

RESEARCH ARTICLE

Quality of Life of Patients with Advanced Cervical Cancer before and after Chemo-radiotherapy

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Abstract

Background: Cervical cancer is the most frequently diagnosed cancer among women in India. Understanding quality of life (QOL) in women undergoing chemo-radiotherapy for cervical cancer will help in introducing interventions for better care and outcomes in these women. This study assessed QOL before and after chemo-radiotherapy in cervical cancer patients. **Materials and Methods:** This follow-up study covered sixty-seven newly diagnosed women with advanced cervical cancer (stages 2b to 4b). Structured questionnaires (the European Organization for Research and Treatment of Cancer, EORTC QLQ-C30 and EORTC QLQ-CX24) were used to assess the change in QOL after 6 months of treatment. **Results:** The mean age of women at the time of detection of cervical cancer was 52.3±11.29 years (Range 30-75 years). Six months survival was 92.53%. The mean global health score of cervical cancer patients after six months of treatment was 59.52, which was significantly higher than the pre-treatment score of 50.15 (p=0.00007). Physical, cognitive and emotional functioning improved significantly (p<0.05) after treatment. Fatigue, pain, insomnia and appetite loss improved but episodes of diarrhea increased after treatment. The mean "symptoms score" using EORTC QLQ-CX24 post treatment was 20.0 which was significantly lower as compared to the pre-treatment score 30.0 (p<0.00001). Sexual enjoyment and sexual functioning decreased significantly after treatment. **Conclusions:** QOL of newly diagnosed cervical cancer patients improved significantly following chemo-radiotherapy. Enhancement was also demonstrated on three of the five functional scales of EORTC QLQ-C30. To further improve QOL, interventions focusing on social and psychological support and physical rehabilitation may be needed.

Keywords: Cervical cancer - chemo-radiotherapy - quality of life - India

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Introduction

Cervical cancer is a major public health problem in many developing countries. Besides contributing significantly to mortality rates, it leads to loss of productive years due to prolonged disability (Lozano et al., 2012). The absolute burden of cervical cancer is expected to increase in future unless effective preventive measures are undertaken. Globally, cervical cancer is the fourth commonest cancer in women with nearly 528,000 new cases reported in 2012 (Ferlay et al., 2012). Nearly 85% of the global burden occurs in the less developed regions, where it accounts for almost 12% of all female cancers. High-risk regions, with estimated Age standardized rate (ASRs) over 30 per 100,000 include Eastern Africa (42.7), Melanesia (33.3), Southern (31.5) and Middle (30.6) Africa. There were an estimated 266,000 deaths from cervical cancer worldwide in 2012, accounting for 7.5% of all female cancer deaths (Ferlay et al., 2012).

Cervical cancer is one of the leading cancers among

Indian women with estimated 123000 new cases and 67477 deaths in 2012 (Ferlay et al., 2012). Cancer is preventable and curable, if detected at an early stage. The five-year survival rate of cervical cancer when diagnosed at the earliest stage is 92% and the combined 5-year survival rate of all stages is 71% (American cancer society, 2006). It is currently believed that the persistent infection with one of the 15 oncogenic types of Human papilloma virus (HPV) is the central and necessary cause of almost all cervical cancers and its precursor, cervical intra epithelial neoplasia (CIN). A proportion of CIN, if not detected and treated, progresses to invasive cervical carcinoma over a period of 10-20 years owing to the effect of other cofactors (Bosch et al, 2002; Boyle and Lewin, 2008) Unfortunately, despite the availability of methods for prevention and early diagnosis, many women in India have never been screened for cervical cancer due to lack of periodic screening program.

Though the diagnosis and treatment of cervical cancer has been developed, there are important consequences

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from the disease and its treatment among survivors, especially the impact on quality of life (QOL). Some functional disorders occur following therapies such as surgery, which involves the female genital anatomy affecting directly their perception of body image and sexual functions; radiotherapy which could damage the vaginal mucosa and epithelium; and chemotherapy which could induce various adverse effects like nausea, vomiting, diarrhea, constipation, mucositis, weight changes and hormonal changes. Various psychological factors including low self-esteem, changes in self-image, beliefs about the origin of cancer, marital tensions, fears and worries can affect the patients (Fernandes et al., 2015). Need to measure QOL has become important due to broadening concept of measuring health status beyond traditional indicators such as mortality and morbidity. Assessing QOL is potentially valuable in identifying patients' problems and addressing them in the existing health systems. Taking into account the impact of early screening methods on long term survival of cancer patients, studies assessing QOL and its related factors have become critical. Limited studies have been done to evaluate QOL among cervical cancer survivors diagnosed in advanced stages. This study assessed the QOL in such patients before and after treatment with chemotherapy and radiotherapy.

Materials and Methods

This was a follow-up study covering 67 women who were newly diagnosed with cervical cancer between 1st January 2014 and 30th June 2014 at the Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi. The inclusion criteria were all women who were newly registered and diagnosed cases of cervical cancer of any histological type and advanced cancer stages (2b to 4b). Critically ill patients, those not willing to give informed consent and those who underwent surgery

and did not require radiotherapy and chemotherapy were excluded. All consecutive cervical cancer patients fulfilling the inclusion criteria during the six month period (January to June, 2014) were eligible for recruitment.

Quality of life of the study subjects was assessed using the questionnaires developed by the European Organization for Research and Treatment of cancer (EORTC) QLQ-30 and EORTC QLQ-CX24 (Aaronson et al., 1993; Sprangers et al., 1993; Fayero et al., 2001; Greimel et al., 2006; Jayasekara et al., 2008)

a) EORTC QLQ- CX30

The EORTC QLQ-C30 is a questionnaire developed in 1993 to assess the quality of life of generic cancer patients. It has been translated and validated into several languages including Hindi and has been used in numerous studies worldwide. This questionnaire has undergone extensive testing in multicultural and multidisciplinary research settings, and has been confirmed to be a reliable and valid tool. The EORTC QLQ C-30 questionnaire comprises of 30 questions assessing functions viz. physical, role, cognitive, emotional, social; symptoms viz. fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulty; and a global health status score which assesses the overall QOL.

b) EORTC QLQ-CX24

EORTC Quality of Life Group has adopted a "modular" approach to QOL assessment for overcoming the limitations of generic tool and for disease specific treatment measurements. Consequently, modules specific to tumor site locations, management modality, or a QOL dimension have been developed that are administered in addition to the core questionnaire. The EORTC QLQ CX-24 is a complementary questionnaire specific for cervical cancer patients that consists of 24 questions categorized as functional scales viz. body image, sexual activity, sexual enjoyment, sexual/vaginal functioning and symptom

Table 1. Comparison of Pre and Post Treatment EORTC QLQ CX-30 Quality of Life Scores in Women Treated for Cervical Cancer (N=56)

EORTC CX30 SCALE	Pre-Treatment (Mean ± SD)	Post-Treatment (Mean ± SD)	't' Value	p Value
Global health scale				
Global health status	50.2±13.1	59.5±10.9	4.1	0.00007*
Functional scale				
Physical functioning	80.0±22.8	89.8±17.4	2.6	0.012*
Role functioning	85.7±16.0	91.7±14.9	2.0	0.044*
Emotional functioning	58.2±17.0	71.7±15.6	4.4	0.00026*
Cognitive functioning	81.3±17.1	91.1±11.9	3.5	0.00062*
Social functioning	67.3±15.2	69.3±17.9	0.7	0.51
Symptom Score	30.0±8.2	20.0±10.8	5.5	<0.00001*
Fatigue	57.3±15.1	v	8.4	<0.00001*
Nausea & vomiting	4.2±13.2	7.8±18.3	1.2	0.24
Pain	42.1±14.1	20.5±16.4	7.5	<0.00001*
Dyspnea	3.0±11.5	2.4±8.7	0.3	0.75
Insomnia	16.1±16.8	10.1±17.9	1.8	0.072
Appetite loss	65.5±15.5	30.4±21.3	10.0	<0.00001*
Constipation	10.1±21.9	15.5±29.8	1.1	0.28
Diarrhea	0.6±4.5	19.6±28.3	5.0	<0.00001*
Financial difficulty	35.7±15.4	31.0±17.8	1.5	0.13

* statistically significant

scales viz. symptoms experience, lymphedema, peripheral neuropathy, menopausal symptoms and sexual worry. Both the tools utilize a 4-point response scale namely "Not at all", "A little", "Quite a bit" and "Very much" to assess each functional or symptom item, and a 7-point response scale to assess global health status ranging from very poor to excellent.

These study instruments were administered to patients at baseline and again at 6 months to ascertain changes in QOL after treatment.

Institutional Ethics Committee (IEC) approval was obtained prior to initiation of study. Prior to enrollment, written informed consent was obtained from patients after detailed explanation about the study. Patient confidentiality was assured and the study participants had the right to abstain from participation without affecting on the quality of care being provided to them.

Statistical analysis

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 18. Qualitative data was expressed in proportions while mean and standard deviation were calculated for quantitative data. The student's t test and Chi-square tests were used for comparing the characteristics of the study participants and the quality of life scores before and after chemo-radiotherapy. The scoring of the questionnaire data was performed according to the scoring manual. All scores were transformed to a 0-100 scale. For the functional

scales, a good function was indicated by higher scores. For symptom scales, more severe symptoms were indicated by a higher score. A p-value under 0.05 was considered statistically significant.

Results

This study included 67 patients of advanced cervical cancer who met the eligibility criteria. Six deaths were reported during the course of the study and 5 patients were lost to follow up. The final sample that was analyzed consisted of 62 patients and the quality of life was assessed in 56 patients. The mean age of study participants was 52.28±11.29 years (Range 30-75 years). Squamous cell carcinoma was the most common cancer (97%) while remaining 3% patients were diagnosed with adenocarcinoma/ adeno-squamous carcinoma. Majority (53.73%) of the study subjects were in stage 3b and 40% in stage 2b and remaining in stage 3a and 4a. Metastasis was present in only one patient. Combination of radiotherapy and chemotherapy was the most common (77.67%) modality of treatment. Nearly 12% of the study subjects were treated only by radiotherapy while another 10.45% cases received radiotherapy after surgery. Palliative treatment was given to four patients.

Six-month survival among those who could be followed up was 92.53%. The global health score improved significantly after treatment (p=0.00007). The mean global health score of cervical cancer patients following

Table 2. EORTC QLQ CX-24 cervical cancer module scores in cervical cancer woman before and after treatment

Parameter	n	Pre-treatment Score	Post-treatment Score	't' value	p value
		(Mean ± SD)	(Mean ± SD)		
Functional Scale					
Body image	56	72.0±15.7	59.5±22.5	3.4	0.0009
Sexual activity	47	86.5±21.6	83.0±19.5	0.8	0.41
Sexual enjoyment	11	87.9±16.8	63.6±27.7	N.A	N.A
Vaginal functioning	11	75.0±12.4	25.0±12.4	N.A	N.A
Symptom Scale					
Symptoms experience	56	25.7±13.5	12.6±9.5	6	<0.00001
Lymphoedema	56	3.6±15.2	10.1±19.0	2	0.046
Peripheral Neuropathy	56	10.1±19.0	7.1±15.2	0.9	0.36
Menopausal symptoms	56	4.8±17.3	1.2±6.2	1.5	0.15
Sexual worry	47	60.3±37.2	17.0±19.5	7	<0.00001

N.A- For some variables t and p value not calculated due to small sample size

Table 3. Overall Health and Quality of Life of the Study Subjects before and after Treatment according to Stage of Cancer Cervix and Modality of Treatment

Parameter	n	Pre-treatment Response*							Post-treatment Response*							Yate's Corrected Chi-sqaure	p value (df=1) #
		1	2	3	4	5	6	7	1	2	3	4	5	6	7		
		Poor-Average				Good-Excellent			Poor-Average				Good-Excellent				
Ca Cx Stage 2B																	
Overall Health Score	24	0	1	2	13	8	0	0	0	0	0	7	16	1	0	5.34	0.021
Quality of Life Score	24	0	1	2	13	8	0	0	0	0	0	7	16	1	0	5.34	0.021
Ca Cx Stage 3A, 3B, 4A																	
Overall Health Score	32	0	1	8	16	7	0	0	0	0	2	16	12	2	0	2.55	0.11
Quality of Life Score	32	0	1	10	13	8	0	0	0	0	2	16	12	2	0	1.73	0.19
Treatment Modality: Radiotherapy																	
Overall Health Score	12	0	0	2	7	3	0	0	0	0	1	4	6	1	0	1.54	0.21
Quality of Life Score	12	0	0	2	7	3	0	0	0	0	1	4	6	1	0	1.54	0.21
Treatment Modality: Radio & Chemotherapy																	
Overall Health Score	44	0	2	8	22	12	0	0	0	0	1	19	22	2	0	5.69	0.017
Quality of Life Score	44	0	2	10	19	13	0	0	0	0	1	19	22	2	0	4.66	0.03

#Statistically significant p<0.05; *1 is very poor and 7 means excellent

treatment was 59.52, which was significantly higher than pre-treatment values of 50.15. (Table 1).

The patients' quality of life of patients in the functional scales comprising physical, role, emotional and cognitive functioning improved significantly after treatment of cervical cancer ($p=0.012, 0.044, 0.000026, 0.00062$ respectively). There was no difference in social functioning score. Symptom like fatigue, pain and loss of appetite improved significantly, but no significant improvement was seen in nausea/vomiting, dyspnea, insomnia and constipation. However, diarrhea worsened in the post treatment phase (Table 1).

There were significant changes in cervical cancer specific EORTC QLQ CX-24 module scores for cervical cancer patients (Table 2). There was significant decrease in body image, sexual enjoyment and vaginal functioning after treatment, though sexual activity as a whole did not change significantly.

Overall symptom experience showed significant improvement after treatment with score reducing from 25.70 to 12.55 indicating improvement ($P=0.00001$). There was no difference in symptoms indicative of peripheral neuropathy and menopausal symptoms after treatment. On the other hand, sexual worry decreased significantly with the mean score declining from 60.28 to 17.02 after treatment.

Overall health score and quality of life score improved significantly ($p<0.021$) following treatment in stage 2b of cervical cancer but this improvement was not significant in stage 3 and 4 (Table 3). Improvement in overall health score and quality of life score was significant ($p=0.017$ and 0.030) in patients who received both radio & chemotherapy, while patients who received only radiotherapy (including 6 patients who had surgery before radiotherapy) did not show significant improvement.

Discussion

Indicators of quality of life measure the impact of a disease and its treatment on a patient's daily activities, behavior, perceived health and functional status. Quality of life indices, which focus on patient's own perception of disease, provide further information that cannot be obtained solely from conventional clinical and functional measurements. Therefore tools to measure quality of life have been framed by various organizations for comprehensive assessment of patients under treatment.

Many factors may contribute to QOL of women diagnosed with a gynecological cancer. In our study most common modality of treatment was combination of radio and chemotherapy. Radiation therapy damages the vaginal mucosa and epithelium which leads to decrease in sexual functioning and pleasure. Additional side-effects of radiotherapy are nausea, vomiting, diarrhea and mucositis among others (Barros and Labate, 2008)

Our study compared the pre-treatment and the post-treatment QOL for advanced cervical cancer patients. The Global health score showed a significant increase after treatment making it apparent that quality of life improves after treatment. Similar results were also seen in a recent study published by (Kumar et al., 2014) In functional

scales, all the items showed a significant increase after treatment including physical, emotional, cognitive and role except social functioning which was nearly same before and after treatment. This finding was in contrast to a study by (Greimel et al., 2002), which showed that the global health status, emotional and social functioning remained low. This difference could be because of enrollment of all stages of cervical cancer in their study and the fact that majority of study subjects underwent surgery as a part of treatment modality. The symptom scale analysis revealed that there was a significant decrease in fatigue, pain, insomnia and appetite loss after treatment. This was in contrast with another study done by (Klee et al., 2000) in which pain, appetite loss, nausea & vomiting increased after 3 months of treatment. This variation could be because of differences in time gap between initiation of treatment and post therapy QOL assessment. Episodes of diarrhea worsened after treatment in the present study which may due to radiotherapy. Radiotherapy has been shown to be associated with diarrhea while constipation may be ascribed to injury to the parasympathetic nerves during surgical interventions (Klee et al., 2000; Possover and Schneider, 2002). Another study by (Tokzaharani et al., 2013) also showed that scores were negatively associated with symptoms including short breathing, lack of appetite, nausea and vomiting, sleep disorder, peripheral neuropathy and menopausal symptoms. In our study, financial difficulties had not changed significantly after treatment. Other studies have shown that financial difficulties increased after treatment which can affect the QOL of the patients (Park et al., 2007). As the study subjects were being treated in a government supported institution, out-of-pocket expenses are likely to be low. This aspect of assessment becomes especially important in resources limited settings in developing countries like India.

Sexuality is an important aspect in patients suffering from any gynecological cancer and thus a crucial determinant of QOL. In our study, there was a significant decrease in sexual enjoyment and sexual and vaginal functioning score in EORTC QLQ CX -24 which was also demonstrated in the study conducted by (Kumar et al., 2014). Another study by (Park et al., 2007) stated that 40% to 100% individuals face sexual dysfunction after treatment. This is because cervical cancer and its treatment affect the same areas of the body which are involved in sexual response. Both chemotherapy and radiotherapy has been associated with sexual problems like dyspareunia, insufficient lubrication and anxiety about sexual performance. Beside this, psychological factors also have an important role in sexual behaviors, and we found that cervical cancer patients had more anxiety about sexual performance. Overall symptoms experience reduced significantly after treatment but lymphedema, peripheral neuropathy & menopausal symptoms did not change significantly. In contrast, Kumar et al demonstrated significant increase in these symptoms after treatment. In another study done by (Frumovitz et al., 2005), frequency of menopausal symptoms increased and sexual functioning decreased after treatment. These symptoms may follow from oophorectomy or radiation damage to the ovaries.

In our study patients had perceived poor body image after treatment. These results were similar to those reported by of (Park et al., 2007).

In our study overall health score and quality of life score improved significantly ($p < 0.021$) following treatment in stage 2b of cervical cancer but the improvement was not significant in stage 3 and 4. This was expected since treatment of cervical cancer done in early stages results in better QOL outcomes than if detected and treated at later stages. This signifies the importance of screening for early detection and timely appropriate treatment of cervical cancer. In our study improvement in overall health score and quality of life score was significant in patients who received both radio & chemotherapy, while patients who received only radiotherapy failed to report significant improvement. This could be attributed to the fact that radiotherapy alone was given to patients who were in advanced stages of cervical cancer or had poor general condition in whom only palliative treatment was possible.

It is suggested that further studies and interventions focusing on improving the QOL in survivors should be encouraged. Although, the overall QOL after treatment in cervical cancer survivors was good, management of related problems can further improve it. By detecting the problems associated with the quality of life after treatment of cervical cancer, health care professionals will be able to undertake intervention programs that will help to prevent or ameliorate specific problems and adverse effects.

Acknowledgements

Although our study revealed that cervical cancer patients undergoing treatment with radiotherapy and chemotherapy are satisfied with their global quality of life, attention should be paid to specific dimensions like sexual functioning during post-treatment period. To further improve QOL, interventions focusing on social and psychological support and physical rehabilitation may be needed.

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