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Identifying and predicting distinct distress trajectories following a breast cancer diagnosis - from treatment into early survival

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ABSTRACT

Objective: Most longitudinal studies on distress in breast cancer (BC) patients reported a continuous decrease after diagnosis, however masking individual variations in patterns of adjustment. We sought to identify distinct trajectories of distress during primary treatment into survivorship and to identify variables that are determinants of which patient follows which type of adjustment trajectory.

Methods: Psychological distress was measured at four significant time points (after surgery/biopsy, at treatment completion, two and six months thereafter) among 181 newly diagnosed BC patients. A latent growth mixture modeling approach was used to identify distinct distress trajectories.

Results: Four distress trajectories were identified: a 'resilient' pattern (73.1%), a 'high-remitting' (7.7%) trajectory, a 'delayed' increase in distress (7.9%), and a constantly high 'chronic' distress (11.3%) pattern. High perceived burden from physical symptoms at treatment completion encompassed a higher chance for the 'high-remitting' and 'chronic' distress trajectory. High self-efficacy at baseline increased chances for the 'high-remitting' pattern. Neither type of treatment, demographic or medical characteristics, nor baseline distress reliably predicted distress trajectories.

Conclusion: The majority of BC patients adjust well through a demanding treatment period. High patient-perceived burden from physical symptoms, and high coping self-efficacy is suggesting a transient, self-limiting distress trajectory, while patients experiencing constant 'chronic' distress, and those developing distress following treatment completion only cannot be identified by a single, initial assessment. Only systematic tracking with repeated measurement extending into survivorship can eliminate this problem. Interventions should aim at reducing the impact of symptom burden on women's every-day life and on strengthening coping-self efficacy.

1. Introduction

The physical and psychosocial exigencies of experiencing a cancer diagnosis and undergoing treatment are well documented, including evidence from prospective studies that assess large samples of individuals after a cancer diagnosis, most of them dealing with breast cancer (BC) patients [1]. As shown in longitudinal studies, psychological distress, e.g. symptoms of anxiety and depression, usually was found to peak around the time of diagnosis until treatment aiming for cure is started, followed by a continuous decrease during the first year [2–4].

However, an overall decrease in distress over time detected on a group level may mask variation in individual patterns of adjustment. When 'looking beyond the mean' [5] several longitudinal studies using growth curve modeling found distinct trajectories of psychological distress over months or years after BC diagnosis [5–11]. However, these studies yield considerably varying results on the distinct distress trajectories, the proportion of individuals belonging to a subgroup representing a particular pattern of adjustment, as well as on the factors characterizing and/or predicting a distinct trajectory. Some of this heterogeneity may be due to variation in time points and number of measurements, short observation intervals not extending into early

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survivorship e.g. [5,9,12], assessments not linked to illness-related key events e.g. [5,6,13] or selected samples regarding treatment modality, e.g. with neoadjuvant chemotherapy not included e.g. [5,11]. Therefore this study's *primary goal* was to prospectively determine the course of distress experienced by early BC patients during and beyond the period of active cancer treatment, and to determine whether distinct trajectories of psychological distress will be confirmed as found in previous research [5–13].

Second, the study aims to identify factors that allow to reliably characterizing patients assigned to a particular distress trajectory. Therefore, the type of (neo-)adjuvant cancer treatment and patient-perceived burden due to physical symptoms will be examined as will the impact of patients' pre-cancer conditions (previous mental disorder, current physical comorbidity, psychological well-being in the year preceding BC diagnosis) in addition to demographic data. Also, the impact of patient-perceived general self-efficacy (GSE) and self-efficacy specific to adjusting to cancer (CRSE) on the course of distress will be tested as self-efficacy was found to predict emotional well-being and depression in cancer patients [14,15]. Considering the interactional context of cancer treatment, a potential impact of trust in physician (TIP) on the course of adjustment will be determined.

Third, we examined potential mediators by looking at the course of self-efficacy, physical symptom burden and TIP, in order to identify potential targets and time points for screening and intervention.

The study was conducted at two certified German BC centers. It linked assessments to key treatment-related events at four time points starting from diagnosis through (neo-) adjuvant treatment until six months after treatment completion rather than to employ pre-determined time points. Current standards in BC treatment such as neoadjuvant chemotherapy increasingly used among young women were considered and a growth-mixture modeling approach for determining distress trajectories was applied.

Knowledge of distinct trajectories of distress during and after completion of treatment is expected to provide further information at what time points and which at-risk groups are in need for continued monitoring and for targeted psychosocial and behavioral interventions. In settings with limited resources, knowing which patients are likely to follow a stable trajectory will help to avoid unnecessary screening and providing treatment to those, whose distress would remit by its own.

2. Method

2.1. Data collection and participants

For this prospective, longitudinal cohort study BC patients were consecutively recruited at two BC centers, certified by the German Cancer Society [16] upon diagnosis of invasive BC from May 2013 to March 2016. Eligible patients were younger than 70 years, had received a first BC diagnosis following surgery/biopsy, and were assigned a neo−/adjuvant treatment modality specific to their clinical and histopathological risk profile based on current guidelines [17] by a multidisciplinary tumor board: (1) radiation of the remaining breast tissue following breast-conserving surgery (rad), (2) neoadjuvant chemotherapy followed by surgery of the breast and radiation therapy (neocht), (3) surgery followed by adjuvant chemotherapy and radiation therapy (adj-cht). Assessment at four time points was linked to the course of treatment: after surgery/biopsy (T1), upon completion of neo−/adjuvant treatment (radiotherapy, chemotherapy or both) (T2), two months (T3) and again six months (T4) following treatment completion. Potential participants were contacted in person prior to receiving information on neo−/adjuvant treatment as recommended by the tumor board from a gynecologist. They were informed verbally and using written material on the purpose of the study. Consenting study participants were contacted in-person at the first assessment (T1), whereas questionnaires were mailed at T2 to T4. To adjust for individual variation of treatment duration, patients were contacted by phone/email to assure that treatment was completed before T2 questionnaires were sent.

Based on preceding sample size calculation an overall sample size of $n = 170$ patients (40% rad only, 30% each undergoing adj-cht and neocht) was required [18]. Initially, patients were recruited regardless of type of treatment. Once the adequate rate of rad patients had been recruited, only neo−/adj-cht patients were recruited until the desired sample size was achieved.

2.2. Measures

2.2.1. Main outcome

We assessed *psychological distress* as primary outcome using the 12-item version of the General Health Questionnaire (GHQ) [19], which has been validated, among others, in cancer patients [20] and shows a good congruousness with other common distress measurements [21]. Patients are asked to state how they felt in the last week compared their usual state on a 4-point Likert scale. A total value is calculated, ranging from 0 to 36 and a recommended cut-off of 11/12, with higher scores indicating more severe distress. Good psychometric properties of the GHQ were reported [22,23]. In the current sample, Cronbach's α at T1 was 0.92.

2.2.2. Predictor variables

Cancer related self-efficacy (CRSE) was assessed using the 14-item Cancer Behavior Inventory (CBI) [24]. Patients indicate how confident they feel regarding various aspects of coping with cancer and treatment on a 9-point Likert scale. Total scores range from 14 to 126, with higher values indicating higher CRSE. In a German study (on cancer patients) the CBI proved to be sufficiently reliable (Cronbach's α 0.87, present study 0.92), valid and sensitive to change [24]. We further assessed *generalized self-efficacy* (GSE) using the Generalized Self-Efficacy Scale (GSE) [25] in order to determine the predictive role of this comprehensive construct. All ten GSE items are rated on a 4-point Likert scale with scores ranging from 10 to 40. In the German version Cronbach's α ranged from 0.80 and 0.90, [26], in this study it was 0.92.

Physical symptom burden, as perceived by patients was measured using the interference scale of the MD Anderson Symptom Inventory (MDASI II) [27]. This subscale evaluates the extent to which physical symptoms assessed by the symptom scale (part I) interfered with the patient's daily living within the last 24 h. The six items are evaluated on an 11-point Likert scale. Mean scores are used representing overall burden due to physical symptoms. Adequate psychometric properties with good reliability (Cronbach's α part I of 0.82 and part II of 0.84, present study part I 0.89 and part II 0.91) and validity were reported for the German MDASI version [28].

Trust in physician (TIP) was assessed using the Trust in Physician Scale (TIPS) [29]. The scores of the 11 items are aggregated and transformed to values from 0 to 100, higher values indicating higher TIP. Compared to Cronbach's α 0.90 reported in the original study, in the current sample it was 0.80.

Treatment characteristics and *demographic data* assessed at T1 were derived from patients' own reports and from medical records. Psychological well-being in the year preceding BC diagnosis, previous mental disorder, current physical comorbidity and regular psychotropic and/or opioid medication at time of BC diagnosis were enquired from the patients.

2.3. Statistical analysis

To identify distinct distress trajectories, a latent growth mixture modeling approach (GMM) was used, which allows to determine whether a sample is composed of two or more different subgroups (latent classes) of individual growth trajectories, with class membership defined by the growth parameters intercept and slope [30,31]. First, a single-class GMM without covariates (unconditional model) was