THE DISTRESS THERMOMETER FOR DISTRESS SCREENING IN PATIENTS WITH FEMALE CANCER:

IMPLICATIONS FOR CLINICAL PRACTICE

FLOOR PLOOS VAN AMSTEL

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Floor Ploos van Amstel

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"Ineens is alles anders"

Rosemarie Jansen

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General introduction and outline of the thesis

General introduction and outline of the thesis

Cancer is the leading cause of death in the Netherlands. Over the last three decades the number of patients diagnosed with cancer in the Netherlands doubled, from respectively 56.000 in 1989 to 116.000 in 2018.[1] Due to improved treatments the overall survival, and consequently the number of cancer survivors, has improved significantly with an increase in 5 years survivors from 45% in 2000 to almost 60% in 2013.[2] At this moment, approximately 800.000 people have or had cancer in the Netherlands.[2] Cancer and its treatment can cause short-term side effects, for example nausea and hair loss. Moreover, they can cause long-term side effects, such as neuropathy or lymph edema. In addition, cancer and its treatment can have psychosocial consequences, such as fatigue, anxiety and fear of recurrence, and an unknown percentage of patients experience practical problems, such as difficulties in returning back to work or insurance problems, resulting in financial problems.[3] All these issues may lead to *distress.*

Distress

'Distress is a multifactorial unpleasant experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis.'[4]

Receiving a cancer diagnosis by itself is a major stressor in someone's life. According to Lazarus and Folkman's psychological stress and coping theory, the way patients cope with a new health situation depends on the appraisal of the threat posed by this (health) situation. The difference in coping strategies is driven by primary and secondary appraisal of the situation. The primary appraisal depends on the level of seriousness, harmfulness and/or challenge of the diagnosis. Three levels of reactions are distinguished among patients: negative, neutral and positive. The distress increases with the level of threat. The secondary appraisal depends on the resources available to the patient, which will determine how the patient is able to cope with the new health situation.[5] Ultimately the patient's full reaction to the stressor cancer is the result of the accumulated primary and secondary appraisal, as well as her/his personal and demographic characteristics, such as age, gender, origin, personality traits and social environment.[5] Experiencing distress could have serious implications, as it is a potential risk factor for poorer *quality of life* and non-adherence to treatment.[4]

Quality of Life

'An individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment'.[6]

Patients with cancer may perceive distress after diagnosis, during treatment and also after treatment. In addition, distress often varies through the cancer treatment trajectory and problems may remain for months or even years after diagnosis.[7-10] Patients may expect to return smoothly to their former life. However, after end of treatment patients often start to reflect on the period of diagnosis and treatment. This so-called re-entry phase can be a time of disruption and increased distress.[11-14] Patients struggle with questions how to manage the (long-term) consequences, such as the changes of their body, the fear of recurrence and changed relationships with family and friends. Therefore, the period after treatment can be marked by elevated distress levels.[7,10,13] For survivors, who have to deal with short and long-term side effects of cancer and its treatment, timely attention to quality of life is of crucial importance.[15] To ensure that distress management becomes routine part of cancer care, the National Comprehensive Cancer Network (NCCN) defined distress as the 'sixth vital sign'.[16] Early detection and treatment of distress could counteract these negative consequences and may also lead to better communication between patient and professional and to fewer calls and visits to the hospital.[4] Consequently, this results in less demand of care. Therefore, it seems important to screen for distress in patients with cancer.

Screening for distress

There are many validated self-report screening tools available to detect distress in patients with cancer.[17,18] In their review Carlson and colleagues described several tools that were used in studies to screen for distress. Examples of screening tools to identify distress are the Brief Symptom Inventory-18 (BSI-18), General Health Questionnaire (GHQ), Distress Thermometer (DT) (including problem list) and Screening Inventory of Psychosocial Problems (SIPP).[17] The BSI-18 and GHQ aim to screen only for psychologic distress and/or psychiatric disorders. The DT and SIPP focus more on psychosocial problems (physical and emotional) and global distress. A common characteristic of short distress tools (like the DT) is that they have high negative predictive value and lower positive predictive value. Therefore, one cannot rely on the distress screening tool alone and an additional conversation with a healthcare professional is needed.[4,18,19] Worldwide, the most recommended screening tool for distress is the DT, developed by the NCCN.[4]

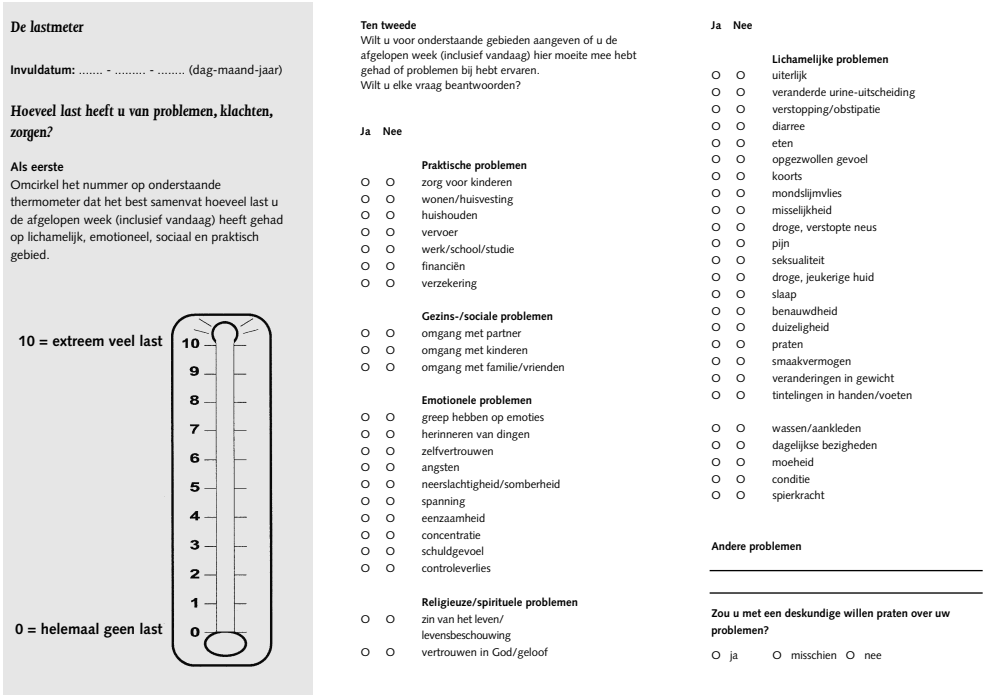
Guidelines for distress screening

In 1999, the NCCN published the first guideline about screening for distress in patients with cancer.[4] They developed the DT as a short screening instrument for distress. On a thermometer, patients score their distress on a visual analog scale (0 = no distress; 10 = extreme distress) and a problem list. Since then, the NCCN DT has been translated and validated into different languages and in different cancer populations.[20] In the Netherlands, a Dutch distress management guideline "detection of need for psychosocial care" has been developed by different psychosocial cancer professionals in 2010.[3] They have established requirements to which a distress screening instrument must comply. According to them, the instrument must (1) measure distress in a general sense, (2) be suitable for all cancer types, (3) be intended for adults, (4) be reliable and valid, (5) feature a cuttoff point, (6) be manageable in daily practice and (7) be available in the Dutch language. They concluded that the DT (including the problem list and referral question) is most suitable to screen distress.[3] This is consistent with the NCCN guideline, which also advises to implement the DT in daily oncology practice.[4] The Dutch DT has been validated with a cuttoff score of 5. The problem list contains 47 problems and concludes with an extra question: 'would you like to talk about the problems with a professional' (yes, maybe or no).[21] Notably, the DT has been validated with different cuttoff scores in different countries, which is the result of language, culture and cancer population. A cuttoff score is necessary to make a distinction between patients with and without distress. Most frequently a cuttoff score of 4 or 5 is recommended for use in daily oncology practice.[4] In some studies, a cuttoff score of 7 is used as extreme distress.[22,23] Following the Dutch distress guideline, screening for distress should be carried out shortly after cancer diagnosis and after each treatment modality, and at fixed time points during follow-up.[3] From the literature and experience in daily practice, we know that most patients experience higher levels of distress shortly after diagnosis than during follow-up.[7,24] This raises the question as to whether one general cuttoff score is appropriate to detect distress at different time points, for example shortly after diagnosis, when high levels of distress can be expected. In research, the DT has been used mainly to measure the impact or incidence of distress or as part of an intervention.[10,21-23,25,26] Although the recommendation was to implement the DT in daily practice, studies with evidence by (longitudinally) randomized controlled trials are scarce. The lack of efficiency of using the DT in daily oncology practice makes implementing the DT in daily practice a challenge. Therefore, more studies are needed about the effectiveness of the use of the DT. Figure 1 shows the Dutch DT.

Distress and the role of the (oncology) nurse

The results of the DT serve as a tool for the conversation between professional and the patient. It is not well-defined which healthcare professional should discuss the DT with the patient. However, in daily practice it is usually a task of oncology nurses who have the skills, time and competences to focus on the identification of multiple needs of patients.[27] Galway et al. support this in their review, in which

they conclude that nurse-delivered interventions on psychosocial aspects can positively affect quality of life.[28] According to them, an advantage of nurses offering psychosocial support is that no stigma of mental disorder is attached, as opposed to support provided by psychological services.[28] A training in the nurse-led DT intervention and communication skills is necessary.[29] Besides that, it must be clear what the nurse should do with the issues that the patients experience and how to act on that, particularly when a referral to another professional is indicated.



De lastmeter

Invuldatum: ..... - ..... - ..... (dag-maand-jaar)

Hoeveel last heeft u van problemen, klachten, zorgen?

Als eerste
Omcirkel het nummer op onderstaande thermometer dat het best samenvat hoeveel last u de afgelopen week (inclusief vandaag) heeft gehad op lichamelijk, emotioneel, sociaal en praktisch gebied.

10 = extreem veel last
0 = helemaal geen last
10 9 8 7 6 5 4 3 2 1 0

Ten tweede
Wilt u voor onderstaande gebieden aangeven of u de afgelopen week (inclusief vandaag) hier moeite mee hebt gehad of problemen bij hebt ervaren.
Wilt u elke vraag beantwoorden?

Ja	Nee	
		Praktische problemen
O	O	zorg voor kinderen
O	O	wonen/huisvesting
O	O	huishouden
O	O	vervoer
O	O	werk/school/studie
O	O	financiën
O	O	verzekering
		Gezins-/sociale problemen
O	O	omgang met partner
O	O	omgang met kinderen
O	O	omgang met familie/vrienden
		Emotionele problemen
O	O	greep hebben op emoties
O	O	herinneren van dingen
O	O	zelfvertrouwen
O	O	angsten
O	O	neerslachtigheid/somberheid
O	O	spanning
O	O	eenzaamheid
O	O	concentratie
O	O	schuldgevoel
O	O	controleverlies
		Religieuze/spirituele problemen
O	O	zin van het leven/ levensbeschouwing
O	O	vertrouwen in God/geloof

Ja	Nee	
		Lichamelijke problemen
O	O	uiterlijk
O	O	veranderde urine-uitscheiding
O	O	verstopping/obstipatie
O	O	diarree
O	O	eten
O	O	opgezwollen gevoel
O	O	koorts
O	O	mondslijmvlies
O	O	misselijkheid
O	O	droge, verstopte neus
O	O	pijn
O	O	seksualiteit
O	O	droge, jeukerige huid
O	O	slaap
O	O	benauwdheid
O	O	duizeligheid
O	O	praten
O	O	smaakvermogen
O	O	veranderingen in gewicht
O	O	tintelingen in handen/voeten
O	O	wassen/aankleden
O	O	dagelijkse bezigheden
O	O	moeheid
O	O	conditie
O	O	spierkracht

Andere problemen

Zou u met een deskundige willen praten over uw problemen?

O ja O misschien O nee

Figure 1 The Distress Thermometer (Dutch version).

Distress in breast cancer patients

With an incidence of 14.882 breast cancer patients in 2018, breast cancer is the most common cancer in women in the Netherlands, affecting one in seven adult females.[1] Even though the probability of survival is relatively high for breast cancer, studies have shown that the disease and its treatment can have a significant long-term impact on a person's life.[8,11] Treatment for breast cancer varies, and may consist of surgery, radiotherapy, chemotherapy, targeted therapy and/or hormonal therapy and often a combination of these. Each of these treatments have their specific treatment-related side effects, which are sometimes temporarily, but may also persist. Some research has already shown increased

levels of distress in breast cancer patients shortly after diagnosis, during active treatment, but also until approximately 4 years after treatment.[7,8,10,22,23,30] A longitudinal nationwide study in the Netherlands showed that one in five patients with breast cancer reported clinical distress (DT ≥ 5) at 6 and 15 months after diagnosis.[31] Predictors of distress in female breast cancer survivors, defined as women who have finished primary treatment with curative intent, are advanced cancer at diagnosis and treatment with chemotherapy, longer primary treatment duration and a more recent transition into survivorship.[32] Treatment-related symptoms associated with distress included (post)menopausal symptoms, pain, fatigue, and sleep disturbance. Lower socioeconomic status, younger age, non-Caucasian ethnicity or being unmarried were sociodemographic characteristics that increased distress.[32] Often other questionnaires instead of the DT were used to measure distress.[17,18] In 2009, at the start of this thesis, there were no studies using the DT to measure the prevalence of distress in breast cancer survivors in the Netherlands.

Distress in ovarian cancer patients

Globally, ovarian cancer is the seventh most common cancer in women, the eight most common cause of cancer death, and most common cause of gynecological cancer death.[33,34] In 2018, 1417 women were diagnosed with ovarian cancer in the Netherlands.[1] Most ovarian cancer patients are diagnosed at an advanced stage and prognosis is poor with a five year survival rate of 25- 35%. Ovarian cancer survivors and recurrent ovarian cancer patients experience high levels of distress, depression and anxiety, which is associated with poorer quality of life.[35,36] Younger ovarian cancer survivors are likely to suffer from greater distress and lower quality of life compared to older ovarian cancer survivors.[35] Despite the impact of ovarian cancer, there is only a limited number of studies on psychosocial problems and the distress (measured with the DT) patients are experiencing. This might be explained by the lower incidence of ovarian cancer, in contrast with breast cancer. It is unclear whether the disease status of ovarian cancer patients influences distress and quality of life. Therefore, it is of special interest to know whether in the approach and support of ovarian cancer patients in daily clinical practice a distinction should be made between patients with and without recurrence of ovarian cancer.

Outline of the thesis

The aim of this thesis is to investigate distress in patients with breast and ovarian cancer. In each study the DT will be used as an instrument to measure distress. In **Chapter 2** we will assess the different parts of the DT in breast cancer survivors. We will explore the prevalence of distress and the relationship between reported distress and demographic, treatment and psychosocial variables. In **Chapter 3** the focus is on patients with ovarian cancer. In a cross-sectional study we will assess if the self-reported distress, severity, experienced problems and, furthermore, quality of life is correlated with the disease status of the patients. In **Chapter 4** we will discuss whether a specific cuttoff score should be used shortly after breast cancer diagnosis. The cuttoff score of 5 is generally used for distress screening. High levels of distress are expected shortly after the diagnosis of breast cancer. Therefore, we will establish the optimal DT cuttoff score for detecting high distress, shortly after breast cancer diagnosis and to correlate this score with the reported problems.

Despite the high number of studies on the DT worldwide, assuming the added value of this instrument, there is no evidence that patients' quality of life improves by using the DT in daily oncology practice. This was the reason to design and perform a randomized controlled trial to assess the effectiveness of a nurse-led intervention with the DT on the quality of life of breast cancer patients treated with curative intent. In **Chapter 5** the design is described of this randomized controlled trial on the effectiveness of a nurse-led intervention with the distress thermometer for patients with primary breast cancer treated with curative intent. In **Chapter 6** the results are described of the nurse-led DT intervention trial on quality of life at two years after the end of treatment. **Chapter 7** describes the summary of the thesis and **Chapter 8** comprises a general discussion of the thesis, supplemented by lessons learned from the use of the DT in routine oncological care and suggestions are made for further research.

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2

Distress screening remains important during follow-up after primary breast cancer treatment

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Abstract

Background

To improve psychosocial care, the National Comprehensive Cancer Network recommends the use of the Distress Thermometer (DT) to detect distress among cancer patients.

Objectives

The objectives of this study were to describe the prevalence of distress in breast cancer survivors (BCSs) and to investigate demographic, treatment, and psychosocial variables associated with distress and problems most often reported on the problem list. Moreover, we assessed how many BCSs requested referral to a professional for additional support.

Methods

In a cross-sectional study, 258 BCSs identified at an outpatient clinic of a university hospital were asked to complete the following questionnaires: DT, Quality of Life Questionnaire, Hospital Anxiety and Depression Scale, and Illness Cognition Questionnaire.

Results

Of the 258 identified BCSs, 129 (50%) completed all questionnaires. After a mean follow-up period of 5.6 (SD 10) years, 47 (36%) of these 129 BCSs experienced distress as assessed by the DT. BCSs experienced significantly more distress in the first 2 years than in the period between 2 and 5 years after surgery. Also, more distress was experienced in BCSs treated with surgery, radiotherapy, and chemotherapy compared to those treated with surgery only. Problems most frequently encountered were fatigue (57%), decrease in muscle strength (47%), and lack of physical fitness (42%). Thirty one (69%) of the distressed BCSs requested or considered referral to a professional. Regression analysis showed that reduced quality of life, reduced cognitive function, and fatigue were predictors of distress.

Conclusion

The current study found that more than one third of all BCSs experienced distress. Screening remains an important part of BCSs' care. The professional should be aware of the potential problems and distress patients may experience.

Introduction

Breast cancer is the most common type of cancer among women in western society.[1] In 2008, the incidence was 1.38 million new cases globally.[1] In the Netherlands, the incidence of breast cancer in 2009 was approximately 13.000. At the end of 2020, it is expected that the incidence of breast cancer will increase to almost 18.000 in this country.[2] The probability of survival has risen in the Netherlands in recent years due to screening and new treatment modalities.[2] Even though the probability of survival is relatively high, breast cancer has a significant long-term impact on a person's life both during and after treatment.[3] Today, most patients with breast cancer undergo surgery and/or radiotherapy, chemotherapy, hormonal therapy, and sometimes targeted therapy (trastuzumab). Each treatment has specific treatment-related side effects, some temporarily and some lingering, such as loss of energy, tiredness, pain, change in sexuality, and infertility problems.[4-6] Besides having to deal with potential long-term treatment-related physical problems, breast cancer survivors (BCSs) may also experience emotional, social, and practical difficulties. Common emotional problems among survivors include coping with the cancer diagnosis and fear of recurrence, issues such as "loss of control" of their life, increased health worries, anxiety, or depression.[7-9] Social problems can develop if family and friends do not know how to deal with cancer and subsequently cannot support the patient.[8] Practical problems are seen for instance with work and health insurance.[10,11]

Distress

The overall burden of cancer diagnosis and treatment is referred to as distress, which is defined by the National Comprehensive Cancer Network (NCCN) as follows:

> *Distress is a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment.*[12]

According to the stress-coping model of Lazarus and Folkman, distress arises when the appraisal of the threats (in this case, breast cancer) outweighs the resources of the patient.[13] If distress arises, this can have a negative impact on quality of life and speed of recovery after treatment.[14-16] Particularly in the first year after diagnosis, anxiety and depression are common psychological problems.[17] Emotional problems such as anxiety and depression may influence the experience of short-and long-term side effects of cancer and its treatment. Evers et al. mentioned that illness cognitions are an important mediator between the disease and patients' well-being and that the way patients perceive and think about their disease accounts for many of the individual differences in their physical and psychological health status.[18] After treatment concludes, it is assumed that patients will return to their former lives. However, in this period, reflection on the diagnosis and treatment often influences psychosocial recovery.[9,19] Patients struggle with questions as how to manage (long-term) side effects, changes of their body image, fear of recurrence, and the altered relationships with family and friends.[7-9]

Each of these aspects influence the quality of life and could result in distress.[7,9,20] Prior research has demonstrated increased levels of distress in cancer patients after diagnosis, during active treatment, and until approximately 4 years after treatment.[9,20-23]

The NCCN guideline for distress management recommends screening of all cancer patients on distress with the Distress Thermometer (DT).[12] The DT is a short self-report measure assessing distress and problems encountered in the domains of emotional, practical, physical, spiritual, and social functioning. The DT has been tested and validated in patients with different types of cancer and treatments.[12,24-30] The Dutch DT has been validated for cancer patients with different diagnoses and treatments and is recommended in the Dutch guideline "detection of need for psychosocial care" to screen non-hospitalized patients on distress.[25,31] The goal of this study is to describe the prevalence of distress in BCSs measured with the thermometer. We investigated which problems on the problem list were reported most frequently and whether distressed BCSs request referral to a professional. In addition, we wanted to investigate which demographic, treatment, and psychosocial variables are associated with distress. We expected that BCSs with distress would report lower quality of life, more anxiety and depression, and reduced illness cognitions.

Methods

Study type

A cross-sectional study was conducted in July 2009.

Participants

Participants of this study were treated for breast cancer at the Radboud university medical center in the Netherlands. In order to be eligible, patients should have been treated with curative intent and finished their primary treatment. Adjuvant hormonal therapy or trastuzumab was permitted, and the participants needed to be free of local recurrence or distant metastases at the time of participation. In addition, participants had to be able to read and write in Dutch. The collected demographic variables were: age, marital status, educational level, and employment status. Treatment variables collected by self-report were: surgery, radiotherapy, chemotherapy, hormonal therapy, trastuzumab, and the date of primary surgery. All treatment regimens were described in the questionnaire, and the patient marked the treatment received.

Recruitment

Self-report questionnaires were sent to 258 eligible BCSs. An accompanying letter explained the goal of the study. The questionnaires were filled out anonymously. Returning the questionnaire implied informed consent to participate. After 2 months, a reminder was sent to all eligible BCSs.

Instruments

Distress Thermometer

The Distress Thermometer (DT) consists of three parts, namely a thermometer, a problem list, and a question about referral. The thermometer requires the participants to identify the level of distress they experienced in the past week, including the day of the screening. Patients indicate on a scale of 0 (no distress) to 10 (extreme distress) how they feel. A cutoff point of five and above yields the best sensitivity and specificity for having distress.[25] The DT has a good internal consistency and reliability ($\alpha = 0.90$). The problem list investigated whether the indicated level of distress is related to physical, familial/social, psychological, practical needs or spiritual domains and lists 47 problems. The Dutch version has one extra question: "Would you like to talk with a professional about your problems?" [25]

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) is a 14-item, self-report measure of psychological distress.[32,33] The HADS is widely used in cancer patients and is an accepted measurement in the medical setting. The HADS has two subscales (anxiety and depression), each ranging from 0 to 21, and a total score. Each item is rated on a scale from 0 (not at all) to 3 (very much). Higher scores imply more anxiety or depression, and more psychological distress. The scale has been translated and validated for the Dutch population ($\alpha = 0.84–0.90$).[34]

EORTC QLQ-C30 version 2.0 and EORTC QLQ-BR23

The European Organization for Research and Treatment of Cancer Quality of Life (EORTC) QLQ-C30 questionnaire was developed to assess the quality of life of patients with cancer.[35] It consists of 30 statements divided into five functional scales (physical, role functioning, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea/vomiting), six single symptom items (dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties), and a general quality of life scale. The items of the global quality of life scale use a 7-point linear analog scale (very poor to excellent). All other items are scored on a 4-point scale from 1 (not at all) to 4 (very much). The scoring is from 0 to 100. For the functional and general score, this means higher scores correspond with a better level of functioning. However, for the symptom scales, higher scores correspond with more severe symptoms ($\alpha = 0.82$).[35,36] The EORTC QLQ-BR23 is a breast cancer-specific self-report questionnaire consisting of 23 items and is complementary to the QLQ-C30 ($\alpha = 0.57–0.89$).[37] Questions address breast cancer treatment-specific problems, like physical and emotional problems, sexual function, and arm and/or shoulder problems. Because chemotherapy and hormonal treatments may result in additional side effects, two items of the ovarian (OV) EORTC QLQ version were added (abnormal blood loss and vaginal dryness).[38]

Illness Cognition Questionnaire

The Illness Cognition Questionnaire (ICQ) measures three different cognitions: helplessness (a way of emphasizing the aversive meaning of the disease, six items), acceptance (a way to diminish the aversive meaning, six items), and perceived benefits (a way of adding positive meaning to the disease, six items). The ICQ was developed to measure how people ascribe meaning to their chronic illness.[18,39] The items can be scored between 1 (not agree) and 4 (totally agree). A higher score on a subscale of helplessness represents a higher degree of helplessness; a higher score on the other subscales means better acceptance and more perceived benefits. This questionnaire has a good internal consistency (0.84–0.91) and test–retest reliability.[18,39]

Ethics

The ethical committee of the hospital approved the study.

Statistical analysis

Based on clinical experience and the Dutch breast cancer guideline, we divided the total group into three follow-up periods.[40] BCSs frequently visit their physician during the first 2 years following diagnosis. In this phase, BCSs are recovering from treatment and try to return to their normal lives. Moreover, patients know that in the first 2 years following diagnosis, they are at the highest risk for recurrence and therefore these patients might need more psychosocial support in this period. During the second period (> 2 to ≤ 5 years), most of the patients return to normal life, but a substantial majority have to deal with the side effects of treatment (for example hormonal therapy). In this phase, the patient has to visit the physician once or twice a year. In the third period (> 5 years), BCSs have usually finished all cancer-related therapy. They only have yearly mammography, and many return to the national breast screening program. We assume, therefore, that distress can be different in these three periods. We compared the reported distress with demographic variables (age, marital status, educational level, and employment) and treatment variables (type of treatment and time since first primary surgery) and the used instruments. Data analysis was performed using SPSS version 16. Descriptive statistics were used for demographic and treatment variables. An independent sample t-test was performed to measure differences between mean distress and the variables age (subcategorized in < 55 and ≥ 55 years to distinguish pre- and postmenopausal women[41]), marital status (married/cohabiting and living alone), and employment (paid and unpaid work). The chi-square test was used to discover differences between distressed BCSs and non-distressed BCSs in relation to the demographic and treatment variables. A chi-square test was also performed for time since surgery (0 to ≤ 2, > 2 to ≤ 5, and > 5 years) in relation to the experienced problems on the problem list. We performed an ANOVA with distress as dependent variable and treatment modalities and time since first primary surgery as fixed factors (conducted separately). When a significant difference ($p < 0.05$) was found, Bonferonni post hoc test was used to compare the different groups. Distress was defined as DT score ≥ 5.[25] Pearson correlations were used

to investigate the association between the total distress score and the subscale scores of the additional questionnaires. For each questionnaire, we performed an explorative linear multivariate analysis (enter method) to assess which subscale of that questionnaire (predictor) was most strongly associated with the distress score (the dependent variable), when adjusting for the other subscales in that questionnaire. The available number of participants limited the number of the independent variables that we could include in the multivariate analysis.[42] As our study involved 129 participants, we could enter a maximum of nine independent variables in each explorative multivariate analysis. Therefore, the functional items and the symptom items of the EORTC QLQ-C30 questionnaire were investigated separately. All subscales significant in the first regression analysis were included in a second regression analysis (enter method). In this way, we assessed which of the subscales were most strongly associated with distress, when adjusting for the other subscales of the different questionnaires.

Results

Response

Two hundred and fifty-eight BCSs were contacted for this study. Between July and November 2009, 150 questionnaires were returned, and after a reminder, we received another five questionnaires (total response rate of 60%). Twenty-six questionnaires were excluded since the date of surgery and/or the thermometer was not filled in. Therefore, 129 (50%) BCSs had complete data available for analysis.

Demographic and treatment variables

Demographic and treatment characteristics are listed in Table 1. Mean age (N = 129) was 57 (SD 10) years. One hundred-two BCSs (79%) were married or cohabiting, and 114 (88%) had children. Mean time since primary surgery was 5.6 years (SD 4.7). Thirteen BCSs (10%) underwent surgery only, and 48 (37%) were still treated with hormonal therapy at the time of participation in this study.

Prevalence of distress in BCSs and the relationship between distress, demographic, and treatment variables

The mean score on the DT of the total group was 3.82 (SD 2.6). Distress (DT ≥ 5) was present in 47 BCSs (36%). There was no significant relation in mean distress scores and the demographic variables. Mean distress scores and prevalence of distress in relation to treatment modalities and time since primary surgery are presented in Table 2. BCSs who underwent surgery only experienced significantly less distress compared with survivors who received a combination of surgery, radiotherapy, and chemotherapy (0 versus 45%) ($p < 0.05$). BCSs were significantly more distressed in the first 2 years after primary surgery than BCSs who underwent primary surgery between 2 and 5 years ago ($p < 0.05$).

Table 1 Demographic and treatment variables of study participants (N = 129).

	Breast cancer survivors (%)
Age, mean (SD) in years	57 (10)
Marital status	
Married/cohabiting	102 (79)
Divorced	10 (8)
Widowed	10 (8)
Living independently	7 (5)
Educational level	
Primary school	4 (3)
Lower vocational	22 (17)
Secondary school	21 (16)
Secondary vocational	23 (18)
Higher general	9 (7)
Higher vocational	34 (26)
University	16 (13)
Employment*	
Paid work	58 (45)
Voluntary work	4 (3)
Housewife	31 (24)
Sick leave	10 (8)
Disability insurance	16 (12)
Retirement	22 (17)
Time elapsed since surgery, mean (SD) in years	5.6 (4.7)
Treatment	
Surgery	13 (10)
Surgery and RT	14 (11)
Surgery and CT	37 (29)
Surgery, RT and CT	65 (50)
Hormonal therapy	
Active treatment	48 (37)
Past	14 (11)
Trastuzumab	
Active treatment	3 (2)
Past	4 (3)

Abbreviations: RT = radiotherapy, CT = chemotherapy.

* Percentages do not add up to 100% because more options are possible.

Relation of distress with anxiety, depression, illness cognitions, and/or decreased quality of life

Comparisons between distressed and non-distressed BCSs are shown in Table 3. All subscale scores of the HADS, ICQ, and functional scales of the EORTC QLQ-C30 differed significantly between distressed and non-distressed BCSs. These subscales correlated significantly with level of distress. The function scales sex function and sex enjoyment (BR23) and symptom scales constipation and nausea (QLQ-C30), hair loss (BR23) and OV questions were not significantly different for patients with or without distress. The explorative regression analysis indicated that in total, eight subscales (anxiety, depression, disease benefits, helplessness, cognitive function, quality of life, diarrhea, and fatigue) were significantly related to the degree of distress. The second linear regression showed that impaired quality of life ($p < 0.017$), cognitive function ($p < 0.041$), and fatigue ($p < 0.018$) were predictive of the level of distress (total $R^2 = 0.571$).

Table 2 Mean and prevalence distress in time since primary surgery and treatment modalities.

	N	Distress	
		Mean (SD)	n (%)
Time since primary surgery (years)			
0 to ≤ 2	25	5.0 (3.0)[a]	13 (52)
> 2 to ≤ 5	52	3.4 (2.5)[a]	16 (31)
> 5	52	3.7 (2.5)	18 (35)
Total	129	3.8 (2.6)	47 (36)
Type of treatment			
Surgery only	13	2.1 (1.3)	0 (0)[b]
Surgery and RT	14	2.7 (2.0)	3 (21)
Surgery and CT	37	3.7 (2.6)	15 (41)
Surgery, RT and CT	65	4.4 (2.7)	29 (45)[b]
Total	129	3.8 (2.6)	47 (36)

Abbreviations: RT = radiotherapy, CT = chemotherapy.

[a] ANOVA, Bonferonni test: ($p < 0.05$), 0 to ≤ 2 years vs > 2 to ≤ 5 years.

[b] Chi-square ($p < 0.05$), surgery only vs the combination of surgery, RT, and CT.

Most reported problems by BCSs on the problem list of the DT

BCSs with more distress also reported more problems on the problem list ($r = 0.714$; $p < 0.001$). The ten most frequently reported problems of the total group are shown in Figure 1; the number of problems between the distress and non-distress group differed significantly. However, the type of problems did not differ between distressed and non-distressed BCSs. The ten problems were part of the physical and emotional domains of the problem list. For all BCSs, distressed and non-distressed, fatigue was the most frequently reported problem after treatment (n = 73, 57%). In addition to problems listed in Figure 1, the non-distressed BCSs also mentioned the problems tingling in hands/feet (n = 21, 26%) and pain (n = 17, 21%).

The distressed group more frequently mentioned *housekeeping* (n = 24, 51%) as a problem compared to the non-distressed group. An explorative analysis found significant differences between time since surgery (three groups) and the problems: *work/school/study, emotional control, nervousness, loneliness, sleep, and muscle strength* (see Table 4). There was no correlation between the total number of problems experienced by BCSs and the time elapsed since first primary surgery (p = 0.14).

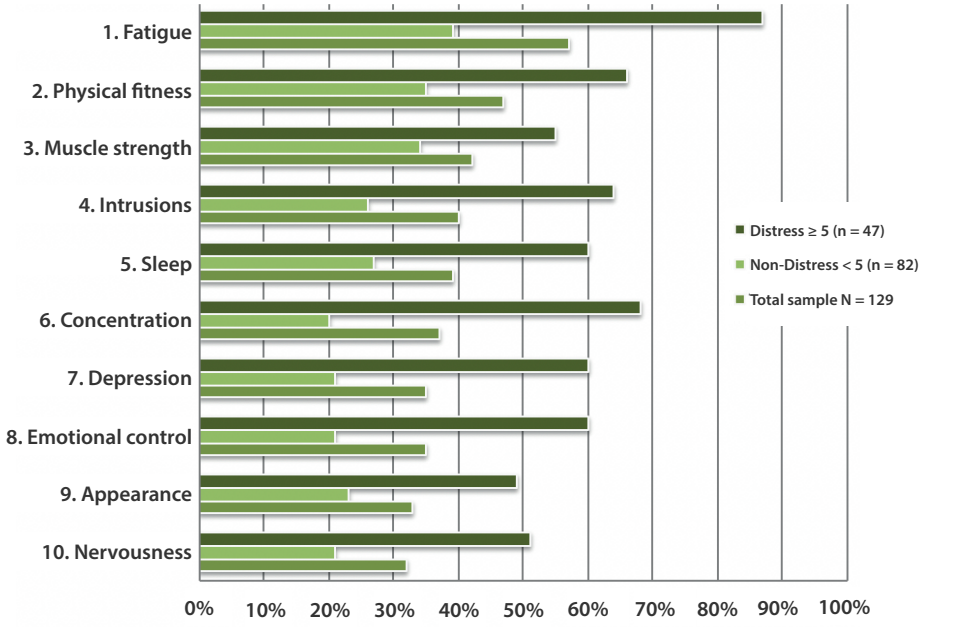

Figure 1 The top ten most reported problems by breast cancer survivors on the problem list ($p < 0.05$, between distress and non-distress).

Request for referral to a professional

Of all BCSs, three patients in this study left this part of the questionnaire unanswered. Six percent of the BCSs who reported no distress made a request for referral, 24% reported that they would consider a referral, and 70% reported they did not wish to be referred. Of the BCSs who were identified as distressed, 25% requested to be referred and 44% reported that they were considering a referral. BCSs who reported they would like a referral (DT mean score, 5.9) or would consider a referral (DT mean score, 4.6) had significantly ($p < 0.05$) more distress than BCSs who reported that they do not wish to be referred (DT mean score, 2.9).

Table 3 Comparisons between non-distressed (DT < 5) and distressed (DT ≥ 5) breast cancer survivors on anxiety, depression, illness cognitions, and quality of life.

	Non-distress mean (SD)	Distress mean (SD)	p value	Pearson's correlation
HADS (n = 128)				
HADS total	6.9 (4.8)	14.2 (8.3)	0.001	0.603[a]
Anxiety subscale	4.4 (3.0)	8.1 (4.8)	0.001	0.511[a]
Depression subscale	2.5 (2.5)	6.1 (4.4)	0.001	0.599[a]
ICQ (n = 127)				
Helplessness	7.6 (1.9)	11 (4.2)	0.001	0.551[a]
Acceptance	19.7 (3.3)	16.7 (4)	0.001	–0.427[a]
Disease benefits	18.0 (4.2)	15.2 (4.8)	0.001	–0.323[a]
EORTC QLQ-C30 function scales (n = 129)				
Cognitive	85.8 (18.7)	59.9 (31)	0.001	–0.512[a]
Emotional	86.4 (17.4)	63.5 (30.4)	0.001	–0.534[a]
Social	91.3 (15.1)	73.2 (27.8)	0.001	–0.519[a]
Physical	87.6 (14.4)	76 (15.8)	0.001	–0.424[a]
Role function	88.5 (17.6)	62.1 (32.4)	0.001	–0.548[a]
Quality of life	81.8 (12.8)	59.2 (19)	0.001	–0.670[a]
Symptom scales (n = 129)				
Financial difficulties	8.1 (18.6)	17.7 (26.8)	0.033	0.196[b]
Dyspnea	6.5 (19.2)	11.3 (18.7)	0.167	0.191[b]
Pain	14.8 (20.1)	32.6 (29.5)	0.001	0.411[a]
Fatigue	18.7 (17.8)	50.4 (26.8)	0.001	0.625[a]
Sleep	22 (27.8)	46.1 (35.1)	0.001	0.436[a]
Appetite loss	4.1 (11)	7.8 (15.9)	0.157	0.204[b]
Nausea/vomiting	1.8 (5.7)	5.7 (16.0)	0.119	0.108
Constipation	11.8 (21.1)	9.2 (15.1)	0.425	–0.003
Diarrhea	3.6 (12.4)	16.3 (13.2)	0.006	0.325[a]
EORTC QLQ-BR23 function scales				
Body image (n = 121)	82.9 (20)	67.6 (32.4)	0.006	–0.349[a]
Sex function (n =121)	25.8 (21)	20.5 (22.1)	0.183	–0.131
Sex enjoyment (n = 69)	53.1 (24.5)	48.3 (27.5)	0.485	–0.139
Future perspective (n =121)	71.9 (26.7)	50.4 (33)	0.001	–0.428[a]
Symptom scales				
Side effects (n = 124)	14.1 (14.4)	20.6 (23.6)	0.001	0.336[a]
Breast (n = 129)	12.7 (14.4)	20.6 (23.6)	0.042	0.298[a]
Arm (n = 129)	17.7 (18.5)	29.3 (24.3)	0.006	0.319[a]
Hair loss (n = 28)	25 (35.5)	33.3 (31.8)	0.526	0.009
EORTC OV questions				
Vaginal dryness (n =72)	2.2 (1.0)	2.1 (1.0)	0.485	–0.036
Abnormal blood loss (n =128)	1.0 (0)	1.0 (0)	0.929	–

Abbreviations: HADS = Hospital Anxiety and Depression Scale, ICQ = Illness Cognition Questionnaire, EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30, QLQ-BR23 = Quality of Life Questionnaire Breast Cancer 23, OV = Ovarian questions from the EORTC.

[a] Correlation is significant at the 0.01 level (two-tailed). [b] Correlation is significant at the 0.05 level (two-tailed).

Table 4 Reported problems by breast cancer survivors on the problem list of the DT and time since primary surgery.

	A 0 to ≤ 2 years (n = 25; mean age, 52)	**B** > 2 to ≤ 5 years (n = 52; mean age, 58)	**C** > 5 years (n = 52; mean age, 58)
Work/school/study	50%[b,c]	12%[a]	12%[a]
Emotional control	54%[b]	22%[a]	38%
Nervousness	46%[b]	16%[a,c]	40%[b]
Loneliness	31%[b]	8%[a]	17%
Sleep	58%[c]	43%[c]	20%[a,b]
Muscle Strength	69%[b,c]	31%[a]	38%[a]

[a] Significantly different from group A, chi-square ($p < 0.05$).

[b] Significantly different from group B, chi-square ($p < 0.05$).

[c] Significantly different from group C, chi-square ($p < 0.05$).

Discussion

In this study, we assessed the different parts of the DT in BCSs. Additionally, the relationship between reported distress and demographic, treatment, and psychosocial variables was explored. Of the 129 BCSs investigated, 36% experienced a high level of distress as indicated by their scores on the DT. Intensity of treatment and time since primary surgery were positively correlated with distress. Problems of the emotional and physical domains were mentioned most frequently. Distress was correlated with various psychosocial variables including quality of life, illness cognitions, anxiety, and depression. The majority of the distressed BCSs indicated that they made a request for referral or considered a referral to a professional. The validation study of the Dutch DT by Tuinman and colleagues reported more distress than we found in our study: 43 vs 36%, respectively. This may be due to the fact that they investigated both male and female cancer patients with varying tumor types, and a substantial proportion of patients were on active treatment at the time of investigation.[25]

This study demonstrated that BCSs who received their treatment more recently experienced significantly higher levels of distress. The first 12 to 18 months after cancer treatment are called re-entry phase, in which patients try to return to their former lives.[9] This can be a time of disruption and increased distress. Patients struggle with questions such as how to manage (long-term) side effects, changes to their body, fear of recurrence, and changed relationships with family and friends.[7-9,20]

The explorative regression analysis demonstrated that lower cognitive functioning, impaired quality of life, and increased fatigue predicted higher levels of distress. However, which problem or combination of problems contributed most to the distress is unknown. Further studies on the nature and occurrence of possible combinations of problems are needed before effective measures for prevention can be recommended.

Our results showed that BCSs still experienced many problems. Distressed as well as non-distressed BCSs most frequently mentioned fatigue, decrease in muscle strength, and lack of physical fitness. Fatigue is one of the most common long-term side effects of cancer and its treatment. In this study, 75% of all BCSs and 87% of distressed BCSs indicated fatigue as a problem. These figures are much higher than those found in other studies in which fatigue was reported to be present in 34 and 38% of the BCSs. In these studies, however, they used a specific scale to measure fatigue.[5,43] In our study, the patients could only answer yes or no about the problem fatigue on the problem list of the DT. The DT aims to give an overview of the self-reported problems and does not provide any information about the severity of the reported problems. It might be possible that patients got adjusted to their problems and therefore experienced less distress. This could explain the fact that there is no relationship between the total number of problems and time elapsed since surgery.

Twenty-five percent of the distressed BCs indicated that they had made a request for referral to a professional, and 44% of the distressed BCSs considered a referral compared to 6 and 24% of the non-distressed patients. When interpreting the results of the DT and the request for referral of the patient, some considerations should be taken into account. First of all, endorsing problems on the problem list does not mean that BCSs experience distress or that they request referral. Secondly, a high score on the DT does not automatically mean BCSs wish to be referred. Some patients with a high distress score on the DT may have felt empowered enough to manage their problems without outside intervention (or perhaps they relied on other sources of supportive intervention such as friends/family and did not consider it a true intervention for that reason). Therefore, it is important to discuss the results of the DT with the patient in order to clarify the nature and severity of the distress, the existing problems, and to what degree the patient needs assistance with these problems. This is in line with NCCN and Dutch guidelines recommending the use of this instrument to enhance the communication between health professional and patient.[12,31]

Several methodological issues should be considered in reviewing the results of the present study. Firstly, there was found to be a large standard deviation between the time since primary surgery and the time of assessment. Due to the length of time between initial surgery and evaluation, it is possible that the problems and distress reported by BCSs are related to other problems or life events rather than to cancer treatment. Due to the cross-sectional design of the present study, it is not possible to interpret the direction of the causal relation between distress and the correlation with other variables. Results from the regression analysis should therefore be regarded as exploratory and interpreted with caution. In a recent meta-analysis, Norton and colleagues showed that the HADS does not provide good separation between the subscales anxiety and depression.[44] Therefore, future research should use specific questionnaires for anxiety and depression to examine a relation with the DT. Finally, as with any self-report investigation of this nature, response bias may have affected our results. It is possible that women with problems and/or distress are more willing to complete questionnaires.

This study has some important strengths. First of all, it is the first study which used the DT to explore distress and problems in BCSs in the Netherlands and, to the best of our knowledge, also worldwide. Secondly, almost all studies are focused on validating the DT, or they only used the thermometer to measure distress. However, we also described specifically all components of the DT in BCSs.

Implications for practice

A major advantage of the DT is that it is a simple screening tool to use. This study indicated that more than one third of the BCSs who participated experienced distress at an average of 5 years after primary surgery. Thus, screening on distress is an integral aspect of care of survivors. The professional, such as the oncologist and/or nurse, should be aware of the (potential) problems and the distress patients experience. The Dutch guideline recommends assessment of psychosocial care needs with the DT, and the nurses have an important role in this assessment and in the discussion of distress.[31] In daily practice, we experience that patients approach nurses more easily than physicians. Nurses have proven capable of screening survivors on distress and can refer patients to the proper professionals when needed in order to ensure proper patient care. This could prevent or lower distress and thereby improve the quality of life. Systematic use of the DT during follow-up will give the nurses an overview of the distress and problems experienced by the patients. The DT can monitor evolving problems in order to intervene early, with more chance to be successful. It helps patients to categorize their problems and makes it easier for the patient as well as for the nurse to discuss the reported problems. Patients may therefore feel more empowered to take a more active role in their own care and the management of their treatment. It also can act as a backbone for referral to a rehabilitation program for cancer survivors and may provide the opportunity to offer the patients in these programs a more personalized treatment program in contrast to the more traditional fixed ones.

Further research is needed, for example to compare the level of distress measured with the DT in healthy women. Longitudinal studies are required to more accurately determine the course of distress with the DT. This kind of research will enable the identification of early determinants and risk factors of distress and may facilitate the development of new, as well as the improvement of existing, interventions. Ultimately, this may lead to a decreased incidence of serious distress in BCSs.

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3

Self-reported distress in patients with ovarian cancer: is it related to disease status?

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Abstract

Objective

Patients with epithelial ovarian cancer have a poor prognosis and often undergo intensive treatment. These patients are therefore at risk for experiencing distress and reduced quality of life. The aim of this study was to explore the self-reported distress severity, experienced problems, and quality of life in relation to their disease status.

Methods

This cross-sectional study was conducted in 2011 at a University Medical Center. Women with ovarian cancer (n = 273), both during and after treatment, were asked by mail to fill in self-report questionnaires. Distress was measured using with the Distress Thermometer (DT), Hospital Anxiety and Depression Scale, and Impact of Event Scale. Problems and quality of life were assessed with the problem list of the DT, and European Organization for Research and Treatment of Cancer Quality of Life C30 and OV28.

Results

The questionnaire data of 104 patients were analyzed. Screening with the DT revealed distress in 32% [mean (SD), 3.1 (2.6)]. Distress was found with the Hospital Anxiety and Depression Scale in 14% [8.6 (5.9)] and with the Impact of Event Scale in 18% of the patients [17.5 (15.5)]. No significant differences were found in distress severity and self-reported problems between patients with and without recurrence. In both groups, the problems fatigue, condition, and neuropathy were most reported. Patients with distress (DT $\geq$ 5) experienced significantly worse functioning, more problems, and lower quality of life than patients without distress ($p < 0.01$).

Conclusions

This study showed that disease status in patients with ovarian cancer seems to have no influence on distress, quality of life, and the problems encountered. However, distressed patients experienced more problems, with physical and emotional functioning, and had lower quality of life. The problems fatigue, physical condition, and neuropathy are the most prevailing.

Introduction

Epithelial ovarian cancer (EOC) is known as the seventh most common type of cancer among women with an incidence of 225.000 cases per year worldwide.[1] The advanced stage of disease at diagnosis, the treatment and its adverse effects, and the relatively unfavorable prognosis leave patients with EOC at increased risk of experiencing distress and decreased quality of life.[2-4] To improve cancer care in terms of overall well-being, quality of life is an important patient reported outcome to explore. Overall, patients with EOC report good quality of life but impaired quality of life seems to be associated with distress.[4] Arden-Close and colleagues reported a relationship between psychological distress (increased levels of anxiety and depression) and younger age of onset, presence of advanced disease at diagnosis, more physical symptoms, and shorter time since diagnosis in patients with EOC.[3]

Distress is increasingly being recognized as an important factor and positioned as the sixth vital sign in cancer care.[5,6] The National Comprehensive Cancer Network (NCCN) defined distress as: *"a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment".*[7] Distress negatively impacts quality of life, speed of recovery after treatment, and survival. It is also a known risk factor for non-adherence to treatment, leading to decreased cost-effectiveness of therapies.[7-9] Early detection and treatment of distress in patients results in less hospital calls and visits, better adherence to treatment, and better communication between the patient and the treating physician.[7] The NCCN guideline for distress management recommends screening for distress of all cancer patients with the Distress Thermometer (DT).[7] Also, in the Netherlands, more attention for psychosocial problems in patients with cancer is strongly recommended by national guidelines and the Healthcare Inspectorate.

The DT is a short self-report screening instrument assessing both the severity of distress and problems encountered in the domains of emotional, practical, physical, spiritual and social functioning.[7] The nurse or physician discusses the distress score and the encountered problems and offers intervention(s) if required. The DT could be an important instrument to increase the quality of life for these patients but studies into its use in patients with EOC are scarce. Most studies concern the validation of the DT in different languages or per tumor type.[7,10-12] To our knowledge, to date, only one study reported about the DT in gynecologic cancer in general.[13] In this study, because of the lack of knowledge about the DT specifically in EOC, we compared the DT with well-known and validated questionnaires focusing on distress and quality of life.

The aim of this study was to investigate distress, the nature of the self-reported problems, and quality of life in patients with EOC. The influences of disease status and distress on quality of life and problems are explored.

Material and Methods

Study design and Patients

This cross-sectional study was conducted in a University Medical Center in May 2011. Patient eligibility criteria for the study were (1) 18 years or older; (2) able to read and write Dutch, and (3) seen by the gynecologic or medical oncologist for EOC in the last 5 years.

Recruitment Procedure

A letter explaining the goal of the study, a set of self-report questionnaires, and a stamped return envelope were sent to 273 patients who were treated for EOC. To verify whether the patients were still alive at the time of sending out the questionnaires, all eligible patients were checked in the national database of municipal personal records. Hospital identification numbers were used to code the questionnaires as this enabled the researchers to link the questionnaires to the patient medical records. Return of the questionnaires indicated consent to participate in the study. After one month, a reminder was sent to all non-responders.

Measures

Demographic characteristics and medical history

In a general questionnaire, the following variables were collected: demographic variables included age, marital status, educational level and employment status. Treatment-related variables included surgery and/or chemotherapy. From the medical records, treatment phase was collected.

Distress

To measure distress, we used the Dutch version of the DT, the Impact of Event Scale (IES), and the Hospital Anxiety and Depression Scale (HADS).

The DT is a screening instrument and consists of three parts, namely, a thermometer, a problem list, and a question concerning referral.[11] The thermometer part of the DT requires participants to identify the level of distress experienced in the past week, including the day of the screening. Patients indicate the level of distress on a scale of 0 (no distress) to 10 (extreme distress). In Dutch cancer patients, a cuttoff value of five and above was found to yield the best sensitivity and specificity for distress.[11] The DT has a good internal consistency ($\alpha = 0.90$).[10, 11] The problem list investigates whether the indicated level of distress is related to physical, familial/social, psychological, practical or spiritual needs and lists 47 problems. The Dutch version has added an extra question: 'Would you like to talk with a professional about your problems?' with answer options yes, maybe, and no.[11]

The HADS is a 14-item, self-report measure of anxiety and depression.[14, 15] Each item is rated on a scale from 0 (not at all) to 3 (very much). The HADS has two subscales (anxiety and depression) and a total score. The HADS has been translated and validated for the Dutch population.[16] A recent meta-analysis of

Norton et al. showed that the HADS does not provide good separation between the subscales anxiety and depression.[17] Therefore, we only used the total score to describe the psychological distress of the patients.[18] Higher scores imply more psychological distress. A cuttoff point of 15 is used for emotional distress.

The IES is a 15-item self-report measure to assess the impact of traumatic events. The instruction referred to the event as the diagnosis and treatment of cancer. Each item was rated on a 4-point scale from "not at all" to "often" (score 0-1-3-5) with a cuttoff point of 35 for distress.[19] The IES was adapted to measure cancer-specific distress and used in several studies with cancer patients.[20, 21] Higher scores mean more cancer-specific distress.

Quality of Life

The European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30 version 2.0) and the ovarian specific module EORTC QLQ-OV28 were assessed to measure quality of life of patients with EOC. The EORTC QLQ-C30 consists of 30 statements divided into five functional scales, three symptom scales, six single symptom items, and a general quality of life scale. The items of the general quality of life scale use a 7-point linear analog scale (very poor to excellent). All other items are scored on a 4-point scale from 1 (not at all) to 4 (very much). The scoring is from 0 to 100. For the functional and general score, this means that higher scores correspond with a better level of functioning. For the symptom scales, higher scores correspond with more severe symptoms.[22, 23] The EORTC QLQ-OV28 ovarian cancer module consists of 28 items that assess (chemo)therapy-related side effects, abdominal symptoms, hormonal symptoms, body image, sexual functioning, and attitudes towards disease and treatment.[24]

Ethics

Permission to conduct the study was obtained from the institutional ethics review board.

Data analysis

Data were analyzed using IBM SPSS version 20. Descriptive statistics were generated to summarize the demographic variables, medical variables, and problems on the DT problem list. Outliers were identified with a boxplot of time since surgery and were not included within the analysis. Because of the different prognosis and treatment modalities, this study investigated the differences in distress and quality of life between patients with EOC who are recurrence free (RFOC) and patients with recurrence (ROC). Also, differences were made between distressed (DT ≥ 5) and non-distressed patients with EOC. Independent sample t-tests and chi-square test were performed to determine differences between the groups. We corrected for multiple testing by using $p < 0.01$. Pearson correlations were used to investigate the association between quality of life and distress. Missing data on the problem list of the DT (yes/no) were included in the analysis as no problem.

Results

Description of the sample

Two-hundred and seventy-three patients with EOC were initially contacted for this study. The questionnaires were filled out and returned by 117 patients (43%). One patient was excluded because family mentioned that they filled out the questionnaire for the patient. Two patients were excluded due to complaints from another malignancy. Ten outliers based on time since surgery (> 12 years) were excluded. Thus, 104 (38%) questionnaires were used for the analyses. Information about the demographic and treatment characteristics are listed in Table 1 (N = 104). Median age was 61 years (range 20 - 90), 71 patients (68%) were married or cohabiting and 34 patients (33%) had paid work. Median time since surgery was 3.3 years (range 0.5-12). Of the total group, 59 (57%) were patients with RFOC and 45 patients (43%) with ROC. Eighty-seven patients (84%) had been treated with chemotherapy. There were no significant correlations between distress and the variables age, education, and time since surgery.

Table 1 Patients' demographics and medical characteristics (N = 104).

Characteristics	Patients (%)
Age, median (range) in years	61 (20 – 90)
Marital status	
Married/cohabiting	71 (68)
Divorced/widowed/other	32 (31)
Unkown	1 (1)
Education[a], median (range)	4 (2 – 7)
Occupation[b]	
Paid work	34 (33)
Retirement	31 (30)
Disablement insurance act or sick leave	19 (18)
Other[c]	38 (37)
Medical	
Time elapsed since surgery, median (range) in years	3.3 (0.5 – 12)
0 - 2 years since surgery	27 (26)
2 - 5 years since surgery	42 (40)
5 - 10 years since surgery	31 (30)
> 10 years since surgery	4 (4)
Received chemotherapy	87 (84)
Diagnosis	
Recurrence free of ovarian cancer (RFOC)	59 (57)
Recurrence of ovarian cancer (ROC)	45 (43)

[a] According to the Dutch standardized scoring system (range, 1 – 7) in which 1 is no education and 7 is university.
[b] Multiple answers possible, answers do not add up to 100%. [c] No (paid) work, student, housewife.

Prevalence of distress in patients with EOC

Seven patients did not fill in a DT score, and four and three patients did not complete the HADS and IES, respectively. On the basis of the DT, the patients with EOC (n = 97) had a mean score of 3.1 (SD 2.6) and 33 (32%) of them scored 5 or higher on the thermometer of the DT. Psychological distress measured with the HADS showed a mean score of 8.6 (SD 5.9) (n = 100). Fifteen patients (14%) scored 15 or higher. The IES scale showed a mean score of 17.5 (SD 15.5) with 19 patients (18%) scoring 35 or higher (n = 101). There were no significant differences in distress between RFOC and ROC patients, measured with the DT, HADS and IES.

Problem List of the DT and request for referral to a professional

All patients with EOC reported a median of 6 problems (range 0 - 20). Patients with RFOC reported a median of 4 (range 0 - 20) and patients with ROC had a median of 7 (range 0 - 20) ($p = 0.461$) problems per patient. The top five of problems of patients with RFOC and ROC are shown in Table 2. Fatigue, condition, and tingling in hands/feet were most mentioned as a problem in both groups.

Compared to patients with EOC without distress (DT < 5), patients with EOC with distress (DT ≥ 5) more frequently reported fatigue (45% and 73%, respectively; $p < 0.01$), tingling in hands/feet (33% and 61%, respectively; $p < 0.01$) and condition (31% and 73%, respectively; $p < 0.01$) as a problem. Patients with distress reported more problems on the problem list pertaining to patients with non-distress ($r = 0.601$, $p < 0.001$). Five of the patients with EOC (N = 104) left the question about referral unanswered. Eight patients (8%) with EOC had a referral request (RFOC: 5, ROC: 3), 19 patients (18%) considered a referral and 72 patients (69%) did not want to be referred to a professional. Of the patients with EOC with distress (n = 33, DT ≥ 5), 7 patients (21%) requested to be referred and 7 patients (21%) were considering it.

Quality of life

In the total sample, a mean quality of life global health score of 75.3 (SD 20.8) was found. No differences were found between RFOC and ROC patients (78.5 and 70.9, respectively). The quality of life global health status was negatively correlated with the DT score ($r = - 0.558$, $p < 0.001$), HADS score ($r = -0.567$, $p < 0.001$), and IES score ($r = -0.284$, $p < 0.001$). Also, the total of problems on the problem list were negatively correlated with the quality of life global health status ($r = -0.550$, $p < 0.001$) and the function scales ($p < 0.001$). Table 3 shows the relation between the quality of life of patients with and without distress. Significant differences were found on all functions and on some symptom scales between both groups.

Table 2 Top five of problems on the DT of RFOC and ROC patients (N = 104).

	RFOC (n = 59)	**ROC (n = 45)**
1	Fatigue (58%)	Fatigue (49%)
2	Condition (47%)	Tingling in hands/feet (44%)
3	Tingling in hands/feet (39%)	Condition (42%)
4	Sleep (36%)	Muscle strength (40%)
5	Muscle strength (31%)	Emotional control (40%)

Abbreviations: RFOC = Recurrence free of ovarian cancer, ROC = Recurrence of ovarian cancer.

Table 3 Differences in quality of life in patients with EOC with (DT ≥ 5) and without distress (DT < 5).

	N = 104	Total group Mean (SD)	n = 63	DT < 5 Mean (SD)	n= 33	DT ≥ 5 Mean (SD)	p
EORTC QLQ-C30							
***Function scales*[1]**							
Physical	103	78.4 (20.7)	63	87.4 (14.4)	33	65.7 (21.9)	<0.001*
Role	103	78.6 (25.9)	63	88.4 (20.2)	33	62.1 (27.4)	<0.001*
Emotional	103	82.4 (18)	63	89.3 (12.6)	33	71.5 (19.1)	<0.001*
Cognitive	103	85.8 (16.2)	63	89.2 (13.8)	33	79.3 (18.6)	0.006*
Social	103	84.6 (20.8)	63	90.7 (15.2)	33	73.2 (26.3)	<0.001*
***Symptom scales*[2]**							
Fatigue	103	31.1 (23.3)	63	22.6 (21.5)	33	43.6 (19.2)	<0.001*
Nausea/vomiting	102	6.7 (16.3)	63	3.4 (10.4)	33	8.3 (15.8)	0.077
Pain	103	18.4 (25.8)	63	11.1 (18.2)	33	30.8 (30.9)	<0.001*
Dyspnea	101	12.9 (24.5)	63	8.5 (18.9)	33	20.8 (32.5)	0.026
Insomnia	103	24.3 (28.8)	63	18 (25.3)	33	33.3 (30)	0.002*
Appetite Loss	102	11.8 (23.8)	63	6.9 (17.1)	33	17.7 (31.7)	0.049
Constipation	103	17.2 (25.1)	63	15.9 (25.3)	33	17.2 (23.7)	0.704
Diarrhea	103	8.4 (22.2)	63	7.9 (21.3)	33	9.1 (25.4)	0.673
Financial difficulties	102	6.5 (14.9)	63	4.8 (13.3)	33	8.1 (16.7)	0.301
***Quality of life*[1]**							
Global health status/QoL	103	75.3 (20.8)	63	81.6 (18.3)	33	62.6 (21.6)	<0.001*
EORTC QLQ-OV28 Scales[2]							
Abdominal/GI	103	18.4 (18.2)	63	15.1(14.8)	33	22.1 (21.9)	0.106
Peripheral neuropathy	92	24.6 (25.7)	57	18.5 (23.5)	29	33.3 (23.6)	0.007*
Hormonal	92	28.3 (31.5)	57	27.8 (31.9)	29	28.2 (31.5)	0.958
Body Image	102	16.8 (20.2)	63	12.7 (17.4)	32	24.5 (24.7)	0.008*
Attitude to disease/treatment	103	44 (29.6)	63	34 (26.7)	33	60.3 (28.1)	<0.001*
Chemotherapy side effect	103	16.2 (17.5)	63	13.9 (16.2)	33	17.2 (15.5)	0.334
Sexual function	101	22.3 (24.1)	62	30 (24.1)	33	11.9 (19.5)	<0.001*

Abbreviations: DT = Distress Thermometer, EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30, OV = Ovarian questions from the EORTC.

[1] Higher scores represent better functioning.

[2] Higher scores represent more problems.

* Significant different p < 0.01.

Discussion

To the best of our knowledge, this is the first study to explore distress and problems measured with the DT in a specific sample of patients with EOC. We compared distress (with different instruments) and quality of life between patients with RFOC and ROC. An additional evaluation of differences between distressed en non-distressed patients with EOC was performed.

With a screening instrument, distress was measured in 32% of all patients with EOC, which is much lower than the 57% that Johnson and colleagues reported in their study which measured distress in gynecologic cancer.[13] These differences may be due to the sample of patients with different gynecological tumors, the fact that their patients filled out the DT before the first chemotherapy treatment and the use of a lower distress cuttoff point of 4.[13] In other studies from the Netherlands, using a DT cuttoff point of 5 in patients with different tumor types during treatment or follow-up, distress scores were reported between 36% and 43%.[10, 11, 25] These scores are more in line with our results, although still higher.

Patients reported higher percentages of distress on the DT in comparison to the HADS and IES. We have, however, to keep in mind that the HADS and IES are diagnostic instruments and the DT is an instrument designed only for screening.[7, 16, 19] In contrast with the HADS and IES, which only measure emotional problems, the DT also measures problems in the social, practical, spiritual and physical domains. In case the patient reports distress and emotional problems on the DT, further diagnostic testing with HADS, IES, or other questionnaires like Center for Epidemiological Studies Depression Scale should be considered to further identify serious emotional problems.[26] Eventually, a specific referral can be arranged.

This study showed that disease status in patients with EOC was not related to distress and the problems encountered. This corresponds with the study of Johnson and colleagues who found no differences in DT scores between patients who were receiving treatment for the first time and who had recurrence of their cancer.[13] On the other hand, our data showed that distressed patients with EOC experienced more problems and lower quality of life than non-distressed patients. Distress seems related to the number of problems in patients with EOC. These results were similar with a study about the DT in breast cancer survivors.[25] Also, Roland and colleagues mentioned in their review that having more physical symptoms was related to higher levels of distress and lower functioning which affects quality of life.[4] In our study, the physical problems fatigue, decreased condition, and peripheral neuropathy were reported as most problematic on the DT, confirmed by the data of the EORTC quality of life questionnaire. These problems are long lasting familiar side effects of the treatment and the disease itself. Studies about reducing fatigue, improving condition and peripheral neuropathy of patients with EOC are limited. Physical exercise and cognitive behavioral therapy is effective for relieving fatigue in cancer survivors and could be considered in patients with EOC.[27, 28] Unfortunately, well-accepted proven therapy for peripheral neuropathy does not yet exist.[28] In daily practice, early detection by monitoring patient-reported outcomes during treatment may lead to earlier interventions, with delaying or type or dose of the chemotherapy.[29-31]

Almost half of the patients with distress mentioned that they wanted or would consider a referral to a professional. It is unclear if the needs were unmet and what kind of referrals were needed. Unfortunately we had no information on whether patients already received professional help for the problems

reported. Stafford and colleagues described in their study a high rate of referral refusal during screening program for depression and anxiety.[32] For further research, it is important to explore the unmet needs and what kind of care the patients received and would like to receive from other caregivers, for example the nurse, general practitioner, or social worker.
The quality of life scores reported in our sample of patients with EOC were similar to normative data of the general population, which were also described in a review about ovarian cancer survivors.[4,33] Because most of the patients experienced no distress and median time after first surgery was 3.3 years, patients probably have learned to cope with their feelings, experienced personal growth, had positive personal transition, adjusted to the disease or changed perspectives on life, and anxiety and depression symptoms improved over time.[4, 32, 34, 35]

Our study had several limitations. This study was cross-sectional, used self-reported questionnaires which resulted in missing data. Patients were both under treatment or in late follow-up, and the sample size of the patients with RFOC and ROC was small. In addition, we do not know why the non-response group declined to complete the questionnaires. Thus, the results may be affected by selection bias of our sample. More longitudinal research and prospective studies are needed to identify distress trajectories and problems during and after treatment, comparable to trajectory studies in patients with breast cancer and colorectal cancer.[36,37,38] To offer adequate care for patients with EOC with (severe) distress, interventions are needed and should be developed to prevent deterioration in their situation. Ameliorating or solving these problems in an early phase by regular screening with the DT could decrease distress and increase thereby quality of life. For now, this study is a step forward in the development of personalized psychosocial care which can fulfill unmet needs in the patients with EOC.

In conclusion, in this cross-sectional study, patients with recurrence ovarian cancer are not more distressed than patients without recurrence. However, if patients are distressed, they have more problems and their quality of life is worse than those who are not distressed.

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4

A specific distress cutoff score shortly after breast cancer diagnosis

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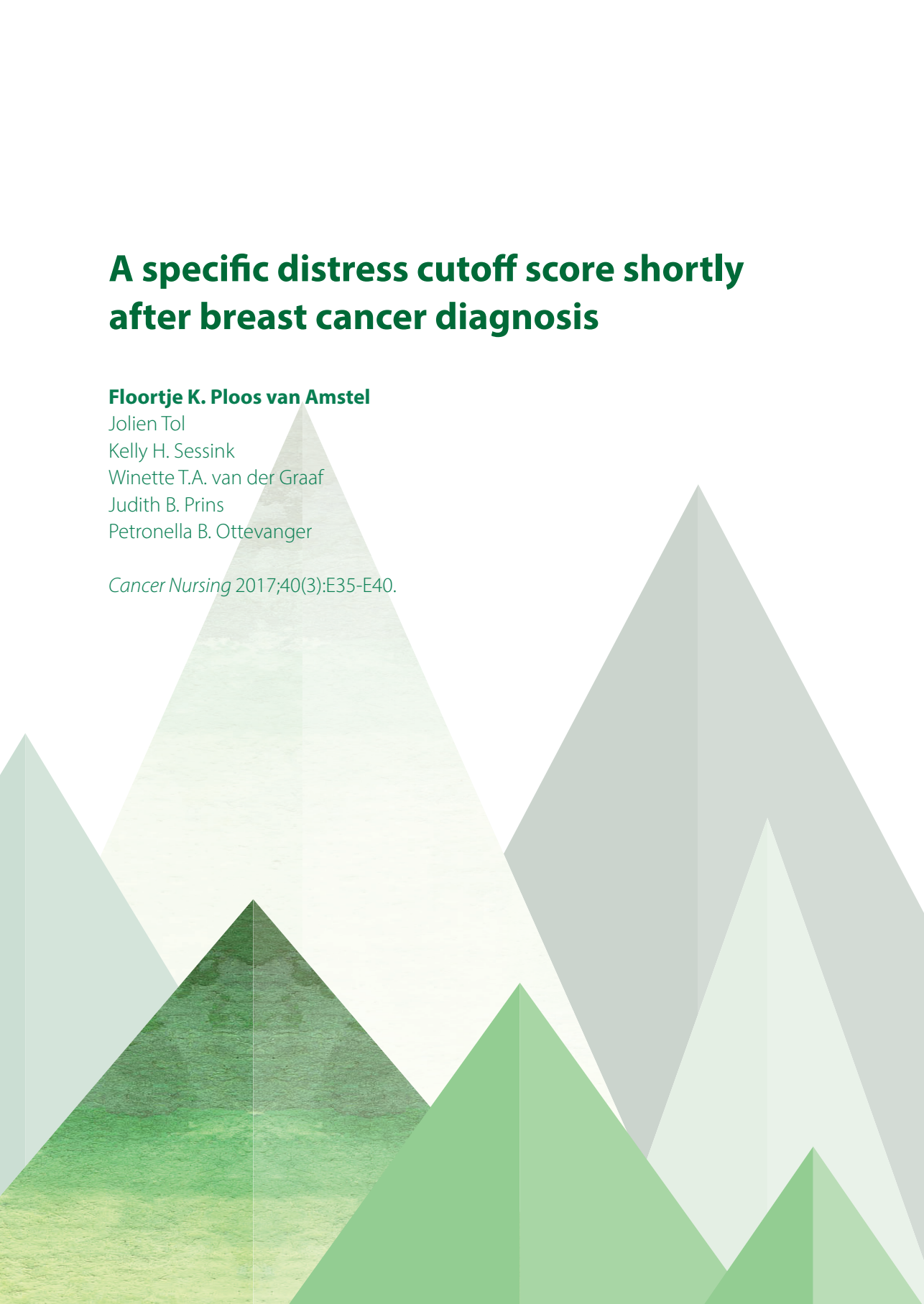

Abstract

Background

High levels of distress are expected shortly after the diagnosis breast cancer. The Distress Thermometer (DT) is commonly used to screen for distress, using a cutoff score of 4 or 5; however, this score might not be appropriate for detecting distress in women with recently diagnosed breast cancer.

Objectives

The aims of this study were to establish the optimal DT cutoff score for detecting high distress shortly after breast cancer diagnosis and to correlate this score with the reported problems.

Methods

We selected for this study Dutch women who completed the DT and the Hospital Anxiety and Depression Scale within 1 month after breast cancer diagnosis. Receiver operating characteristic analysis of DT scores was performed, with the Hospital Anxiety and Depression Scale being used as the criterion standard for the level of distress. The sensitivity, specificity, positive predictive value, and negative predictive value of each DT score were calculated.

Results

In total, 181 women participated in the study. The optimal DT cuttoff score for detecting distress was 7 with a sensitivity of 0.73, specificity of 0.84, positive predictive value of 69%, and negative predictive value of 87%. Emotional problems were the most frequently reported concerns.

Conclusion

We consider a cutoff score of 7, shortly after breast cancer is diagnosed, optimal to identify those women with high distress and therefore at risk of chronic distress.

Implications for Practice

The findings are clinically important because they can enable healthcare professionals to direct their time and resources to those most in need of their assistance.

Introduction

Breast cancer is the second most common cancer overall, with incidence rates varying between 27 per 100.000 in Middle Africa and East Asia and 96 per 100.000 in Western Europe.[1] Many women are distressed shortly after diagnosis – life is suddenly uncertain, and treatment must start within weeks.[2] The early detection and treatment of distress in these women could probably decrease or even prevent the long-term psychological effects of the diagnosis and treatment. Paying attention to the psychosocial well-being of patients meets with widespread acceptance, and many countries have developed and implemented guidelines to screen for distress.[3-8] The Distress Thermometer (DT), developed by the National Comprehensive Cancer Network (NCCN) in 1998, is generally considered to be the best screening instrument available for this purpose.[9,10] With this instrument, the patient scores his/her distress on a visual analog scale (no distress to extreme distress; 0 – 10) and his/her problems on a problem list; results are then discussed with the healthcare provider.[9,10] Screening is important to assess the presence of distress and its associated problems, thus enabling the timely referral of individuals to appropriately trained professionals, if needed.[5,9,10] The ultimate goal is to reduce the risk of distress during the course of the disease and hence improve the quality of life of the patient.[9]
The original English DT has been translated into 17 languages and has been validated in different cancer populations, both during and after cancer treatment, and against different instruments, although the Hospital Anxiety and Depression Scale (HADS) has been used most often as criterion standard for distress.[8,11] In validation studies, different cuttoff scores for distress have been determined, influenced by language, country, and cancer population.[8,11] The DT has been used in several Dutch studies.[12-18] For example, Tuinman et al. translated and validated the DT in a mixed cancer population, using a cuttoff score of 5.[12] Since then, several studies have assessed cuttoff scores for distress in specific types of cancer, to determine whether the level of distress experienced is specific to a certain type of cancer.[13,14,16-18]

Having received a diagnosis of cancer is a high-impact event that leads to distress and because of empirically derived risk factors, such as family or a personal history of a psychiatric disorder, lack of support, low socio-economic status, and younger age.[2,9,19-22] Levels of distress are higher just after diagnosis than later in the course of the disease.[2,23] Henselmans et al. reported that at the time of breast cancer diagnosis 48% of patients experienced high levels of distress, measured with the General Health Questionnaire; in most patients, levels of distress declined in the months after diagnosis.[23] However, in 15% of these patients, distress remained high during the first year after diagnosis.[23] Patients with high distress are more at risk of longer-term psychological and cancer-related distress and poorer social adjustment.[24] To try to prevent chronic distress, it is important to detect patients with high levels of distress in an early phase. According to the Dutch distress management guideline, 'detection of need for psychosocial care', screening for distress should be carried out shortly after cancer diagnosis and after each treatment modality and at fixed time points during follow-up, by a nurse or medical specialist.[10] Knowledge of the distress score at this stage may help identify those patients who are at increased risk of becoming chronic distressed, having psychosocial morbidity, or of having poor resilience. This raises the

question as to whether one general cuttoff score is appropriate to detect distress at different time points after diagnosis, such as shortly after diagnosis, when high levels of distress can be expected and patients may need extra support. We therefore investigated the optimal DT cuttoff score for identifying high distress in breast cancer patients shortly after diagnosis, which problems they reported, and whether patients' reported symptoms and problems are associated with the initial distress score.

Methods

Participants and recruitment procedure

In the current study, we investigated the optimal DT cuttoff score for detecting high distress, using the baseline data of a randomized controlled trial about the effectiveness of the DT, the Nurse Intervention Project (NIP) (NCT01091584). This study included all patients with newly diagnosed breast cancer at the Radboud university medical center between March 2010 and February 2013. Patients received verbal and written information about the NIP immediately after the diagnosis breast cancer, and several days later, a researcher explained the study in greater detail and asked for written informed consent. At study entry, the patients were asked to complete different questionnaires, preferably before the start of first treatment. In the case of non-response, a reminder was sent within 2 weeks by mail. The NIP inclusion criteria were age 18 years or older, histology proven invasive breast cancer, treatment with curative intent, and competence in Dutch. Exclusion criteria were treatment for a previous malignancy, except adequately treated cervical carcinoma in situ, basal cell carcinoma of the skin, and psychiatric comorbidity hindering study adherence. In this study, we included only those patients who completed the questionnaires within a month after diagnosis.

Measures

Patients were asked to fill in self-report questionnaires about demographic, psychological, and medical characteristics, such as age, marital status, education, employment, the expected medical treatment, and past and current psychological support. Distress was measured with the validated Dutch versions of the DT and the HADS. Both questionnaires asked about the patients' situation in the past week.

The DT is a screening instrument consisting of a visual analog scale (ranging from 0 [no distress] to 10 [extreme distress]), a list of 47 questions (yes/no) about problems in different domains (physical, familial/social, psychological, practical, and spiritual), and a question about a request for referral. For this study, we only used the results of the thermometer and the problem list.[12]

The HADS is a self-report measure with 14 items. Each item is rated from 0 (not at all) to 3 (very much). Higher scores indicate more emotional distress.[25-27] The HADS is commonly used for patients with cancer and was used as criterion standard in 95% of the studies validating the DT.[8] Different cuttoff scores for the total HADS are described in the literature, but as most DT validation studies used a cuttoff score of 15, we also used this cuttoff score for detecting clinically relevant emotional distress.[8,12,13,28]

Ethical considerations

The NIP study was approved by the Medical Ethics Committee (CMO) of Radboud university medical center, Nijmegen, the Netherlands (CMO 2009/293). Registration number of the clinicaltrials.gov is NCT01091584.

Statistical analysis

Data were analyzed using Statistical Package for Social Science (SPPS; version 20, Chicago, Illinois). Descriptive statistics were used to describe the sample. For every DT score, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using the HADS total score of 15 or greater as criterion standard.[12] The correlation between sensitivity and specificity was visualized using a Receiver Operating Characteristic (ROC) curve in which we plotted sensitivity versus 1-the specificity for each cuttoff score. Sensitivity is the probability that a patient with distress is screened as being distressed. Specificity is the probability that a non-distressed patient is screened as not being distressed. The PPV and NPV represent the probability of a positive or negative diagnosis of distress after a positive or negative outcome of the DT, respectively.[29] Further analyses were performed with the calculated optimal cuttoff score for distress. To differentiate non-distressed from distressed patients, an optimal score needs a high sensitivity and specificity, to maximize the proportion of patients whose test results are accurate.[30] In our study, the optimal score was defined as a proper balance between sensitivity and specificity and a PPV of 50% or greater. Pearson correlations and Chi-square analyses were performed to investigate the association between patient characteristics, the problems on the problem list, and the distress score. Cronbach's α was calculated for the five domains and total problem list, to investigate the internal consistency of the DT. Significance was defined as $p < 0.05$.

Results

Sample characteristics

In total, 366 patients received a diagnosis of breast cancer during the inclusion period, of whom 264 met the eligibility criteria and were asked to participate in this study. Ultimately, 199 of these 264 patients (75%) were included; 65 patients (25%) refused to participate. Of these 199 patients, the data of 18 patients were excluded from the current analysis because these patients did not complete the baseline questionnaires within a month of diagnosis. Consequently, the data of 181 patients (69%) were included in this analysis. The patients' characteristics are shown in Table 1. All 181 patients were women, 136 (75%) were married/cohabiting, 90 (50%) were highly educated and 106 (59%) were in paid employment. The first expected treatment modality was surgery (91%) or neo-adjuvant chemotherapy (7%). At baseline, 14 patients (8%) had received psychosocial support.

Table 1 Baseline patient and treatment characteristics (N = 181).

Characteristics	Patients (%)
Demographics	
Age, median (range) in years	55 (30 – 87)
Marital status	
Married/cohabiting	136 (75)
Divorced/widowed/other	45 (25)
Having children	141 (78)
Children living at home	73 (40)
Education	
Low	26 (14)
Medium	65 (36)
High	90 (50)
Occupation[a]	
Paid work	106 (59)
Retirement	31 (17)
Disablement insurance act or sick leave	23 (13)
Other[b]	55 (30)
Medical[c]	
First expected treatment modality reported by the patients	
Surgery: lumpectomy breast	87 (48)
Surgery: ablatio breast	47 (26)
Surgery: amputation breast + axillary lymph node dissection	30 (17)
Neo-adjuvant chemotherapy	12 (7)
Unknown	5 (3)
Psychological[d]	
Any psychosocial support in the past	60 (33)
Psychosocial support at baseline	14 (8)

[a] Because multiple answers were possible, answers do not add up to 100%.

[b] No (paid) work, student, housewife.

[c] Because of rounding decimals off to whole numbers, the total does not add up to 100%.

[d] Psychological support by social worker, psychologist or psychiatrist.

DT: the cuttoff score

The mean DT score was 5 (SD 2.7). The mean HADS score was 11.7 (SD 7.9), and 59 patients (33%) had scores of 15 or greater. The outcomes of the DT and the HADS were significantly correlated ($r = 0.70$; $p < 0.01$). Figure 1 lists the distribution of the scores on the DT. The ROC curve is shown in Figure 2. The area under the curve was 0.83 (standard error 0.03; 95% confidence interval, 0.77–0.90; $p < 0.001$). Of the 181 patients, 109 patients (60%) had a DT score of 5 or greater, resulting in a sensitivity of 0.86, specificity of 0.53, PPV of 47%, and NPV of 89% for a positive HADS outcome (Table 2). Seventy-seven patients (43%) had a DT of 6 or greater, resulting in a sensitivity of 0.76, specificity of 0.74, PPV of 58%, and NPV of 87%; 62 patients (34%) had a DT score of 7 or greater, resulting in a sensitivity of 0.73, specificity of 0.84, PPV of 69%, and NPV of 87%. While sensitivity was almost equal with a cuttoff score of 6 or 7, specificity was 10% higher with a cuttoff score of 7, implying that an extra 10% of patients without significant distress would be identified at cuttoff score of 7. On the basis of these results, 7 would seem to be the optimal DT cuttoff score for identifying high distress in breast cancer patients shortly after diagnosis. This cuttoff score was used in subsequent analyses.

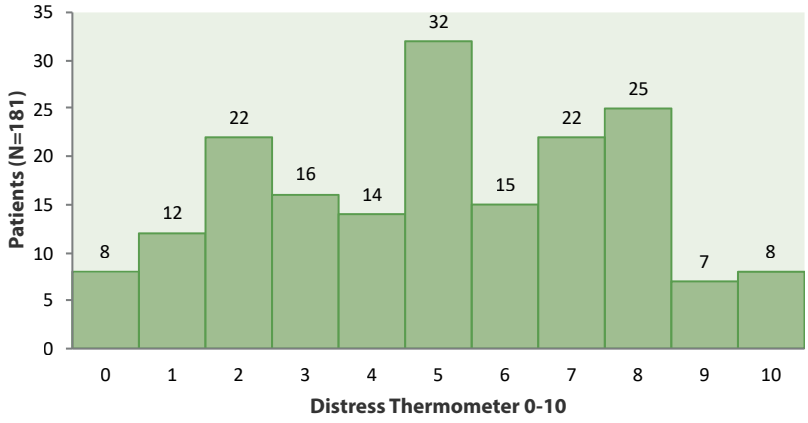

Figure 1 Distribution of the scores on the Distress Thermometer shortly after breast cancer diagnosis (N = 181).

Distress in relation to patient characteristics

Younger patients experienced more distress than older patients ($r = -0.303$; $p < 0.01$), whereas there were no differences in marital status, education, paid employment, treatment modality, and receipt of psychosocial support at baseline between distressed and non-distressed women. Patients with children living at home experienced more distress than patients without children living at home ($X^2 = 10.3$; $p < 0.001$). Patients who had previously received psychosocial support were more distressed than were patients who had not previously received psychosocial support ($X^2 = 4.6$; $p = 0.03$).

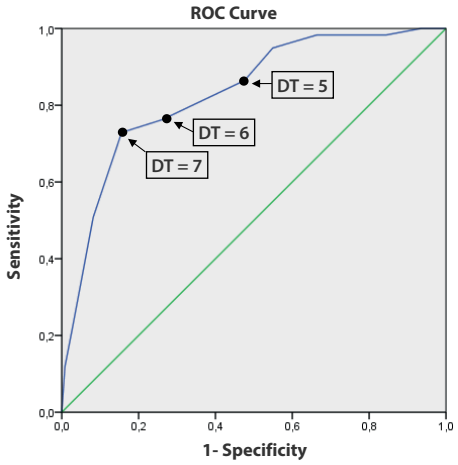

Figure 2 Receiver Operating Curve (ROC) analysis comparing Distress Thermometer (DT) with the Hospital Anxiety and Depression Scale (total score ≥15). Diagonal segments are produced by ties.

Table 2 Distress Thermometer (DT) scores (N = 181): Sensitivity, Specificity, PPV, and NPV.

DT score	Sensitivity	Specificity	PPV %	NPV %
0	1.00	0.00	33	0
1	1.00	0.07	34	100
2	0.98	0.16	36	95
3	0.98	0.34	42	98
4	0.95	0.45	46	95
5	0.86	0.53	47	89
6	0.76	0.74	58	87
7	0.73	0.84	69	87
8	0.51	0.92	75	79
9	0.20	0.98	80	72
10	0.12	0.99	88	70

Abbreviations: NPV = Negative Predictive Value; PPV = Positive Predictive Value.

Distress in relation to the problem list

The internal consistency of the total problem list was α = 0.88, with the physical and emotional domains showing a high internal consistency (α = 0.81 and α = 0.77, respectively). The internal consistency of the other domains was moderate: practical domain 0.56, social domain 0.67, and spiritual domain 0.52.

The DT score was significantly correlated with problems in the practical ($r = 0.377$; $p < 0.01$), social ($r = 0.187$; $p < 0.05$), emotional ($r = 0.571$; $p < 0.01$), spiritual ($r = 0.182$; $p < 0.05$), and physical ($r = 0.302$; $p < 0.01$) domains and with the total number of problems ($r = 0.494$; $p < 0.01$). Twenty-four of the 47 items on the problem list were significantly associated with distress ($p < 0.05$), 9 (38%) of which were in the emotional domain.

The top five self-reported problems were nervousness (81%), anxiety (60%), sleep disturbances (56%), emotional control (50%), and concentration (41%). Non-distressed patients reported significantly less often each of these mentioned problems than distressed patients ($p < 0.01$): nervousness (73% vs 97%), sleep disturbances (46% vs 74%), anxiety (45% vs 89%), concentration problems (34% vs 56%), and loss of emotional control (35% vs 81%).

Discussion

In the present study, we investigated the optimal DT cuttoff score for detecting high distress in women shortly after they had received a diagnosis of breast cancer. Our findings suggest that a cuttoff score of 7 is optimal for distress screening in these patients, rather than the cuttoff score of 5, which is currently recommended in the Dutch national guideline for distress detection in patients with cancer.[10] It is debatable which cuttoff score is best for screening for distress shortly after diagnosis. Because distress in this early diagnosis situation is a normal reaction, we think it is important to identify those patients at risk who will remain severely distressed. A higher cuttoff score at diagnosis would lead to fewer findings of false positive patients, and we hypothesize that the distress of patients with DT scores of 7 or greater is not likely to diminish in the first year. Screening shortly after diagnosis may make it possible to identify those patients at highest risk of being chronically distressed, and therefore allows us to start early interventions in order to prevent or decrease distress in the course of treatment and follow-up.

Other studies have also investigated the appropriate cuttoff score at the time of diagnosis with breast cancer.[31,32] In a Danish study, Bidstrup et al. reported a DT cuttoff score of 7 as being optimal for confirming distress, with a sensitivity of 81% and a specificity of 79%; the PPV and NPV were similar to those reported here. However, Bidstrup et al. recommended a cuttoff score of 3 for screening purposes, because they preferred a high sensitivity (99%) and recommended the cuttoff score of 7 for detecting severe distress.[31] Similarly, a study by Hegel et al. reported a DT cuttoff score of 7 as being optimal for detecting depression in breast cancer patients.[32]

In contrast with Denmark[31], in the Netherlands we use a distress guideline that recommends screening at fixed time points for every patient. Patients with low to moderate distress (< 7) will all have a short conversation with a nurse who will discuss whether the patient is sufficiently in control of her situation

and if the patient wishes to be referred to another professional. Patients with high distress (≥ 7) will receive an extensive exploratory conversation with the nurse, the patient will be discussed in a psychosocial multidisciplinary team meeting, and a treatment plan is developed. Interpreting the test characteristics of each cuttoff value, the DT cuttoff of 7 enables the healthcare providers to help identify patients at risk of chronic distress and start with early interventions, keeping resources available, for those in need of it, without spoiling them to patients who can manage themselves.

The NCCN recommends a cuttoff score of 4, and this is worldwide the most frequently used cuttoff score to screen for distress.[9] The DT was validated with a cuttoff score of 5 for the general cancer population in the Netherlands by Tuinman et al.[12] However, Admiraal et al. concluded that a cuttoff score of 4 was needed for Dutch patients with prostate cancer, because of the low level of distress in this group.[13] Another Dutch study identified a cuttoff score of 5 as being optimal for identifying distress in long-term survivors of thyroid carcinoma.[16] On the basis of our findings and those of international studies, we conclude that the best cuttoff score is not only dependent on the tumor type and screening moment, but probably also on cultural and psychosocial factors.[8,13,31] Therefore, it is seems inappropriate to generalize cuttoff scores across different cancer populations. Instead, cuttoff scores should be established for specific cancer populations, by tumor type and treatment phase. It is important to describe these cuttoff scores mentioning the time points of assessment, the population and tumor types. This will ensure that healthcare professionals know what cuttoff score is important at different time points throughout the disease and in different cancer populations.

In our patients, emotional problems were the most frequently reported problems immediately after the diagnosis of cancer. With high distress scores, these problems were more reported; therefore, early support seems to be needed for patients with high distress scores. After the first shock, most patients learn how to cope with the diagnosis and subsequently experience particularly (late) effects of treatment to be of influence on their quality of life, which may cause distress.[14,33,34]

In recent years, it has been debated whether the HADS should be used as criterion standard for the DT.[28,35] Although both questionnaires measure distress, they are fundamentally different. The HADS is a diagnostic instrument for emotional distress and the DT is a global screening instrument for various types of distress, not solely emotional distress. As already mentioned, patients in our study experienced mainly emotional problems shortly after diagnosis, and for this reason, comparison with the HADS is appropriate. On the other hand, validating the DT with an extensive interview might be better to explore the construct validity of distress. However, this is not practical in day-to-day patient care, and especially not in the diagnostic phase of cancer. Moreover, interviews are more difficult to interpret in a standardized manner.

It is important to note that our results were probably influenced by some bias. First, only patients meeting the specific inclusion and exclusion criteria were approached for the study. Second, most patients filled out the questionnaire within a month of diagnosis and not on a specific moment after diagnosis; patients might experience more distress several days after diagnosis or just before the first treatment. Also, some patients did not know their treatment plan at the time of assessment, which

might have caused additional uncertainty and distress. In this study, we did not further investigate the reported distress and problems in a conversation with the patients. This would have given us more insight into the severity of the experienced distress. However, this would not have changed problems or the DT cuttoff score.
A strength of this study is the large sample size, which facilitates generalization of findings to the Dutch breast cancer population and increases their relevance to the breast cancer community at large.

Implications for practice

The cuttoff score of 7 is optimal for distinguishing between distressed and non-distressed patients shortly after the diagnosis of breast cancer. The DT guideline recommends discussing DT outcomes with patients. It is important to investigate the causes of distress. Knowledgeable healthcare professionals, such as nurses, can empower patients by informing them about the natural course of distress. In addition, it is recommended that DT findings should be discussed in a psychosocial multidisciplinary team meeting.[10] Distressed patients should be referred to a psychologist or a social worker, if appropriate, and attention should be given to their psychosocial well-being during and after treatment. Our findings are clinically important because they can enable healthcare professionals to direct their time and resources to those most in need of their assistance.

Conclusion

An appropriate cuttoff score for screening for distress with the DT shortly after the diagnosis of breast cancer enables the accurate identification of distressed patients and the associated problems they experience. A DT cuttoff score of 7 is recommended for screening for distress shortly after diagnosis in the Dutch breast cancer population. The optimal cuttoff score of the DT is highly variable across patient groups and should be assessed separately in specific cancer populations.

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5

The effectiveness of a nurse-led intervention with the distress thermometer for patients treated with curative intent for breast cancer: design of a randomized controlled trial

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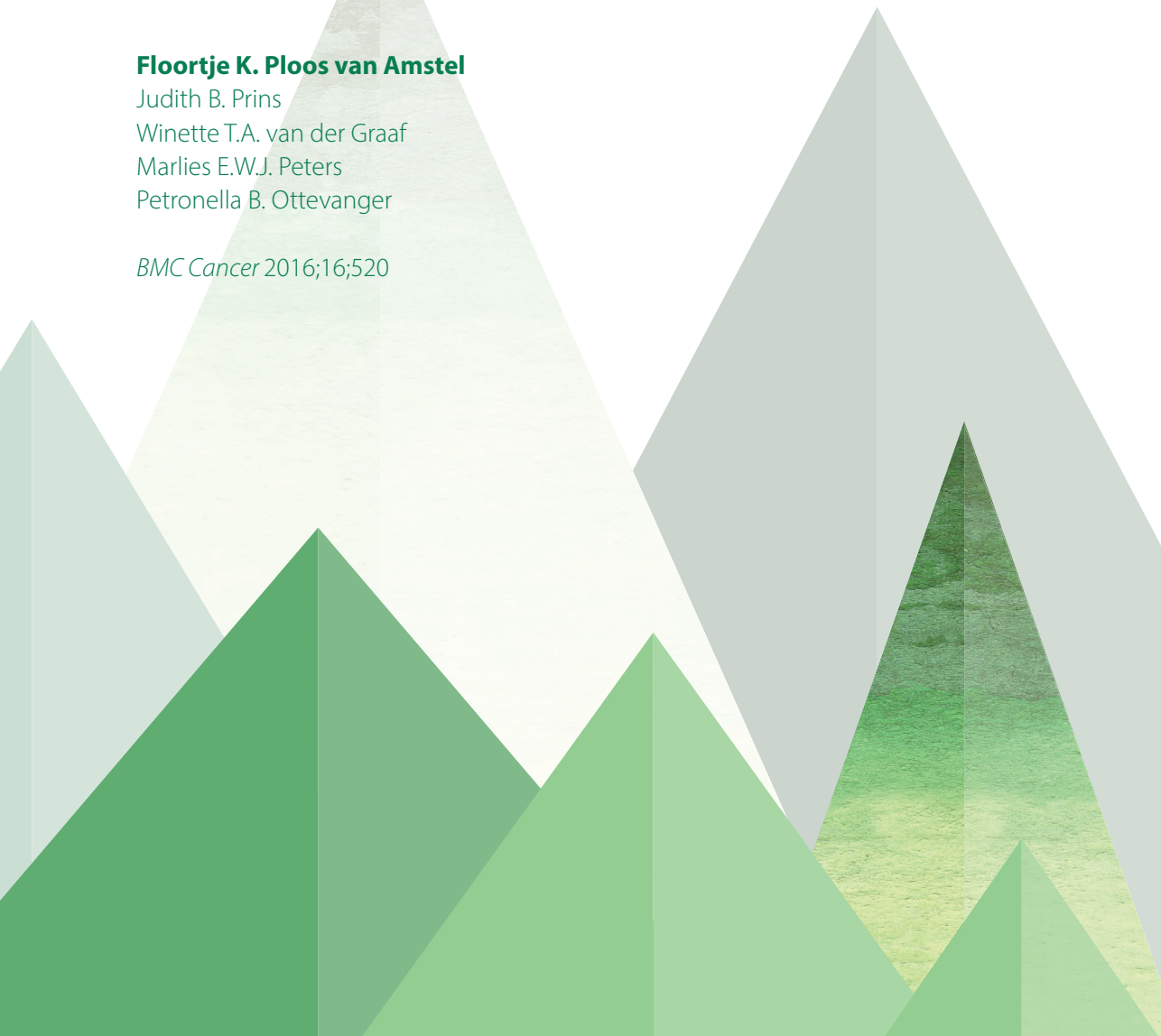

Abstract

Background

Distress in patients with cancer influences their quality of life. Worldwide, screening on distress with the Distress Thermometer (DT) in patients with cancer is recommended. However, the effects of the use of the DT on the psychosocial well-being of the patient are unknown. A study to assess the psychosocial consequences of the systematic use of the DT and its discussion by a nurse as compared to the usual care provided to outpatients who are treated for primary breast cancer is needed.

Methods/design

The effectiveness of a nurse-led intervention with the DT will be tested in a non-blinded randomized controlled trial. Patients treated with curative intent for breast cancer will be recruited from the Radboud university medical center. The intervention consists of the DT together with discussion of the results with the patient by a trained oncology nurse added to the usual care. Patients will be randomly allocated (1:1) to either receive usual care or the usual care plus the intervention. Primary outcome measure is global quality of life measured with the EORTC QLQ-C30. The functional and symptom scales of the EORTC QLQ-C30 and BR23, Hospital Anxiety and Depression Scale, Impact of Event Scale, Illness Cognition Questionnaire and DT (baseline and final measurement only) will be used to measure secondary outcomes. Questionnaires are obtained in both arms at baseline, after completion of each type of cancer treatment modality and during follow-up, with a three and six months' interval during the first and second year respectively.

Discussion

This study will be the first randomized controlled longitudinal study about the effectiveness of the DT as nurse led-intervention. In case of proven effectiveness, future implementation and standardization of use of the DT as part of routine care will be recommended.

Trial registration

This study is registered at clinicaltrial.gov march 17, 2010 (NCT01091584).

Background

With an incidence of more than 1.67 million women yearly, breast cancer is the second most frequently occurring type of all cancers in the world.[1] Despite the reported increase in survival rate, the diagnosis breast cancer has a serious impact on a woman's life.[2,3] The National Comprehensive Cancer Network (NCCN) summarizes the problems that patients with cancer may encounter with the word "distress" and defines it as '*a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling such as depression, anxiety, panic, social isolation, and existential and spiritual crisis*'.[4] When patients experience distress it impinges on their quality of life and the time for recovery during and after treatment.[5-10] The current NCCN guideline describes that 20-47% of patients with newly diagnosed and recurrent cancer experience a significant level of distress.[4] Offering basic psychosocial care is a core task for physicians and nurses. Psychosocial care could consist of education about the disease and treatment process, emotional support, as well as support in choosing treatment modalities. For optimal support, it is important to screen for levels of distress and the unmet needs of the patient.[11,12]

Screening for distress

The Distress Thermometer (DT) has become a worldwide standard screening tool for distress in cancer patients that facilitates a systematic approach to distress detection.[4,9,10,13-20] It consists of a Visual Analog Scale (VAS) score and a problem list. Without a systematic distress assessment patients are at risk of under diagnosis and treatment.[4] Its use can assist in the timely detection of distress and facilitate early intervention. A screening instrument like the DT provides guidance for discussions with patients. Its use gives attention and focus to psychosocial issues, an increased awareness of distress and more effective communication between healthcare professionals and patients.[4]

Recently, an increasing number of papers have been published on the validity of the DT in different languages and on different cuttoff points.[4,14-18,21] Additionally, the DT is used in studies to measure distress related to various tumor types[19,20] and at different time points during treatment and follow-up.[9,10,22,23] Studies about the effectiveness of the utilization of the DT are scarce. Based on current knowledge, only one study described a non-blinded randomized controlled trial about the DT in comparison to standard care.[24] In this study the DT was assessed once at baseline and patients filled out questionnaires at 1, 6 and 12 months of follow-up. No effect on costs and no significant improvement on the mood states among patients were found.[24] Due to this lack of evidence on effectiveness there is an ongoing discussion about the use of the DT.[25-27] Internationally, it is recommended to implement guidelines to address psychosocial care, with for example the DT, to manage the psychosocial impact of cancer as part of daily oncology care.[4,28,29] However, it is still unconfirmed that systematic screening with the DT and a subsequent discussion of the results will lead to improved patients' quality of life. It is striking that the use of the DT is implemented as standard care worldwide without any

evidence of effectiveness. We therefore decided to investigate the added value of using the DT systematic to improve their quality of life by a nurse in oncology care in a randomized controlled trial, in patients diagnosed with breast cancer. The decision to focus on patients with breast cancer was made for the following reasons; (1) breast cancer has a high incidence, (2) most patients undergo a long treatment process and (3) patients have high survival rates. The high survival rate is essential to be able to measure the effects of the intervention in preventing long-term psychosocial problems.

Objective

The primary objective of this randomized controlled trial is to evaluate the effect of a nurse-led DT intervention on improving the quality of life of patients with breast cancer who are treated with curative intent, compared to usual care, after approximately two years of follow-up.

Methods

This study will be reported in accordance with the SPIRIT guideline.[30]

Study design

The design of the study (also called Nurse Intervention Project) is a non-blinded randomized controlled trial (Figure 1). In the intervention group, a thorough assessment using the DT and a discussion of the results by a trained oncology nurse will be added to the usual care. Actions based on the outcomes of the DT will be taken as necessary. The control group will receive the usual care without using the DT. By comparing the results of the intervention group with the control group the effect of the intervention can be determined.

Participants eligibility

Inclusion criteria: women with histology proven malignancy of the breast; who will receive treatment with curative intent, written and oral fluency in the Dutch language and aged ≥ 18 years. Exclusion criteria: men, women who have been treated previously for a malignancy (except adequately treated cervix carcinoma in situ and basal cell carcinoma of the skin) and women with psychiatric problems that impair adherence to this study.

Recruitment

Patients will be recruited from the population of newly diagnosed breast cancer patients at the Radboud university medical center. Women who have been diagnosed with breast cancer and meet the inclusion criteria, will be asked to participate in this study. The patients will be monitored after surgery, during adjuvant treatment and approximately two years during the follow-up. Immediately following diagnosis participants will be verbally briefed by a clinical nurse specialist about the study and given an information pack containing a detailed information sheet and letter of invite to participate in the study. This timing

is crucial as it is preferable to collect baseline measurement before start of the first treatment modality. Following receipt of the information package the patient has several days to consider participation in the study. If the patient gives consent for further discussion about the study, the investigator will then be in contact with the patient by telephone or during the next hospital visit to discuss further potential participation. In the time frame between the diagnosis and the start of treatment, the patient usually visits the responsible healthcare professional (surgeon, clinical nurse specialist or oncologist). On that day, if appropriate, the patient will be asked to confirm her participation and baseline measurements will be taken in the hospital or at home. There are paper-and-pencil and electronic versions of the assessment available. Electronic completion reduces the risk of missing data because the patient has to answer each questions before sending. A paper-and-pencil version of the questionnaires will be available for those who are not capable of filling it out electronically.

Randomization

The expectation is that approximately 75% of the patients will receive hormonal therapy. Since mood swings and fatigue are known side effects of hormonal therapy, we will stratify for hormonal treatment.[31] We therefore will use a randomized block design, prepared by an independent statistician. The patients will be randomized in a 1:1 ratio, immediately after assessment of the adjuvant treatment plan, which includes the use of adjuvant hormonal therapy. Random assignment using sequentially numbering will be done by a physician not involved in the study. The result of the randomization will be communicated by e-mail or mail to the patient by the investigator.

Intervention

The intervention comprises of support by the trained oncology nurse based on the discussion of the DT in accordance to the protocol for assessing the need for psychosocial care for cancer patients.[13] The intervention is combined with the (follow-up) visit to the outpatient clinic. The DT consists of a thermometer ranging from 0 (no distress) to 10 (extreme distress). In addition the tool contains 47 questions (yes / no answers) related to different issues. The issues have been categorized into: practical issues, family / social issues, emotional issues, religious / spiritual issues, physical issues. The DT concludes with the question: "Would you like to talk with a professional about your problems?" (yes/maybe/no). The cuttoff point is 5.[14]

The following steps will be made for each screening moment with the DT:

1. The patient will receive an e-mail or mail about the appointment with the trained oncology nurse, which will take place in combination with regular visits in the outpatient clinic.
2. The patient will fill out the DT in the outpatient clinic a few minutes before the appointment.
3. The trained oncology nurse will discuss the DT with the patient before or after the visit with the attending healthcare professional. The nurse will ask on which problems the DT score is based and the mentioned problems on the problem list will be discussed. If the patient reports a lot of problems, the nurse will ask the patient to prioritize the problems indicated. At the end, the nurse will ask if the patient would like to be referred to a professional.
4. Time allocated to these meetings will last between 5 - 30 min, depending on the severity of the distress and the nature of the problems.
5. If the patient reports a DT score of < 5 the trained oncology nurse will inquire whether the patient is sufficiently in control of her situation. The low distress score and the issues marked on the problem list are discussed briefly. At a score ≥ 5 on the DT, an extensive exploratory conversation between the nurse and the patient will take place. The outcome of this conversation will be discussed in a psychosocial Multi Disciplinary Team (MDT). The MDT has been established to discuss all patients of the intervention group with a score of ≥ 5 on the DT and to discuss patients who personally request additional support. The participants of the MDT are the attending healthcare professional and/or oncologist, the trained oncology nurse, a social worker and clinical psychologists. During the MDT a treatment plan is composed when needed. The nurse will propose this plan to the patient by phone.

Three oncology nurses will be trained by a clinical psychologist to perform the intervention over three sessions. A specific manual will be developed during the training sessions and the intervention. In order to apply consistency in the content and the discussion of the DT with the patients, those three nurses will receive the same training. They should be qualified as a nurse and be knowledgeable in the course and treatment of breast cancer. For financial reasons an independent trained study nurse cannot be hired for this study. Because oncology nurses from the wards have a high risk of contamination the intervention group while being in contact with patients from both the intervention and the control group, they are not suited to deliver the intervention themselves. Therefore, we will select three oncology nurses who are not bedside nurses and are involved in other than breast cancer patient groups on the out-patient clinic. In order to build a trustworthy relationship and give continuity to the care whenever possible the patient will meet the same oncology nurse at every visit. During this study the DT is not implemented in daily care so the oncology nurses of the departments involved in the study will not use it in daily practice. A short standard report (as incorporated in the manual) will be filled out after each conversation. To prevent contamination with other professionals, the report of the conversation will not be included in the medical record of the patient. The investigator of the study is also one of the trained oncology nurses who will deliver the interventions. In order to minimize the

influence of the investigator on the results of the study, an independent database will be created and an independent statistician will analyze the data.

Usual care

As already mentioned, the DT will not be implemented in daily care for patients with breast cancer during this study period, therefore no professionals taking care of breast cancer patients will use the DT. The usual care consists of routine follow-up visits with the attending healthcare professional (physician or clinical nurse specialist) according to the Dutch breast cancer guideline (see also measuring time points).[32] Depending on the judgment of the responsible healthcare professional, the patients may be referred to other healthcare professionals, if indicated. No psychosocial MDT is available in usual care.

Measuring time points

The baseline measurement will take place preferably before breast surgery or start of the neo-adjuvant chemotherapy. During the first year of treatment the assessments will take place at the end of each treatment modality. In the second and third year, the follow-up visits will be in line with the recommendations of the Dutch breast cancer guideline.[32] This means that data will be collected approximately every 3 months during the first and every 6 months in the second year after the completion of adjuvant treatment (except for trastuzumab or hormonal therapy). This will result in a total of 8 - 10 measurements, depending on the number of adjuvant therapies (see Figure 1). In order to monitor the effects of treatment on the patients' well-being in both the short- and long- term, patients will be followed for two years after completion of the primary (adjuvant) treatment. At all measuring time points both groups will receive questionnaires. The DT is included for both groups at baseline and at the end of the study. At those time points the results will not be discussed with the patients. Approximately two days before the regular visit to the attending healthcare professional, the patient will be asked to fill out the questionnaire electronically (Radquest software, department of Medical Psychology) or on paper in the hospital or at home. It takes 10 – 30 min to fill out the questionnaires. Additionally, a diary will be provided to the patient in which the consumed care and work absence has to be noted and recorded. At the moment the patient hands in the diary, a new one is provided by mail or personally. In case of non-response, a reminder will be send within 2 weeks by e-mail or mail.

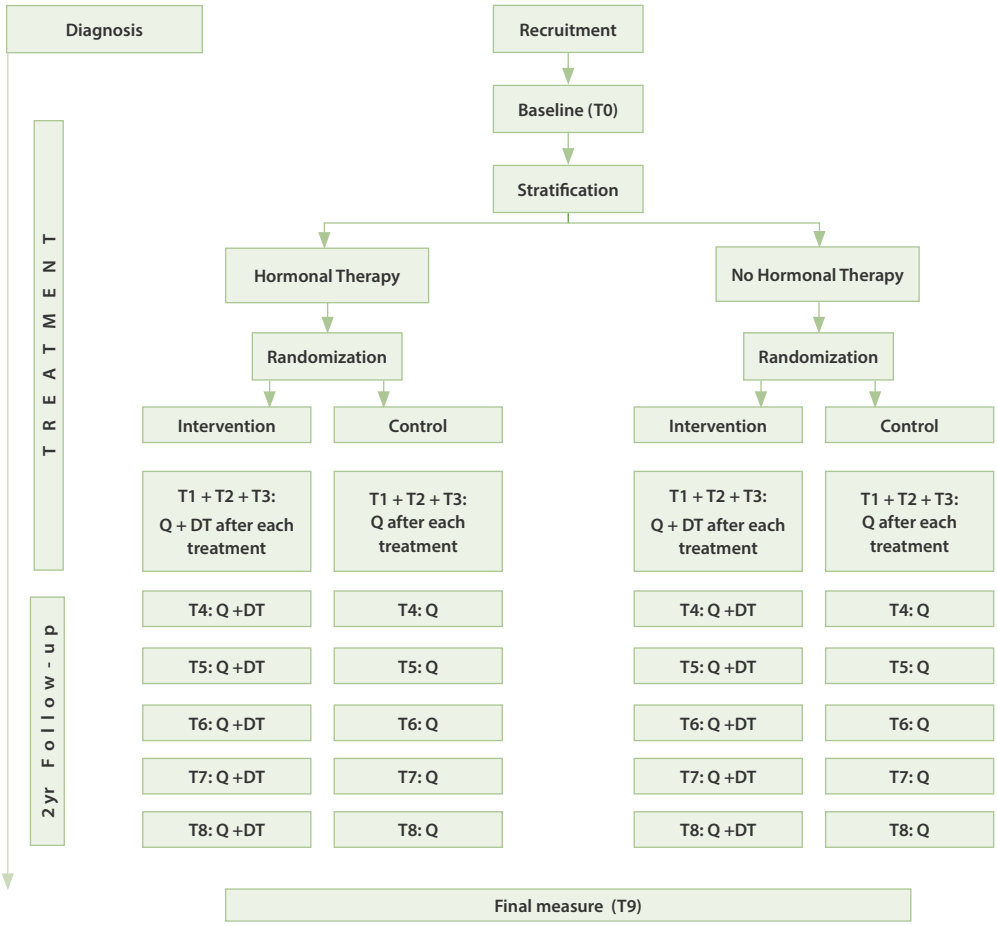

Figure 1 Flow-chart of the Nurse Intervention Project.

Abbreviations: Q = Questionnaires, DT = Distress Thermometer Intervention includes a thorough assessment using the DT and a discussion of the results by a trained oncology nurse. The questionnaires are: EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, QLQ-BR23 = Quality of life- Breast Cancer, HADS = Hospital Anxiety and Depression Scale, IES = Impact of Event Scale, ICQ = Illness Cognition Questionnaire, EQ-6D = EuroQol-6D, and a diary.

Table 1 Measurements and time points of the Nurse Intervention Project.

Questionnaires	Target	T0	T1-T8	T9	Response format
Demographic & medical characteristics	Descriptive of the population	X	X	X	Multiple answers
EORTC QLQ-C30	Functional scales: physical, role, emotional, social, and cognitive functioning (15 items)	X	X	X	4 point Likert scale range 15-60
	Symptom scales: fatigue, pain, nausea/vomiting (7 items)	X	X	X	range 7-28
	Single symptom items (6 items)	X	X	X	range 6-24
	Global Health and global quality of life* (2 items)	X	X	X	7 point linear analog scale range 2-14
EORTC QLQ-BR23	Functional scales: body image, sexual functioning, sexual enjoyment, future perspective (8 items)	X	X	X	4 point Likert scale range 8-32
	Symptoms scales: arm symptoms, breast symptoms, systemic therapy side effects, upset by hair loss (15 items)	X	X	X	range 15-60
DT	General distress	X	X[1]	X	11 point visual analog scale range 0-10
	Problem list (47 items)	X	X[1]	X	Yes/no
	Question: wish for referral (1 item)	X	X[1]	X	Yes/maybe/no
HADS	Emotional distress (14 items) Subscales: Anxiety (7 items) Depression (7 items)	X	X	X	4 point Likert scale range 0-42 (total scale) range 0-21 range 0-21
IES	Coping with the cancer (15 items) Subscales: Intrusion (7 items) Avoidance (8 items)	X	X	X	4 point scale range 0-75 (total score) range 0-35 range 0-40
ICQ	Illness perceptions (18 items) Subscales: Helplessness (6 items) Acceptance (6 items) Perceived benefits (6 items)	X	X	X	4 point Likert scale range 6-24 range 6-24 range 6-24
Diary	Healthcare use and work absence		X	X	Yes/no, frequency and reason
EQ-6D	Quality of life in relation to economic evaluations (1 item)	X	X	X	Visual analog scale range 0-100
	Dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression and cognition (6 items)	X	X	X	range 1-3 for each dimension

Abbreviations: T0 = baseline measurement, T1-T3 measurement after each treatment and T4-T8 follow-up, T9 = final measure, EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, QLQ-BR23 = Quality of life- Breast Cancer, DT = Distress Thermometer, HADS = Hospital Anxiety and Depression Scale, IES = Impact of Event Scale, ICQ = Illness Cognition Questionnaire, EQ-6D = EuroQol-6D.

* Primary outcome.

[1] Only in the intervention group.

Study outcome measures

Demographic data and the use of psychosocial care are measured with general questionnaires. Medical disease-specific data will be collected from the electronic medical record. A checklist will be used to collect the relevant medical records from the patients' status.

Primary outcome measure

The primary outcome will be the global quality of life subscale as defined by the European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire-C30 (EORTC QLQ-C30).[33] The items of the global health and global quality of life scale use a 7-point linear analog scale (very poor to excellent).[34]

Secondary outcomes

The secondary outcomes will be: breast cancer related quality of life, anxiety, depression, emotional distress, coping, illness cognitions and distress (Table 1). Functional and symptom scales of the EORTC QLQ-C30 will be used to assess the other dimensions of quality of life (see Table 1). Higher scores on the global and function scales implies good quality of life. On the symptom scales, low scores indicates less intense symptoms hence higher quality of life. [33-35] Breast cancer related quality of life will be assessed with the breast cancer related questionnaire EORTC- BR23 which consists of 23 questions and complements the C30.[36] Anxiety, depression and emotional distress will be measured with the Hospital Anxiety and Depression Scale (HADS). The HADS has two subscales (anxiety and depression) and a total score of emotional distress. The questionnaire consists of 14 questions with scores ranging from 0 (not at all) to 3 (very much).[37-39] The presence of coping problems will be measured with Impact of Event Scale (IES). This questionnaire provides an inventory of the effects of a shocking event and focuses on the person's feelings and thoughts over the previous seven days. The IES has two subscales: intrusion and avoidance. The scores range from 'not at all', 'rarely', 'sometimes' and 'often'.[40] To identify the role of illness cognitions in relation to the treatment effectiveness we will use the Illness Cognition Questionnaire (ICQ). There are three subscales: helplessness, acceptance and perceived benefits. The scores range from 1 (none) to 4 (entirely).[41] Distress will also be measured with the DT at baseline and final measurement for both groups (see Figure 1).[14] In case we will find differences between both groups on quality of life we will further explore the healthcare utilization. These data will be gathered with a diary that the patients will take home between measurement time points. Patients will register their healthcare utilization, cancer-related absence from work, specific medication and care. Quality of Life in relation to economic evaluations will be measured using the EuroQol-6D (EQ-6D). The EQ-6D comprises both the EQ-5D and an additional dimension namely, cognition. The EQ-5D measures health on five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). Every dimension is differentiated in three levels: no problems, some problems, and extreme problems. The EuroQol Visual Analog Scale (EQ-VAS) will also be used. The EQ-VAS provides a subjective assessment of quality of life on a scale ranging from 0 (worst health) to 100 (best health).[42]

Evaluation

At the end of the study, patients will be asked to evaluate their experiences during the study period. In addition, the intervention group will be asked to evaluate their experience of the intervention. The control group will be asked about their need for more psychosocial support during treatment or follow-up.

Data management

We expect most patients will fill out the questionnaires electronically. The results of the questionnaires will be converted to SPSS by a data manager. Only the investigators have access to the coding, storage of all questionnaires and the final dataset. The paper and pencil questionnaires and medical characteristics will be entered in the SPSS database by a research assistant. For the validity of these data, for 10% of the data double entry of data will be done. A statistician will check data value ranges. All source data will be stored for 15 years.

Power calculations

Based on prior clinical studies a difference of 10 points in the EORTC QLQ-C30 and its subscales is considered a clinically relevant difference for patients with cancer.[34] The power of the study to detect an effect of 10 points or more is calculated as follows. The primary outcome is the global quality of life subscale of the EORTC QLQ-C30 (SD = 22.7) at the end of the study.[43] However, we aim for sufficient power for the most important secondary outcomes – the subscales: role function, emotional function, cognitive function and social function of the EORTC QLQ-C30 (clinically relevant difference 10 and SD = 18.7 – 22.8).[43] Therefore, we are aiming for 84 patients per group. The power of the primary outcome then becomes more than 96%, and for the relevant subscales at least 80%, when analyzing these outcomes with adjustment for baseline (i.e., an ANCOVA which has as much power as the *t*-test or more depending on the correlation of the baseline measurement with the measurement at the end of the trial). Taking a drop-out of at most 15% into account, a total number of 193 patients needs to be included to have sufficient power for the primary and secondary outcomes.

Statistical analysis

The primary analysis is the comparison of the primary outcome global quality of life subscale of the EORTC QLQ-C30 as measured at the end of the research period analyzed by ANCOVA, i.e., an adjustment for baseline will be included. The secondary analysis of the primary outcome is a repeated measurements analysis of the sequence of the repeated measurements in order to compare the trends between the two groups (mixed model for repeated measurements). Similar analysis will be carried out on the secondary outcomes. Subgroup analysis will be performed on demographic and treatment characteristics. Missing data will be analyzed with the last observation carried forward method for the ANCOVA and a sensitivity analysis assuming missing data to be missing-at-random will be performed using a mixed model for repeated measurements. Patients who have died, had recurrence or metastasis of the breast cancer, or

were diagnosed with another malignancy during the study will be considered to have dropped out of the study from that event onwards.

Discussion

This study will evaluate the effect of an oncology nurse-led DT intervention compared to usual care on improving the quality of life of patients who are treated for breast cancer with curative intent. The results will contribute to the actual knowledge and the current discussion about using the DT in daily oncology practice, as most previous studies were performed for validation of the DT.[25-27] Even though Hollingworth et al. performed an RCT to measure the efficacy of the DT, they used the DT once.[24] In our study, we will offer a nurse-led DT intervention repeatedly in a period of more than two years, which makes our study unique and complementary to the existing literature. Despite a natural recovery of quality of life over time, we will expect additional improvement when using the DT systematically during a longer period. As a primary endpoint, we will use the EORTC QLQ-C30 global quality of life scale. In order to compensate for probable response shift, we will also inspect the secondary outcomes to measure distress reduction. Additionally, the results of this study will give us insight into the trajectories of distress and quality of life from diagnosis to 2 year follow-up in the usual care group. The short- and long-term problems of patients with breast cancer will become apparent. Therefore, the outcome of our study may have impact on the future implementation of the DT both nationally and internationally. The strengths of our study are: (1) we will follow the guideline about distress management, (2) we will systematically assess and discuss the DT for approximately 2 years follow-up, (3) we will discuss the DT results of all patients in the intervention group with high distress in a psychosocial MDT.

Conclusion

In conclusion, the aim of our study is to determine the effectiveness of the systematic use of the DT and the subsequent discussion of the results with a trained oncology nurse compared with usual care on the quality of life of the patient with breast cancer. It is anticipated that the results of the study will have impact on the future implementation and standardization of the use of the DT as part of routine care. It is expected that the data collection will be completed early 2016.

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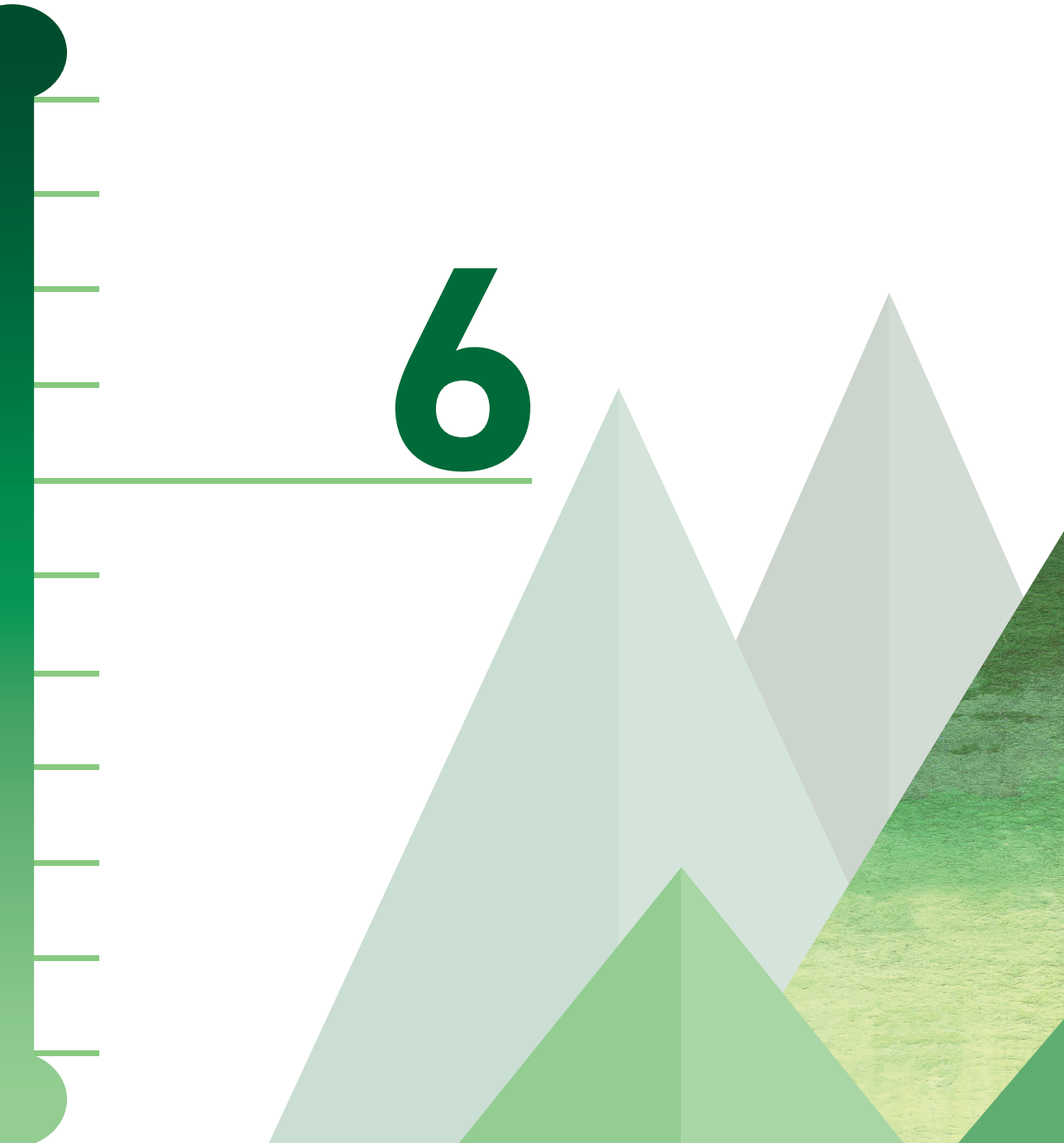

Does a regular nurse-led distress screening and discussion improve quality of life of breast cancer patients treated with curative intent? A randomized controlled trial

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Abstract

Objective

We performed a randomized controlled trial (RCT) to investigate whether regular screening with the Distress Thermometer (DT) by a nurse improved global quality of life (QOL) of patients with breast cancer (BC) treated with curative intent.

Methods

BC patients were randomized between regular screening for distress with a nurse-led DT intervention (NDTI) and usual care (UC). Both groups filled out questionnaires at baseline, after each received treatment modality and at follow-up visits up to 2 years. At these points, the intervention group received also the NDTI. The primary outcome was the global QOL of the EORTC QLQ-C30 at 2 years after the end of treatment. Analyses were done on an intention-to-treat basis, using analysis of covariance (ANCOVA), generalized least squares, and interaction analyses.

Results

Of 194 randomized patients, 153 filled out the questionnaires up to 2 years after treatment. There was no significant difference between NDTI and UC in global QOL 2 years after the end of treatment (mean diff. -1.273, $p = 0.610$; 95% CI [-6.195; 3.649]). Subgroup analysis of patients who received multimodality treatment (surgery, radiotherapy, and chemotherapy, $n = 66$) showed a significant between-group difference in global QOL over time (mean diff. -10, $p < 0.001$; 95% CI [-14.835; -5.167]) together with other secondary outcomes measures in favor of the NDTI.

Conclusion

NDTI did not lead to a significant improvement in global QOL 2 years after the end of treatment for patients with BC. However, the findings indicate that BC patients who received multimodality treatment may benefit from NDTI.

Background

The diagnosis cancer and its subsequent treatment have a tremendous impact on patients.[1, 2] The National Comprehensive Cancer Network (NCCN) defines distress as *'a multifactorial unpleasant experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment.*[1] The first NCCN guideline about distress screening with the Distress Thermometer (DT) was published in 1999.[1] Since then more attention has been given to the impact of the diagnosis of cancer.[1] The DT has been validated in different languages and cancer populations.[3] Patients should rate their distress on a scale from 0 (no distress) to 10 (extreme distress) and provide information about issues that contribute to their distress.[1, 4] When patients experience distress, it can negatively affect their health-related Quality of Life (hrQOL).[5-7] HrQOL is a multidimensional concept which covers the subjective perceptions of cancer patients' symptoms including physical, emotional, social, cognitive functions, disease symptoms, and side effects of treatment, whereas global QOL is a general perception of the experience of QOL.[8] Patients with good physical functioning will most likely experience less distress. On the other hand, distress may result in impaired physical and psychosocial functioning, which can be measured with a hrQOL questionnaire.[9] This relationship was also discussed in a review about predictors of distress in cancer patients.[7] Randomized controlled trials (RCTs) that focused on the period of treatment and the first year of follow-up did not establish evidence that distress screening with the DT improves hrQOL.[10-14] At the start of our study, longitudinal screening on distress with a DT in cancer patients during and up to 2 years after treatment in an RCT was never performed. The assumption was that regular assessment of distress would help identifying patients who suffered from distress or were at risk of distress and that timely intervention may impact positively on hrQOL. Our aim was to determine if early psychosocial interventions for those patients who experience distress could prevent or halter deterioration in hrQOL during the first 2 years of recovery from cancer. Although it is not specified which healthcare professional should ask patients about distress, in practice oncology nurses frequently do this.[15-17] An advantage of nurses addressing distress is that there is less stigma of mental health problems, which might be the case if distress screening is provided by psychological services.[18] In our RCT, we selected the nurse to regularly screen for distress with the DT and discuss results, the so-called nurse-led DT intervention (NDTI). Breast cancer (BC) patients were chosen because of the high incidence of the disease, increased distress,[5, 19-21] frequent requirement of multimodality treatment, and good survival rates, which makes distress relief an important issue.

Methods

This RCT is reported in accordance with the CONSORT statement and the study protocol has been published elsewhere.[22, 23] The study was approved by the Medical Ethics Committee of our institution (2009/293). Registration number of the clinicaltrials.gov is NCT01091584.

Study design and participants

We performed a non-blinded RCT to evaluate the effect of the NDTI on improving global QOL in patients with BC treated with curative intent compared to usual care (UC). Participants were women diagnosed with BC at a university medical center. Inclusion criteria were age ≥18 years with histology-proven invasive BC and eligible for curative treatment. Exclusion criteria were previous malignancy (except adequately treated cervix carcinoma in situ and basal cell carcinoma of the skin), a psychiatric disorder, or lack of competence in the Dutch language. Patients received verbal and written information about the study immediately after being diagnosed with BC from a clinical nurse specialist (CNS) at the outclinic. Several days later, the investigator contacted the patients by telephone to make an appointment to explain the study. Written informed consent was obtained. The baseline assessment (T0) was done before treatment started. Thereafter, the assessments were scheduled after each treatment modality which included surgery and/or (neo) adjuvant chemotherapy, and/or radiotherapy. During follow-up, patients could be treated with hormonal therapy or trastuzumab. After the first treatment modality, questionnaires were completed by the patients, and interventions deemed necessary were carried out (T1). Subsequently, if applicable, after the second treatment modality (T2) and third treatment modality (T3), again questionnaires were completed and necessary interventions were carried out. This was repeated every 3 months during the follow-up visits in the first year (T4 - T7) and every 6 months during the second year of follow-up (T8 - T9). This resulted in a total of 8 to 10 measurements for each patient, depending on the number of treatment modalities. These intervals were recommended by the Dutch distress guideline and corresponded with the NCCN guideline.[1, 24] Three oncology nurses (study nurses) were responsible for collecting data.

Intervention

The NDTI comprised a discussion of the DT results by a study nurse according the Dutch distress guideline.[24] Three qualified oncology nurses were trained in how to use the DT to become study nurses for this study. After each assessment, the nurse reviewed the DT score and explored which problems were particularly important to the patient. The intervention encompassed providing emotional support and education about cancer and its treatment. It also included giving practical advice on emotional, social, practical, and/or physical issues raised. A close family member or the caregiver was encouraged to join the NDTI sessions. If the patient had a DT score of < 5, the nurse inquired whether the patient indeed did not feel distressed. If the score was ≥ 5, the nurse had a more focused conversation on the problems indicated by the patients. In a psychosocial multidisciplinary team (MDT) meeting, all NDTI patients with a score ≥ 5 or who personally request additional support were discussed. After this meeting, the nurse explained the proposed plan to the patient by telephone. Appendix A and the study protocol give more details about the NDTI.[22]

Usual care

UC consisted of routine follow-up visits with the attending healthcare professional according to the Dutch BC guideline. The DT was not used. The treating healthcare professional decided whether the

patient should be referred to other professionals for additional psychosocial and physical support. The patients in the UC group were not discussed in the MDT meetings.

Outcome measures

Questionnaires were completed online with RadQuest software or with paper and pencil.[25] Information about demographics and the use of psychosocial care was collected by general questionnaires, and medical disease-specific data were collected from the electronic medical records.

The primary outcome measure was global QOL, as assessed with the European Organization for Research and Treatment of Cancer, QOL Questionnaire-C30 (EORTC QLQ-C30). The items were scored on a seven-point linear scale (1–7, very poor to excellent).[8, 26] Secondary outcomes included (breast) cancer hrQOL, anxiety, depression, emotional distress, coping, illness cognitions, general distress, and healthcare utilization. We used the EORTC QLQ-C30 and the BC-specific EORTC-BR23 to explore other dimensions of hrQOL (physical, role, emotional, social, and cognitive functioning).[26, 27] Anxiety, depression, and emotional distress were measured with the Hospital Anxiety and Depression Scale (HADS).[28] The Impact of Event Scale (IES) was used to measure coping problems, and the Illness Cognition Questionnaire (ICQ) was used to measure illness cognitions in relation to cancer treatment.[29, 30] In the UC group, general distress and problems were only measured with the DT at baseline and at the end of the study.[4] Healthcare utilization was monitored by means of self-report information and the EuroQol-6D (EQ-6D).[31] More details about the questionnaires are described in the protocol of this study.[22] At the end, the intervention group was additionally asked to evaluate the NDTI.

Randomization and sample size

An independent statistician prepared a randomized block design. Patients were stratified by the use of hormonal treatment. Patients were randomized in a 1:1 ratio, immediately after the hormonal status was known, and the adjuvant treatment plan was established. Random assignment using sequential numbers was done by a physician not involved in the study.

Based on prior clinical studies, a difference of 10 points or more in the EORTC QLQ-C30 and its subscales is considered a clinically relevant difference for patients with cancer. The primary outcome was the global QOL subscale of the EORTC QLQ-C30 (SD = 22.7) at the end of the study after 2 years of follow-up.[26, 32] We aimed for sufficient power for the most important secondary outcomes the subscales: role function, emotional function, cognitive function and social function of the EORTC QLQ-C30 (clinically relevant difference of 10 and SD = 18.7–22.8).[32] We calculated that we needed 84 patients per group with a power of 96% and at least 80% for the primary outcome and for the relevant subscales, respectively.[22] With an expected drop-out of at most 15%, we needed to include minimally 193 patients to have sufficient power for the primary and some secondary outcomes.

Data analysis

Statistical analyses of intention-to-treat data were performed using IBM SPSS, version 24. Missing values on the primary outcome measure at T9 were imputed using last observation carried forward and a sensitivity analysis was used to evaluate the impact of the missing values. End-of-follow-up outcomes were analyzed using a one-way between-groups ANCOVA with the baseline measurement of the outcome and hormonal therapy as covariates and the intervention as variable. Secondary analyses of all post-baseline measurements were done using a generalized least squares model with condition, time, and the interaction between condition and time as fixed factors and the baseline measurement as covariate. We assumed an unstructured correlation matrix for the residuals. Thereafter, we performed the same post hoc analysis in a subgroup of patients who received surgery, radiotherapy, and chemotherapy.

Results

The CONSORT diagram (Figure 1) shows the number of patients approached, screened, randomly assigned, and retained. Between March 2010 and February 2013, all women who received a diagnosis of BC (n = 366) were assessed for inclusion criteria. Of these patients, 103 did not meet the inclusion criteria and 65 declined to participate. Four patients were erroneously enrolled and therefore excluded after randomization.[33] Overall, 96 BC patients were assigned to NDTI and 98 to UC. Baseline characteristics are shown in Table 1. Of the 194 patients, 25 (13%) dropped out during the study because of further treatment in another hospital (n = 2), no further interest (n = 3), death (n = 1), local recurrence, distant metastases, or second malignancy (n = 10), or too burdensome (n = 9). Of the remaining 168 patients, 153 patients completed the final measure.

NDTI

Ninety-six patients allocated to the intervention group. Table 2 shows the results of the experienced distress of the patients at each time point. In total, 688 DT's were filled out, 215 (31%) patients (some patients more than once) were discussed in the MDT because of the distress score. Most of the patients did not wish to receive a referral to psychooncology services, but indicated that the conversation with the nurse was sufficient. Twenty-four patients (25%) received a referral to a psychooncology services. Patients with anxiety and/or depression were referred to a psychologist (n = 10). Other patients with, for example, coping, family or financial problems were referred to a social worker (n = 9). One patient was referred to a sexologist. Because of chronic fatigue, three patients were referred to an expert center for cancer-related fatigue. Some patients had already psychological support before start of treatment, which they continued during the study.

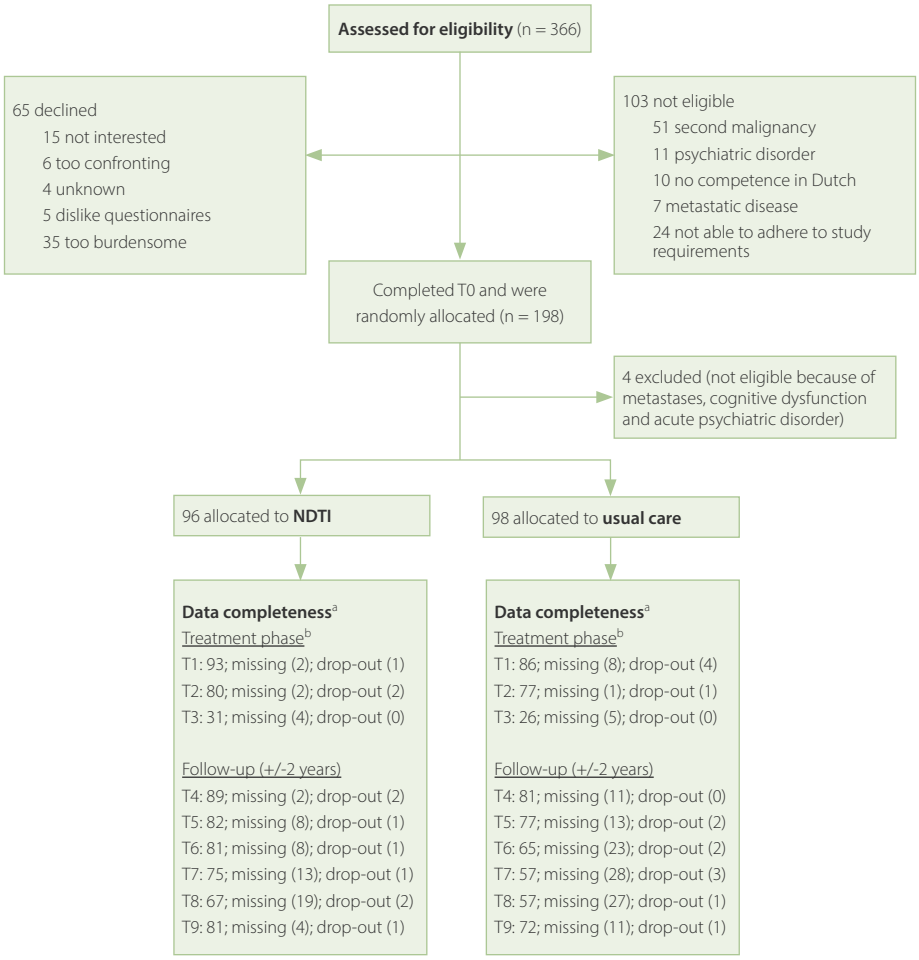

Figure 1 CONSORT flow chart showing recruitment and enrolment.

Abbreviation: NDTI = Nurse-led Distress Thermometer Intervention.

[a] Data completeness: patients who filled out at least the global QOL of the EORTC QLQ-C30 at the mentioned time point.

[b] T1:after one treatment modality, T2: after two treatment modalities, T3:after three treatment modalities.

Table 1 Patient and treatment characteristics at baseline (N = 194).

	NDTI (n = 96)	UC (n = 98)
Age, median (range) in years	52.5 (30 - 86)	53.1 (26 - 75)
Marital status, n (%)		
Married/cohabiting	77 (80)	74 (76)
Divorced/widowed/other	19 (20)	24 (24)
Education, n (%)[a]		
Low (ISCED 0-1-2)	17 (18)	10 (10)
Medium (ISCED 3-4-5)	41 (43)	49 (50)
High (ISCED 6-7-8)	35 (36)	38 (39)
unknown	3 (3)	1 (1)
Occupation[b]		
Paid work	58	54
Retirement	13	16
Disablement insurance act or sick leave	16	10
Other[c]	32	24
Treatment (received), n (%)		
Surgery	9 (9)	14 (14)
Surgery + radiotherapy	24 (25)	26 (27)
Surgery + chemotherapy	27 (28)	27 (28)
Surgery + radiotherapy + chemotherapy	35 (36)	31 (32)
unknown	1 (1)	
Hormone therapy	66 (69)	66 (67)
Global Quality of life[d] (mean, SD)	70.8 (23)	74.3 (20)
Distress[e] (mean, SD)	5.2 (2.7)	4.6 (2.8)

Abbreviations: NDTI = Nurse-led Distress Thermometer Intervention, UC = usual care.

[a] ISCED = International Standard Classification of Education, 2011.

[b] Multiple answers possible.

[c] No (paid) work, student, housewife.

[d] Measured with EORTC QLQ-C30.

[e] Measured with DT.

Effect of the NDTI

At the 2-year time point following completion of cancer treatment (T9), there was no significant effect of the intervention on global QOL (mean diff. -1.273, p = 0.610; 95% CI [-6.195; 3.649]) or on any of the secondary outcome variables. There was no clinically relevant difference in global QOL between patients receiving NDTI and UC. Primary and secondary outcomes at the different time points are given in Appendix B. Figure 2A shows the mean global QOL of the different time points over time. At T3, a decrease of global QOL was seen. Only patients who received surgery, radiotherapy and chemotherapy (multimodality treatment) had an assessment at T3 (Figure 2A). We found a significant interaction effect on global QOL over time between the NDTI and the UC patients, which was attributed to the assessment on T3 (p = 0.011). An additional exploratory post hoc subgroup analysis was performed in this group of patients (n = 66).

Table 2 Percentages of NDTI patients without (DT < 5) and with distress (DT ≥ 5) at the different time points.

	DT < 5 n (%)	DT ≥ 5 n (%)
T1 n = 95	49 (52)	44 (46)
T2 n = 82	50 (61)	31 (39)
T3 n = 35	17 (49)	17 (49)
T4 n = 91	63 (69)	24 (26)
T5 n = 90	66 (73)	18 (20)
T6 n = 89	58 (65)	23 (26)
T7 n = 88	52 (59)	22 (25)
T8 n = 86	57 (66)	17 (20)
T9 n = 85	61 (72)	19 (22)

Abbreviations: NDTI = Nurse-led Distress Thermometer Intervention, DT = Distress Thermometer.

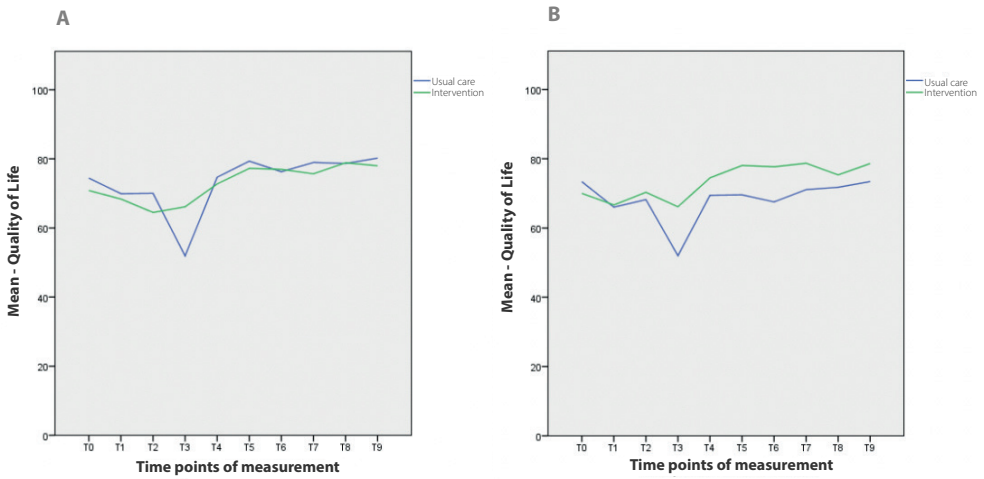

Figure 2 Mean difference in global QOL between patients who received NDTI or UC.
A: total group N = 194, B: Patients who received multimodality treatment n = 66.

Exploratory post hoc subgroup analysis of patients who received multimodality treatment

After 2 years of follow-up, there was no clinically relevant difference in global QOL between this subgroup of patients who received the NDTI when compared to those that received UC. The mean global QOL scores of these two groups showed a clinically meaningful difference at time points T3 and T6. Appendix C shows the mean scores of the primary and the secondary outcomes for the subgroup. Figure 2B shows the trajectory of the mean differences in global QOL scores of NDTI and UC patients receiving multimodality treatment (n = 66). At T9, there was no significant difference in global QOL between the patients having had multimodality treatment who received NDTI when compared to those who received UC. We found a significant improvement in coping ($p = 0.021$), cognitive functioning ($p = 0.047$), and less constipation in the patients having received the NDTI ($p = 0.029$). Over time, a significant difference on global QOL (mean diff. -10, $p < 0.001$; 95% CI [-14.835; -5.167]), emotional functioning ($p < 0.001$), cognitive functioning ($p < 0.01$), sexual functioning ($p = 0.017$), future perspective ($p < 0.01$), anxiety ($p = 0.033$) and avoidance ($p = 0.013$) in favor of the NDTI.

Evaluation of the NDTI

Eighty NDTI patients (83%) completed the evaluation form. Sixty-one of the 80 patients (76%) recommended that the use of the DT should be part of UC, 18 patients (23%) were hesitating and 1 person did not recommend it.

Discussion

In this study, we evaluated the effect of a NDTI intervention on improving hrQOL in patients with BC. We focused on patients with BC treated with curative intent because we were interested in the long-term effects of the intervention and, therefore, we needed high survival rates and a relevant post-therapy phase. In the metastatic setting, patients have a different life perspective and will be on treatment for most, if not all, of the time.

The main result is that using the DT by a nurse at regular time points did not improve global QOL 2 years after the end of treatment. This finding is in line with other (nurse) intervention studies with the DT.[10-14] Albeit, they used the DT in a different way and with a shorter follow-up period.[10-14] In this study, 20% to 49% of the patients experienced distress (DT ≥ 5) at one or more time points. In line with the literature, most patients were not keen on receiving a referral to a specialist such as a psychologist or social worker.[34-36] A potential explanation for our findings is that in our study, both groups completed the questionnaires at regular intervals. Although the UC group only completed the DT at baseline and at the end, this may have helped them to understand their actual feelings and unmet needs.[37] However, a more likely explanation is that the patients had a relatively good global QOL at baseline (mean scores were between 71 and 74), which makes it hard to establish a clinically relevant improvement of 10 points.[26, 32] Another explanation might be that the patients adapted to their new health situation,

which is known as response shift.[38] On the other hand, it might be questioned whether the EORTC QLQ-C30 was sensitive enough to measure differences in the higher range of QOL. For future studies, we suggest the use of another primary endpoint, like cancer-related fatigue, measured with a specific multidimensional questionnaire, as we observed that fatigue was one of the most frequently mentioned issues on the problem list of the DT.[5, 21]

Although the intervention did not result in an overall effect, it seemed beneficial to patients who received multimodality treatment. It is possible that these patients, who have more risk for recurrence of BC, experience more side effects due to more intensive therapy and have more unmet needs and emotional problems.[39] Although this is a subgroup analysis (n = 66), our findings suggest that a NDTI may have a positive impact on QOL of patients undergoing this intensive therapy. This is partly endorsed by the wide range of endpoints on which the intervention had a positive effect. We also showed that the patients receiving this intensive treatment recovered faster during the re-entry phase (first year, T4-T7) and thereafter compared to UC. During this phase, patients start to recover physically and emotionally and learn how to deal with (long-term) side effects and return to work.[40] While it is known that younger patients and patients with lower education levels are more likely to become distressed,[7] our study showed that multimodality treatment is another factor that may induce increased distress, which may be an important reason to provide additional psychosocial support during and after treatment.

Limitations

All patients came from one university medical center and the study was delivered and evaluated by their own healthcare providers, which may have resulted in selection and response bias. The study patients were females, relatively young, mostly Caucasian, and well educated, which may be a selection of the BC population as a whole. During this study, the guideline for BC follow-up changed, recommending fewer visits. Therefore, we had to skip some time points and we collected fewer data than planned. Possible Type 1 errors cannot be excluded due to the number of secondary analyses. For logistic and financial reasons, the investigator (FPvA) was one of the study nurses. To minimize the impact of this limitation, an independent database was created and all analyses were performed by an independent statistician. Finally, contamination was possible because participants of the MDT saw NDTI patients as well as UC patients. Although UC may differ between countries, we have no reason to believe that our UC differs much from the majority of other countries where the DT has been subject of research.

Despite these limitations, this study is the first RCT in which the DT was used longitudinally as NDTI at regular intervals during treatment and follow-up until 2 years after the end of treatment. By doing so, we followed the (inter)national guidelines on distress management, which gave us a unique opportunity to investigate the added value of the DT in clinical practice.[1, 24] Moreover, the number of dropouts was low, especially in the intervention group. Finally, despite the lack of significant improvement in outcome of this NDTI, 76% of the patients, who responded to the evaluation questionnaire, would recommend the NDTI as part of UC.

Clinical implications

Although, we found no differences in global QOL, most patients appreciated the extra attention from a competent healthcare professional. However, in times of budgetary constraints, it is important to focus resources on those patients who are in need. Our study indicates that patients that are most likely to benefit from the NDTI are those receiving multimodality treatment. Even though we investigated the effects of the NDTI only in patients with BC, it might be that patients with other types of cancer managed with multimodality treatment may also benefit from this intervention.

Conclusions

This study showed that the NDTI is not effective in improving global QOL in BC patients 2 years after the end of treatment. The findings from this study contribute to the existing knowledge underpinning the discussions in the literature and amongst clinicians as to the benefits of introducing the DT as part of standard care in oncology practice. The findings indicate that not all patients need or benefit from the DT and that those most likely to benefit are those who received multimodality treatment, during and in the first year after treatment. To confirm our findings, more studies focusing on distress screening in cancer patients who received multimodality treatment are needed.

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Appendix A

Methods of the nurse-led DT intervention

Summarized the followings steps were followed to establish the intervention, more detail information you can find in the study protocol:

1. Three qualified oncology nurses were trained in how to use the DT to become study nurses for this study. In order to build a trustworthy relationship and give continuity to the care, whenever possible the patient met the same nurse at every visit. During this study, the DT was not implemented in daily care in our hospital, so the oncology nurses of the departments involved in the study were not using it in daily practice.
2. The NDTI was given at regular time points combined with scheduled visits at the outpatient clinic. The patient completed the DT before the actual appointment with the nurse, before or after the patient had been seen her healthcare professional (medical specialist or CNS). The nurse and patient reviewed the DT score and discussed distress-related problems. If the patient had a DT score of < 5, the nurse inquired whether the patient felt sufficiently in control of her situation. If the score was ≥ 5, the study nurse had a more extensive conversation and asked whether the patient could prioritize the problems indicated. The nurse advised the patient how to cope with the issues mentioned. Time allocated to these meetings was depending on the severity of the distress and the nature of the problems.
3. A short standard report (as incorporated in the manual) was filled out after each conversation. To prevent contamination with nursing professionals, the report of the conversation was not included in the electronic medical record of the patient.
4. The results of the DT and the conversation with the nurse were discussed in a weekly psychosocial multidisciplinary team (MDT) meeting. This team was specifically established for this study to discuss all patients with a DT score of ≥ 5 and patients who personally requested additional support. The participants of the MDT were a representative of the medical staff (medical oncologist and/or CNS), one of the study nurses, a social worker, and a clinical psychologist. At these meetings, distress treatment plans were drawn up as needed, and after this meeting, the nurse explained the proposed plan to the patient by telephone. Each patient received a personal plan, and depending on the problems, a referral to some other healthcare professional (like a psychologist or physiotherapist) was needed.

Appendix B

Differences of means (SD) between patients receiving NDTI and UC (N = 194).

	T0		T1		T2		T3		T4		T5		T6		T7		T8		T9	
	NDTI (n=96)	UC (n= 98)	NDTI (n=93)	UC (n=86)	NDTI (n=80)	UC (n=77)	NDTI (n=31)	UC (n=26)	NDTI (n=89)	UC (n=81)	NDTI (n=82)	UC (n=77)	NDTI (n=81)	UC (n=65)	NDTI (n=75)	UC (n=57)	NDTI (n=67)	UC (n=57)	NDTI (n=81)	UC (n=72)
Primary outcome																				
Quality of life[a]	71 (23)	74 (20)	68 (19)	70 (19)	64 (21)	70 (20)	66 (19)*	52 (19)	73 (20)	75(19)	77(19)	79 (16)	77(18)	76(19)	76 (19)	79 (17)	79(16)	79 (18)	78(17)	80(16)
Secondary outcomes																				
Distress[b]	12 (8)	10 (7)	10 (8)	8 (6)	8 (7)	7 (6)	7 (8)	11 (7)	8(7)	7 (6)	7 (7)	5(4)	7(7)	6(6)	7 (6)	6 (5)	7 (6)	7 (5)	6 (6)	6 (5)
Anxiety[b]	8 (5)	7 (4)	6 (4)	5 (3)	4 (3)	4 (4)	4 (4)	6 (4)	5(4)	4 (4)	4 (4)	3(3)	4 (4)	4(3)	4 (4)	3 (3)	4 (4)	4 (4)	4 (4)	3 (3)
Depression[b]	4 (4)	3 (3)	4 (4)	3(3)	4 (4)	3 (3)	4 (4)	5 (4)	3 (4)	3 (3)	3 (4)	2(2)	3(3)	2(3)	3 (3)	2 (2)	3 (3)	2 (2)	2 (3)	2 (3)
Physical functioning [a]	93 (11)	92 (14)	83 (18)	85 (14)	78 (19)	82 (17)	73 (18)	74 (16)	86 (13)	86 (15)	86 (15)	88 (13)	88 (15)	88 (13)	85 (17)	88 (14)	87 (12)	90 (13)	87 (16)	87 (14)
Emotional functioning[a]	63 (23)	69 (21)	73 (20)	77 (19)	76 (19)	78 (20)	80 (22)*	64 (25)	78(22)	83 (15)	81 (17)	86 (15)	84 (17)	86 (15)	82 (18)	84 (18)	83 (15)	85 (17)	83 (18)	86 (16)
Social functioning[a]	91 (15)	90 (18)	82 (24)	80 (25)	78 (24)	76 (26)	70 (27)	65 (27)	87 (20)	85 (19)	89 (18)	90 (18)	92 (15)	89 (17)	90 (17)	87 (20)	91 (14)	92 (13)	93 (16)	93 (17)
Role functioning[a]	84 (24)	86 (24)	64 (26)	65(25)	63 (32)	69 (27)	52 (29)	50 (32)	75 (24)	72 (27)	77 (27)	82 (23)	79 (23)	78 (25)	79 (24)	80 (25)	79 (25)	82 (27)	84 (24)	85 (23)
Cognitive functioning [a]	80 (23)	83 (22)	82 (22)	79 (21)	78 (23)	76 (26)	78 (21)*	67 (24)	78 (21)	82 (20)	85 (17)	83 (22)	85 (19)	84 (20)	84 (18)	83 (21)	86 (17)	88 (19)	85 (18)	83 (21)
Body Image[c]	91 (16)	92 (13)	83 (23)	86 (19)	80 (25)	82 (24)	78 (26)*	68 (28)	82 (23)	85 (20)	84 (20)	87 (19)	83 (22)	88 (16)	84 (19)	83 (23)	86 (19)	89 (17)	88 (16)	88 (18)
Sexual functioning[c]	22 (18)	26 (22)	17 (17)	25(24)	18 (18)	23 (22)	13 (17)	11 (14)	21 (19)	24 (23)	23 (22)	24 (23)	22 (18)	24 (21)	22 (20)	23 (22)	26 (22)	22 (20)	24 (20)	23 (19)
Future Perspective[c]	51 (31)	52 (31)	62 (29)	62 (28)	66 (24)	65 (26)	65 (28)*	49 (29)	72 (23)	68 (24)	70 (21)	75 (21)	72 (22)	75 (22)	76 (20)	77 (21)	72 (20)	70 (25)	73 (19)	75 (24)
Sexual Enjoyment[c]	56 (27)	57 (26)	51 (23)	53 (26)	48 (22)	50 (22)	42 (25)	39 (25)	49 (24)	54 (26)	50 (25)	54 (22)	49 (23)	48 (23)	52 (25)	56 (26)	57 (26)	57 (22)	53 (23)	56 (20)
Intrusion[d]	15 (9)	14 (8)	13 (10)	11 (8)	10 (8)	9 (8)	8 (7)	12 (8)	8 (7)	8 (8)	8 (7)	7(6)	8(8)	7 (7)	6 (7)	7 (7)	7 (7)	7 (7)	5 (6)	5 (6)
Avoidance[d]	12 (9)	13 (8)	9 (8)	10 (8)	8 (7)	9 (9)	6 (7)	12 (9)	7 (7)	7 (8)	7 (7)	6(7)	7(7)	5 (6)	6 (7)	6 (8)	5 (6)	6 (7)	4 (5)	5 (7)
Helplessness[e]	10 (4)	9 (3)	11 (4)	10 (3)	11 (3)	10 (3)	12 (5)	12 (4)	9 (3)	9 (3)	8 (3)	8(3)	8(3)	8 (3)	8 (3)	8 (3)	8 (3)	8 (2)	8 (2)	8 (3)
Acceptance[e]	14 (5)	15 (5)	16 (5)	17 (4)	17 (5)	17 (5)	16 (5)	15 (4)	17(5)	18 (4)	17 (5)	19 (4)	17 (4)	19 (4)	18 (4)	19 (4)	18 (4)	19 (4)	19 (4)	19 (4)
Perceived Benefits[e]	12 (5)	14 (5)	14 (5)	16 (5)	14 (4)	15 (5)	15 (5)	15 (4)	15 (5)	16 (5)	15 (5)	16(5)	14(4)	16 (5)	14 (5)	17 (4)	15 (5)	17(5)	15 (5)	17 (5)

Abbreviations: NDTI = Nurse-led Distress Thermometer Intervention, UC = Usual Care.

Questionnaires: [a]EORTC QLQ-C30, [b]HADS, [c]EORTC BR23, [d]IES [e]ICQ.

* Difference of ≥ 10 points between both groups (= clinically relevant).

Appendix C

Differences in means (SD) between patients receiving NDTI and UC of patients who were treated with surgery, radiotherapy and chemotherapy (n = 66).

	T0		T1		T2		T3		T4		T5		T6		T7		T8		T9	
	NDTI (n=35)	UC (n=31)	NDTI (n=33)	UC (n=26)	NDTI (n=32)	UC (n=27)	NDTI (n=31)	UC (n= 25)	NDTI (n=32)	UC (n=24)	NDTI (n=30)	UC (n=23)	NDTI (n=28)	UC (n=19)	NDTI (n=27)	UC (n= 17)	NDTI (n=25)	UC (n=18)	NDTI (n=30)	UC (n=21)
Primary outcome																				
Quality of life[a]	70 (24)	73 (22)	67 (22)	66 (18)	70 (20)	68 (18)	66 (19)*	52 (19)	74 (20)	69 (17)	78 (21)	70 (13)	78 (18)*	68 (21)	79 (19)	71 (17)	75(18)	72 (17)	79 (17)	73 (16)
Secondary outcomes																				
Distress[b]	12 (9)	11 (6)	10 (8)	10 (6)	8 (7)	9 (6)	7 (8)	11 (7)	7 (7)	10 (7)	6 (8)	7 (4)	7 (7)	9 (7)	6 (6)	8 (5)	8 (8)	9(5)	6 (6)	7(6)
Anxiety[b]	8 (5)	7 (4)	5 (5)	6 (3)	4 (5)	5 (4)	4 (4)	6 (4)	3 (4)	6 (4)	3 (4)	4 (3)	4 (4)	5 (4)	3 (3)	5 (4)	5 (4)	6 (4)	4 (3)	4 (4)
Depression[b]	4 (4)	3 (3)	4 (4)	4 (3)	4 (4)	4 (3)	4 (4)	5 (4)	3 (4)	4 (3)	3 (5)	3 (2)	3 (4)	4 (3)	2 (3)	3 (2)	3 (4)	3 (3)	3 (3)	3 (3)
Physical functioning [a]	94 (11)	93 (11)	81 (21)	86 (13)	81 (17)	86 (12)	73 (18)	74 (16)	85 (11)	84 (14)	87 (13)	82 (14)	86 (17)	84 (12)	86 (19)	83 (14)	82 (16)	85 (15)	86 (17)	84 (13)
Emotional functioning[a]	63(20)	66 (24)	75 (19)	69 (18)	79 (17)	71 (21)	80 (22)*	66 (24)	86 (16)	77 (14)	85 (19)	81 (14)	88 (13)	79 (17)	88 (15)*	78 (20)	81 (17)	78 (19)	85 (15)	83 (18)
Social functioning[a]	90 (16)	86 (22)	84 (19)	78 (22)	81 (22)	77 (28)	70(27)	66 (27)	89 (17)	81 (19)	89 (23)	87 (19)	92 (15)	81 (20)	91 (16)	83 (24)	86 (18)	91 (12)	93 (13)	87 (24)
Role functioning[a]	88 (23)	82 (23)	63 (27)	62 (29)	67 (30)	67 (28)	52 (29)	49 (32)	77 (24)*	61 (25)	83 (23)*	68 (23)	77 (25)*	65 (28)	80 (24)*	65 (23)	74 (28)	73 (26)	82 (24)	75 (27)
Cognitive functioning[a]	84 (20)	81 (29)	84 (23)	78 (22)	85 (20)*	67 (30)	78 (21)*	67 (24)	84 (17)	75 (21)	88 (15)*	75 (22)	85 (16)*	75 (23)	90 (14)*	72 (23)	85 (17)	84 (19)	88 (15)	80 (18)
Body Image[c]	94 (9)	92 (14)	88 (17)	87 (15)	86 (20)	87 (16)	78 (26)*	68 (28)	83 (24)	84 (14)	84 (24)	85 (17)	84 (24)	83 (18)	86 (20)	85 (18)	84 (24)	93 (10)	89 (14)	89 (15)
Sexual functioning[c]	20 (19)	26 (22)	17 (18)	25 (25)	19 (20)	21 (23)	13 (17)	11 (14)	20 (17)	21 (26)	21 (20)	19 (22)	20 (16)	21 (23)	20 (19)	16 (22)	24 (24)	16 (18)	23 (17)	15 (16)
Future Perspective[c]	46 (29)	49 (30)	61 (28)	58 (26)	66 (26)	58 (24)	65 (28)*	49 (29)	75 (24)*	61 (23)	73 (24)	71 (23)	77 (20)	70 (22)	79 (21)	75 (19)	73 (19)*	63 (28)	71 (19)	68 (27)
Sexual Enjoyment[c]	48 (29)	57 (29)	48 (24)*	58 (31)	50 (24)	58 (27)	42(25)	40 (26)	44 (25)*	61 (29)	53 (28)	58 (22)	46 (24)	43 (27)	44 (24)	50 (36)	62 (29)*	48 (18)	50(27)	59 (22)
Intrusion[d]	14 (9)	14 (7)	11 (9)	12 (7)	9 (8)	10 (7)	8(7)	12 (8)	7 (7)	10 (7)	7 (8)	8 (6)	7 (7)	9 (8)	6 (7)	8 (5)	7 (7)	9 (7)	4 (4)	7(6)
Avoidance[d]	11 (10)	14 (8)	9 (9)	12 (8)	7 (7)	10 (8)	6(7)	12 (10)	6 (7)	9 (8)	5 (7)	8 (9)	5 (6)	7 (6)	5 (8)	9 (9)	5 (6)	10 (9)	3 (4)	7 (9)
Helplessness[e]	10 (4)	9 (3)	11 (4)	11 (3)	10 (3)	10 (3)	12 (5)	11 (4)	9 (4)	10 (3)	9 (4)	9 (2)	8 (3)	9 (3)	8 (3)	9 (3)	9 (3)	9 (2)	8 (3)	9 (3)
Acceptance[e]	15 (5)	15 (5)	16 (5)	16 (4)	17 (4)	16 (4)	16 (5)	15 (4)	17 (4)	16 (4)	18 (5)	17 (4)	17 (4)	17 (4)	18 (4)	18 (4)	18 (5)	18 (4)	18 (4)	18 (4)
Perceived Benefits[e]	13 (4)	13 (5)	14 (5)	15 (4)	14 (4)	14 (4)	15 (5)	15 (4)	15 (5)	15(5)	15 (5)	15 (4)	15 (5	14 (5)	16 (5)	16 (4)	15 (5)	16 (4)	16 (5)	16 (5)

Abbreviations: NDTI = Nurse-led Distress Thermometer Intervention, UC = Usual Care.

Questionnaires: [a]EORTC QLQ-C30, [b]HADS, [c]EORTC BR23, [d]IES, [e]ICQ.

* Difference of ≥10 points between both groups (=clinically relevant).

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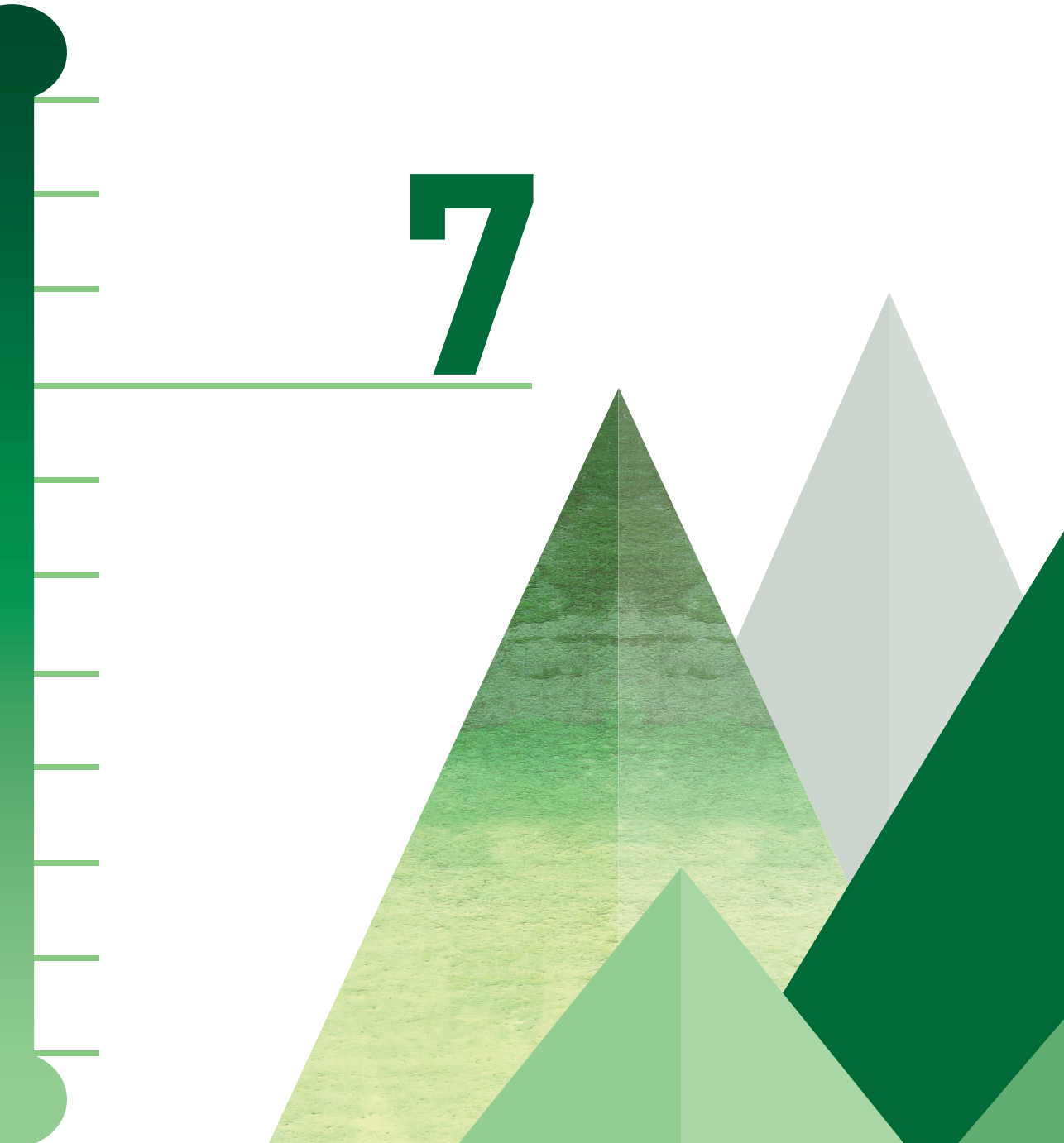


Summary

Summary

The studies presented in this thesis focused on distress in patients with cancer, especially on women with breast and ovarian cancer. The NCCN developed a short validated screening instrument for distress, the so-called Distress Thermometer (DT). The distress guideline titled *'Detection of the need for psychosocial care',* was published in the Netherlands in 2010. This guideline was developed in collaboration with different cancer healthcare professionals and organizations. Since then, implementation of the DT at the outpatient clinic of the hospitals started and several studies on the DT were performed in the Netherlands. In this thesis we used the DT to measure the distress level and related problems in cancer patients. Based on the first Dutch distress management guideline, screening for distress should be carried out shortly after cancer diagnosis, after each treatment modality and at fixed time points during follow-up. Patients with a DT score of 5 or higher should be discussed in a psychosocial multidisciplinary team (MDT) meeting.

In **Chapter 1** a general introduction related to distress screening and distress screening instruments in cancer patients is provided. **Chapter 2** describes a cross-sectional study with Dutch breast cancer survivors (BCSs). This chapter focused on the three different parts of the DT, the thermometer, the problem list and a question concerning need for help. Of the 258 BCSs, 129 (50%) completed the questionnaires, of which, one third experienced distress, even several years after diagnosis. Mean distress score measured with the DT was 3.8 (SD 2.6). Intensity of treatment and time since primary surgery were positively correlated with distress. The most frequently reported problems were physical problems such as fatigue, decreased muscle strength and impaired physical fitness. Distress was correlated with various psychosocial variables such as global and health-related quality of life, illness cognition, anxiety and depression. The majority of the BCSs did not wish to be referred to a specialized healthcare professional to discuss their distress or problems. While in chapter 2 all patients were breast cancer survivors, **Chapter 3** focuses specifically on patients with ovarian cancer, either with or without recurrence of the cancer. In contrast to breast cancer, ovarian cancer is mostly diagnosed in an advanced stage of disease and patients have a relatively unfavorable prognosis. This leaves patients with ovarian cancer at an increased risk of experiencing high levels of distress. In this cross-sectional study patients (N = 273) with and without recurrence of ovarian cancer were asked to fill out questionnaires about their psychosocial well-being including the DT. In total, 104 patients (38%) completed the questionnaires and were analyzed. Fifty-nine (57%) of the patients were without recurrence and 45 (43%) had experienced a recurrence or progression of the ovarian cancer. The disease status in patients with ovarian cancer was not related to distress. Most reported problems were in the physical domain, namely fatigue, decreased condition and peripheral neuropathy. These problems are known adverse effects of the treatment and the disease itself, and are long-lasting. The mean global quality of life was 75.3 (20.8), which is comparable to the population norm. No differences were found between patients with and without recurrence of ovarian cancer. The global quality of life was negatively correlated with the DT score (r =

-0.558; $p < 0.001$). Distressed patients with ovarian cancer experienced more problems on the problem list. Moreover, their quality of life was lower compared to those who were not distressed.

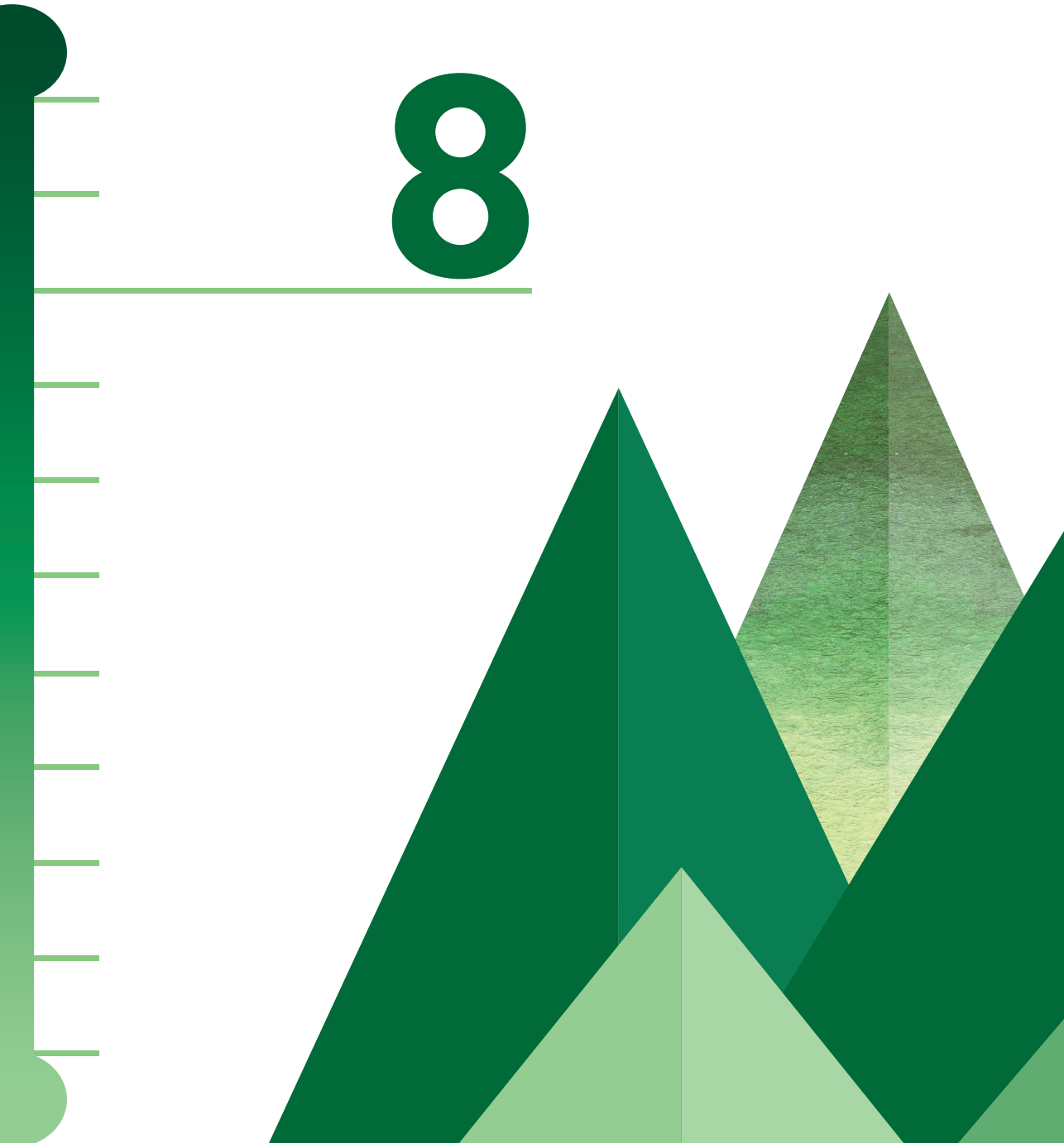
In **Chapter 4** breast cancer patients were asked for their level of distress and problems shortly after breast cancer diagnosis in order to establish the optimal DT cuttoff score for detecting distress shortly after diagnosis. This study explored in 181 breast cancer patients whether one general cutoff score of 5, as advised in the Dutch distress management guideline, is appropriate to detect distress shortly after diagnosis when high levels of distress are expected. The mean DT score was 5 (SD 2.7). The Hospital Anxiety and Depression Scale (HADS) was used as the golden standard for distress. The results showed that a cuttoff score of 7 for the DT seemed more appropriate to identify those women with high distress shortly after breast cancer diagnosis. A higher cuttoff score at diagnosis would lead to fewer findings of false-positive patients and make it possible to start early interventions for those who really need it. In contrast to the findings from the studies reported in chapter 2 and 3, emotional problems were the most frequently reported problems for patients in this study. Younger patients experienced significantly more distress than older patients.

Though screening for distress with the DT in patients with cancer is recommended worldwide, evidence about the effectiveness of the use of the DT in breast cancer care on quality of life is limited. **Chapter 5** describes the design and rationale for a randomized controlled trial to assess the psychosocial consequences of systematic use of the DT and its discussion by a nurse, in patients who were treated for primary breast cancer with a curative intention. The nurse-led DT intervention consisted of usual care in combination with assessment of the DT, together with a discussion on the results with the patient by a trained oncology nurse. In case of a DT score of 5 or higher the patient was discussed in a psychosocial MDT. The control group received usual care without regular distress screening with the DT. The study was stratified for hormonal treatment. The primary outcome was global quality of life measured with the EORTC QLQ-C30. Secondary outcomes were the functional and symptom scales of the EORTC QLQ-C30 and BR23, HADS, Impact of Event Scale and Illness Cognition Questionnaire. Outcomes were assessed in both arms at baseline, after completion of each cancer treatment modality, e.g. surgery, radiotherapy, chemotherapy and during follow-up, with a three and six months' interval during the first and second year respectively. **Chapter 6** describes the results of this randomized controlled trial. In total 194 patients were randomized, 96 patients were assigned to the nurse-led DT intervention and 98 to usual care. The findings revealed that systematic use of the DT by a nurse at regular time points did not improve global QOL of cancer patients two years after end of medical treatment. In total, 688 DT's were completed, 215 (31%) patients (some patients more than once) were discussed in the MDT, because of a high distress score. Most of the patients did not wish to receive a referral to psycho-oncology services, but indicated that the conversation with the nurse was sufficient. Although the intervention did not result in an overall effect, an exploratory post hoc subgroup analysis showed that the nurse-led DT intervention seems beneficial to patients who received multimodality treatment. The findings from this RCT contributes

important information to the existing literature, in particular, the discussion about whether or not to use the DT as standard care in daily practice.

In **Chapter 7**, all studies reported in this thesis are summarized and the findings are discussed in **Chapter 8**. In **Chapter 8**, the practical implications of the findings are also considered in more detail along with methodological considerations and recommendations for future research.

8



General discussion and future perspectives

General discussion and future perspectives

In the Netherlands, a distress guideline *'Detection of the need for psychosocial care',* which was developed in collaboration with different cancer care professionals and organizations, was published in 2010.[1] A central part of this guideline is the use of the Distress thermometer (DT). The DT has been developed to timely detect distress and unmet needs in order to offer appropriate support to prevent serious problems. In addition, the DT is a tool to discuss problems with the patient, discuss eventual need for extra care and determine who will provide this.
Since 2010, implementation of the DT at the outpatient clinic of the hospitals started and over the last nine years several DT studies were conducted. However, some important questions following the results of studies we and others conducted still remain and these will be discussed in this chapter.

Distress screening with the DT in cancer patients: what is the effect?

The main result of our randomized controlled trial (RCT) is that distress screening with the DT and Problem List (PL) did not improve psychosocial well-being. These results are in line with the results of other RCTs that used the DT as an instrument for screening distress compared to usual care. Hollingworth et al. conducted an RCT with cancer patients who started with radiotherapy or chemotherapy.[2] The intervention group completed the DT together with a problem list, which was followed by a discussion of these outcomes with a trained radiographer/nurse. The intervention was conducted once and on request twice. The follow-up time was 12 months and they concluded that distress screening was not cost effective in improving patient's mood states over this time-period.[2] In an RCT with lung cancer patients, the DT/PL were completed before the scheduled outpatient clinic appointment at several timepoints: after randomization (baseline) and additionally after 7, 13 and 24 weeks. After completion of the DT/PL, patients met face-to-face with a psychosocial nurse to discuss their response pattern. Patients were offered referral to psychosocial and/or paramedical caregivers (depending on the problem(s)) if the DT score was 4 or higher or when the patients answered the referral wish question with a yes. They concluded that distress screening with the DT did not improve the QOL or other patient-reported outcomes when compared to usual care alone.[3] Another RCT was performed by van der Meulen et al. in patients with head and neck cancer. The intervention consisted of three to four screenings with the DT/PL plus nurse-guided follow-up. No effects on patient outcomes as depressive symptoms, health-related QOL (hrQOL) and worry of cancer were seen.[4] Schuurhuizen et al. performed a multicenter RCT in patients with metastastic colorectal cancer.[5] They screened distress with the Hospital and Anxiety Depression Scale (HADS) and DT, followed by a stepped care program. They showed that screening for distress and offering subsequent treatment did not result in a reduced distress outcome after 48 weeks. Additionally, they described that the absence of effect of the intervention was likely due to the low uptake of the stepped care in the intervention group.[5] All above mentioned RCTs followed the patients with a maximum of 12 months. Despite the fact that we and the group of van der Meulen et al.

did not find any improvement in psychosocial well-being with the use of the DT in routine cancer care, the patients of both studies appreciated the intervention and would recommend it for daily practice. One could ask the question why this may be the case. Do we need evidence of the effect of distress screening or is patient satisfaction enough? It seems that patients appreciate more attention to their psychosocial well-being and unmet needs. But why did distress screening with the DT not show to have an effect on QOL? Global and hrQOL are common secondary outcomes in medical treatment trials. It might be questioned whether global or hrQOL is sensitive enough as a primary endpoint of an RCT with the DT and a nurse-led intervention. Probably we should focus more on specific problems instead on the broader construct as global QOL is. For example, we should better focus on cancer-related fatigue and an adjusted intervention, as we observed that fatigue was one of the most frequently mentioned issues on the problem list of the DT. Another explanation might be that the patients adapted to their new health situation, which is known as response shift. Eventually, the nurse-led DT intervention is low intensive, which makes it less likely to result in measurable effects.

When do we have to screen on distress and which patients may benefit from screening?

The evidence for the effectiveness of distress screening with the DT is thus limited. Thereby, since there is a limited budget for healthcare and a shortage of nursing staff we probably have to re-think if it is necessary to screen all patients at fixed time points. We should ask ourselves whether we should discuss the DT with every cancer patient or whether we can identify patients at risk for increased distress, based on previous distress studies. In our cross-sectional studies we found that distress was present in 60% of the breast cancer patients shortly after diagnosis and in 36% of breast cancer survivors.[6, 7] Higher treatment intensity and shorter time since primary surgery correlated positively with distress in breast cancer survivors. Shortly after diagnosis younger patients experienced more distress than older patients and patients with children living at home experienced more distress than patients without children living at home. Thereby, patients who had previously received psychosocial support were more distressed than patients who had not previously received support.[6] Our longitudinal RCT showed that 20-49% of the breast cancer patients experienced distress at one or more time points. Distress was measured in 32% of the patients with ovarian cancer with and without recurrence of the cancer. These percentages were in line with results from other DT studies.[8]

Distress trajectories of breast cancer patients were examined in several studies. Helgeson et al. found in their observational study with 287 breast cancer patients an improvement over time in mental health functioning measured with the SF-36 up to four years after diagnosis. A subgroup of 12% of patients experienced a poorer mental health.[9] Henselmans et al. identified four distress trajectories measured with general health questionnaire in the first year after breast cancer diagnosis (N = 171). They also found a subgroup of 15% patients who experienced chronically severe distress up to six months after end of treatment.[10] Bidstrup et al. described five distress trajectories in newly breast cancer patients

(N = 323) measured with the DT up to eight months. A subgroup of 8% of the women maintained severely distressed throughout the eight months.[11] In our RCT, 25% (n = 88) of the intervention group experienced distress (DT ≥ 5) 1 year after end of treatment and 22% (n = 85) of them after 2 years. Studies showed that more than half of the patients did not experience distress, but that a small subgroup experienced severe distress during a longer period.[7, 9-12] Therefore, we would like to suggest to select those patients for DT screening who are most at risk for developing distress. Based on our RCT this is the group of patients who will receive multimodality treatment. Literature has shown that cancer patients are at increased risk for distress if they had a history of psychiatric disorder, depression, severe comorbid illness and/or communication barriers.[8] In addition, social risk factors are younger age, living alone, financial problems, having young children and prior trauma and/or abuse.[8] The nurse can use the first structured screening with the DT prior to start of treatment to assess the patient and make an inventory of the risk factors and problems. Screening shortly after diagnosis may make it possible to identify those patients at highest risk of being chronically distressed and therefore allows to start early interventions in order to prevent or decrease distress in the course of treatment and follow-up. This first screening moment will give the patient more insight into which problems can be put forward to discuss with the nurse during treatment and follow-up. Nurse-led DT intervention can then be offered to those at risk, to those who are seeking for additional support and to those who actually experience a high level of distress. Next, how often should patients be screened for distress? Releasing fixed time points asks for more empowerment and self-management of patients to express their problems. One other logical moment for screening seems at the end of treatment, before the re-entry phase, where the nurse-led DT intervention gives the opportunity to integrate the results into aftercare plans for physical as well as psychosocial rehabilitation.

Screening on distress with the DT; do we need a cuttoff score?

Worldwide, the original NCCN DT has been translated into different languages and applied in different cancer populations.[13] Notably, different cuttoff scores for distress have been determined, which are influenced by language, country and cancer population.[13] In the Netherlands, the DT is validated in a mixed cancer population by Tuinman et al. which led to a cuttoff score of 5.[14] Afterwards, other validation studies were performed in the Netherlands. Roerink et al. identified 5 as an optimal cuttoff score for identifying distress in long-term survivors of thyroid carcinoma.[15] A cuttoff score of 4 is recommended for the Dutch prostate cancer patients.[16] Distressed childhood cancer survivors were identified with a DT ≥ 3.[17] In our study, we validated the DT with breast cancer patients shortly after diagnosis, with a cuttoff score of 7.[6] All these studies used the HADS as golden standard, therefore it is likely that there is a focus on emotional distress. However, validation studies of the DT for physical distress in breast cancer survivors showed an appropriate concurrent validity for the screening of physical problems with a DT ≥ 5.[18] Ma et al. suggest an optimal cuttoff score of 4 in their meta-analysis. Nevertheless, they mention that

more studies are needed to examine the accuracy and optimal cuttoff score in different regions globally and different cancer subtypes.[19]

In 2017, the Dutch distress guideline was revised.[1] In the pursuit of clarity, the authors recommended the cuttoff score of 4 to identify patients with distress which they based on the meta-analysis of Ma et al.[19] They described that the cuttoff score of 4 is an essential indication of the patient's referral requirement. The chance that a patient with a score above a cuttoff point has a desire to be referred to another healthcare professional is three times higher than for a patient with a score below the cuttoff point. However, there are patients with a score below the cuttoff point who have a referral request.[1, 7] Consequently, with a cuttoff score of 4, more patients were screened false positively. It could also be questioned whether one cuttoff score for all cancer patients is beneficial and/or if we really have to use one cuttoff score at all time points. Experiencing some distress at diagnosis is a normal reaction. It is therefore an important task for the nurse to explore if the experienced distress is a normal reaction to the cancer diagnosis or whether it dominates the life in such a way that additional support is needed. Using a higher cuttoff score of the DT will facilitate the selection of patients who are in need of nurse led or other professional interventions. Studies showed that majority of patients scoring above the cutoff score on the DT declined extra professional help with the mentioned problems.[5, 7] Therefore, Dekker et al. argued that distinction between adaptive and maladaptive emotional responses may aid to understand the low uptake of interventions for distress.[20] They mention that psychosocial interventions must be tailored to the nature of emotional responses (adaptive versus maladaptive emotions), instead of their intensity. This seems like an interesting turn in the reconceptualization of distress and how to detect the patients in need. More research is needed to determine the best indicators of patients with high levels of distress, who need support, or indicators of maladaptive emotions.[20]

Implementation of the DT; what are the barriers and what is needed?

Implementation can be defined as 'a planned process and systematic introduction of innovations and/or changes of proven value, the aim being that these are given a structural place in professional practice, in the functioning of organizations or in the healthcare structure'.[21] In routine clinical practice implementation of the DT following the distress guideline is difficult to organize. Given the lack of evidence of distress screening with the DT on patients-reported outcomes, it is difficult to convince healthcare professionals to further implement the DT. Several studies have found barriers for implementation of distress screening, such as lack of time, lack of training and low personal skills or confidence of the clinician.[22-24] In our university medical center cancer care is organized in care pathways per tumor type, with diversity in the organization of in tumor type focused clinics. In this context a barrier is the fact that contact between nurses and patients at the outpatient clinic is not always standardized in each cancer specific pathway.[25] According to the Dutch distress guideline, a psychosocial multidisciplinary meeting at regular time points should be organized to discuss the results of the DT conversations with distress or if the patient asks for more help.[1] In daily practice, however, it turns out

that, because of financial and logistic reasons, this is difficult to organize. [25] Mitchell et al. mentioned also that acceptability and resources are the key factors to make distress screening a success.[22] In order to implement the DT properly, it is important that finances and nursing staff are available for distress screening. Given the challenging pressure on costs in cancer care, the focus on distress screening may not be seen as priority.[25]

Methodological considerations and future research

Based on progressive insights gained from the studies described in this thesis, several methodological considerations and recommendations for future directions can be formulated. **Chapter 2, 3** and **4** were cross-sectional studies. The advantage of this design was that it gave us the opportunity to gain information from a larger sample size, which facilitated generalization of findings of Dutch breast and ovarian cancer patients. Though, this design also has some limitations. First, it is not possible to interpret the direction of the causal relation between distress and other variables. Second, we used self-reported questionnaires which resulted in missing data because patients did not always reply on our request to fill in the questionnaires. Third, the results may be affected by response bias because it is unknown why the non-response group declined to complete the questionnaires (non-response was 50% and 57% in chapter 2 and 3, respectively). Fourth, it is possible that the self-reported problems and distress are related to other problems or life events rather than to the cancer treatment. Fifth, in the cross-sectional studies we did not further investigate the reported distress and problems in a conversation with the patients. This would have given us more insight into the severity of the experienced distress. The protocol of the non-blinded RCT design is described in **chapter 5** which we conducted in **chapter 6**. The main strength was that it is the first RCT in which the DT was used longitudinally as nurse-led DT intervention (NDTI) at regular intervals during treatment and follow-up until 2 years after end of treatment. We followed the national distress guideline, which gave us the opportunity to investigate the added value in clinical practice. Despite the strengths, there were some methodological limitations to consider. The results were probably affected by selection bias because we used specific selection criteria for inclusion. Most exclusion criteria were known as risk factors for distress, for example second malignancy and psychiatric comorbidity. It could be that the intervention would have had a positive effect in this group. In future studies it should be interesting to select patients who are at risk for distress beforehand and include them in a NDTI trial. Contamination was possible because participants of the psychosocial multidisciplinary team saw NDTI patients as well as UC patients. For logistic and financial reasons, the investigator was one of the study nurses. To minimize the impact of this limitation, an independent database was created and all analyses were performed by an independent statistician. The ideal situation for future study should be to involve oncology nurses specifically to perform the NDTI in an RCT in different cancer pathways. The results of the RCT suggest that breast cancer patients who received multimodality treatment, might have some benefit of a NDTI during and in the first year after treatment. This suggestion is based on an exploratory post hoc analysis. More studies focusing on

distress screening with cancer patients who received multimodality treatment are needed to confirm this. In this study we focused on an intervention performed by a nurse with face-to-face contact. Nowadays, there are more web-based self-management applications available like the Oncokompas or BREATH in the Netherlands.[26, 27] It is also interesting to do more research on the PREMS and PROMS of the cancer patients using the DT with various interventions. For example, whether e-health combined with the DT or only face to face NDTI are most suitable and effective. Another interesting suggestion is made by Kaal in her dissertation where she proposed to measure empowerment by means of a '(em) power(ment)' thermometer. She described that focusing on measuring resilience instead of problems or distress might be more appealing and more informative to assess a positive hrQOL. Thereby, a power thermometer has a more positive connotation than a distress thermometer.[28] It should be interesting to compare the DT and a power thermometer in a study.

Clinical implications

This thesis does not provide strong evidence for structural use of the DT at fixed time points in breast cancer patients. Despite the lack of the evidence, patients and nurses are satisfied with the instrument. The DT provide insight into the experience of the level of distress and problems for the patient as well for the healthcare professional. It gives an overview of what is important for the patient on that specific moment. Nowadays, there is more focus on person-centered care which is a way of thinking that the healthcare professional puts patients and their families at the center of decisions. It means that we have to be more flexible to meet patients' needs and find the best way to provide care. This means not just focus on cuttoff scores of the DT at fixed time points but create a psychosocial healthcare plan together that fits the needs of the patients. For the creation of a personal care plan, it is important that the nurse knows the person behind the patient in order to engage the person as an active partner in his/her care and treatment. The DT can be a useful instrument to explore the needs and feelings of the patient. At the time of screening and creation of the personal care plan, it is important that the nurses knows which patients' group is at high risk for distress and which resources are available for which problem. In addition, it is a multidisciplinary task to build collaborative partnerships that encourages and empowers patients actively so that they can take part in finding solutions for their unmet needs.[29] A major component of the medical care is communication. Training of the healthcare professionals on their communication skills about how to identify distress and the related problems should be an important element of delivering oncology care. Successful implementation of person-centered care depends on informed and involved patients, receptive and responsible healthcare professionals and a coordinated and well-integrated healthcare environment.[30]

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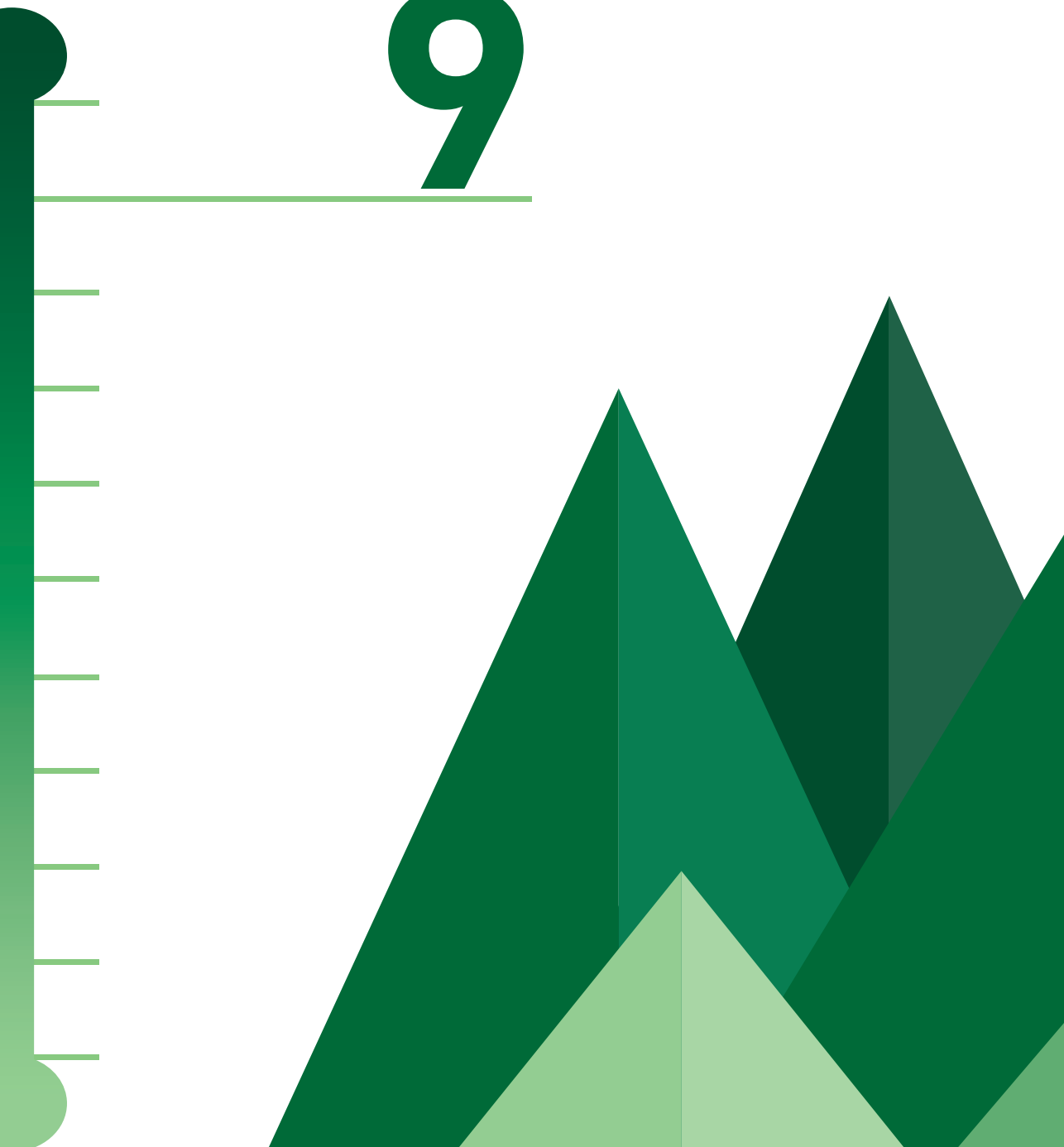


Nederlandse samenvatting

Nederlandse samenvatting

In Nederland wordt jaarlijks bij ongeveer 116.000 mensen kanker vastgesteld. Hoewel de overlevingskansen steeds groter worden, heeft het krijgen van kanker een grote impact op iemands leven. De diagnose kanker en de behandeling kunnen op lichamelijk gebied zowel op korte als op lange termijn bijwerkingen geven. Voorbeelden van bijwerkingen die ervaren worden op korte termijn zijn misselijkheid en kaalheid. Bijwerkingen die gedurende langere periode, ook na afronding van de behandeling, ervaren kunnen worden zijn tintelingen in handen en voeten, vermoeidheid en problemen met seksualiteit. De emotionele impact kan zich uiten in angst voor terugkeer van ziekte, depressie, eenzaamheid, spanning en concentratieproblemen. Mogelijke praktische gevolgen zijn re-integratie op het werk, verzekerings-en financiële problemen. Daarnaast kunnen sociale problemen ontstaan in de omgang met de kinderen, partner, vrienden en/of familie. Deze totale last die mensen met kanker kunnen ervaren op lichamelijk, emotioneel, sociaal, praktisch en levensbeschouwelijk gebied wordt samengevat in de term *distress*.

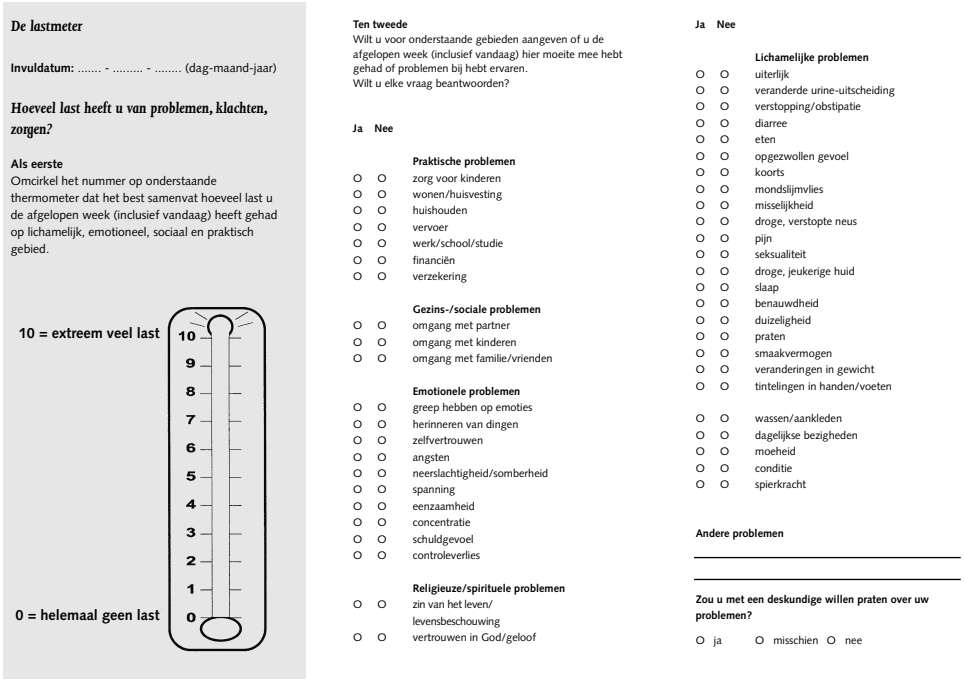
Een screeningsinstrument om distress vast te stellen kan ervoor zorgen dat de problemen die mensen ten gevolge van kanker ervaren tijdig worden gesignaleerd en interventies sneller kunnen worden ingezet. Het systematisch inzetten van een dergelijk screeningsinstrument heeft als voordeel dat er structureel aandacht is voor mogelijke problemen. Dit kan bijdragen aan een verbeterde communicatie tussen patiënt en zorgverlener, aangezien het instrument een houvast is voor het gesprek. Wereldwijd wordt de *Distress Thermometer* aanbevolen als screeningsinstrument om te gebruiken voor het screenen op distress. In Nederland is de Distress Thermometer vertaald en gevalideerd onder de naam **Lastmeter**. Vanaf 2010 wordt landelijk geadviseerd om de Lastmeter te gebruiken voor het screenen op distress volgens de richtlijn 'Detecteren behoefte psychosociale zorg'.

Lastmeter

De Lastmeter is een korte vragenlijst die bestaat uit drie verschillende onderdelen. Allereerst de thermometer waarbij de vraag wordt gesteld '*Hoeveel last heeft u ervaren in de afgelopen week, inclusief vandaag?*'. Op de thermometer kan de patiënt tussen de 0 (geen last) en 10 (extreem veel last) aangeven. Vervolgens bevat het instrument 47 items (ja/nee antwoorden) van problemen die zijn onderverdeeld in verschillende domeinen. De domeinen betreffen: praktische problemen, gezins-/sociale problemen, emotionele problemen, religieuze/spirituele problemen en lichamelijke problemen. Ten slotte sluit het af met de vraag: '*Zou u met een deskundige willen praten over uw problemen?*' (antwoord mogelijkheden ja/misschien/nee).

In de richtlijn 'Detecteren behoefte psychosociale zorg' (versie 1) staat beschreven dat de Lastmeter afgenomen moet worden net na diagnose, na afronding van elk soort behandeling en in de follow-up

op vaste controle momenten. Het afkappunt voor verhoogde last is 5. Patiënten die op de thermometer een 5 of hoger scoren dienen vervolgens besproken te worden in een psychosociaal multidisciplinair overleg. Dit is een overleg waarbij een arts, verpleegkundige en psychosociale hulpverleners zoals psycholoog, maatschappelijk werker en/of pastorale medewerker aanwezig zijn. In afbeelding 1 staat een afbeelding van de Lastmeter.



De lastmeter

Invuldatum: ..... - ..... - ..... (dag-maand-jaar)

Hoeveel last heeft u van problemen, klachten, zorgen?

Als eerste
Omcirkel het nummer op onderstaande thermometer dat het best samenvat hoeveel last u de afgelopen week (inclusief vandaag) heeft gehad op lichamelijk, emotioneel, sociaal en praktisch gebied.

10 = extreem veel last

10 9 8 7 6 5 4 3 2 1 0

0 = helemaal geen last

Ten tweede
Wilt u voor onderstaande gebieden aangeven of u de afgelopen week (inclusief vandaag) hier moeite mee hebt gehad of problemen bij hebt ervaren.
Wilt u elke vraag beantwoorden?

Ja	Nee	
		Praktische problemen
O	O	zorg voor kinderen
O	O	wonen/huisvesting
O	O	huishouden
O	O	vervoer
O	O	werk/school/studie
O	O	financiën
O	O	verzekering
		Gezins-/sociale problemen
O	O	omgang met partner
O	O	omgang met kinderen
O	O	omgang met familie/vrienden
		Emotionele problemen
O	O	greep hebben op emoties
O	O	herinneren van dingen
O	O	zelfvertrouwen
O	O	angsten
O	O	neerslachtigheid/somberheid
O	O	spanning
O	O	eenzaamheid
O	O	concentratie
O	O	schuldgevoel
O	O	controleverlies
		Religieuze/spirituele problemen
O	O	zin van het leven/ levensbeschouwing
O	O	vertrouwen in God/geloof

Ja	Nee	
		Lichamelijke problemen
O	O	uiterlijk
O	O	veranderde urine-uitscheiding
O	O	verstopping/obstipatie
O	O	diarree
O	O	eten
O	O	opgezwollen gevoel
O	O	koorts
O	O	mondslijmvlies
O	O	misselijkheid
O	O	droge, verstopte neus
O	O	pijn
O	O	seksualiteit
O	O	droge, jeukerige huid
O	O	slaap
O	O	benauwdheid
O	O	duizeligheid
O	O	praten
O	O	smaakvermogen
O	O	veranderingen in gewicht
O	O	tintelingen in handen/voeten
O	O	wassen/aankleden
O	O	dagelijkse bezigheden
O	O	moeheid
O	O	conditie
O	O	spierkracht

Andere problemen

Zou u met een deskundige willen praten over uw problemen?

O ja O misschien O nee

Afbeelding 1 De Lastmeter.

De onderzoeken die beschreven staan in dit proefschrift richten zich op de last (distress) die ervaren wordt door vrouwen met borstkanker of eierstokkanker op verschillende momenten tijdens en na behandeling.

Bij het gebruik van de Lastmeter hoort ook dat patiënten hun ervaren last en problemen kunnen bespreken met een zorgverlener. We hebben onderzocht of het bespreken van de Lastmeter met een verpleegkundige invloed heeft op onder andere de kwaliteit van leven van vrouwen tijdens en na hun behandeling voor borstkanker.

Ervaren last van vrouwen met borstkanker na afronding van de behandeling

De studie beschreven in **Hoofdstuk 2** richt zich op vrouwen met borstkanker die de behandeling voor borstkanker hebben afgerond. Het doel van dit onderzoek was om te bestuderen hoeveel vrouwen last en/of problemen ervaren en wat de relatie is met persoonlijke kenmerken (zoals opleiding, behandeling en leeftijd). Ook is onderzocht welke problemen het vaakst voorkwamen en of er behoefte was aan extra hulp. Om antwoorden te krijgen op bovenstaande vragen hebben we 258 vrouwen die voor borstkanker behandeld waren in het Radboudumc aangeschreven en gevraagd om een vragenlijstboekje in te vullen. In totaal werden 129 vragenlijsten compleet ingevuld retour ontvangen (response percentage 50 %). Ongeveer een derde van deze groep vrouwen gaf aan dat ze verhoogde last ervoeren (een score van 5 of hoger op de Lastmeter). Onderscheid werd gemaakt tussen vrouwen tot 2 jaar na operatie, vrouwen die 2 tot 5 jaar na de operatie waren en vrouwen waarbij de operatie meer dan 5 jaar geleden was. Vrouwen tot 2 jaar na operatie ervoeren meer last dan vrouwen die 2 tot 5 jaar na behandeling waren. Vrouwen die een gecombineerde behandeling hadden ondergaan (operatie en chemotherapie en/of bestraling) rapporteerden meer last dan vrouwen die alleen geopereerd waren. De top 3 van meest gerapporteerde problemen van de gehele groep bevond zich in het lichamelijke domein, namelijk vermoeidheid, verminderde spierkracht en verminderde conditie. De hoogte van de last hing samen met onder andere kwaliteit van leven, angst en depressie. De meerderheid van de vrouwen gaf aan geen behoefte te hebben om met een deskundige te praten over hun problemen.

Ervaren last van vrouwen met eierstokkanker

Hoofdstuk 3 richt zich specifiek op de last en problemen die vrouwen met eierstokkanker ervaren. In tegenstelling tot vrouwen met borstkanker wordt eierstokkanker meestal gediagnosticeerd in een vergevorderd stadium van de ziekte waardoor zij vaak een ongunstige prognose hebben. In ons onderzoek hebben we ons gericht op vrouwen met eierstokkanker die in het Radboudumc zijn behandeld. Het doel van het onderzoek was om te bestuderen wat hun last en problemen waren, waarbij gebruik gemaakt werd van de Lastmeter. Daarnaast hebben we met vragenlijsten onderzocht of er sprake was van angst en/of depressie en hoe hun kwaliteit van leven was. Van de 273 hebben 117 vrouwen de vragenlijst teruggestuurd waarvan 104 vragenlijsten (response 38%) gebruikt zijn voor de analyse. Van de 104 vrouwen die de vragenlijsten hebben ingevuld, was bij 45 vrouwen de terugkeer van de ziekte inmiddels vastgesteld. We hebben onderzocht of het al dan niet terugkeren van de ziekte invloed had op de ervaren last en kwaliteit van leven, wat niet zo bleek te zijn. De meest gerapporteerde problemen bevonden zich in het lichamelijke domein, namelijk vermoeidheid, verminderde conditie en perifere neuropathie (tintelingen in handen en/of voeten). Dit zijn bekende bijwerkingen die samenhangen met de chemotherapie die deze patiënten krijgen en deze kunnen vaak langdurig of zelfs blijvend aanwezig zijn. De ervaren kwaliteit van leven van de vrouwen met eierstokkanker was gelijk aan die van de gemiddelde persoon zonder kanker. Vrouwen die aangaven hoge last te ervaren (een score

van 5 of hoger op de Lastmeter) scoorden meer problemen op de probleemlijst en hadden een lagere kwaliteit van leven dan vrouwen met een lage last.

Gebruik van de Lastmeter net na de diagnose borstkanker

In de richtlijn 'Detecteren behoefte psychosociale zorg' (versie 1) wordt aanbevolen om de Lastmeter te gebruiken net na de diagnose. In de richtlijn staat ook dat het afkappunt voor het wel/niet ervaren van verhoogde last op alle meetmomenten hetzelfde is. Wij vroegen ons echter af of het afkappunt van 5 een geschikt afkappunt is net na diagnose. De diagnose kanker heeft namelijk in het algemeen sowieso een grote impact op iemands leven en hoge last wordt dan ook vaak gezien net na diagnose. In de studie, beschreven in **hoofdstuk 4**, hebben we onderzocht welk afkappunt op de Lastmeter het meest geschikt is om vrouwen met duidelijk verhoogde last te onderscheiden van vrouwen die last hebben zoals je kan verwachten net na de diagnose borstkanker. Het doel hiervan was om alleen die vrouwen te selecteren die ook daadwerkelijk verhoogde last ervaren en die daarom mogelijk extra ondersteuning nodig hebben. Hiervoor hebben we bij 181 vrouwen met borstkanker gekeken hoe hoog de ervaren last was en welke problemen zij rapporteerden. De hoogte van de last hebben we vergeleken met een andere veelgebruikte vragenlijst voor het meten van last (distress), angst en depressie, namelijk de Hospital Anxiety and Depression Scale, kortweg HADS. Hieruit kwam naar voren dat een afkappunt van 7 het meest geschikt lijkt te zijn om vrouwen met hoge last te selecteren. Het gebruik van een hoger afkappunt dan 5 zorgt ervoor dat vrouwen met hoge last gerichter geselecteerd kunnen worden en dat vroegtijdig zorg kan worden ingezet bij vrouwen die het daadwerkelijk nodig hebben. In tegenstelling tot wat we in **hoofdstuk 2** en **hoofdstuk 3** constateerden, waren de meest voorkomende problemen, problemen uit het emotionele domein. Daarnaast kwam naar voren dat leeftijd samenhangt met distress. Jongere vrouwen ervoeren namelijk meer distress dan oudere vrouwen.

Het gebruik van de Lastmeter: wat is het effect op de kwaliteit van leven?

Hoewel screening met de Lastmeter bij mensen met kanker wereldwijd wordt aanbevolen, is het bewijs voor het effect van het gebruik van de Lastmeter op de kwaliteit van leven beperkt. In **hoofdstuk 5** staat beschreven waarom wij ervoor hebben gekozen om een studie op te zetten om het effect van het regelmatig gebruik van de Lastmeter en het bespreken hiervan door de verpleegkundige op de kwaliteit van leven van vrouwen die in opzet curatief worden behandeld voor borstkanker te onderzoeken. De hypothese was dat door het vroegtijdig signaleren van verhoogde last het mogelijk zou zijn om tijdig gerichte interventies in te zetten en daardoor problemen op lange termijn te voorkomen.
Daarnaast staat beschreven hoe wij dit onderzoek precies hebben opgezet en welke stappen we hiervoor hebben ondernomen (protocol). Om een effect te kunnen meten heeft er een loting plaatsgevonden (randomisatie) waarbij een groep vrouwen de standaard zorg ontving (controlegroep) en een groep

vrouwen de standaard zorg ontving aangevuld met op vastgestelde momenten een gesprek met de verpleegkundige aan de hand van de ingevulde Lastmeter (interventiegroep). De vrouwen uit de interventiegroep werden besproken in een psychosociaal multidisciplinair overleg indien zij op de Lastmeter een 5 of hoger scoorden. Aan beide groepen werd gevraagd om op verschillende momenten tijdens en na behandelingen vragenlijsten in te vullen over onder andere kwaliteit van leven, angst en depressie, ziektebeleving en borstkanker specifieke problemen. Uiteindelijk was het doel om vast te stellen of er verschil was in de ervaren kwaliteit van leven tussen beide groepen twee jaar na afronding van de behandeling.

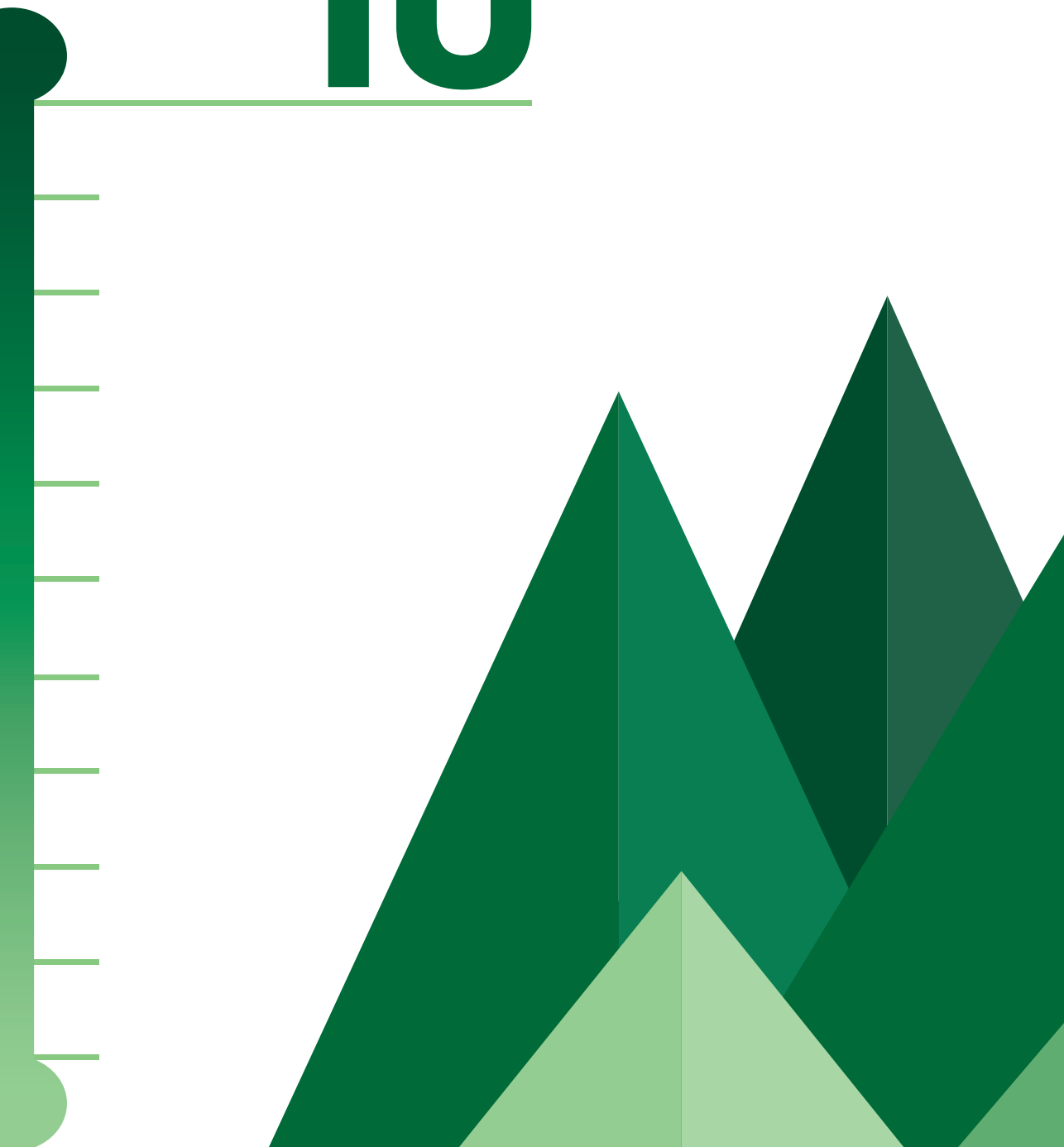
In **hoofdstuk 6** worden de resultaten getoond van het onderzoek dat in **hoofdstuk 5** staat beschreven. In totaal deden 194 vrouwen mee aan deze studie. Van de 194 vrouwen werden 98 vrouwen toegewezen aan de standaard zorg zonder gebruik van de Lastmeter en 96 aan de standaard zorg met extra gesprekken met de verpleegkundige aan de hand van de ingevulde Lastmeter. De resultaten lieten zien dat het regelmatig gebruik van de Lastmeter door een verpleegkundige geen effect had op de ervaren kwaliteit van leven twee jaar na afronding van de behandeling. In totaal werden 688 Lastmeters ingevuld en besproken waarvan 215 vrouwen (sommige vrouwen meerdere keren) zijn besproken in het psychosociaal multidisciplinair overleg in verband met een score van 5 of hoger. De meeste vrouwen gaven aan dat zij geen behoefte hadden aan een verwijzing om met een deskundige te praten over hun problemen en dat het gesprek met de verpleegkundige voldoende was. Hoewel de interventie niet resulteerde in een positief effect twee jaar na afronden van de behandeling (het zogenaamde 'primaire eindpunt van de studie'), werd in een verkennende subgroep analyse aangetoond dat de interventie mogelijk wel effect had op de groep vrouwen die een behandeling met zowel operatie, bestraling als ook chemotherapie hadden ondergaan. De resultaten van deze studie sluiten aan bij het reeds bestaande bewijs over het effect van het gebruik van de Lastmeter en kunnen worden meegenomen in de discussie over het al dan niet gebruik van de Lastmeter als standaardzorg in de dagelijkse praktijk.

Het gebruik van de Lastmeter in de dagelijkse praktijk: hoe nu verder?

In **hoofdstuk 8** wordt bediscussieerd wat de resultaten van de verschillende onderzoeken betekenen voor de dagelijkse praktijk. Ook worden de voor-en nadelen beschreven van de methoden van de onderzoeken die zijn gebruikt. Daarnaast worden er aanbevelingen gedaan voor verder onderzoek. Dit proefschrift laat zien dat er geen sterk bewijs is voor een positief effect op de kwaliteit van leven door het bespreken van de resultaten van de Lastmeter op vastgestelde momenten door de verpleegkundige bij vrouwen met borstkanker. Hoewel er geen effect gezien wordt op de kwaliteit van leven, geven zowel patiënten als verpleegkundigen aan dat de Lastmeter hen helpt het gesprek aan te gaan over de ervaren last en de problemen op dat moment. Tegenwoordig is er steeds meer aandacht voor persoonsgerichte zorg waarbij de zorgverlener de patiënt en zijn/haar familie in het middelpunt zet en gelijkwaardig mee laat denken in de beslissingen van hun behandeling. Hierbij is het belangrijk dat de behoeften

en de wensen van de patiënten goed in kaart worden gebracht aan het begin en het einde van het behandeltraject. De Lastmeter kan dan een hulpmiddel zijn bij het formuleren van een persoonlijk (psychosociaal) plan dat aansluit bij de ervaren last en de behoeften van de patiënt. Het betekent dat de focus in het gebruik van de Lastmeter niet ligt op het afnemen van de Lastmeter op standaard vaste momenten en/of afkappunt maar dat de patiënt aangeeft wat hij/zij nodig heeft. Hierbij is het van belang dat de verpleegkundige weet wie een verhoogd risico heeft op verhoogde last en welke mogelijkheden voor ondersteuning beschikbaar zijn bij bepaalde problemen. Daarnaast zijn goede communicatieve vaardigheden nodig om de ervaren last en (onvervulde) behoeften te ontdekken en te bespreken.

10



PhD Portfolio | Research data management | List of publications | Dankwoord | Curriculum Vitae

PhD portfolio

Name PhD student: F.K. Ploos van Amstel
Department: Medical Oncology
Graduate School: Radboud Institute for Health Sciences
PhD period: 01-9-2009 – 31-12-2019
Promotors: Prof. dr. W.T.A. van der Graaf, Prof. dr. J.B. Prins
Copromotor: dr. P.B. Ottevanger

	Year(s)	ECTS
TRAINING ACTIVITIES		
Courses & Workshops		
• *Basiscursus regelgeving en Organisatie voor klinisch onderzoekers (BROK)*	2010	1.75
• *Presenteren eigen onderzoek*	2011	1.5
• *Schrijven van Wetenschappelijke Teksten*	2012	3.0
• *Academic Writing*	2012	3.0
• *Herregistratie BROK*	2014, 2018	0.4
• *European Academy Nursing Science Summer School*	2012, 2013, 2016	5.25
Seminars & Lectures		
• *Expertmeeting over de Lastmeter IKO (oral)*	2010	0.5
• *Palliatieve zorg- intuitie, wijsheid en wetenschap (oral)*	2012	0.5
• *Werkgroep oncologieverpleegkundigen, Radboudumc (oral)*	2014	0.25
• *6e Nationaal Congres Palliatieve Zorg (oral)*	2016	0.5
• *Anna Reynvaanlezing (oral)*	2017	0.25
Symposia & Congresses		
• *V&VN oncologiedagen, Utrecht (oral)*	2010	0.75
• *IPOS congress, Antalya, Turkey (poster)*	2011	1.0
• *NVPO congress, Utrecht (oral)*	2012	0.5
• *V&VN oncologiedagen Ede (oral & poster)*	2013	1.0
• *IPOS congress, Amsterdam (poster)*	2013	1.0
• *ESGO congress, Torino, Italy (oral)*	2014	1.25
• *IPOS congress, Lisbon, Portugal (poster)*	2014	1.25
• *V&VN oncologiedagen, Ede (oral)*	2014	0.75

Other		
• *Gammaraad psychosocial oncology, secretary*	2010-2012	3.0
• *Journal reviewer 'Psycho-Oncology'*	2014	0.1
• *Member of Deskundigheidscommissie NVPO*	2014-2015	1.0
• *Congresredactie verpleegkundig deel van WOG/DGOG congres*	2014	1.0
• *Journal Club psychosocial oncology*	2012-2015	3
• *Congresredactie Oncologiedagen V&VN*	2015	1.0
TEACHING ACTIVITIES		
Lecturing		
• *Gastdocent 'maken van een poster en schrijven van een abstract', Erasmus Medisch Centrum Zorgacademie, Rotterdam*	2011	0.8
• *Gastdocent' verpleegkundig onderzoek, EBP en kritisch lezen', Vervolgopleiding Oncologie Verpleegkundige, Radboudumc Health Academy, Nijmegen*	2015-2018	1.2
Supervision of internships / other		
• *Docentbegeleider, Hogeschool Arnhem en Nijmegen, Nijmegen*	2014	2.0
• *Opdrachtgever HBO-V kwaliteitsprojecten, Hogeschool Arnhem en Nijmegen, Nijmegen*	2015-heden	4.0
TOTAL		**41.5**

Research data management

This thesis is based on the results of human studies, which were conducted in accordance with the principles of the declaration of Helsinki. The medical and ethical review board Committee on Research Involving Human Subjects Region Arnhem Nijmegen, Nijmegen, the Netherlands has given approval to conduct these studies (2009/293). Informed consent was obtained from all participants.

This project and the patient data for analyses are stored on the Radboudumc, department server: (H):ONCOdata$ in the folder H:\VerpleegkundigOnderzoek\VIP. This folder is specifically for this project to which access is only granted to authorized personnel. All paper informed consent and questionnaires (chapter 4 and 6) are stored in a locked cabinet at the department of Medical Oncology. The paper data of chapter 2 are stored in the department archive of Medical Psychology. The paper data of chapter 3 are stored in the department archive of Medical Oncology. Data management and monitoring were performed using a Microsoft Excel file and 'Statistical Package for the Social Sciences' (SPSS) files which are also stored in the folder Verpleegkundig Onderzoek. During the course of this thesis, databases were created to save the patient derived data. All databases were encrypted and created using the latest versions of SPSS. The databases did not contain information regarding the identity of the patient (such as name or social security number) and only contained coded anonymous information. The privacy of the participants in this study is warranted by use of encrypted and unique subject codes. This code correspondents with the code on the patients booklets. Data where converged from Radquest to SPSS. The data will be saved for 15 years after termination of the study. Using these data patient data in future research is only possible after a renewed permission by the patient as recorded in the informed consent. The datasets analyzed during these studies are available from the corresponding author on reasonable request.

List of publications

Ploos van Amstel FK, Peters MEWJ, Donders R, Schlooz-Vries MS, Polman LJM, van der Graaf WTA, Prins JB, Ottevanger PB. Does a regular nurse-led distress screening and discussion improve quality of life of breast cancer patients treated with curative intent? A randomized controlled trial. *Psychooncology* 2020;1-10.

Rietveld MJA, Peters EJ, Husson O, **Ploos van Amstel FK**, Kamm Y, Sijtsema S, Diepenbroek M, Heler J, Zoetbrood C, Zielstra M, Lambert SD, Prins JB, Ottevanger PB. Psychometric properties of the 45-item supportive care needs survey – partners and caregivers – Dutch (SCNS-P&C45-D) in partners of patients with breast cancer. *J Patient Rep Outcomes* 2019;11,3:1.

Ploos van Amstel FK, Tol J, Sessink KH, van der Graaf WTA, Prins JB, Ottevanger PB. A specific distress cutoff score shortly after breast cancer diagnosis. *Cancer nurs* 2017;40(3):E35-E40.

Ploos van Amstel FK, Prins JB, van der Graaf WTA, Peters MEWJ, Ottevanger PB. The effectiveness of a nurse-led intervention with the distress thermometer for patients treated with curative intent for breast cancer: design of a randomized controlled trial. *BMC Cancer* 2016;16;520.

Ploos van Amstel FK, van Ham MAPC, Peters EJ, Prins JB, Ottevanger PB. Self-reported distress in patients with ovarian cancer: is it related to disease status? *Int J Gynecol Cancer* 2015;25(2):229-35.

Ploos van Amstel FK, Merkx-Kokshoorn A, Slot S, Ottevanger PB. Het signaleren van distress en behoefte aan zorg voor patiënten met kanker. *Tijdschrift psychosociale oncologie* 2014;22(3).

Ploos van Amstel FK, van den Berg SW, van Laarhoven HWM, Gielissen MFM, Prins JB, Ottevanger PB. Distress screening remains important during follow-up after primary breast cancer treatment. *Support Care Cancer* 2013;21(8):2107-2115.

Van den Berg SW, **Ploos van Amstel FK,** Ottevanger PB, Gielissen MFM, Prins JB. The Cancer Empowerment Questionnaire: Psychological Empowerment in Breast Cancer Survivors. *J Psychosoc Oncol*. 2013;31(5);565-583.

Ploos van Amstel FK, van Vliet M, Potting CMJ, Donnelly JP, Blijlevens N, Schoonhoven L. Detecteren van koorts bij de hematologische patient in de neutropene fase. *Tijdschrift Verpleegkunde* 2011;26(2);13-18.

Dankwoord

Het is nu echt zover. Mijn proefschrift over de Lastmeter is klaar. Daarmee is een LAST van mijn schouders afgevallen. Ik heb in mijn promotie periode echter veel KRACHT ervaren door rondom de lastmeter samen te werken met collega's en mij gesteund te weten door familie en vrienden.

Voor dit dankwoord blik ik aan de hand van de lastmetersystematiek graag terug op mijn persoonlijk ervaren last en kracht in de afgelopen jaren. Jaren waarin ik veel heb geleerd en zowel pieken als dalen heb gekend. Het traject begon met weinig last (score 1). Ik startte als jonge verpleegkundig onderzoeker aan het project over de Lastmeter. De last nam toe (score 5) bij het afronden, als er artikelen te submitten en re-submitten waren. De last werd verder verhoogd (score 7) als ik afwijzingen te incasseren kreeg en/of mocht re-submitten met inachtneming van de opmerkingen van de referenten. De ervaren last daalde naar aanvaardbaar (score 3) als daar uiteindelijk het verlossende mailtje kwam dat het artikel geschikt was bevonden voor publicatie in een internationaal vakblad. Wat de score op de lastmeter ook was en welke problemen hier dan ook bij hoorden, er stonden lieve collega's voor mij klaar die mij hielpen, motiveerden en er mede voor hebben zorg gedragen dat ik nu met trots dit proefschrift verdedig. In dit dankwoord wil ik dan ook iedereen bedanken die direct en indirect betrokken waren bij het tot stand brengen van dit proefschrift.

Allereerst wil ik mij richten tot alle patiënten, die vragenlijsten met betrekking tot de Lastmeter hebben ingevuld en gesprekken met mij over de Lastmeter hebben gevoerd. Zonder hen had ik dit proefschrift niet kunnen schrijven. Ik wil dan ook alle vrouwen bedanken die open stonden om hun last en ook hun kracht met mij te delen en te bespreken. Ik heb veel van hen mogen leren, ik heb door hen beter inzicht gekregen in welke problemen wanneer het meest werden ervaren en welke zorg er al dan niet beschikbaar is. In gedachten sta ik ook stil bij de vrouwen die in de afgelopen jaren zijn overleden of waarbij de ziekte teruggekomen is.

Speciaal woord van dank gaat uit naar mijn promotieteam: **prof. dr. Winette van der Graaf**, **prof. dr. Judith Prins** en **dr. Nelleke Ottevanger**.
Winette, je kritische blik en vragen zorgden uiteindelijk altijd voor meer diepgang en betekenis van mijn onderzoek. Je steun in het schrijven en het intensieve mail- en whatsapp-contact op de piekmomenten in met name het afgelopen jaar hielpen mij om toch de finale sprint te maken en het proefschrift echt af te ronden. Bedankt voor het laatste duwtje in de rug.
Judith, bedankt voor je kennis en ervaring die je deelde over de psychosociale zorg en de bestaande literatuur, de Lastmeter trainingen en de discussies die we hebben gehad over hoe de psychosociale zorg voor de patiënt met kanker verbeterd kan worden. De rol die je mij gaf in het project 'Implementatie van de Lastmeter Radboudumc breed' heeft bijgedragen aan mijn inzicht in hoe de psychosociale zorg in elke keten weer anders georganiseerd is en heeft mij ook een enthousiast netwerk van gemotiveerde (oncologie) verpleegkundigen opgeleverd.

Nelleke, bedankt voor al jouw steun aan en vertrouwen in mij, zowel op het werk als privé. Je hebt mij de kans gegeven om onderzoeker te worden, verpleegkundig expert en casemanager. Ook nu motiveer en steun jij mij in de keuzes die ik maak. Wat hebben we samen veel meegemaakt. We hebben ontzettend veel gelachen en soms ook een traan gelaten. Ik bewonder je voor je inzet, positiviteit en je enorme kennis. Mooi om te zien hoe jij je volledig inzet om élke patiënt de best passende behandeling te geven. Bedankt voor je geduld, je inhoudelijke bijdrage en het allerbelangrijkste: je vriendschap. Ik hoop dat we in de toekomst nog veel projecten samen mogen opzetten om de kwaliteit van zorg te verbeteren.

Dr. Marlies Peters, vanaf het eerste moment dat ik op de afdeling Medische Oncologie kwam, stond jij voor mij klaar. Je hielp mij met het onderzoek en het schrijven. Je hebt mede mijn (onderzoeks)lasten lichter gemaakt en je deur stond altijd open en niet alleen voor mij. Jouw bijdrage aan dit proefschrift is niet te beschrijven en ik ben er dan ook trots op dat jij vandaag naast mij staat als een krachtige paranimf.

Ik dank de leden van de manuscriptcommissie, **prof. dr. Hester Vermeulen**, **prof. dr. Hans de Wilt** en **prof. dr. Irma Verdonck-de Leeuw** voor het beoordelen en goedkeuren van dit proefschrift.

Het onderzoek kon niet uitgevoerd worden zonder de hulp van de verschillende medewerkers van de afdeling Heelkunde. In het bijzonder de mamma-chirurgen **Margrethe Schlooz-Vries** en **Annelies Werner** en de verpleegkundig specialisten **Renate Besselink**, **Lenny Polman** en **Kelly Sessink**. Bedankt voor jullie hulp bij de inclusie en de begeleiding van de vrouwen met borstkanker. Ik heb veel geleerd van jullie met betrekking tot de problemen die patiënten kunnen ervaren na een operatie. Renate en Kelly, niet alleen op het werk heb ik veel aan jullie gehad. Een fijne vriendschap is eruit ontstaan en ik kijk uit naar onze volgende RenFloKel date.

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Co-auteurs, dank jullie wel voor jullie bijdrage in het krachtig meedenken aan het opzetten en uitvoeren van dit soms lastige onderzoek en het schrijven van de artikelen. **Prof. dr. Hanneke van Laarhoven**, je was betrokken bij mijn eerste artikel en je kritische en motiverende feedback hielp mij verder in de zoektocht naar het goed schrijven van een artikel. **Dr. Jolien Tol**, bedankt voor je fijne samenwerking met het schrijven van het artikel en ook de zorg die we samen gaven aan de vrouwen met borstkanker. **Dr. Maaike van Ham**, ik leerde je kennen toen ik casemanager werd binnen de gynaecologische oncologische keten. Mooi om te zien hoe jij samenwerkt met de verschillende verpleegkundigen en hoe jij je inzet om de psychosociale zorg voor de vrouwen met gynaecologische kanker continu te verbeteren. **Dr. Marieke Gielissen**, jouw fijne en gezellige begeleiding, als ook kennis van onderzoek en bestaande literatuur hielpen mij elke keer weer verder. Voor de statische analyse en ondersteuning wil ik graag **dr. Rogier Donders** en **dr. Steven Teerenstra** bedanken.

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De groep **gespecialiseerde verpleegkundigen**. Wat een fijne en diverse groep casemanagers en verpleegkundig specialisten zijn jullie. We hebben allemaal hetzelfde doel: aanspreekpunt zijn voor patiënten en ervoor zorgen dat hun pad zoveel mogelijk aansluit bij hun individuele behoeften en wensen. Jullie zorgen ook voor een fijne en vertrouwde werksfeer waarin ik met plezier met jullie samenwerk en mijn steentje kan bijdragen aan het verbeteren van zorg. Ik wens dat we in de toekomst nog meer verpleegkundig leiderschap kunnen laten zien, waarbij jullie als casemanagers en verpleegkundig specialisten een steeds duidelijkere en meer prominente rol krijgen in elke keten en op de afdeling.

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Mijn interesse voor de psychosociale zorg voor mensen met kanker is ontstaan op de afdeling Hematologie van het Radboudumc. De leerzame en gezellige tijd op deze afdeling heeft mij gevormd als verpleegkundige. Mijn eerste onderzoek is uitgevoerd op de afdeling Hematologie en ik wil dan ook alle medewerkers van de afdeling Hematologie, die daar toen werkzaam waren, bedanken voor de veilige en gezellige werksfeer en ik ben blij met de vriendschappen die ik eraan over heb gehouden. In het bijzonder, **dr. Maarten van Vliet**, bedankt voor de zure sluwe sleutel en ESCAPE (espresso met cappuccino) momenten waarin we onze promotietrajecten bespraken.

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I would like to thank my colleagues from the European Academy of Nursing Science (EANS). I had a great time with you discussing our studies and similarities and differences between our countries. It is great to see that we still help each other, even years after the summer school.

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Curriculum vitae

Floor Ploos van Amstel werd geboren op 9 februari 1983 te Wijk bij Duurstede. Zij behaalde haar VWO diploma in 2001 aan het Revius Lyceum te Doorn. Datzelfde jaar begon ze aan haar opleiding Verpleegkunde aan de Hogeschool Arnhem en Nijmegen en behaalde in 2005 haar diploma. Floor werkte vervolgens tussen 2005 en 2009 als verpleegkundige op de afdeling Hematologie van het Radboudumc. In 2006 startte ze met de deeltijd opleiding verplegingswetenschap aan de Universiteit Utrecht. In 2007 behaalde ze de pre-master en in 2009 de master Verplegingswetenschap. Voor haar afstudeeronderzoek in de Verplegingswetenschap ontving zij in 2010 de Johanna Diepeveen-Speekenbrink Wetenschaps Prijs. Daarnaast werd zij voorgedragen om lid te worden van de Sigma Theta Tau International. Dit is een organisatie die verpleegkundig leiderschap stimuleert. Na het behalen van haar master kreeg ze een baan als verpleegkundig expert op de afdeling Medische Oncologie. Binnen deze functie startte ze haar onderzoek naar de Lastmeter bij vrouwen met kanker, onder begeleiding van dr. P.B. Ottevanger, prof. dr. J.B Prins en prof. dr. W.T.A. van der Graaf. Tussen 2009 en 2013 richtte zij zich op haar onderzoek, begeleidde zij studenten met kwaliteitsprojecten en hielp zij o.a. bij een implementatieproject van de Lastmeter binnen het Radboudumc. Samen met dr. P.B. Ottevanger verwierf zij in 2012 een subsidie voor de inventarisatie van de behoeften van de partners van vrouwen met borstkanker en het opzetten van extra zorg voor hen. Naast de functie van verpleegkundige expert werd zij ook casemanager voor patiënten met gynaecologische kanker en gemetastaseerd schildklierkanker. Zij was voor hen hun eerste aanspreekpunt, nam de begeleiding en informatieverstrekking op zich en coördineerde hun zorg. Voor de psychosociale begeleiding gebruikte zij regelmatig de Lastmeter. Naast haar werk op de afdeling Medische Oncologie gaf zij als gastdocent les over verpleegkundig onderzoek op de vervolgopleiding Oncologie Verpleegkundige van de Radboudumc Health Academy in Nijmegen. In 2012 werd zij geselecteerd voor deelname aan de European Academy for Nursing Science Summer School die zij tussen 2012-2016 volgde. Voor haar artikel *'A Specific Distress Cutoff Score Shortly After Breast Cancer Diagnosis'* werd zij in 2017 genomineerd voor de Anna Reynvaan Wetenschapsprijs. In 2017 besloot zij dat ze zich verder wilde richten op de kwaliteit van zorg en werd zij kwaliteitsfunctionaris en projectleider op de Afdeling Medische Oncologie. In deze functie werkt zij nauw samen met de verschillende disciplines van de afdeling om zo de kwaliteit van zorg(processen) voor de oncologische patiënten te verbeteren.
Floor woont samen met haar partner Paul en hun twee zoons Kaj (2015) en Sep (2017).


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