% and 50%. It was noted that there was no evidence of residual diseases in stage IB and IIA. Although CCT demonstrated a high complete response rate and low residual diseases but it also showed a higher incidence of radiation morbidities (Pesee et al., 2010). Both radiation morbidities and high complete response might be influenced by HDR fractionation brachytherapy. The 5 year survival rate of stage IIIB in CCT revealed approximately 54.8% (Pesee et al., 2010).

In conclusion, CCT resulted in an incidence of 3.5% residual diseases and 96.5% of complete response. The residual diseases of stage IIB, IIIB and IVA were 2.78%,

3.37% and 50%. It was noted that there was no evidence of treatment failure in stage IB and IIA. These data allow for a proposal to improve outcome primarily through early detection. Routine checking by a cervical screening program should be encouraged in asymptomatic women in order to detect the early cases before tumor progression.

Acknowledgements

We would like to express our deep appreciation to Prof. Kawee Tungsubutra, The founder Dean, Faculty of Medicine Khon Kaen University. Appreciation acknowledgement for Assoc.Prof. Vorachai Tungvorapongchai, Ass. Prof. Varodom Boonvisuth, and Ass.Prof. Dr. Wichit Kirdpon for noble advise. The authors thank Emeritus Professor Dr. James A. Will, Department of Pathobiology, School of Veterinary Medicine and Animal Science, College of Agriculture and Life Sciences, University of Wisconsin, Madison, Wisconsin, for his valuable comments and critical reviews of the manuscript.

References

Bermudez RS, Huang K, Hsu IC (2010). Cervical cancer. In: handbook of evidence- based radiation oncology, second edition. Hansen EK, Roach III M, eds. New York: *Spinger*, 499-512.

Franckena M, Lutgens LC, Koper PC, et al (2009). Radiotherapy and hyperthermia for treatment of primary locally advanced cervix cancer: results in 378 patients. *Int J Radiation Oncology Biol Phys,* **73**, 242-50.

Hassele MD, Rose BS, Kochanski JD, et al (2011). Clinical outcomes of intensity-modulated pelvic radiation therapy for carcinoma of the cervix. *Int J Radiation Oncology Biol Phys,* **80**, 1436-45.

International Federation of Gynecologists and Obstetricians (1995). Staging announcement: FIGO staging of gynecologic cancers: cervical and vulva. *Int J Gynecol Cancer,* **5**, 319.

Mabuchi S, Ugaki H, Isohashi F, et al (2010). Concurrent Nedaplatin, external beam radiotherapy and high-dose-rate brachytherapy in patients with FIGO stage IIIB cervical cancer: A comparison with a cohort treated by radiotherapy alone. *Gynecol Obstet Invest*, **69**, 224-32.

Matsuura K, Tanimoto H, Fujita K, et al (2007). Early clinical outcomes of 3D- conformal radiotherapy using accelerated hyperfractionation without intracavitary brachytherapy for cervical cancer. *Gynecologic Oncology*, **104**, 11-4.

Perez CA (1997). Uterine cervix. In: Textbook of principles and practice of radiation oncology, third edition. Perez CA, Brady LW, eds.New York, *Lippincott-Raven Pub*, 1806-8.

Perez CA, Grigsby PW, Chao KS, et al (1998). Tumor size, irradiation dose, and long-term outcome of carcinoma of the uterine cervix. *Int J Radiat Oncol Biol Phys*, **41**, 307-17.

Pesee M,Tangvoraphonkchai V, Reamsiri T, et al (1995).Low dose rate brachytherapy Caesium -137 afterloading in the treatment of carcinoma of uterine cervix in Srinagarind hospital:Analysis of a actuarial survival rate. *Thai J Radiol*, **1**, 125-30.

Pesee M, Krusun S, Padoongcharoen P (2010). High dose rate Cobalt-60 afterloading intracavitary therapy of the uterine cervical carcinoma in Srinagarind hospital, analysis of complications. *Asian Pac J Cancer Prev*, **11**, 491-4.

Pesee M, Krusun S, Padoongcharoen P (2010). High dose rate Cobalt-60 afterloading intracavitary therapy of the uterine cervical carcinoma in Srinagarind hospital, Analysis of survival. *Asian Pac J Cancer Prev*, **11**, 1469-71.

Sundfor K, Trope CG, Hogberg T, et al (1996). Radiotherapy and neoadjuvant chemotherapy for cervical cancer. A randomized multicenter study of sequential cisplatin and 5-fluorouracil and radiotherapy in advanced cervical carcinoma stage IIIB and IVA. *Cancer*, **77**, 2371-8.

Sriamporn S, Swaminathan R, Parkin DM, et al (2004). Loss-adjusted surivival of cervix cancer in Khon Kaen, Northeast Thailand. *Bri J Cancer*, **91**, 106-10.

Symonds RP (2003). Cancer of the cervix and vagina. In: Text book of evidence- based oncology.Williams C, ed. London: *BMJ*, 402-9.

Visser AG, Symonds RP (2001). Dose and volume specification for reporting gynaecological brachytherapy: time for a change. *Radiother Oncol*, **58**, 1-4.

Veldeman L,Madani I, Hulstaert F, et al (2008). Evidence behind use of intensity-modulated radiotherapy: a systematic review of comparative clinical studies. *Lancet Oncol*, **9**, 367-75.