Late Presentation at Primary Diagnosis of Breast Cancer: Patients' Personality Characteristics and Attitudes

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Keywords

Breast cancer · Delayed presentation · Exulceration · Psychological characterization · Personal characteristics

Abstract

Introduction: Breast cancer (BC) is the most common cancer in women worldwide. Despite screening and information efforts, about 10% of patients present with tumor size T3 or T4 at primary diagnosis. Late presentation is associated with more advanced tumor stage and consecutively with worse survival rates. **Objective:** This study aimed to evaluate whether patients with a late presentation at primary BC diagnosis differ in their personality from those with early diagnosis. **Methods:** In this bicentric, observational study, personality traits, positive and negative affectivity, anxiety, spirituality, illness beliefs, and sociodemographic characteristics were assessed in BC patients who presented with T-stages 3 or 4 (late presenters) and T-stages 1 or 2 (controls) at initial diagnosis. **Results:** Forty patients (20 controls, 20 late presenters) were interviewed. "Late presenters" perceived their disease as long lasting and had significantly more "positive affectivity" in the current trait. Although no significant associations were found, there was a trend for late presenters to have higher education levels, less spiritual longing, less accurate explanation of their illness, less anxiety in the trait

scale, and more conscientiousness than the controls. **Conclusion:** As patients with late presentation for BC differ in specific psychological and sociodemographic characteristics from patients with early BC, the findings of this pilot project warrant additional investigations to identify further specific characteristics and motivations. Identifying patients at risk for late presentation and encouraging them to accept an earlier diagnosis could help to improve their therapy and, finally, their outcome.

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Introduction

Worldwide, breast cancer (BC) is the most common cancer in women and the most common reason for cancer-related deaths [1]. Known prognostic factors in BC predicting patient outcome are lymph node status, histologic grade and subtype, as well as tumor size [2].

Tumor burden at presentation is a key factor for outcome. According to the UICC staging system, 5-year relative survival rates for patients with stage 1 or 2 at presentation range from 95 to 70%. Five-year survival rates for

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patients presenting with stage 3 (locally advanced and/or highly nodal positive) and stage 4 (metastatic BC) range from 52 to 18% [3]. Using multimodal tumor therapy, it is possible to extend the 5-year survival rate for patients with stage 4 disease up to 41%, which is still poor compared to those with earlier disease stages [4, 5]. These figures show that it is of utmost importance to diagnose BC as early as possible. Most patients in the western world are diagnosed at an early stage due to BC screening programs [6, 7]. Nevertheless, there are around 10% of patients who present with stage 3 and 4, including locally advanced BC [3, 7–9]. Late presentation of patients with BC is associated with shorter survival [10]. There is strong evidence for an association of late presentation with older age, whereas associations with socioeconomic status and ethnicity could not unequivocally be demonstrated [10].

The understanding of the relative risk of developing BC, of the associated risk factors, and of the diversity of potential symptoms of BC seems to be limited in women of all ages. However, older women (65 years and older) have a lower perception of their personal risk of developing the disease and are less able to identify BC symptoms or risk factors [11]. In addition, negative beliefs about the disease and its treatment are more common among this group than among younger women. Such beliefs include concerns about disability, disfigurement, and adverse economic consequences [12].

Another factor leading to a delay in primary diagnosis seems to be a reluctance of these women to bother their general practitioner. Burgess et al. [13] further described a higher tendency among them not to express explicit fears and to be hesitant because of fearing the consequences of diagnosis and treatment of BC. Bish et al. [14] tried to build a theoretical model to explain late presentation based on self-regulation theory, the theory of planned behavior and implementation intentions. That model includes stages of symptom appraisal, attitudes towards help-seeking, and translating intentions into behavior.

In a retrospective study assessing sociodemographic characteristics, medical history, and psychological issues in 67 BC patients, younger (≤ 40 years) and older (≥ 70 years) age, use of alternative medicine, and psychiatric comorbidities were associated with locally advanced BC at primary diagnosis [15].

An overview of the current literature shows that there are factors that are associated with late presentation, such as older age, special health beliefs, and fears. But there has not yet been any investigation about the personality of women with locally advanced BC at presentation. To our knowledge, data regarding late presentation and personality characteristics in other cancer subtypes are missing as well. Due to these findings, the aim of this study was to determine differences of personality traits between patients who consult a physician only after symptoms of BC

have persisted for an extended period of time (late presenters [LP]) and those who promptly seek medical help. Therefore, LP were defined by T-stage of T3 or T4. Their tumors were definitely to be noticed by the patients themselves earlier, especially in locally exulcerated cases. We further compared positive and negative affectivity, anxiety, spirituality, and illness beliefs of these patient groups. We defined “no difference in regard to personality characteristics” between control (C) group and LP as the null hypothesis. An alternative hypothesis was defined as “difference in regard to personality characteristics” between C group and LP. Knowledge about characteristics of women who are at risk of delay in seeking medical help for BC may help to tailor information targeting this patient population and to improve treatment options by detection of the disease at an earlier stage.

Patients and Methods

Patient Characteristics

In this bicentric study, 20 patients with locally advanced BC (T3 or T4) who presented at the Breast Center of the University of Munich (LMU) and the clinic “Dritter Orden” Munich between August 2013 and July 2017 were enrolled. Patients with histopathologically confirmed BC and locally advanced tumors (T3 or T4, particularly locally exulcerated and definitely palpable) at initial diagnosis were included. Thirteen of 20 patients presented with an ulcerated tumor. The tumor size, especially exulceration, was selected as inclusion criterion, since this allowed to identify patients who most probably had knowledge of the tumor at least for several months before presentation. Patients had to be ≥ 18 years old, and informed consent was obtained from all individual participants included in the study.

A cohort of 20 patients with T-stage T1 or T2 at primary diagnosis and matched in age (± 5 years) to each of the patients with late presentation was recruited as a C group. The target of 40 patients (20 LP and 20 C) was determined in advance after estimating the occurrence of LP in our center respecting the low incidence of advanced tumors.

Exclusion criteria were inadequate German language knowledge, evidence of psychosis, and history of cancer other than basal-cell carcinoma or dysplasia of the cervix.

Patients were recruited during the in-patient stay before surgery and after the consultation hours in the participating hospitals. This date of recruiting was selected as in this setting, enough time for disclosure and interview was guaranteed. All patients with T3 or T4 were asked for participation, no one refused to participate. After achieving the targeted number of 20, the recruitment was closed. The same procedure was applied for the C group.

Ethics Approval

The participation in the study was not associated with any risk, disadvantage, or stress. Patient data were anonymized. The study was approved by the LMU ethics committee (reference number 322-13) and was conducted in accordance with the Declaration of Helsinki.

Statistics

All statistical analyses were performed by SPSS, version 23.0 (released 2015; IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, USA). To compare the characteristics and attitudes of the patient

Table 1. Sociodemographic data in the late presenters and controls

	Late presenters	Controls	<i>p</i> value	Test statistics
Mean age (SD), years	66 (9.62)	65.3 (10.17)	0.824	T = 0.224
Mean number of children (SD)	1.4 (1.14)	1.35 (1.26)	0.896	T = 0.131
Educational level, <i>n</i> (%)			0.840	T = 0.206
Secondary school/lower	5 (25)	7 (35)		
Higher than secondary school	15 (75)	13 (65)		
Religion, <i>n</i> (%)			0.370	T = 0.777
No religion	3 (15)	5 (25)		
Any religion (christian/muslim)	17 (85)	15 (75)		
Relationship status, <i>n</i> (%)			0.800	T = 0.255
Single	2 (10)	0 (0)		
Married	11 (55)	9 (45)		
Divorced	1 (5)	9 (45)		
Widowed	6 (30)	2 (10)		

groups, *t* tests or nonparametric testing (Mann-Whitney U test) were used depending on whether the data were normally distributed. For statistical significance, *p* had to be <0.05. Due to the low number of patients, we also report trends detected in the analysis.

Assessments

This study was designed as a cross-sectional, observational, bi-centric study. Between August 2013 and July 2017, patients who matched the inclusion criteria were assessed with different questionnaires between initial diagnosis and surgery. Five validated questionnaires were used, and patients' sociodemographic background was assessed. In order to collect information about patients' characteristics and personalities, the questionnaires asked for positive and negative feelings, personal assumptions regarding the illness, current and habitual feelings, personality factors (openness to experience, conscientiousness, extraversion, agreeableness, neuroticism), spiritual and religious engagement, education, symptoms, relationship to doctors, and attempts to explain.

Sociodemographic Questionnaire

A questionnaire regarding sociodemographic data, such as age, place of residence, nationality, religion, family, education, other diseases, symptoms, date and reason for first medical presentation, experience with cancer, and contact to alternative medicine, was developed for this study.

Positive and Negative Affect Schedule

Negative and positive affectivity in the current trial was assessed by the Positive and Negative Affect Schedule (PANAS) on 2 scales. Twenty feelings, described by 10 adjectives for the positive and 10 adjectives for the negative affect scale, were selected by Krohne et al. [16], such as active and irritable, proud and afraid, or strong and nervous. Patients were asked for the intensity of their feelings regarding these items and should relate them to a scale between 1 (not at all) and 5 (very much). Points were given in correlation to the intensity scale. For each scale (positive or negative affect), the points were summarized in the end and varied between 10 and 50 [16, 17].

Illness Perception Questionnaire-R

The Illness Perception Questionnaire-R (IPQ-R) aims to evaluate patients' personal assumptions and suppositions regarding the illness. The patients were asked for 14 current symptoms (e.g., pain, dyspnea, nausea, and others) and if they suspected these symptoms were associated with the illness. Furthermore, the pa-

tients were asked to estimate the time to a response to the treatment and the controlling of the treatment, to estimate consequences, personal controlling, coherence, cyclic appearance, emotional representation, and causes of their illness. The estimations were scaled into 5 groups between "not at all" and "completely." For each scale (time to response, consequences, etc.), the points varied from 5 ("not at all") to maximally 15 points ("completely") [18, 19].

State-Trait Anxiety Inventory

The State-Trait Anxiety Inventory (STAI) consists of 20 questions measuring current anxiety (= "state anxiety"; e.g., nervous, relaxed and happy) and 20 questions assessing the persistent tendency to experience anxiety (= "trait anxiety"; e.g., calm, happy and secure) [20, 21]. Each scale contains positive and negative items. Patients have to choose between 4 intensities for each item. Points differ between 20 and 80; higher scores are related to greater anxiety. The method tries to differentiate between current and habitual anxiety.

NEO Five-Factor Inventory

The NEO Five-Factor Inventory (NEO-FFI), a short-version of the NEO-PI-R, consists of 60 items, which measure the personality traits openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism [22]. Twelve questions for each personality trait exist and can be scaled between 0 (e.g., no openness for experience) and 4 (e.g., strong openness to experience). The result is the mean and can vary between 0 and 4.

Spiritual and Religious Attitudes in Dealing with Illness-15

The Spiritual and Religious Attitudes in Dealing with Illness (SPREUK-15) questionnaires analyze the individual spiritual involvement. In 15 questions, the 3 scales desire for spirituality or access to spirituality, trust in a higher power, and reflection are questioned. For each item, 5 questions exist that can vary between 0 (no spiritual and religious attitudes) and 4 (strong spiritual and religious attitudes). Finally, the calculated value ranges between 0 and 100 [23, 24].

Results

Sociodemographic Data (Table 1)

A total of 20 patients each were included in the LP and in the C groups. The mean age was 65.5 years for

Table 2. Questionnaire items with differences and significances between late presenters and controls

	Late presenters, mean (SD)	Controls, mean (SD)	<i>p</i> value	Test statistics, T/Z
PANAS				
Positive affect $\alpha = 0.843^*$	37.10 (5.07)	32.00 (7.78)	0.019	T = 2.46
Negative affect $\alpha = 0.841^*$	18.05 (7.70)	19.85 (7.35)	0.314	Z = -1.03
IPQ-R $\alpha = 0.651$				
Timeline	14.80 (4.89)	12.00 (4.72)	0.038	Z = -2.08
Consequences	13.70 (4.18)	13.85 (4.85)	0.917	T = -0.11
Personal control	15.60 (2.92)	14.30 (3.98)	0.247	T = 1.18
Control by treatment	16.40 (2.92)	16.70 (1.72)	0.820	Z = -0.23
Coherence	14.20 (5.79)	16.3 (3.77)	0.182	T = -1.36
Appearance	9.60 (3.76)	9.30 (3.99)	0.808	T = 0.25
Emotion	14.65 (6.61)	17.75 (4.89)	0.100	T = -1.69
STAI $\alpha = 0.742$				
State	49.05 (17.30)	50.70 (13.26)	0.737	T = -0.34
Trait	34.55 (12.19)	37.70 (10.23)	0.174	Z = -1.37
NEO-FFI $\alpha = 0.617$				
Neuroticism	1.50 (0.99)	1.51 (0.72)	0.978	T = -0.03
Extraversion	2.16 (0.55)	2.35 (0.68)	0.431	T = -0.94
Openness to experience	2.32 (0.59)	2.39 (0.46)	0.668	T = -0.43
Agreeableness	2.85 (0.42)	2.96 (0.43)	0.353	T = -0.80
Conscientiousness	3.19 (0.43)	2.94 (0.48)	0.107	T = -1.65
SPREUK-15 $\alpha = 0.796$				
Religious/spiritual desires	29.50 (32.44)	26.75 (28.39)	0.925	Z = -0.11
Trust	50.50 (34.82)	50.00 (26.25)	0.959	T = 0.05
Reflection	53.75 (28.64)	54.56 (28.08)	0.928	T = -0.09

For interpretation of values, see Methods section. α = Cronbach's alpha. * Separate α for positive affect and negative affect due to 2 scales.

the entire sample with no statistically significant differences between the groups (LP: mean 66.0, SD 9.62 vs. C: mean 65.3, SD 10.17; $p = 0.824$) due to matching. As presented in Table 1, in the LP group, more women had different educational level regarding school graduation, and the number of women not believing in any religion was lower in this group (15 vs. 25% in C; $p = 0.370$). These differences were not statistically significant. There was also not statistically significant difference regarding number of children (LP: mean 1.4, SD 1.14 vs. C: mean 1.35, SD 1.26; $p = 0.824$) and relationship status ($p = 0.80$).

Positive and Negative Affect Schedule (Table 2)

The measured level of positive affectivity was statistically significantly higher in the LP (mean 37.10, SD 5.07 vs. C: mean 32.00, SD 7.78; $p = 0.019$). In contrast, regarding the negative affect values, both groups had a similar level of negative affectivity (LP: mean 18.05, SD 7.70 vs. C: mean 19.85, SD 7.35; $p = 0.314$).

Illness Perception Questionnaire-R (Table 2)

The values of the item "timeline" differed significantly between the LP and the C groups (LP: mean 14.80, SD

4.89 vs. C: mean 12.00, SD 4.72; $p = 0.038$). So, patients with late presentation think their illness will last for a long time or is likely to be permanent.

Regarding causes of the disease, patients with late presentation seemed to have a less accurate understanding of their illness (coherence; LP: mean 14.20, SD 5.79 vs. C: mean 16.30, SD 3.77; $p = 0.182$), even if the difference was not significant.

Negative emotional response tended to be lower in the LP (mean 14.65, SD 6.61) than in the C group (mean 17.75, SD 4.89; $p = 0.10$).

No trend was detectable regarding consequences (LP: mean 13.70, SD 4.18 vs. C: mean 13.85, SD 4.85; $p = 0.917$), personal control (LP: mean 15.60, SD 2.92 vs. C: mean 14.30, SD 3.98; $p = 0.247$), control by treatment (LP: mean 16.40 vs. C: mean 16.70; $p = 0.820$), and cyclic appearance (LP: mean 9.60 vs. C: mean 9.30; $p = 0.182$).

State-Trait Anxiety Inventory (Table 2)

Regarding the state scale, no statistically significant difference between both groups was detectable (LP: mean 49.05, SD 17.3 vs. C: mean 50.7, SD 13.26; $p = 0.737$), meaning that both groups did not differ regarding their state anxiety.

In contrast, in the trait scale, the mean of the LP (34.55, SD 12.19) was lower than the mean of the C group (37.70, SD 10.23). Although the difference was not significant ($p = 0.174$), this trend suggests that patients with late presentation show less trait anxiety.

NEO Five-Factor Inventory (Table 2)

The LP tended to show higher values regarding conscientiousness than the C group (LP: mean 3.19, SD 0.43 vs. C: mean 2.95, SD 0.48) even if the difference was not significant ($p = 0.107$).

No differences between the LP and the C groups were detectable regarding neuroticism (LP: mean 1.50, SD 0.99 vs. C: mean 1.51, SD 0.72; $p = 0.978$), extraversion (LP: mean 2.16, SD 0.55 vs. C: mean 2.35, SD 0.68; $p = 0.431$), openness to experience (LP: mean 2.32, SD 0.59 vs. C: mean 2.39, SD 0.46; $p = 0.668$), and agreeableness (LP: mean 2.85, SD 0.42 vs. C: mean 2.96, SD 0.43; $p = 0.353$).

Spiritual and Religious Attitudes in Dealing with Illness-15 (Table 2)

Comparing spiritual and religious attitudes in both groups, the absolute number of patients in the LP group searching for religious or spiritual sources was higher than in the C group, but there was no significance (LP: mean 29.5, SD 32.44 vs. C: mean 26.75, SD 29.40; $p = 0.925$). Neither this finding nor the differences in the scales “trust” (LP: mean 50.50, SD 34.82 vs. C: mean 50.00, SD 26.25; $p = 0.959$) and “reflection” (LP: mean 53.75, SD 28.64 vs. C: mean 54.56, SD 28.08; $p = 0.928$) were statistically significant.

Discussion

As late presentation with BC is associated with poor survival, many studies were performed to find personal or structural reasons for this behavior [25]. This study aimed to analyze personal characteristics and attitudes of patients with delay in presentation.

Regarding religious and spiritual attitudes, previously performed studies could not detect any significant associations with the time of first presentation for BC [26]. In our cohort, patients with late presentation tended to have more desire for spiritual and religious sources, and there were fewer patients with late presentation not believing in any religion.

More patients with late presentation assumed that their disease would last for a long time compared to the C group. In case of T4 tumors, the risk for involved lymph nodes or distant metastasis is higher, which then leads to more extensive therapy with surgery, radiation, and/or systemic therapy [27]. Due to its systemic nature, advanced breast carcinoma is often declared as a chronic

disease [28]. Even though patients who present late are aware of the chronicity of their disease, it is not clear if they would have also suspected BC to be longer lasting if they had presented earlier with a potentially good opportunity of shorter treatment and cure.

In our study, patients with late presentation had less understanding of their disease in general. Other studies showed that insufficient explanations could be a psychological reaction to save mental health, or that the attempt to explain reasons for BC is related to a lower educational level [15]. A low educational level has also been correlated with advanced T-stage [29, 30]. We could not confirm this finding, as in our study patients with delayed presentation rather had a higher educational level than the participants in the C group. Nevertheless, this difference was not significant, and we did not ask for advanced education (e.g., university degrees), so this topic may need to be further investigated.

Regarding “anxiousness” as a trait, patients with early presentation at first diagnosis showed higher levels, which may cause a higher need for safety and professional medical care. As a consequence, they may see their physician more often and participate more frequently in screening programs, which may then contribute to an earlier diagnosis in this patient group [31]. In contrast, other studies postulated that the state “anxiety” led to a late presentation, also in patients with other malignant diseases [32], but this effect was not detectable in our study. It is well known that cancer patients in general have higher levels of negative emotional response to the illness like anxiety and depression [33]. In our study, however, we could not verify a difference in negative emotional response between late and early presenters. Patients with locally advanced BC at the initial diagnosis had relatively more positive feelings and a statistically significantly higher positive affect compared to the C group, which may be related to lower trait anxiety. Nevertheless, cancer patients in general tend to have a higher probability of negative emotional states compared to the healthy population, because they are afraid of the consequences of the diagnosis [12, 13, 34].

LP showed more conscientiousness compared to BC patients presenting early. As this feature in the context of the NEO-FFI is defined as responsibility, sense of duty, self-discipline, and reliability, its assessment is often related to performance [22]. In contrast, health is not as well measurable. Additionally, in the western world, breasts are symbols of maternity and beauty [35]. Both items can be connected to self-discipline and responsibility and are better measurable by their visibility than health. So, patients may fear being perceived as unconscientious and may therefore present even later.

A limitation of this study is the small sample size. However, the study was planned as a pilot project focusing on patients with locally advanced and even exulcer-

ated BC at primary diagnosis. Given the fact that this patient group is quite rare in breast centers and is often not willing to participate in a clinical study, acquiring a higher number of patients was not considered feasible. Consequently, the statistical analysis and conclusions are more of a descriptive than a quantitative nature.

In summary, patients with locally advanced BC at initial diagnosis were found to have significantly higher positive affectivity and more frequently perceived their illness as long-lasting or permanent. Other personal characteristics, such as educational level, spirituality, explanation of the illness, trait scale, and conscientiousness, also differed numerically but not statistically between early and late presenting patients. In summary, statistically significant differences between the groups justified acceptance of the alternative hypothesis for the parameters “positive affect” and “timeline,” whereas no such differences could be shown and, thus, the null hypothesis was maintained for all other parameters under investigation. However, the findings of this pilot project warrant further investigations to identify characteristics and motives of patients with late presentation for BC. The understanding of patients’ reasons for not visiting a physician at first symptoms may help to identify the patient group that does not tend to see a physician early. Identifying this patient group might help to establish specific screening and health education programs to contact this hardly reachable patient group. By improving the awareness of this patient group and by simplifying the approach to a breast specialist, this might lead to an earlier contact if symptoms appear. If we were thereby able to provide this patient group with an earlier diagnosis in case of BC, this could help to improve their therapy and probably their outcome.

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Statement of Ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the LMU ethics committee (reference number 322-13) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study.

Conflict of Interest Statement

Thomas Kolben holds stock of Roche AG and has a relative employed at Roche AG. Theresa M. Kolben is employed at Roche AG and holds stock of Roche AG. Tom Degenhardt has received grants from Pfizer, Roche, GSM, and Daiichi Sankyo. Rachel Wuerstein has received research and travel support as well as honoraria from Roche, Celgene, AstraZeneca, MSD, Lilly, and Pfizer Oncology. Sven Mahner has received research and travel support and honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, Jenapharm, GSK, Janssen-Cilag, Medac, MSD, Pharmamar, Roche, Tesaro, and Teva. Anna Hester has received research grants from the “Walter Schulz” foundation and travel support from Roche and Pfizer Oncology. All other authors declare that they have no conflicts of interest.

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Author Contributions

Thomas Kolben designed the experiment and wrote the manuscript. Susanne Beyer analyzed and interpreted the data and wrote the manuscript. Sanaz Ghasemi performed the experiment and analyzed the data. All authors analyzed and interpreted the results and read and approved the manuscript. Anna Hester read and revised the manuscript.

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