Gynecologic Oncology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Review Article

A study of chronic fatigue in Norwegian cervical cancer survivors

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HIGHLIGHTS

- 23% of the cervical cancer survivors reported chronic fatigue mean 11 years after diagnosis.
- Among those treated by minimal invasive or radical surgery 19% had chronic fatigue.
- Among those treated by chemoradiation 28% had chronic fatigue.
- Depressive symptoms and poorer quality of life were associated with chronic fatigue.

ARTICLE INFO

Article history:
Received 6 March 2017
Received in revised form 19 May 2017
Accepted 21 May 2017
Available online xxxx

Keywords:
Cervical cancer
Chronic fatigue
Surgery
Chemotherapy
Radiotherapy
Cancer survivor
Long-term survivors

ABSTRACT

Objective. Chronic fatigue after treatment is a common adverse event in cancer patients, but there are few studies in long-term survivors of cervical cancer. The aim of this investigation was to explore the prevalence of chronic fatigue and its association with various clinical and treatment-related factors in a population-based cohort of Norwegian cervical cancer survivors treated by any modality.

Methods. All patients, treated for cervical cancer from 2000 through 2007 in the Health Region of South-Eastern Norway, cancer-free, alive and aged ≤75 years by the end 2013 ($n = 822$) received a questionnaire covering chronic fatigue and other clinical variables.

Results. 461 of 822 survivors (56%) completed the questionnaire and 382 entered the analyses. Chronic fatigue was reported by 23% (95% confidence interval 19%–27%) with a median age of 52 years (range 32–75) at survey, 11 years (range 7–15) after diagnosis. Among survivors treated by minimal invasive- or radical surgery, 19% had chronic fatigue, while the prevalence was 28% in those treated with radiation and concomitant chemotherapy (chemoradiation). The chronic fatigue group reported significantly more cardiovascular disease, obesity, less physical activity, more treatment-related symptom experience, more menopausal symptoms, higher levels of anxiety and depressive symptoms, and poorer quality of life than the non-fatigued group. In multivariate analysis only increased level of depression and poorer global quality of life were significantly associated with chronic fatigue.

Conclusions. Chronic fatigue was reported by 23% of long-term survivors after cervical cancer at a mean of 11 years after treatment. Some of the associated factors are amenable to prevention and/or treatment and should be subjects of attention at follow-up.

Contents

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http://dx.doi.org/10.1016/j.ygyno.2017.05.028
0090-8258/

1. Introduction

Chronic fatigue is a common and distressing symptom in several groups of cancer survivors [1]. However, chronic fatigue has not been extensively studied in survivors of cervical cancer. Although chronic fatigue contributes considerably to impaired health-related quality of life (HRQoL), Vistad et al. [2] reported only one study of such fatigue [3] in their review of 23 studies on HRQoL in long-term survivors of cervical cancer. Cull et al. [3] reported that 33% of women treated for cervical cancer by surgery and radiotherapy, complained of chronic fatigue 2 years after treatment. In their study of long-term (>5 years) survivors after radiotherapy, Vistad et al. [4] found 30% with chronic fatigue. These women had significantly lower HRQoL, higher levels of anxiety and depression, and more physical impairment than women without chronic fatigue, but in multivariable analysis only depression remained significantly associated with chronic fatigue.

In a long-term study, Le Borgne et al. [5] observed that compared with women from the general population, survivors of cervical cancer had a higher level of mental fatigue at 15 years after diagnosis, but not at 5 and 10 years after. Tveit Sekse et al. [6] observed that 25% of women treated for cervical cancer were fatigued at a mean of 16 months post-treatment. However, their sample included only 29 subjects and their response rate was only 19%. Therefore, larger studies of women treated for cervical cancer are needed in order to determine the prevalence of chronic fatigue and its associations to type of treatment, severity of the disease (stage), and physical, psychological and socio-demographic factors. This was the aim of the present study.

2. Material and methods patient sampling

The Cancer Registry of Norway identified all patients with cervical cancer diagnosed between January 1, 2000 and December 31, 2007 and treated at hospitals located in the Health Region of South-Eastern Norway (2.8 million inhabitants). They were included in the present study if they were alive, aged ≤75 years, had no recorded history of second cancer, were considered tumor-free and not on any cancer treatment as of December 31, 2012. Co-operating gynaecologists responsible for the management of these patients at the relevant hospitals identified the patients to be included, and approved that they were contacted by mail. Accordingly, 822 patients were eligible for the study. They all received an invitation letter including information about the study together with a consent document and the survey questionnaire. Non-responders got one reminder.

2.1. Treatment for cervical cancer in Norway

Treatment for cervical cancer includes surgery, radiation and chemotherapy, or a combination of the three modalities. Generally, the choice of modality for primary treatment was based on tumor stage and grade according to the International Federation of Gynecology and Obstetrics (FIGO) staging system, which classifies the tumor according to its size and extension. In patients with minimal disease (FIGO stage Ia), minimal invasive surgery i.e. removal of a large conus (conisation) was considered as adequate treatment (Group 1). Patients with disease of limited volume [FIGO stages Ib–IIa except stage Ib2 (tumor > 4 cm)] usually underwent major surgery consisting of radical hysterectomy with pelvic lymph node dissection with or without bilateral salpingo-oophorectomy (Group 2).For several years, the standard treatment of patients with locally advanced disease (FIGO stage IIb-IVa) has been external-beam pelvic radiation to the tumor and the regional lymph nodes, combined with intra-cavitary radiation targeting the tumor [7]. In addition, low-dose cisplatin-containing chemotherapy has been given concomitantly to enhance the efficacy of the radiation [8]. Such treatment (chemoradiation) was given to Group 3. A small sub-sample received neoadjuvant chemotherapy (5-fluorouracil, etoposide and cisplatin), followed by standard major surgery (Group 4). Another few patients had combinations of surgery and external beam pelvic radiation along with chemotherapy (Group 5). In the analyses, Group 4 and 5 were merged into the group of surgery combined with either chemoradiation and/or neoadjuvant chemotherapy due to small sample sizes.

2.2. Measurements

2.2.1. The Fatigue Questionnaire (FQ)

The FQ is a validated questionnaire for measuring fatigue severity and contains questions concerning mental- (4 items) and physical fatigue (7 items) for the last 4 weeks. Each item is rated from 0 (as before) to 3 (very much worse). The mental fatigue score ranges from 0 to 12 and the physical score from 0 to 21, with higher scores signifying more fatigue. The total fatigue score represents the sum of these scale scores and ranges from 0 to 33. An additional item covers the duration of the fatigue experience with 4 response alternatives one of them being “6 months or more” [9]. For the definition of chronic fatigue, a dichotomized score for each response alternative (0 = 0, 1 = 0, 2 = 1, 3 = 1) is used, and chronic fatigue is defined as a dichotomized sum score of ≥4 with a duration of ≥6 months [9]. Internal consistency measured by Cronbach's coefficient alphas were 0.90 for physical, 0.76 for mental,

Please cite this article as: R. Steen, et al., A study of chronic fatigue in Norwegian cervical cancer survivors, Gynecol Oncol (2017), http://dx.doi.org/10.1016/j.ygyno.2017.05.028