(Ex-)breast cancer patients with (pre-existing) symptoms of anxiety and/or depression experience higher barriers to contact health care providers during the COVID-19 pandemic

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Abstract

Purpose To identify factors associated with (perceived) access to health care among (ex-)breast cancer patients during the COVID-19 pandemic.

Methods Cross-sectional study within a large prospective, multicenter cohort of (ex-)breast cancer patients, i.e., UMBRELLA. All participants enrolled in the UMBRELLA cohort between October 2013 and April 2020 were sent a COVID-19-specific survey, including the Hospital Anxiety and Depression Scale (HADS) questionnaire.

Results In total, 1051 (66.0%) participants completed the survey. During COVID-19, 284 (27.0%) participants reported clinically relevant increased levels of anxiety and/or depression, i.e., total HADS score ≥ 12. Participants with anxiety and/or depression reported statistically significant higher barriers to contact their general practitioner (47.5% vs. 25.0%, resp.) and breast cancer physicians (26.8% vs. 11.2%, resp.) compared to participants without these symptoms. In addition, a higher proportion of participants with anxiety and/or depression reported that their current treatment or (after)care was affected by COVID-19 compared to those without these symptoms (32.7% vs. 20.5%, resp.). Factors independently associated with symptoms of anxiety and/or depression during COVID-19 were pre-existent anxiety (OR 6.1, 95% CI 4.1–9.2) or depression (OR 6.0, 95% CI 3.5–10.2).

Conclusion During the COVID-19 pandemic, (ex-)breast cancer patients with symptoms of anxiety and/or depression experience higher barriers to contact health care providers. Also, they more often report that their health care was affected by COVID-19. Risk factors for anxiety and/or depression during COVID-19 are pre-existent symptoms of anxiety or depression. Extra attention—including mental health support—is needed for this group.

Keywords Breast cancer · COVID-19 · Depression · Anxiety · UMBRELLA · Patient-reported outcomes
Introduction

The COVID-19 pandemic is having a major impact on global health. During the early months of the COVID-19 pandemic in the Netherlands, a 46% decline in general practitioner consultations, and a sharp decrease in cancer diagnoses were reported [1, 2]. Increased (perceived) thresholds to health care access may negatively affect patients’ (psycho)social and physical well-being as well as their prognosis.

Symptoms of anxiety and depression among cancer patients and survivors have been reported to affect their health care behavior and health care consumption during a health threat of the magnitude of COVID-19 [3].

The aim of this study was to assess the prevalence of anxiety and depression among a large cohort of breast cancer patients and survivors during the COVID-19 pandemic. In addition, we assessed the association between the presence of symptoms of anxiety and/or depression and COVID-19-specific concerns, including health care behavior and consumption.

Materials and methods

The present study was conducted within the prospective observational multicenter ‘Utrecht cohort for Multiple BREast cancer intervention studies and Long-term evaluation’ (UMBRELLA), including patients with histologically proven invasive breast cancer or ductal carcinoma in situ (DCIS) referred from regional and tertiary referral hospitals to the University Medical Center Utrecht (UMCU) for adjuvant radiation therapy [4, 5]. All participants completed self-reported UMBRELLA questionnaires, including the Hospital Anxiety and Depression Scale (HADS), at regular time intervals during and after their breast cancer treatment.

All active participants, who enrolled in the UMBRELLA cohort between October 2013 and April 2020 and consented to receiving online questionnaires, were sent a survey (April 7, 2020), including the HADS and COVID-19-related questions [6, 7]. Ethical approval was obtained from the Medical Ethics Committee of the UMCU (NL52651.041.15, METC 15/165). The UMBRELLA study is registered on clinicaltrials.gov (NCT02839863).

HADS is a 14-item questionnaire using a 4-point Likert scale. Scores ≥ 12 on the total HADS, and scores ≥ 8 on the 7-item anxiety and depression subscales indicated increased risk of depression or anxiety disorder [8].

Demographic and clinical data, including age, highest educational level, type of surgery, most invasive axillary treatment, (neo-)adjuvant systemic treatment, radiotherapy, and pathological T and N stage (AJCC 7th edition), were collected in the context of UMBRELLA and provided by the Netherlands Cancer Registry (NKR) [9].

Frequencies, proportions, means with standard deviation, or medians with interquartile ranges were used to describe patient demographics, treatment characteristics and HADS scores. A Chi-square test was performed to compare differences in proportions of patients scoring above the clinically relevant HADS threshold scores before and during COVID-19 [10]. Univariable and multivariable logistic regression analyses were used to evaluate to what extent relevant clinical demographic, tumor- and treatment characteristics affected clinically relevant symptoms of anxiety and/or depression during COVID-19. Two-sided \( p \) values < 0.05 were considered statistically significant. Statistical analyses were performed with IBM Statistical Package for Social Sciences (SPSS) software, version 25 (IBM Corp, Armonk, NY).

Results

Of the 3239 participants enrolled in the UMBRELLA cohort between October 2013 and April 2020, 1595 participants met the inclusion criteria. Of those, 1051 (66.0%) participants completed the COVID-19-specific questionnaire, of which 4.9% \( (n = 51) \) were under active treatment for their breast cancer.

Prevalence and risk factors for anxiety and/or depression during COVID-19

Overall, 284 (27.0%) participants experienced clinically relevant symptoms of anxiety and/or depression during COVID-19 (Table 1). Of all participants who experienced symptoms of anxiety and/or depression during COVID-19,
| Table 1 Baseline characteristics of participants with or without a clinically relevant increase in total HADS score (≥ 12), i.e., symptoms of anxiety and/or depression, as measured by the HADS questionnaire during the COVID-19 pandemic (n = 1051) |
|-----------------------------------------------|
| **Patient characteristics**                  |
| Baseline characteristics                      |
| Age in years at inclusion, mean (SD)          | Participants with a total HADS score < 12a (n = 767) | Participants with a total HADS score ≥ 12a (n = 284) | p value |
| Female                                        | 57 9.6 | 55 10.1 | 0.003 |
| Male                                          | 6 0.8 | 0 0.0 | 0.135 |
| Sex, No. (%)                                  | 0.135 |
| Highest educational level                     | 0.185 |
| Primary or (post-)secondary school            | 326 42.5 | 133 46.8 | 0.698 |
| College or university                         | 434 56.6 | 147 51.8 | 0.005 |
| Unknown                                       | 7 0.9 | 4 1.4 | 0.008 |
| Time since diagnosis (months), median (IQR)   | 24 6-42 | 24 6-42 | <0.001 |
| Unknown, No. (%)                              | 0.83 |
| **Tumor characteristics**                    |
| Pathological T stadium                        | 0.112 |
| In situ (IS), 0, I or II                      | 698 91.0 | 256 90.1 | 0.698 |
| III or IV                                     | 15 2.0 | 8 2.8 | 0.005 |
| X or unknown                                  | 54 7.0 | 20 7.0 | 0.003 |
| Pathological N stadium                        | 0.509 |
| 0                                             | 461 60.1 | 145 51.1 | 0.112 |
| I, II or III                                  | 198 25.8 | 102 35.9 | 0.008 |
| X or unknown                                  | 108 14.1 | 37 13.0 | 0.003 |
| **Treatment characteristics**                |
| Type of breast surgery                        | 0.008 |
| Breast conserving therapy                     | 596 77.7 | 217 76.4 | 0.008 |
| Mastectomy                                    | 70 9.1 | 24 8.5 | 0.008 |
| Mastectomy with direct breast reconstruction   | 65 8.5 | 28 9.9 | 0.008 |
| No breast surgery                             | 0 0.0 | 2 0.7 | 0.008 |
| Unknown                                       | 36 4.7 | 13 4.6 | 0.008 |
| Most invasive axillary treatment              | 0.509 |
| Sentinel node procedure                       | 572 74.6 | 212 74.6 | 0.509 |
| Axillary lymph node dissectionb               | 56 7.3 | 26 9.2 | 0.008 |
| Unknown or not performed                      | 139 18.1 | 46 16.2 | 0.008 |
| Systemic therapyd                             | 0.003 |
| No systemic therapy                           | 168 21.9 | 38 13.4 | 0.003 |
| Chemotherapyd                                 | 261 34.0 | 117 41.2 | 0.003 |
| Endocrine therapy or immunotherapy            | 102 13.3 | 45 15.8 | 0.003 |
| Unknown                                       | 236 30.8 | 84 29.6 | 0.003 |
| Radiation therapy                             | 0.779 |
| Local                                         | 515 67.1 | 163 57.4 | 0.779 |
| Locoregionalc                                 | 158 20.6 | 86 30.3 | 0.003 |
| No radiation therapy or type unknown          | 94 12.3 | 35 12.3 | 0.003 |
| Currently receiving active breast cancer treatmentf | 0.779 |
| Yes                                           | 37 4.8 | 14 4.9 | 0.779 |
| No                                            | 723 94.3 | 266 93.7 | 0.779 |
| Other                                         | 7 0.9 | 4 1.4 | 0.779 |
| **Hospital Anxiety and Depression Scale**     |
| Total HADS score before COVID-19a             | 0.779 |
| Above threshold                               | 64 9.3 | 156 62.7 | 0.003 |
| Below threshold                               | 627 90.7 | 93 37.3 | 0.003 |
62.7% (n = 156) already experienced these symptoms pre-COVID-19. A total of 18.2% (n = 191) of all participants reported symptoms of anxiety and 16.0% (n = 168) symptoms of depression during the pandemic. The proportion of participants experiencing symptoms of anxiety and/or depression was slightly, but significantly lower before the pandemic (23.4%, n = 220).

Lower age, higher pathological N stage, receipt of systemic therapy or radiotherapy and pre-existent symptoms of anxiety or depression were significantly associated with anxiety and/or depression during COVID-19 (Table 1). In multivariable analysis, only pre-existent symptoms of anxiety or depression were independently and significantly associated with symptoms of anxiety and/or depression during COVID-19 (OR 6.1, 95% CI 4.1–9.2 and OR 6.0, 95% CI 3.5–10.2, resp., Table 2).

**COVID-19-specific concerns and health care consumption**

Significantly more participants with anxiety and/or depression experienced higher barriers to contact their general practitioner (47.5% vs. 25.0%, resp.) and breast cancer physicians (26.8% vs. 11.2%, resp.) compared to patients without these symptoms (Table 3). In addition, a higher proportion of participants with anxiety and/or depression reported that their current treatment or (after)care was affected by COVID-19 compared to those without these symptoms (32.7% vs. 20.5%, resp.).

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**Table 1** (continued)

| Participants with a total HADS score < 12<sup>a</sup> (n = 767) | Participants with a total HADS score ≥ 12<sup>a</sup> (n = 284) | p value |
|---|---|---|
| **HADS anxiety score before COVID-19<sup>a</sup><sub>g</sub>** | | <0.001 |
| Above threshold | 57 | 124 | 49.8 |
| Below threshold | 634 | 91.8 | 125 | 50.2 |
| **HADS depression score before COVID-19<sup>a</sup><sub>g</sub>** | | <0.001 |
| Above threshold | 26 | 3.8 | 89 | 35.7 |
| Below threshold | 665 | 96.2 | 160 | 64.3 |

As a result of rounding, percentages may not total to 100%

*<sup>i</sup>Q<sub>r</sub> interquartile range, *<sub>n</sub> number, SD standard deviation, HADS Hospital Anxiety and Depression Score

<sup>a</sup>A clinically relevant total HADS score ≥ 12 (above threshold) indicates a probable depression and/or anxiety disorder

<sup>b</sup>Axillary lymph node dissection (in combination with sentinel node procedure)

<sup>c</sup>Pre- and/or postoperative therapy

<sup>d</sup>Chemotherapy (in combination with other systemic therapy, i.e., immunotherapy, endocrine therapy)

<sup>e</sup>Including supraclavicular and/or axillary lymph nodes

<sup>f</sup>Active treatment includes chemotherapy and/or radiation therapy

<sup>g</sup>Only patients with known HADS scores as obtained in UMBRELLA within 2 years before the first official COVID-19 diagnosis in the Netherlands (February 27, 2020) were included for comparative analyses with HADS scores from the COVID-19-specific questionnaire (n = 940)

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**Table 2** Multivariable logistic regression analysis of risk factors for clinically relevant increase in symptoms of anxiety and/or depression, i.e., total HADS score above threshold (≥ 12), during the COVID-19 pandemic (n = 940)

| Variables | OR 95% CI |
|---|---|
| Age | 0.99 0.97–1.01 |
| Pathological N stadium | Ref. |
| 0 | Ref. |
| I, II or III | 1.12 0.67–1.85 |
| X or unknown | 1.36 0.75–2.45 |
| Systemic therapy<sup>a</sup> | Ref. |
| No systemic therapy | | |
| Chemotherapy<sup>b</sup> | 1.48 0.85–2.55 |
| Endocrine therapy or immunotherapy | 1.55 0.83–2.88 |
| Unknown | 1.41 0.81–2.44 |
| Radiation therapy | Ref. |
| Local | | |
| Locoregional<sup>c</sup> | 1.49 0.89–2.51 |
| No radiation therapy or type unknown | 0.83 0.45–1.55 |
| HADS anxiety score before COVID-19<sup>a</sup> | Ref. |
| Below threshold | 6.12 4.05–9.24 |
| Above threshold | | |
| HADS depression score before COVID-19<sup>a</sup> | Ref. |
| Below threshold | 5.95 3.48–10.18 |
| Above threshold | | |

<sup>a</sup>Pre- and/or postoperative therapy

<sup>b</sup>Chemotherapy (in combination with other systemic therapy, i.e., immunotherapy, endocrine therapy)

<sup>c</sup>Including supraclavicular and/or axillary lymph nodes
Discussion

During the COVID-19 pandemic, 27.0% of the (ex-)breast cancer patients reported clinically relevant symptoms of anxiety and/or depression. (Ex-)breast cancer patients with anxiety and/or depression reported to experience higher thresholds to contact their health care providers. Factors independently associated with anxiety and/or depression during COVID-19 were pre-existent symptoms of anxiety or depression.

In the early months of the COVID-19 pandemic, a sharp decrease in cancer diagnoses and a 46% decline in general practitioner consultations were observed in the Netherlands [1, 2]. In this study, participants with anxiety and/or depression reported higher barriers to contact their health care providers during COVID-19 compared to those without these symptoms. The COVID-19 pandemic might have increased the perceived burden on patients with symptoms of anxiety and/or depression. High levels of anxiety and perceived threat have been shown to be related to increased avoidance behavior [11]. Anxiety for a COVID-19 infection, a higher level of moral concerns about wasting the physicians’ time for non-COVID-19-related symptoms, and assumptions about scarcity in the capacity of health care services for non-COVID-19-related care might also explain these barriers in seeking health care among patients with symptoms of anxiety and/or depression [1]. These results suggest that, in case of subsequent waves or a future pandemic, (ex-)breast cancer patients experiencing anxiety and/or depression are especially at risk for reduced health care consumption and may need extra encouragement to contact their health care providers, when necessary.

The proportion of participants experiencing anxiety and/or depression increased only slightly during COVID-19 (27.0%), when compared to pre-COVID-19 (23.4%). However, there was a considerable shift: quite some patients with pre-existing symptoms of anxiety and/or depression no longer experienced clinically relevant levels of anxiety.
and/or depression during COVID-19 and vice versa. The participants’ perception of the COVID-19 pandemic and different coping mechanisms might play a role in this shift [11]. Higher tolerance for uncertainty is related to better coping strategies and lower threat appraisal. For example, patients who tolerated uncertainty better, experienced lower levels of anxiety during the H1N1 pandemic in 2009 and showed higher levels of problem-focused coping [11]. However, further studies are needed to better understand these coping mechanisms in the context of a major health threat, and their effect on health care consumption.

Our findings that 18.2% of all participants reported symptoms of anxiety and 16.0% symptoms of depression, are in line with outcomes previously reported among UMBRELLA participants with early invasive breast cancer or DCIS prior to COVID-19 at 24 months after diagnosis (anxiety 12.5–17.1%, depression 6.0–16.1%) [12]. Moreover, the observed proportion of (ex-)breast cancer patients with anxiety and/or depression during COVID-19 seemed even lower when compared to the general population. A recent meta-analysis assessing anxiety and depression among a general population in Europe during COVID-19 observed that 32.4% (n = 8,341) experienced symptoms of anxiety and 23.8% (n = 8,341) symptoms of depression [13].

Although previous research showed that mental health can be impaired in the context of a major health threat, there are still insufficient clinical (screening) tools that can help identify those at risk [14]. Pre-existent anxiety and/or depression was reported by 62.7% (n = 156) of the participants with anxiety and/or depression during COVID-19. Similarly, a recent global study among non-cancer patients with pre-existent anxiety or depression (n = 2,734) reported worsening of psychological well-being in at least 50.0% during COVID-19 [15].

With the aim of providing adequate (mental) health support in the context of a health threat of this magnitude, surveillance and clear documentation of symptoms of anxiety and/or depression prior to and during major health threats seem a valuable tool to identify those at risk for reduced health care consumption. Especially in times of lockdown and social distancing, integration of e-mental health applications and digital psychological interventions is important to improve supportive care for those at risk. Last, raising public awareness about the importance of encouraging these particularly vulnerable individuals to contact their health care professionals, when necessary, is warranted.

Conclusion

Reduced health care consumption, and increased thresholds to contact health care professionals following the COVID-19 pandemic are reasons for concern. We found that (ex-)breast cancer patients with symptoms of anxiety and/or depression experienced higher barriers in seeking health care. Patients with pre-existent symptoms of anxiety or depression were particularly at risk for (worsening of) anxiety and/or depression during the pandemic.

Author contributions The corresponding author (HMV) confirms that she had full access to all the data in the study and had final responsibility for the decision to submit for publication. All listed authors did not receive any writing assistance and have approved the manuscript before submission. Each author has contributed significantly to, and is willing to take public responsibility for, the following aspects of the study. Design DRMM, CAB, MCTB, RG, LES, WM, NV, IED, FL, EJPS, MFE, IOB, TD, RB, DAYA, AD, HMV. Data acquisition DRMM, CAB, MCTB, LES, AD, HMV. Analyzes DRMM, CAB, RG, MCTB, DAYA, HMV. Interpretation DRMM, CAB, RG, MCTB, DAYA, HMV. Drafting DRMM, CAB, MCTB, RG, LES, WM, NV, IED, F. van der Leij, EJPS, MFE, IOB, TD, RB, DAYA, AD, HMV.

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Data availability Raw data were generated at the University Medical Center Utrecht. Derived data supporting the findings of this study are available from the corresponding author Prof Dr HM Verkooijen upon reasonable request.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

Ethical approval This study was in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate Informed consent from all individual participants was obtained within the UMBRELLA cohort.

Consent to publish Informed consent from all individual participants was obtained within the UMBRELLA cohort.

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