Prospective Quality of Life Study of South African Women Undergoing Treatment for Advanced-stage Cervical Cancer

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ABSTRACT

Purpose: The majority of South African cervical cancer patients present with advanced-stage disease. Chemoradiation therapy, in comparison with radiation therapy, results in marginally improved survival in women with advanced cervical cancer. The impact on the quality of life due to the addition of a chemosensitizer in a situation of limited survival benefits warrants objective assessment. This prospective study compares the quality of life for women with cervical cancer and treated with radiation or chemoradiation therapy at Tygerberg Hospital, South Africa.

Methods: A prospective study was done in a population with a high incidence of advanced cervical cancer. Quality of life measurements were done at pretreatment, post treatment, and follow-up. The European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire and the Cervix Cancer Module were used.

Findings: The study included 219 women. Forty-four women were treated with primary surgery. A total of 102 women completed primary radiation therapy and 73 women completed primary chemoradiation therapy. The demographic characteristics of the last 2 treatment groups were different. Women receiving chemoradiation therapy had a higher educational level ($P < 0.01$) and had less advanced stage (III or IV) cervical cancer ($P < 0.01$). Radiation therapy was used significantly more in HIV-positive women. The presiding clinicians chose treatment options based on clinical factors unrelated to quality of life. Chemoradiation therapy resulted in statistically more improvement in the pain ($P < 0.05$), fatigue ($P < 0.05$), appetite loss ($P < 0.01$), and nausea and vomiting ($P < 0.05$) quality of life domains. In these domains, pretreatment quality of life scores were significantly higher in the radiation therapy group, implying a poorer quality of life status at the initiation of treatment. In post hoc analysis, the global health domain was significantly more improved ($P = 0.03$) by chemoradiation. Peripheral neuropathy was not increased by chemoradiation.

Implications: Chemoradiation therapy improved quality of life more than radiation therapy in certain domains. This allows for selection of chemoradiation as a treatment option in situations where quality of life is the end point of treatment. (*Clin Ther.* 2015;37:2324–2331)

Key words: Cervical cancer, Chemoradiation, Quality of life.

INTRODUCTION

Cervical cancer remains common in developing countries, where the majority of cases occur.[1] In these developing countries, a high incidence of advanced-stage cervical cancer is found. The advanced stage is not amenable to surgery, and radiation therapy has been the treatment of choice.[2] In 1995, on the basis of 5 randomized controlled trials, the National Cancer Institute recommended that chemoradiation therapy be the preferred treatment for advanced-stage cervical cancer.[3] A meta-analysis by Green et al[4] of available studies showed a 5-year survival benefit of 29% in all stages of cervical cancer for chemoradiation therapy compared with radiation therapy. In a separate meta-analysis, Lukka et al[5] calculated a 26% survival benefit, but subsequent limitations—for example, omission of unpublished studies—challenged this finding.[5,6] A Cochrane review calculated a survival benefit of 13% across all stages of cervical cancer treated with chemoradiation therapy.[7] Limitations in

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all of these meta-analyses were differences in study designs, accrual rates, and treatment schedules. Additional limitations included heterogeneity of the control arms of the studies, including the use of previously conducted studies as controls. These limitations were addressed by performing an individual patient data analysis. This individual patient data analysis found there was a 9% survival benefit with chemoradiation therapy in all stages of cervical cancer. The effect of chemoradiation therapy on survival decreased with increasing tumor stage, with estimated absolute survival benefits of 10% (stage IA–IIA), 7% (stage IIB), and 3% (stage III–IVA) at 5 years.[8]

Despite increased toxicity, chemoradiation therapy is still widely accepted.[9] The increased toxicity relates to specifically increased grade 3 and 4 hematologic toxicity (2-fold increases) and gastrointestinal (3-fold increases) events in the chemoradiation therapy group.[10] The presence of physician-recorded toxicity correlates poorly with patient-reported quality of life.[11] A meta-analysis of chemoradiation therapy toxicity suggests that although the acute toxicity was acceptable, additional studies on the toxicity-related impact on quality of life are needed.[10] The present study aims to describe the impact on quality of life of radiation therapy or chemoradiation therapy for women with cervical cancer treated at Tygerberg Hospital, South Africa.

METHODS

Inclusion Criteria

Newly diagnosed cervical cancer patients referred to the Unit of Gynaecologic Oncology, Tygerberg Hospital were approached to participate in the study. The unit is 1 of the 2 tertiary referral units for public-sector patients of the Western Cape Province. The Western Cape Province has a population of 5.8 million. The majority of the population (85%) does not have private insurance and are dependent on the public facilities provided by the 2 tertiary hospitals (Tygerberg Hospital and Grootte Schuur Hospital) for treatment of invasive cervical cancer.[12]

Patients were eligible if they had histologically proven cervical cancer. Women unable to provide informed consent because of psychiatric disorders were excluded. After informed consent was obtained, the patients completed the questionnaire in the language of their choice, for example, Xhosa, English, or Afrikaans.[13] A research assistant helped patients who could not read or write. To exclude bias, the research assistant had no medical background and was not involved in the clinical management of the patients. Patients completed the questionnaires before treatment, after completion of initial treatment, and at 3-month post-treatment follow-up. Clinical data were extracted from patient records. Ethical approval was obtained from the local committee (S12/06/174).

Confounding variables that could affect quality of life were included in statistical analysis. These were age, race, educational level, employment status, income, stage of cervical cancer, and HIV status. Employment status, marital status, race, income, and educational levels were self-reported by patients. A poverty line income of ZAR3500 per month was used.[12]

The treatment protocol at Tygerberg Hospital for patients with advanced stage IB2 to IVA cervical cancer is 46 to 50 Gy in 23 to 25 fractions of external beam radiation therapy (EBRT). This is delivered to the pelvis with concurrent weekly cisplatin (40 mg/m^2) for 4 to 6 cycles and high-dose radiation brachytherapy at 20 to 26 Gy in 4 to 5 fractions starting in week 5 of EBRT. The cervix, uterus, parametria, and pelvic lymph nodes up to and including the common iliac are delineated by a planning computed tomography scan. The para-aortic lymph nodes (PAN) were delineated up to the renal hilum if the common iliac or lower PANs are involved on imaging. This volume is conformally mapped on the XiO Radiation Treatment Planning System (Computerized Medical Systems, Inc, Maryland Heights, Missouri).

The treatment protocol was EBRT at 2 Gy fractions 5 days a week or, alternatively, at 1.8 Gy fractions if the patient has a history of abdominal surgery, is HIV-positive, or has a PAN field. The PAN field receives 45 Gy and the pelvic area receives 50.4 Gy. Patients who have poor performance status or very advanced local disease with bilateral hydronephrosis or renal compromise are prescribed 40 Gy in 15 fractions at 2.67 Gy fractions. Treatment is with an 18-mV linear accelerator with multiple shielding capabilities. During or after the fifth week of EBRT, each patient is examined under anesthesia. A Smit sleeve is placed in the cervical os, and high-dose rate brachytherapy is planned to a total dose of 20 to 26 Gy in 4 to 5 fractions. The dose is delivered by a Varian GammaMed machine (Varian Medical Systems, Palo Alto, California). Chemotherapy is prescribed based on an evaluation of renal function