COVER SHEET

The Functional Assessment of Cancer-Vulva: Reliability and Validity

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Abstract

Objectives: To assess the reliability and validity of the Functional Assessment of Cancer Therapy-Vulvar (FACT-V).

Methods: Seventy-seven patients treated between January 1996 and January 2001 for cancer of the vulva completed the FACT-V, the Eastern Cooperative Oncology Group Performance Status Rating (ECOG-PSR) and the Hospital Anxiety and Depression Scale (HADS) once, twenty consecutive patients treated between February 2001 and October 2001 completed the questionnaires twice, once before surgery and at two months follow-up. The FACT-V scores were compared by patients' performance status, FIGO stage, recurrence, and age, and correlated to the HADS scores. Changes in the FACT-V from baseline to two-months follow-up were evaluated to establish FACT-V's responsiveness to change.

Results: The FACT-V's internal consistency was adequate (Chronbach's alpha range, 0.75 to 0.87). Patients with lower performance status, higher FIGO-stage or recurrent disease received lower FACT-V scores, indicating discriminant validity. The correlation between the FACT-V and the HADS were in the expected direction, indicating convergent and divergent validity. From pre- to post-surgery, scores in nine out of fifteen items of the vulvar cancer specific subscale improved, while those of five items declined, indicating sensitivity of the vulvar cancer specific items to changes in patients' well-being.

Conclusions: The newly developed FACT-V provides a reliable and valid assessment of the quality of life of women with vulvar cancer. It can be used as a short measure of quality of life within research studies, and to facilitate communication about quality of life issues in clinical practice.

Introduction

About 3,900 women are diagnosed with vulvar cancer each year in the United States [1]. It is a relatively uncommon cancer, with only 3 to 5% of all gynecologic malignancies originating from the vulva [2]. Surgery and radiotherapy are the standard treatments and while effective, the treatment for vulvar cancer still imposes disfigurement and mutilation to the external genitals of patients likely to be associated with significant impairment of patients' quality of life (QOL). During the last 15 to 20 years more conservative surgical techniques were developed and individualized patient management is desirable in order to retain patients' QOL without diminishing survival [3].

At diagnosis, patients with gynecologic cancer report high levels of anxiety, depression, and social isolation [4]. Once treated, a significant proportion of gynecologic cancer patients experience fatigue, emotional distress, reduced social functioning, bladder and vaginal dysfunction [5]. Reductions in global QOL and emotional functioning were observed during and up to 24 month after treatment [6,7]. However, only few or no patients with vulvar cancer were included in studies investigating QOL in gynecologic malignancies [4, 7-9], and only a handful of studies reported on QOL or psychosocial well-being associated with vulvar cancer so far [10-14]. The main focus of these studies was on sexual functioning, and patients with vulvar cancer frequently experience significant reductions in this domain of QOL. After treatment, patients may experience vulva pain or numbness, and lymphedema of the legs [15], which may diminish other aspects of their functioning and QOL.

One of the most widely utilized QOL questionnaires is the Functional Assessment For Cancer General (FACT-G), developed by Cella and colleagues [16]. The FACT-G can be accompanied by cancer-site- and symptom- specific subscales such as those developed for breast cancer [17], ovarian cancer [18], and anemia. [19].

The purpose of the current study was to perform the initial psychometric evaluation of a *vulva cancer subscale* (VCS) measuring concerns of patients with cancer of the vulva and to establish its reliability and validity in combination with the FACT-G.

Materials and Methods

Item generation: We reported on this process in detail elsewhere[15]. Briefly, during semi-structured interviews, fifteen patients with a mean age of 68.8 years (range 52 to 85 years) and a mean time since surgery of 13.7 months (range 2 weeks to 36 months) were asked to describe their experience with vulvar cancer and the effect of illness and treatment on their QOL. All patients received treatment at the Queensland Center of Gynecological Cancer in Brisbane, Australia. These semi-structured interviews were structured according to guidelines provided by the Centre on Outcomes, Research and Education (CORE) [19]. Five experts in the treatment of women with vulvar cancer were also interviewed. Items were collated and redundant items and items idiosyncratic to individual patients were excluded. This process yielded the first version of the VCS (15 items), which together with the FACT-G comprises the FACT-V.

Participants:

Patients for the present study came from two sources: Group one consisted of patients who had surgery for vulvar cancer at the Queensland Center of Gynecological Cancer between January 1996 and January 2001. One hundred and forty-five patients were identified and received the assessment package by mail in March 2001. Thirteen patients had left the address, 3 patients had died, one patient refused participation, no response was received from 51 patients and 77 (59.7%) patients agreed to participate and returned completed questionnaires. No significant difference with respect to age ($p = 0.10$), FIGO Stage ($p = 0.59$), or treatment ($p = 0.11$) between responding and non-responding patients was observed.

Group two (longitudinal sample) consisted of 20 consecutive patients who had surgery for vulvar cancer between February 2001 and October 2001. These patients completed the assessment package twice, once before surgery and again two months thereafter. The second assessment of these 20 patients was considered eligible for the cross sectional analysis resulting in a sample of 97 patients for this analysis.

Patient characteristics:

For patients with squamous cell carcinoma (SCC) tumor stage was recorded using the 1988 International Federation of Gynecology and Obstetrics (FIGO) Stage classification. Patient's treatment and time since treatment was also summarized. All information was extracted from the hospital charts. Eighty-six patients (88.6%) had a radical local excision/radical vulvectomy or a wide local excision as primary treatment. Of these, 63 patients (64.9%) had a groin node dissection. The groin node dissection was bilateral except in those patients with stage 1 disease who had unilateral lesions. Postoperative radiotherapy to the groins and the pelvis was given to patients with positive groin nodes and local radiotherapy to patients with close or positive margins at the vulva (n=7). Primary chemoradiation (n=3) or primary radiotherapy (n=1) was given to patients with unresectable disease/or unfit for surgery. Detailed patients characteristics are given in Table 1.

Assessment package:

The participating patients completed the FACT-G and the newly developed VCS, the Eastern Cooperative Oncology Group Performance Status Rating (ECOG-PSR) and the Hospital Anxiety and Depression Scale (HADS) [20]. The FACT-G is a self-report scale and allows patients to rate their current physical, functional, social/family, and emotional well-being on 5-point Likert scales ranging from "not at all" to "very much" [16]. The FACT-G has well established psychometric properties and is sensitive to changes in cancer patients' well-being. The ECOG-PSR scale allows patients' to rate their subjective performance status on a 5-point scale (0 = no symptoms, 1 = some symptoms, but do not require bedrest during the waking day, 2 = require bedrest for less than 50% of the waking day, 3 = require bedrest for more than 50% of the waking day, 4 = unable to get out of bed). The HADS is a widely used self-assessment scale to assess emotional distress, specifically anxiety (HADS-A, 7 items) and depression (HADS-D, 7 items) on a scale ranging from 0 (no problem) to 3 (maximum distress). Patients are grouped into non-cases (scores up to 10) or cases (scores 11 or above). [20] The HADS is generally well accepted by patients and various studies reported good reliability and validity [21].

Statistical analysis:

Means, SD's and percentages of extreme response were calculated to describe the item characteristics of the VCS.

Reliability: Chronbach alpha coefficients were calculated to assess the internal consistency of each subscale and the total FACT-V scale. Chronbach alpha values above 0.80 were considered to prove good reliability while scores above 0.70 were considered adequate.

Validity: We performed different procedures to evaluate the FACT-V's validity.

First- Patients were collapsed intro three groups based on ECOG-PSR score (ECOG-PSR = 0 (n = 39), ECOG-PSR = 1 or 2 (n = 49), ECOG-PSR 3 or 4 (n = 9)). Univariate analysis of variance (ANOVA) were performed to compare FACT-V scores within these three groups to establish known-group (discriminant) validity. It was expected that patients with better ECOG-PSR status would also report better QOL. A subsequent ANOVA compared patients with more advanced stage of disease (SCC FIGO stage 3/4, n= 13) with patients with SCC FIGO stage 1A n = 28, or FIGO stage 1B/2, n = 29. It was also expected that patients who received treatment for recurrent disease (n=8) would report worse QOL than those patients who received their first treatment for vulvar cancer (n=89) although results could only be used as indicative given the small sample size. T-tests for independent samples were used for these

comparisons. In an earlier qualitative study [15], we observed differences between the QOL of patients younger than 65 years compared to those older than 65 years. We therefore performed t-tests for independent samples to compare the QOL scores of patients' younger than 65 years to those of patients' ≥ 65 years. The proportion of patients within each age group who indicated a preference not to answer questions regarding sexuality was compared by $\chi 2$ test.

Second: For divergent validity, Pearson correlation coefficients were used to assess associations between FACT-V and HADS subscales. The highest correlation was expected between the FACT's emotional functioning subscale and the HADS subscales, measuring related concepts, while lower correlations were expected with other FACT-V subscales.

Third – for sensitivity, in the longitudinal sample only (n=20), we assessed changes of the FACT-V from before to after surgery. Differences between mean item and subscale scores before and 2 months after surgery were investigated using paired samples t-tests. The patients within the longitudinal sample were then collapsed into groups based on changes in their subjective ECOG-PSR ratings. Six women reported an improvement in their PSR from before to after the surgery, 5 women reported no change and 9 women reported a lower PSR at the second time point. Changes in the mean subscale and overall scores of the FACT-V within these three groups were compared by multivariate analysis of variance (MANOVA) and then studied in detail by univariate analysis of variance (ANOVA).

Results

Patients

Patients characteristics are summarized in Table 1. Patients mean age at the time of assessment was 60.9 years and the majority of patients received treatment for SCC of the vulva (n = 70).

Descriptive Statistics

The mean values and standard deviations are presented in Table 2. Item 1 of the VCS (I am bothered by discharge/bleeding from my vulva) had the most skewed distribution with more than 70 percent of all patients answering 'not at all' to this item. All other items received a lower percentage of extreme responses (Table 2).

Mean scores of the subscales, the FACT-G and the FACT-V, the HADS-A and the HADS-D are presented in Table 3 within the cross sectional and longitudinal sample. In the cross sectional sample 15 (19.5%) out of 73 patients with sufficient data for the scale to be computed, had a score above 11 in the HADS-A subscale identifying them as cases, and 3 (3.9%) out of 71 patients were identified as cases through the HADS-D subscale. The respective numbers for the longitudinal sample (n = 20) were preoperatively: HADS-A, 9 (45%) cases, HADS-D, 3 (15%) cases; and postoperatively: HADS-A, 5 (25%) cases, and HADS-D, 1 (5%, n =19) case.

Reliability

The internal consistency scores are summarized in Table 3. Chronbach alpha scores for physical well-being, functional well-being, VCS, and the FACT-G and FACT-V were ≥ 0.80, while the social and emotional well-being subscales had adequate internal consistency with scores of 0.77 and 0.75, respectively.

Validity

Discriminant validity - Patients who reported no symptoms (PSR = 0) had higher scores on all but the social well-being subscale and the FACT-V overall, compared to patients reporting some symptoms (PSR 1, 2), while this group again reported better QOL than patients with a PSR of 3 or 4 (Table 4).

Patients with SCC tumors of the vulva (n=70) were grouped by FIGO Stage. Patients with FIGO stage IB/2 were found to have significantly higher scores in the VCS and the FACT-V compared to those treated for FIGO 1A or FIGO 3/4. Patients treated for SCC of the vulva FIGO 1B/2 had higher FACT-G scores than patients treated for FIGO 1A, while patients treated for FIGO 3/4 vulvar cancer reported the lowest FACT-G scores.

Patients treated for recurrent disease had significantly lower functional well-being, VCS and FACT-V summary scores (Table 4).

No significant difference in any QOL subscale or summary score was observed for women younger or older than 65 years (Table 4). A significantly higher number of women older than 65 years (79.5%) chose not to answer questions regarding sexuality than women younger than 65 years (21.7%) ($\chi 2= 28.2$, $p<0.001$).

Convergent and divergent validity - All FACT-V subscales with the exception of the social well-being subscale correlated significantly with the HADS subscales, and these associations were in the expected direction. The highest negative correlations were observed between the emotional functioning subscale and the HADS anxiety subscale ($r = - 0.75$), as well as the functional well-being subscale and the HADS-D subscale ($r = - 0.81$).

Sensitivity - From baseline (before surgery) to two-month follow-up, significant improvements in emotional well-being ($p <0.001$), the VCS ($p = 0.02$) as well as the FACT-G ($p = 0.03$) and FACT-V ($p = 0.02$) summary scores were observed in the longitudinal sample (see Table 3 for mean scores). Although the mean VCS score improved significantly from before surgery to 2-month follow-up overall ($t = 2.5$, $p = 0.02$), on the item level both improvements and reductions in scores were observed. For example, the item score "I am bothered by odor coming from my vulva" improved from a mean of 2.4 before surgery to 3.2

at two month follow-up ($p = 0.03$). In contrast patients rated the item "I am bothered by discomfort in my groins" lower from a 2.8 pretreatment score to 2.2 at two months follow-up ($p = 0.07$). Significant improvements were observed in 5 out of 15 items of the VCS, and significantly lower scores were recorded for three items at two month's follow up (Table 2). As a second indicator of the FACT-Vs' sensitivity patients were grouped by their pre- and post- surgery PSR into improved ($n = 6$), stable ($n= 5$) and worsened ($n=9$) PSR. The multivariate analysis of variance resulted in a significant difference in the FACT-V scores between the three groups ($F(2,20) = 13.4$, $p < 0.001$). Changes in the mean subscale and overall scores of the FACT-V within these three groups were then compared by ANOVA (Table 6). A significant change was observed for all subscale and summary scores except the social well-being subscale and the functional well-being subscale (Table 5).

Discussion

This study evaluated the reliability and validity of the newly developed FACT-V and presented psychometric data of the FACT-G for a sample of patients with cancer of the vulva. The results demonstrate the instrument's reliability, validity and sensitivity to change. The FACT-V is appropriate to use in clinical trials and descriptive studies aiming to assess the QOL of patients with vulvar cancer.

Treatment for vulvar cancer has become more individualized and less radical in recent years. In an attempt to decrease morbidity, ongoing trials currently evaluate treatments which aim to achieve similar outcomes compared to standard care while using less destructive techniques [22,23]. However, the impact of these treatment modifications on treatment-related morbidity and on patients' QOL have not been fully studied. The FACT-V might assist in facilitating such research with the aim to further improve treatment for patients with vulvar cancer.

The FACT-V is a 33-item questionnaire that can be completed within less than 15 minutes. The general part (FACT-G) allows to compare patients' general QOL with those of other cancer patients and the 15 vulvar cancer specific items give some indication of QOL concerns specific to patients treated for cancer of the vulva. The internal consistency of the VCS was found to be good and FACT-G scores were comparable to those observed within other samples of cancer patients in earlier studies [16,17,19]. For example, a mean FACT-G summary score of 88.8 has been reported for a group of breast cancer patients [17], which is very similar to the score of 88.3 observed within the cross sectional sample of vulvar cancer patients in this study.

The VCS as well as the FACT-V successfully separated patients on the basis of self-reported ECOG performance status. For FIGO stage, the physical well-being subscale, the VCS, the FACT-G and the FACT-V discriminated between patients. Patients who were treated for recurrent disease had significantly lower functional well-being and VCS scores, as well as FACT-V scores, compared to patients treated for primary vulvar cancer. These results indicate that the FACT-V is of value as a measure of QOL in vulvar cancer patients. *However, the number of patients with less favorable stages at diagnosis or recurrent disease in the present sample was small and further studies are needed to more precisely estimate the impact of advanced stage on patients' QOL.*

Previous studies suggested that older women might have better QOL compared to younger women, and that younger women experience significant reductions in their sexual well-being [13,15,24]. While we could not confirm a difference between older and younger patients in overall QOL, a significantly higher number of patients younger than 65 years compared to patients older than 65 years answered the questions regarding sexuality. This indicates that sexual well-being is an important topic for patients less than 65 years of age. Eighty percent of patients older than 65 years used the tick box 'I prefer not to answer the questions regarding sexuality' provided on the FACT-G and opted not to answer these questions. By offering this choice the FACT allows patients to retain their privacy with regards to sexual functioning. In interviews, some patients expressed disapproval of such questions be added to a questionnaire and these women recommended a personal discussion between patient and doctor as more suitable alternative [15].

The strong association between the HADS-A and the emotional functioning subscale of the FACT-G as well as with the VCS supports its convergent and divergent validity. In contrast, the HADS-D was more strongly associated with the functional and physical well-being subscales of the FACT-G. This might indicate that declining functional well-being may increase the likelihood of depression. Overall, 21.8% of patients within the present sample scored above the cut-off level of 11 for severe anxiety and 6.3% for depression. Earlier, in a sample of patients with cervical and vulvar cancer, Corney et al [12], observed 21% of the patients to be anxious and 14% to be depressed. Within a sample of 41 vulvar cancer patients a prevalence of 30% depressed patients was reported using the Prime-MD screening test [13].

Using the Symptom Checklist-90 questionnaire, Anderson and Hacker [11] reported a level of emotional distress at the 88 percentile in fifteen patients who had radical vulvar surgery. In summary, vulvar cancer patients seem to experience significant anxiety, depression and emotional distress but it is still unclear if and which type of intervention may benefit these patients.

FACT-V subscale scores were sensitive to changes in patients' self-reported performance status. Overall, patients mean VCS scores improved significantly from before surgery to 8 weeks after surgery. When compared to scores before the operation, a decrease in performance status was associated with a slight decline in VCS scores. In contrast, VCS scores improved in patients who reported improved or stable performance status. This might indicate that vulvar cancer specific concerns, such as irritating itching, discharge and bleeding or the fear about consequences of treatment had a greater effect on patients self-reported performance status before than after surgery (Table 2). It could however also indicate that the VCS might be more sensitive to improvements in vulvar cancer specific well-being rather than to declines and that additional items sensitive to declines may need to be added in subsequent versions of the scale.

In summary, the FACT-V is a reliable and valid instrument to record QOL in women with vulvar cancer or undergoing radical vulvar surgery. The VCS can be used if a concise measure of vulvar specific concerns is needed or can be combined with the FACT-G to also address physical, emotional, social and functional well-being. As for all FACT scales, psychometric testing is ongoing and further improvements to the FACT-V will be made. The FACT-V in its recent form can be used as a short assessment tool of QOL in vulvar cancer clinical trials.

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