CHAPTER 8

MEASURING SOMATIC SYMPTOMS WITH THE CES-D TO ASSESS DEPRESSION IN CANCER PATIENTS AFTER TREATMENT, VALID OR NOT?

COMPARISON BETWEEN PATIENTS WITH HEAD AND NECK, GYNAECOLOGICAL, COLO-RECTAL, AND BREAST CANCER

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Summary
The prevalence of depression after cancer treatment is high. In literature several authors have raised questions about assessing somatic symptoms after cancer treatment to explore depression. They stated that the somatic sequela are a consequence of cancer treatment and are therefore causing the high depression rates in cancer patients. In this study we analysed the somatic domain on a depression questionnaire (CES-D) in cancer patients after treatment, in comparison with a control group, and we compared between cancer groups. Data of 566 cancer patients (head and neck, gynaecological, colo-rectal and breast cancer), and 255 randomly chosen control patients were analysed. The total score of the CES-D on the domain somatic retarded activity is significantly ($p < 0.01$) different for cancer groups and control group. But the cancer groups score lower (colo-rectal cancer) as well as higher (head and neck, breast) than the control group on the somatic domain. We conclude that cancer patients are not a homogenous group of patients concerning somatic sequela and therefore we can not find evidence to remove somatic items from depression questionnaires for patients after cancer treatment.
Introduction
Survival rates of several cancer types have become higher because of earlier detection and better treatment properties (Brenner, 2002). As a consequence more patients have to cope with the physical and emotional consequences of the diagnosis cancer and the side effects of the treatment. In the last decade more attention has been given to this group of patients. Important topics in post-treatment cancer research are quality of life (Aaronson et al., 1992), coping (Hassanein et al., 2001; Petticrew et al., 2002) depression (Hjerl et al., 2003; Krishnan et al., 2002) somatic morbidity (Saffold et al., 2000; van Wilgen et al., 2003), pain (Caraceni and Portenoy, 1999; Portenoy, 1992; Zaza and Baine, 2002) and fatigue (de Jong et al., 2002; Morrow et al., 2002). This research lead to a better understanding of the physical and emotional problems after cancer treatment, and as a consequence treatment programs have been developed, such as: rehabilitation programs (DeLisa, 2001), psycho-social interventions (Owen et al., 2001; Ronson and Body, 2002), pain management, (Portenoy and Lesage, 1999) and multidisciplinary programs (Van Weert, 2004).

An important outcome after cancer treatment is depression. The prevalence of depression after cancer treatment is about 24 % (range 1.5 % to 50%) (Mc Daniel et al., 1995). Depression affects quality of life, survival, length of hospital stay, and therapy compliance (Bottomley, 1998, Hjerl et al., 2003; Mc Daniel et al., 1995). It is therefore of clinical importance to recognise depression in the post-treatment phase.

According to the DSM IV a depressive episode is assumed if five (or more) out of nine symptoms (Table 1) are present, additionally the symptoms should be present during the same 2-week period and represent a change from previous functioning (American Psychiatric Association, 1994). Symptoms of a clinical depression in patients after cancer treatment can be assessed through a clinical interview, a (semi)standardised interview or a questionnaire. Questionnaires are used most frequently in cancer research.

The prevalence of depression in cancer patients is related to type of cancer, follow-up, medical illness, gender, and method of assessment (Beeber et al., 1998; Bottomley, 1998; Mc Daniel et al., 1995; Stommel et al., 1993). Several authors have suggested that the high prevalence of depression after cancer treatment is due to the fact that the somatic symptoms of depression are identical with the somatic symptoms caused by the cancer treatment.
(Beeber et al., 1998; Dugan et al., 1998; Krishnan et al., 2002; Visser and Smets, 1998). They state that somatic symptoms should not be measured when assessing depression in cancer patients. Some authors even removed somatic items from depression questionnaires when measuring cancer patients (Dugan et al., 1998; Visser and Smets, 1998). In the Hospital Anxiety and Depression Scale somatic symptoms are not added to the questionnaire (Zigmund and Snaith, 1983). Hard evidence for the hypothesis that somatic symptoms should be removed in a depression questionnaire when assessing cancer patients is virtually missing, although some studies have been performed to explore this hypothesis. In one of the studies, to explore the role of somatic items in cancer patients, the Zung self rating scale was divided into a questionnaire with and without somatic items. The outcome on the questionnaire with somatic items was about 5% higher. The authors stated that the Zung self rating scale has 5% more false-positive depressed cancer patients when somatic items are assessed (Dugan et al., 1998). After a factor analyses of the Zung Self Depression scale, Passik et al. stated that fatigue is the only somatic item that is typically considered to be a symptom of depression in cancer patients (Passik et al., 2000). While no relationship between depression and fatigue was found by Visser et al. They stated that fatigue is no valid criterion for depression if patients had received radiation therapy (Visser and Smets, 1998). After analysing a structured interview with cancer patients Akechi et al. described that eating disorders and concentration problems are strongly related to depression while sleep disorders and fatigue are not related to the depression but to the somatic sequela of cancer treatment (Akechi et al., 2003).

Several eating related side effects are described before (pain) and during radiotherapy (xerostomia, dysphagia, pain) in head and neck cancer patients, which may affect outcome on a depression questionnaire (Epstein et al., 2001; Sehlen et al., 2003).

From these performed studies no clear statement about the somatic items, in the assessment of depression in cancer patient, can be made. The statements about fatigue are even conflicting.

Aim of this study was to analyse the influence of somatic sequela on a depression questionnaire (CES-D) in cancer patients after treatment in comparison with a control group, and to analyse the different cancer types.

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Figure 1 DSM IV criteria for depression:

(1) depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others.
(2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
(3) significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
(4) insomnia or hypersomnia nearly every day
(5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
(6) fatigue or loss of energy nearly every day
(7) feelings of worthlessness or excessive or inappropriate guilt
(8) diminished ability to think or concentrate, or indecisiveness, nearly every day
(9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Furthermore:

B. The symptoms do not meet criteria for a mixed episode.
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).
E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterised by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

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Methods and material
The CES-D is a short self-report scale designed to measure depressive symptomatology (Radloff, 1977). The questionnaire is translated to Dutch and contains 20 items divided in four domains: somatic retarded activity (7 items), depressed affect (5 items), positive affect (4 items), and interpersonal affect (2 items) and two single items that complete the total score (Bouma et al., 1995; Hanewald, 1987). The total score ranges between 0 – 60, a score of 16 or higher indicates a depressed symptomatology. The CES-D is often assessed in patient with cancer. The psychometric properties of the CES-D in cancer patients are described by several authors. Hann et al. (1999) found an internal consistence of alpha .89 and the test-retest reliability was .51 (p < 0.001). The outcome in the validity analyses were all satisfactory. Concluded was that the CES-D is appropriate for the use on clinical psycho-social research (Hann et al., 1999). Although the relation with somatic symptoms in cancer patients was, on our knowledge, never investigated with the CES-D. In our study the CES-D was administered in patients at least a year after the first cancer treatment and in a control group. Patients with recurrence of the tumour were excluded. The control patients and patients after breast, colo-rectal and gynaecological cancer were obtained from the database of the Northern Centre for Health Care Research (NCG). The control group was matched for gender and age with the cancer group and lived in the same area as the patients with cancer. Patients with head and neck cancer were assessed in the University Hospital Groningen on the Department of oral and maxillofacial surgery, the Department of otorhinolaryngology head & neck surgery or on the Department of surgical oncology. The CES-D was assessed during a regular appointment on the out patients clinic. Patients received a letter, a week before their appointment in which the study was explained. The medical doctor asked the patients to participate. If patients were willing to participate an informed consent was signed, and the CES-D was filled out. For the statistical analyses SPSS 10.0 was used. Of the CES-D the total score, the somatic retarded activity score and the depressed affect score were analysed. Because the other domains, positive affect and interpersonal affect, were not relevant for this study these were not analysed.
An ANOVA multi-comparison between groups was performed for the control and cancer group on the domain somatic retarded activity. An ANOVA multi-comparison between groups with a Bonferroni post hoc analyses was performed for the control group and four cancer groups. A Kruskal-Wallis tests and median tests was performed. These ordinal tests were performed as control for the outcome on the ANOVA multi comparison tests because the outcomes on the CES-D are not normally divided data. Also regression analyses were performed of the CES-D total score, the somatic retarded activity score and the depressed affect score.

Table 1  Descriptive data of the control group and the cancer groups, and the number of patients at risk for depression according to the CES-D.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Breast cancer</th>
<th>Colo-rectal cancer</th>
<th>Gynaecological cancer</th>
<th>Head and neck cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>255</td>
<td>206</td>
<td>136</td>
<td>69</td>
<td>155</td>
</tr>
<tr>
<td>Female</td>
<td>68% (173)</td>
<td>99% (205)</td>
<td>44% (60)</td>
<td>100% (69)</td>
<td>33% (51)</td>
</tr>
<tr>
<td>Age mean (SD)</td>
<td>58 (15)</td>
<td>55 (13)</td>
<td>66 (12)</td>
<td>53 (16)</td>
<td>61 (12)</td>
</tr>
<tr>
<td>Surgery</td>
<td>-</td>
<td>99% (203)</td>
<td>100% (136)</td>
<td>96% (66)</td>
<td>100% (155)</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>-</td>
<td>55% (114)</td>
<td>10% (13)</td>
<td>45% (31)</td>
<td>69% (107)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>-</td>
<td>46% (94)</td>
<td>10% (13)</td>
<td>20% (14)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>* Patients at risk for depression</td>
<td>11% (28)</td>
<td>21% (43)</td>
<td>5% (7)</td>
<td>20% (14)</td>
<td>16% (25)</td>
</tr>
</tbody>
</table>

* Patients with a score of 16 or higher on the CES-D are at risk for depression.
Results
Data of 566 patients and of 255 randomly chosen control patients were analysed. The descriptive data are presented in Table 1. The breast and gynaecological patients were mainly females. The patients at risk for a possible depression according to the CES-D (score ≥16) are presented in Table 1.

In Table 2 the results of the ANOVA multi-comparison between groups are presented. The cancer group differs significantly from the control group on the domain somatic retarded activity, and depressed affect. The four cancer groups and control group were also significantly different on total score, somatic retarded activity, and depressed affect score (Table 2). The ANOVA with a post-hoc bonferroni analyses (Table 3) shows the differences between the control group and four cancer groups on the domain somatic retarded activity. The colo-rectal patients score significantly lower compared to the breast and head and neck patients. Because the outcomes on the CES-D are not normally divided, we performed a Kruskal-Wallis test to analyse the differences between the cancer groups and the control group. In the ranking of the Kruskal Wallis the colo-rectal patients scored the lowest on all outcome. Head and neck patients and breast patients scored highest for somatic retarded activity. The total score, the somatic retarded activity score and depressed affect score are significantly (p < 0.01) different for cancer groups and control group. This significant difference was also found after a median test. The outcome on the Kruskal Wallis test and the median test were similar to the outcome on the ANOVA multi comparison.
Table 2  Mean scores on the CES-D total, the domains somatic retarded activity (7 items), and depressed affect (5 items). Presented are the ANOVA multi comparison between groups (control – cancer) and an ANOVA multi comparison between groups for the control and four cancer types.

<table>
<thead>
<tr>
<th></th>
<th>CES-D Total</th>
<th>F</th>
<th>p</th>
<th>Somatic Retarded</th>
<th>F</th>
<th>p</th>
<th>Depressed affect</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>8.3 (6.4)</td>
<td>2.3 (2.6)</td>
<td>1.0 (1.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer group total</td>
<td>9.0 (8.5)</td>
<td>1.3 (.26)</td>
<td>3.0 (3.4)</td>
<td>7.5 (.006)</td>
<td>1.6 (2.5)</td>
<td>12.1 (.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>8.3 (6.4)</td>
<td>2.3 (2.6)</td>
<td>1.0 (1.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>10.5 (8.3)</td>
<td>3.3 (3.2)</td>
<td>1.9 (2.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colo-rectal</td>
<td>7.0 (6.7)</td>
<td>1.7 (2.4)</td>
<td>0.9 (1.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gynaecological</td>
<td>9.4 (9.6)</td>
<td>2.6 (3.5)</td>
<td>1.9 (3.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head and Neck</td>
<td>8.3 (8.9)</td>
<td>4.2 (.002)</td>
<td>3.8 (4.0)</td>
<td>8.7 (.000)</td>
<td>1.5 (2.4)</td>
<td>7.1 (.000)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3  An ANOVA multi-comparison with post-hoc analyses with a Bonferroni correction was performed for the four cancer types and the control group for the domain somatic retarded activity. In the cells the p values for the differences are shown.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Breast</th>
<th>Colo-rectal</th>
<th>Gynaecological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>.02</td>
<td>&lt; 0.01</td>
<td>1.0</td>
<td>.88</td>
</tr>
<tr>
<td>Colo-rectal</td>
<td>1.0</td>
<td>&lt; 0.01</td>
<td>.88</td>
<td>.20</td>
</tr>
<tr>
<td>Gynaecological</td>
<td>1.0</td>
<td>1.0</td>
<td>&lt; 0.01</td>
<td>.20</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>&lt; 0.01</td>
<td>1.0</td>
<td>&lt; 0.01</td>
<td>.20</td>
</tr>
</tbody>
</table>
In the regression analyses we estimated the mean CES-D total score, somatic retarded activity and depressed affect as dependent of the variables cancer types, age and gender (Table 4). Somatic retarded activity is related to breast cancer, and head and neck cancer as well as gender. Gender was related to all outcome. Colo-rectal cancer was excluded in all analyses.

**Table 4** Regression analyses for CES-D total, somatic retarded activity and depressed affect.
Significant data (p < 0.05) were entered.

<table>
<thead>
<tr>
<th></th>
<th>CES-D tot</th>
<th>Somatic retarded</th>
<th>Depressed affect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>1.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>8.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td></td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td>-0.9</td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td></td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Gynaecological</td>
<td></td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td></td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td>-0.9</td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td></td>
<td>1.6</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**
Cancer patients are not a homogeneous group of patients with respect to the outcome of the CES-D and the domains somatic retarded activity and depressed affect. In comparison with a control group cancer patients score lower (colo-rectal) as well as higher (breast, and head & neck) on the domain somatic retarded activity. Therefore removing somatic items in a depression questionnaire to assess cancer patients seems not valid. The
influence of gender is also in cancer patients important and strongly related to cancer type (Weissman et al., 1993).

We can assume that regarding to somatic sequela “the cancer patient” does not exist. Cancer patients have similarities, like everyone has to cope with a life threatening disease, interruption of normal daily life, and being exposed to treatments, but there are also differences like type of treatment, place of surgery and radiation therapy, the severity of the cancer, the extensiveness of the treatment and the extent of sacrificed structures. As a consequence the somatic morbidity after cancer treatments is different. Especially the place of the tumour seems important. For instance the surgical removal of a tumour of the tongue including removing of salivary glands, a neck dissection and radiation therapy of the neck, has more somatic consequences than removing the uterus or a part of colon without radiation therapy. These differences in treatment have consequences on somatic morbidity and probably also on the results on the somatic items assessed by a depression questionnaire.

In the analyses between the complete cancer group and the control group the hypothesis that somatic morbidity is affecting the prevalence of depression after cancer treatment seems true. In the multi comparison although only head and neck cancer and breast cancer score high on the somatic domain. Somatic morbidity might increase the prevalence of depression in these groups. This could implicate that in these groups the somatic domain or specific somatic items should be removed. This opportunity seems not valid, because we don’t know which specific items should be removed and removing all somatic items seems conflicting with the construction of depression.

Breast and gynaecological patients are mainly women, the female gender has an important impact on the CES-D total scores. The percentages of patients at risk for depression are the highest in these two patient groups. Also the scores on depressed affect are the highest in these two groups. Head and neck patients score significantly higher on the somatic retarded activity domain. Patients with head and neck cancer often have to undergo extensive surgery. This might contain sacrificing part of the glottis, removing salivary glands, removing the upper trachea (getting a tracheostoma), or removing a part of the mandibula possible restored with part of the fibula bone. These extensive operation seem to clarify the high somatic morbidity rates.
The use of questionnaires to assess depression in the medical setting seems valuable because of the high prevalence of depression. Physicians are not well trained in recognising depressions (Passik et al., 2000), therefore a questionnaire can be a helpful tool to explore a possible depression during the medical follow up. If patients score high on a CES-D a referral to a psychologist, social worker or a peer group must be considered to the patient. If a score is around 16 the physician should further explore the patient by asking specific questions that focus on a depressed mood.

References


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