RESEARCH COMMUNICATION

High Dose Rate Cobalt-60 Afterloading Intracavitary Therapy for Cervical Carcinoma in Srinagarind Hospital - Analysis of Survival

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Abstract

Objective: To evaluate the actuarial survival rates in uterine cervical cancer patients treated with teletherapy combined with high dose rate (HDR) cobalt-60 brachytherapy. Materials and Methods: A retrospective study of uterine cervical cancer patients, stages IB-IVB (International Federation of Gynecologists and Obstetricians recommendations or FIGO), treated by radiotherapy alone between April 1986 and December 1988 was conducted. The patients were treated with teletherapy 50Gy/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 analysed the records of 141 patients with uterine cervical cancer with a mean age of 50.0 years (range 30-78). The mean tumor size was 4.1 cm in diameter (range 1-8). Mean follow-up time was 2.94 years (range 1 month - 6.92 years). The 5 year actuarial survival rates for patients with small size tumors less than 2 cm in diameter and tumor sizes larger than 2 cm in diameter were 100% and 63.2%. The overall 5 year survival rate was 63.3%. For cancer stages IB, IIB, IIIA and IIIB they were 100%, 80.3%, 100% and 54.8% and for squamous cell carcinoma and adenocarcinoma were 58.3% and 31.2%. Conclusion: Combined HDR cobalt-60 brachytherapy and external beam radiotherapy provide a useful modality in the treatment of uterine cervical cancer, feasible for developing countries. The approach demonstrated a slightly elevated radiation morbidity but was most effective in early stages and with small tumor sizes less than 2 cm in diameter.

Keywords: Cervical carcinoma - radiotherapy - high dose rate cobalt-60 brachytherapy - actuarial survival rates

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Introduction

Carcinoma of the uterine cervix has been recognized to be the major problem in developing countries particularly in Thai women (Vatanasapt et al., 1993; 1995; Sriplung et al., 2003). Most of the patients were found to be in advanced stages burdened with large tumor volumes at their first visit (Tungsubutra et al ., 1985; Tangvoraphongchai et al., 1989; Pesee et al., 1995).

The large tumor volumes in addition to the advanced staging of cases resulted in the radioresistant tumors. These 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 and was due to limitation of hospital facilities (Tungsubutra et al., 1985; Tangvoraphongchai et al., 1989; Pesee et al., 1995). These problems were the factors influencing the selection of high dose rate Cobalt-60 brachytherapy fractionation. Definitive radiotherapy alone is the standard treatment in uterine cervical cancer (Symonds 2003). There is no consensus on the best technique of brachytherapy (Visser et al., 2001; Symonds, 2003). Concomitant chemotherapy and radiotherapy improves overall and progression-free survival, reduces local and distant recurrence in selected patients (Green et al., 2001). Acute toxicity, particularly leucopenia and gastrointestinal effects, however, were increased in combined therapy of all trials (Symonds, 2003).

Therefore the retrospective study was conducted to determine whether the actuarial survival rates of uterine cervical carcinoma treatment using combined teletherapy 50Gy/25 fractions together with a high dose rate Cobalt - 60 brachytherapy of 850 cGy/ fraction to point A weekly for 2 fractions improved actuarial survival rates. This is now designated as the current combined treatment (CCT) that occurred between April 1986 and December 1988.

The purpose of this retrospective study was to evaluate the actuarial survival rates in uterine cervical cancer patients treated by using CCT.

Materials and Methods

This study was performed at 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

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1986 and December 1988 (2) using HDR Cobalt -60 afterloading brachytherapy of 850 cGy/ fraction to point A for 2 fractions, once weekly fractionation (3) complete treatment. Exclusion criteria were: (1) uterine cervical carcinoma treated by other fractionation schedules; (2) incomplete treatment.

The staging of the diseases was classified by the tumor clinical committee of gynecologists and radiation oncologists according to International Federation of Gynecologists and Obstetricians (FIGO) recommendations published in 1995. This project has been approved by the Human Ethics Committee of Khon Kaen University (HE470104). The results were analyzed in the aspect of the actuarial survival rates by using Life Table Method.

Table1. Patient Characteristics

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

Table 2 . Tumor Size and 5 Year Actuarial Survival Rates (%)

Tumor diameter	5 year actuarial survival rates
Tumor size less than 2 cm	100
Tumor size more than 2 cm	63.2

Table 3. Stage and Actuarial 1, 3, 5 Year Survival Rates

Stages	1 year (%)	3 year (%)	5 year (%)
All	93.8	76.6	63.3
Stage IB	100	100	100
Stage IIA	81.8	81.8	-
Stage IIB	97.1	90.4	80.3
Stage IIIA	100	100	100
Stage IIIB	93.8	70.4	54.8
Stage IV	33.3	-	-

Table 4. Pathology and Actuarial 1, 3, 5 Year Survival Rates (%)

Pathology	1 year	3 year	5 year
Squamous cell carcinomas	75.2	65.4	58.3
Adenocarcinomas	88.9	31.2	31.2

Radiotherapy

All patients were treated with Cobalt-60 teletherapy units.The prescribed dose of teletherapy was 50 Gy/ 25 fractions, five fractions per week to the whole pelvis through AP and PA 15x15 cm^2 or 16x16 cm^2 ports.The ports were extended to 15 cm x18 cm for the patients with stage IIIA. In addition, parametrial boosts of 200 cGy for 3 -5 fractions were used to treat stage IIIB patients with massive tumors at the parametrium. Brachytherapy was performed by using high dose rate Cobalt -60 brachytherapy (RALSTRON 20-B) about 2-4 weeks after completion of teletherapy with doses of 850cGy/ fraction to point A for 2 fractions, once weekly. The point A doses were approximately 75.50 Gy for early stages, and approximately 81.50-85.50 Gy for advanced stages.

Results

Patient characteristics are summarized in Table 1 and the details of actuarial survival rates are given in Tables 2-4.

Discussion

The factors influencing overall survival are tumor size, staging, hemoglobin level, time interval between external- intracavitary radiation and fractionations (Pesee et al., 1989; Pomros et al., 2007). In reference to the low dose rate (LDR) Caesium-137 brachytherapy, the 5 year actuarial survival rates for small size tumors less than 2 cm in diameter versus tumor sizes larger than 2 cm in diameter were 74% versus 56% (Pesee et al.,1995). The 5 year actuarial survival rates of LDR Caesium-137 brachytherapy for squamous cell carcinoma and adenocarcinoma were 51 % and 58 %(Pesee et al., 1995). The CCT 5 year actuarial survival rates for small size tumors less than 2 cm in diameter versus tumor sizes larger than 2 cm in diameter were 100% versus 63.2 % (Table 2). The overall 5 year survival rate was 63.3% (Table 3). According to staging, the actuarial 5 year survival rates of uterine cervical cancer stages IB, IIB, IIIA, and IIIB were 100%, 80.3%, 100% and 54.8% (Table 3). The overall 5 year survival rates of stage IIIB cervical cancer patients using CCT resulted in a 54.80 % survival rates as compared to 33-52.2 % of historic controls (Piver et at., 1977, Patel et al .,1994, Selke et al .,1993, Pesee et al ,1995., Lorvidhaya et al., 2000 , Arai et al, 1992). The 5 year actuarial survival rates of squamous cell carcinomas and adenocarcinomas were 58.3% and 31.2%(Table 4). This modality demonstrated a slightly higher incidence of radiation morbidities (Pesee et al., 2010).

In conclusion, combined HDR Cobalt-60 brachytherapy and external beam radiotherapy was a useful modality in the treatment of uterine cervical cancer. It was a simple technique and feasible for developing countries. It was effective in early stage and small tumor sizes less than 2

cm in diameter. This modality demonstrated a slightly higher incidence of radiation morbidities.

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References

Arai T, NakanoT, Morita S, et al (1992). High dose rate remote afterloading intracavitary radiation therapy for cancer of the uterine cervix. A 20-year experience. *Cancer*, **69**, 175-80.

Green JA, Kirwan JM, Tierney JF, et al (2001). Systematic review and meta-analysis of randomised trials of concomitant chemotherapy and radiotherapy for cancer of the uterine cervix:better survival and reduced distant recurrence rate. *Lancet*, **358**, 781-6.

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

Lorvidhaya V, Tonusin A, Changwiwit W, et al (2000). High dose rate afterloading brachytherapy in carcinomas of the cervix: an experience of 1992 patients. *Int J Radiat Oncol Biol Phys*, **46**, 118-91.

Perez CA, Kuske RR, Camel HM, et al (1988). Analysis of pelvic tumor control and impact on survival in carcinoma of the uterine cervix treated with radiation therapy alone. *Int J Radiat Oncol Bio Phys*, **14**, 613-21.

Pesee M, Tangvoraphonkchai V, Boonvisuth V, et al (1989). Radiotherapy alone in the treatment of carcinoma of the uterine cervix in Srinagarind hospital: analysis of treatment failure. *Thai J Radiol*, **26**, 67-70.

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.

Pomros P, Sriamporn S, Tangvoraphonkchai V, et al (2007). Factors affecting survival of cervical cancer patients treated at the radiation unit of Srinagarind hospital, Khon Kaen university, Thailand. *Asian Pac J Cancer Prev*, **8**, 297-300.

Piver MS, Barlow JJ, Vongtama V, et al (1977). Hydroxyurea: a radiation potentiator in carcinoma of the uterine cervix. A randomized double-blind study. *Am J Obstet Gynecol*, **147**, 803-8.

Patel FD, Sharme SC, Negi PS, et al (1994). Low dose rate vs. high dose rate brachytherapy in the treatment of carcinoma of the uterine cervix: a clinical trial. *Int J Radiat Oncol Biol Phys*, **28**, 335-41.

Selke P, Roman TN , Souhami L, et al (1993). Treatment results of high dose rate brachytherapy in patients with carcinoma of the cervix. *Int J Radiat Oncol Biol Phys*, **27**, 803-9.

Symonds RP(2003). Cancer of the cervix and vagina.In:Text book of Evidence- based Oncology. Williams C, ed. London: BMJ publishing Books, 402-9.

Sriplung H, Sontipong S, Martin N, et al (2003). Cancer incidence in Thailand.1995-1997. Bangkok, Bangkok Medical Publisher, 13.

Tungsubutra K, Pesi M, Tangvoraphonkchai V (1985). Problems in treatment of cancer in the rural areas and the remedies. In Mould RF, Tungsubutra K, eds. Diagnosis and treatment of carcinoma of the cervix in developing areas. Bristol and Boston: Adam Hilger, 219-22.

Tungsubutra K, Tangvoraphonkchai V, Pesi M (1985). Cancer epidemiology in Thailand. Mould RF, Tungsubutra K, eds. Diagnosis and treatment of carcinoma of the cervix in developing areas. Bristol and Boston: Adam Hilger ,187-90

Tangvoraphonkchai V, Pesee M, Boonvisuth V, et al (1989). Tumor registry: an overview of problems shooting in radiotherapy. *Thai J Radiol*, **26**, 95-8.

Vatanasapt V, Martin N, Sriplung H, et al (1993). Cancer in Thailand. 1988-1991. Khon Kaen: Siriphan Press, 68-9.

Vatanasapt V, Martin N, Sriplung H, et al (1995). Cancer incidence in Thailand. 1988-1991. *Cancer Epidemiol, Biomarkers & Prevention*, **4**, 475-83.

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