

Clinical Manifestations and Treatment Results of Patients with Cervical Cancer: A Report from Iran

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Abstract

Introduction: Cervical cancer is one of the major causes of cancer and death among women aged 40 to 60 in developing countries. There is some difference, however, in the incidence of this cancer in Iranian women compared to women living in western and south-east Asian countries. We aimed at investigating the epidemiologic aspects and treatment results of cervical cancer among Iranian patients.

Methods: Medical records of patients with cervical cancer who were referred to Mortazavi Radiation Oncology Center (Imam Hossein Hospital) between 2000 and 2004 were evaluated retrospectively. Clinical data such as stage of the disease, type of chemotherapy, radiation technique and sequence of treatment was recorded.

Results: A total of 220 patients with a median age of 55 years (range: 28 to 89) were studied. The majority of them (37.3%) were referred with stage IIB of the disease. Other stages, in order of frequency, were IIA, IIIA and IB. Most of the patients (74%) were treated with two opposed field radiotherapy with a dose of 50 Gy or less (64%). Disease recurred in 46 patients (21%), 153 patients (74%) received two opposed field radiotherapy and 54 (36%) patients were treated with four fields. On the other hand, 113 patients (55%) did not receive brachytherapy, 36 (18%) only received ovoid brachytherapy and 56 (27%) were treated with ovoid and tandem brachytherapy. Recurrence was more prevalent if the radiotherapy dose was less than 50 Gy and also in patients treated with four-field box technique. The most frequent site of recurrence was pelvic area (71%).

Conclusion: Our report revealed that most of the patients in Iran are diagnosed in advanced stages, a finding that can influence treatment results. Also, using external beam radiotherapy techniques, accessibility to brachytherapy devices and better patient support may improve treatment results.

Keywords: cervical cancer, radiotherapy, chemotherapy, epidemiology

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Introduction

The incidence of cervical cancer is hugely different in different countries. The highest prevalence is found in the regions which lack an appropriate screening program and have high prevalence rates of human papilloma virus infection associated with unsafe sexual behaviors such as India, South and East Africa and Latin America. Cervical cancer is one of the most common causes of cancer-related mortality in these countries [1]. The lowest prevalence exists among Muslim countries in the Middle East such as Iran [2-4]. The latest report by Iranian Ministry of Health, based on pathology center data, revealed that cervical cancer, with more than 500 new cases diagnosed every year, is the second most common malignancy of females' genital tract.

Surgery and radiotherapy are two important parts of cervical cancer treatment which lead to cure in many cases. For instance a study, performed in United States of America, showed that five year survival rate of cervical cancer was estimated to be 71% at all stages.

Considering the lack of precise statistics on treatment results of patients with cervical cancer in Iran, our study was performed on patients with cervical cancer who were referred to a major Radiation Oncology Center, Mortazavi Radiation Oncology Center (Imam Hossein Hospital, Tehran, Iran) between 2000 and 2004.

Materials and methods

Medical records of 220 patients who were referred to Mortazavi Radiation Oncology Center (Imam Hossein Hospital, Tehran, Iran) between 2000

Table 1: Relationship between various factors and recurrence rate in 220 patients with cervical cancer who were referred to Mortazavi Radiation Oncology Center, Tehran, Iran, between 2000 and 2004

Factor (number of patients with available data)	Type	Without recurrence	With recurrence	P value
Hemoglobin level prior to radiotherapy (26)	Below 10 mg/dl	5	2	0.463
	Above 10 mg/dl	16	3	
Surgery (209)	-	108	29	0.436
	+	60	12	
Dosage of radiotherapy (214)	≤50 Gy	116	21	0.035
	>50 Gy	56	21	
Number of radiotherapy fields (207)	2	134	19	0.05
	4	32	22	
Para-aortic radiotherapy (216)	-	159	41	0.867
	+	13	3	
Brachytherapy (218)	-	90	28	0.555
	<30 Gy	31	6	
	30 Gy ≤	12	51	
Radiotherapy protocol (215)	50 Gy EBRT*	43	9	0.346
	50 Gy EBRT+ brachytherapy	73	13	
	>50 Gy EBRT	44	15	
	>50 Gy EBRT+ brachytherapy	13	5	
Chemotherapy (219)	-	167	44	0.777
	+	6	2	
Time interval between EBRT and brachytherapy (91)	≤2weeks	18	3	0.471
	>2weeks	55	15	
Total duration of radiotherapy (176)	≤8weeks	65	12	0.118
	>8weeks	74	25	

* External beam radiotherapy

and 2004 due to pathologically diagnosed cervical cancer were included in this study.

Data regarding age at the time of diagnosis, stage, hemoglobin level, dosage of radiotherapy, type of radiotherapy (i.e. brachytherapy or external beam radiotherapy (EBRT)), number of fields, type of chemotherapy, time and site of recurrence and the treatment of recurrence were collected.

Results

A total of 220 patients with a mean age of 55 years (range: 28-89) and a follow-up duration between 2 to 105 months (16.8 ± 20.1) were investigated. Squamous cell carcinoma (180 patients, 81.3%) and adenocarcinoma (6 patients, 2.7%) were the most common pathologic subtypes. One patient was diagnosed with undifferentiated carcinoma. Stage IIB (82 patients, 37.3%) and stage IA (4 patients, 1.8%) had the highest and the lowest frequency among patients at the time of admission, respectively. Among 26 patients whose hemoglobin level was measured before radiotherapy, 7 cases had values less than 10 mg/dl, and 19 patients had values more than 10 mg/dl.

Surgery

Of all, 137 patients (62.3%) did not have surgery at the time of admission, while 51 patients (33.2%) had total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO), 11 patients (5%) had hysterectomy and only 10 patients (4.5%) underwent Wertheim surgery.

Radiotherapy

Among 214 patients receiving EBRT, 137 (64%) received a dose of 50 Gy or less, and 77 (36%) were treated with a dose higher than 50 Gy. One hundred and fifty three patients (74%) received two opposed field radiotherapy while 54 (36%) were treated with four fields and only 16 patients (7.3%) received para-aortic irradiation. On the other hand, 113 patients (55%) did not receive brachytherapy, 36 (18%) only received ovoid brachytherapy and 56(27%) were treated with ovoid and tandem brachytherapy,

The duration of external radiotherapy was eight weeks or less in 77 patients (44%) and more than eight weeks in 99 (56%) patients. The time interval between EBRT and brachytherapy was two weeks or

less in 21 patients (23%) and more than two weeks in 70 (77%) patients.

Chemotherapy

Among 219 patients, only 8 (0.04%) received chemotherapy.

Recurrence

A total of 46 patients (21%) experienced recurrence. The most common sites of recurrence were pelvis (38 patients, 71%), bone (6 patients, 3%) and viscera (2 patients). The most frequent therapeutic modalities for recurrence in the 43 patients whose relevant data available included radiotherapy (21 patients, 49%), chemotherapy (12 patients, 28%), supportive treatment (7 patients, 16%) and surgery (2 patients, 7%). Among various factors that significantly influenced recurrence rate (table 1), a radiotherapy dose of lower than 50 Gy ($P=0.035$) and four radiotherapy fields ($P=0.05$) can be mentioned.

Discussion

Mean age of patients in our study was higher than the usual age of cervical cancer in the rest of the world which requires more investigation. In our study, most patients were in stage IIB of the disease at the time of admission. Considering the influence of stage on patients' survival, this finding shows that better screening programs among high risk females would be effective as a tool for earlier diagnosis. Since some years ago chemotherapy was not considered necessary along with radiotherapy protocols, only a few of the investigated patients received a combination of chemotherapy and radiotherapy.

Like other studies, the most common site of recurrence was pelvis. A Hg level below 10 has been correlated with a higher recurrence in several studies [5-8]. It has been suggested that the reason for this correlation is the lower oxygenation of the tumoral tissues and consequently, the lower efficacy. No significant correlation between the hemoglobin level and recurrence rate was found in our study, which might be due to lack of available data on hemoglobin levels. Therefore, measuring, recording and correcting the level of hemoglobin prior to radiotherapy might have an important role in improving patients' outcomes and more precise post-therapy reports.

In our study, like other ones, a low recurrence rate was associated with doses more than 50 Gy which supports the necessity of administering higher doses. We found a higher recurrence rate among patients treated with four fields compared to those treated

Table2- Cervical cancer presentation by stage

Stage	Frequency	Percent
I	21 (IA: 4 IB: 17)	11.9
II	119 (IIA:37 IIB:82)	67.2
III	28 (IIIA:17 IIIB:11)	15.8
IV	9	5.1

with two fields (40.7% versus 12.4%). Some previous studies have also recommended using two fields in order to provide homogenous spread of the specific dosage to all areas of the tumor, as poor preparation of the four fields possibly causes treatment failure of the posterior parts of the tumor located in front of the sacrum.

In our study, patients were treated without computer-based radiotherapy planning which is supposed to be the reason for the high recurrence rate in those treated with four fields. So, we recommend treatment with two fields (anterior and posterior) if computer-based facilities are not available. Considering the influence of the duration of total therapeutic period and the interval between EBRT and brachytherapy on recurrence rates, the intervals shorter than two weeks and a radiotherapy duration shorter than eight weeks were associated with a lower risk in our study. We did not find this association to be statistically significant; however, some studies have showed a significant relationship [9-11]. This correlation might be significant with a larger sample size and a longer follow-up.

It seems that prospective studies could provide more precise data; however, these suggestions can be made according to our study: measuring hemoglobin levels prior to radiotherapy and correcting values below 10 mg/dl, performing brachytherapy as soon as possible after EBRT, and completing the whole period of radiotherapy in less than eight weeks. It is also recommended to use four-field pelvic radiotherapy technique only when computer-based radiotherapy treatment planning is available.

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