

## THE FIRST WAVE OF THE COVID-19 PANDEMIC AND ITS IMPACT ON THE LEVEL OF DISTRESS IN PATIENTS WITH BREAST CANCER, A MULTICENTRIC STUDY

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### SUMMARY

**Background:** Information on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), later termed coronavirus disease (COVID-19), first emerged by the end of 2019. As the pandemic spread, cancer patients were immediately recognized as a high-risk population with regard to COVID-19 infection. Moreover, epidemiological measures, like social distancing and lockdowns, additionally burdened patients with cancer. Even outside pandemic breast cancer patients are prone to psychological distress with prevalence ranging approximately 20-40%. This multicentric study aimed to examine the impact of COVID-19 pandemic on the level of distress among breast cancer patients in Croatia while the first wave of COVID-19 pandemic.

**Subjects and methods:** Five hundred forty-five breast cancer patients were offered to participate in the study. A total of two hundred and one patient, with disease stages ranging I-IV, completed the questionnaire. The questionnaire consisted of disease and socio-demographic characteristics followed by the Distress Thermometer and a problem list. The cut off value of 4 was used to define the high level of distress within Distress Thermometer.

**Results:** High distress level was reported in 54.2% of patients. The most significant problems reported by the participants of our study affected emotions, causing worry, sadness, depression, fear, and nervousness. Additionally, specific practical problems emerged (e.g., child care, housing, and work/school), most probably partly due to the lockdowns and social distancing. Interestingly enough, none of the socio-demographic or disease characteristics were linked to the level of distress.

**Conclusions:** During first wave of COVID-19 pandemic more than half of breast cancer patients, undergoing active oncologic treatment, experienced a high level of distress. Therefore, distress driven by the COVID-19 pandemic should be promptly addressed and additional psychological and social support, targeting specific practical and emotional problems, should be provided for those patients. All the more so as global COVID-19 pandemic far exceeded the duration of the first wave.

**Key words:** breast cancer - COVID-19 pandemic - psychological distress - distress thermometer - chemotherapy

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### INTRODUCTION

Information on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), later termed coronavirus disease (COVID-19), first emerged by the end of 2019. At that time, very few could imagine the influence it would have on multiple aspects of human life, not only affecting physical health but having a great impact on mental health as well (Jakovljevic et al. 2020). The World Health Organization declared a pandemic on March 11, 2020 (World Health Organization 2020). The first COVID-19-positive patient in Croatia was registered on February 25, 2020, which marked the beginning of the COVID-19 epidemic in this country.

Within 2 weeks, the Croatian authorities imposed strict social distancing and lockdown as main epidemiological measures aiming to control the rapid transmission of the virus (Croatian Institute for Public Health 2020). The measures imposed a great burden to patients with cancer, particularly those in need of help with daily activities and those living alone. Public transport outage notably limited the patients' ability to attend regular check-ups and prescheduled treatments at hospitals or outpatient clinics. Meanwhile, information on the nature of COVID-19 confirmed that serious complications are more likely to develop in older individuals or patients with underlying health conditions (Lipsitch et al. 2020, Guan et al. 2019, European Society for Medical Onco-

logy 2020, Dai et al. 2020, Lee et al. 2020, Miyashita et al. 2020). The first scientific article regarding COVID-19 and patients with cancer, published on February 14, 2020, concluded that those patients have a significantly higher risk of developing severe events following COVID-19 infection (Liang et al. 2020).

Psychological distress is common in patients with cancer (Menhert et al. 2018, Carlson et al. 2019). The concept of distress is defined by the National Comprehensive Cancer Network (NCCN) as a “multifactorial unpleasant experience of a psychological (i.e., cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with one’s ability to cope effectively with cancer, its physical symptoms, and its treatment” (National Comprehensive Cancer Network 2020). Unmanaged distress has been shown to negatively affect the quality of life, as well as all-cause and cancer-related mortality (Adler & Page 2008). Distress in patients with cancer is caused by the physical aftermath of the disease, and is also linked to non-somatic distress (Kaiser et al. 2010). The prevalence of psychological distress in patients with cancer ranges 30–52% (Mehnert et al. 2018, Carlson et al. 2019, Herschbach et al. 2004, Hewit et al. 2004, Ng et al. 2017, Mergenthaler et al. 2011). Individuals diagnosed with types of cancer associated with poorer prognosis (e.g., lung cancer, pancreatic cancer) tend to have higher levels of distress (Hewit et al. 2004). Estimates of the prevalence of distress in patients with breast cancer vary depending on the definition and measurement of distress (Hewit et al. 2004). The level of distress among patients with breast cancer ranges approximately 20-40%, with the variation mostly attributed to differences in study populations and assessment tools (Mehnert et al. 2018, Carlson et al. 2019, Hewit et al. 2004). Well-established predictors of distress in patients with breast cancer are age (younger patients), type of treatment (chemotherapy versus other types of treatment), partnership (living alone), and lower income (Mehnert et al. 2018, Kaiser et al. 2010, Hewit et al. 2004, Syrowatka et al. 2017).

COVID-19 pandemic has induced many psychiatric individual problems such as panic, anxiety, depression, post-traumatic stress disorders, ect (Jakovljevic et al. 2020). Recently published studies regarding the psychological impact of the COVID-19 outbreak on the general population in China showed that 35–54% of the respondents experienced distress, while 5–8% were highly distressed (Qiu et al. 2020, Wang et al. 2020). Similarly, a study in Italy found that approximately 13% of the respondents had an extremely high level of stress during the COVID-19 pandemic (Mazza et al. 2020). Addressing and recognizing more vulnerable population prone for developing distress, makes it possible to plan and

create meaningful and effective mental health interventions (Marcinko et al. 2020).

The COVID-19 outbreak led to new circumstances, in which patients with cancer have to deal with the distress of having cancer, as well as that caused by the consequences of the COVID-19 pandemic on their disease trajectory and pathway. The aim of this study was to evaluate the impact of the COVID-19 outbreak on the level of distress among patients with breast cancer. The primary endpoint was to determine the level of distress in patients with breast cancer during the COVID-19 pandemic. Secondary endpoints were to investigate whether socio-demographic and disease characteristics are predictive factors of distress. Furthermore, we also aimed to address typical problems indicative of distress.

## SUBJECTS AND METHODS

### Patients

This academic, multicentric, cross-sectional, and observational study was designed by the Council of Institutions, which is a part of the Croatian Society for Medical Oncology, a collaborative society of the European Society for Medical Oncology. The Council consists of representatives from hospitals that provide medical oncology services throughout Croatia. This study, evaluating distress, is part of a larger research project focusing on different aspects of the influence of the COVID-19 pandemic on cancer patients in Croatia.

Participants were female patients with breast cancer, aged >18 years, who received systemic oncological treatment (adjuvant, neoadjuvant, and metastatic setting) during the COVID-19 outbreak. The study was conducted from April 20, 2020 to May 24, 2020, while all extreme epidemiological measures (lockdown and strict social distancing) were ongoing and equally applied to all regions in Croatia. Eight oncology centers participated in this study: two university hospitals (University Hospital Centre Zagreb and University Hospital Centre Osijek) and six general hospitals (General Hospital Dubrovnik, General Hospital Koprivnica, General Hospital Pula, General Hospital Slavonski Brod, General Hospital Varaždin, and General Hospital Zadar) covering approximately 50% of the Croatian population.

### Data acquisition

The data were obtained from the participants by completing an anonymous self-reporting questionnaire with the following information: 1) socio-demographic characteristics: age, partnership status (single versus in partnership), educational degree (elementary, secondary, university/postgraduate), and household income level

(low, medium, high); and 2) disease characteristics: disease stage (early versus advanced breast cancer), type of treatment (chemotherapy versus other types of treatment), duration of disease (<6 months, 6–12 months, >12 months), distance from the hospital facility where the patient was treated (<50 km, 50–100 km, >100 km), and type of facility where the patient was treated (university versus general hospital). Participants completed surveys while waiting in the clinic or during therapy infusion. The study was approved by the Institutional Ethic Committee Boards (reference number for the ethical approval: 02/1-91/97-2020). All patients provided written informed consent. A total of 545 patients with breast cancer were approached to participate in the study. Approximately 60% of those refused to take part in the study mostly because they were not interested, did not have time, or did not return the questionnaire. Finally, the questionnaire was completed by 216 participants; of those, 15 questionnaires were incomplete.

### Survey instrument

Distress level was measured with the Distress Thermometer, a visual analog scale from 0 to 10 (score 0: “no distress at all”; 10: “extreme distress”). The Distress Thermometer is a well-established instrument used to identify levels of distress from any source, even if not caused by cancer (National Comprehensive Cancer Network 2020). The Distress Thermometer has been validated in various international studies (Mergenthaler et al. 2011), and has been established for patients with different types of cancer and different situations and cultures (Ma et al. 2014, Donovan et al. 2014, Van Hoose et al. 2015). Across different indications and cultural backgrounds, these studies reported different cut-off scores (between >3 and >6), which varied depending on the language, country, clinical settings, and sample characteristics (Mergenthaler et al. 2011, Donovan et al. 2014). In the majority of studies, a score of 4 maximized sensitivity and specificity relative to an established criterion (Donovan et al. 2014). Since this was the first time the Distress Thermometer was used to determine the level of distress among patients with breast cancer in Croatia, we opted for the cut off value of 4 as proposed in the NCCN guidelines (National Comprehensive Cancer Network 2020). The distress scale was followed by a problem list including 39 common problem areas divided into five subgroups: practical, family, emotional, spiritual, and physical.

### Statistical methods

Descriptive analyses were performed to describe the data. All categorical variables were presented as frequen-

cies and percentages. The measurement of the distress level was included in the analyses as a categorical variable of low (0–3) or high (4–10) distress, based on the cut-off value.

Bivariate analyses, specifically chi-squared tests for categorical data, were used to assess the relationships between the level of distress in patients, problems they were experiencing, and sociodemographic and baseline clinical characteristics. The chi-squared test was also used to study the relationship between endorsed problems from the problem list and sociodemographic and baseline clinical characteristics. During the post-hoc analysis, Bonferroni’s correction was used to control for Type I error. All statistical analyses were performed using the SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA) software, and statistical tests were two-sided with a 5% significance level, unless noted otherwise.

**Table 1.** Demographic and baseline clinical characteristics of patients

Characteristic	Number of patients (N=201)
Age	
<40 years	37 (18.4)
41–60 years	100 (49.8)
>60 years	64 (31.8)
Partnership status	
In partnership	142 (70.6)
Single	59 (29.4)
Educational degree	
Elementary	22 (10.9)
Secondary	114 (56.7)
University and postgraduate	65 (32.3)
Household income	
Low	75 (37.3)
Medium	79 (39.3)
High	47 (23.4)
Disease stage	
Early breast cancer	132 (65.7)
Advanced breast cancer	69 (34.3)
Type of treatment	
Chemotherapy	95 (47.3)
Other therapies	106 (52.7)
Duration of disease	
<6 months	64 (31.8)
6–12 months	43 (21.4)
>12 months	94 (46.8)
Hospital	
University hospital	71 (35.3)
General hospital	130 (64.7)
Distance to the hospital	
<50 km	171 (85.1)
50–100 km	13 (6.5)
>100 km	17 (8.5)

Data are presented as N (%), unless noted otherwise

**Table 2.** Description of the Distress Thermometer (N=201) through which the patients were divided based on their level of distress n = n = 92 (45.8%) n = 109 (54.2%)

Problem list	Distress 0-3 (N=92 (45.8%)) n (%)	Distress 4-10 (N=109 (54.2%)) n (%)	p-value
<b>Practical problem</b>			
Child care	21 (10.4)	42 (20.9)	0.017*
Housing	20 (10.0)	42 (20.9)	0.010*
Insurance/financial	19 (9.5)	34 (16.9)	0.091
Transportation	14 (7.0)	25 (12.4)	0.168
Work/school	5 (2.5)	23 (11.4)	0.001**
Treatment decisions	6 (3.0)	18 (9.0)	0.094
<b>Family problem</b>			
Dealing with children	9 (4.5)	17 (8.5)	0.221
Dealing with partner	2 (1.0)	8 (4.0)	0.093
Ability to have children	2 (1.0)	3 (1.5)	0.793
Family health issue	20 (10.0)	39 (19.4)	0.055
<b>Emotional problem</b>			
Depression	2 (1.0)	15 (7.5)	0.003**
Fear	8 (4.0)	50 (24.9)	0.000**
Nervousness	12 (6.0)	52 (25.9)	0.000**
Sadness	12 (6.0)	33 (16.4)	0.004**
Worry	34 (16.9)	82 (40.8)	0.000**
Loss of interest in usual activities	5 (2.5)	25 (12.4)	0.001**
<b>Spiritual/religious concern</b>	3 (1.5)	11 (5.5)	0.058
<b>Physical problem</b>			
Appearance	3 (1.5)	16 (8.0)	0.006**
Bathing/dressing	2 (1.0)	3 (1.5)	0.793
Breathing	2 (1.0)	7 (3.5)	0.147
Change in urination	4 (2.0)	12 (6.0)	0.082
Constipation	7 (3.5)	10 (5.0)	0.691
Diarrhea	5 (2.5)	17 (8.5)	0.022*
Eating	3 (1.5)	18 (9.0)	0.002**
Fatigue	15 (7.5)	56 (27.9)	0.000**
Feeling swollen	9 (4.5)	22 (10.9)	0.042*
Fever	1 (0.5)	1 (0.5)	0.904
Getting around	11 (5.5)	44 (21.9)	0.000**
Indigestion	5 (2.5)	17 (8.5)	0.022*
Memory/concentration	9 (4.5)	33 (16.4)	0.000**
Mouth sore	4 (2.0)	14 (7.0)	0.036*
Nausea	6 (3.0)	16 (8.0)	0.065
Dry/congested nose	16 (8.0)	21 (10.4)	0.733
Pain	2 (1.0)	20 (11.9)	0.000**
Sexual	1 (0.5)	5 (2.5)	0.146
Skin dry/itchy	16 (8.0)	38 (18.9)	0.005**
Sleep	19 (9.5)	48 (23.9)	0.000**
Tingling in hands and feet	12 (6.0)	37 (18.4)	0.001**

Data are presented as N (%), unless noted otherwise. \* a two-sided p<0.05 denoted statistically significant difference;

\*\* a two-sided p<0.01 denoted statistically significant difference

## RESULTS

### Demographic and clinical characteristics

A total of 201 reports were analyzed (N=201). The patient characteristics are listed in Table 1. The median age of the patients was 53.12 years (range: 25-80 years). Approximately half of the female patients were aged between 41 and 60 years (n=100; 49.8%). The majority

were in partnership (n=142, 70.6%) and more than half had secondary education (n=114, 56.7%). Regarding the household income, there were 79 patients with medium income (39.3%), while low and high income was reported in 75 (37.3%) and 47 (23.4%) patients, respectively.

Approximately two-thirds of patients had early breast cancer (n=132, 65.7%) while the rest had advanced breast cancer (n=69, 34.3%). Chemotherapy was the

current treatment for almost half of the patients (n=95, 47.3%). Roughly, half of the patients reported a duration of disease >12 months (n=94, 46.8%).

The majority of the patients were treated at general hospitals (n=130, 64.7%), while the rest were treated at university hospitals (n=71, 35.3%). Distance to the hospital was <50 km, 50–100 km, and >100 km for 171 (85.1%), 13 (6.5%), and 17 (8.5%) patients, respectively.

### Distress levels and problem list

The results of the measurement of distress levels and problem list are provided in Table 2. A total of 92 (45.8%) and 109 (54.2%) patients reported a low and high level of distress, respectively.

Regarding the problem list, as shown in Table 2, practical problems (e.g., child care, housing, and work/school) were significantly correlated with a high level of distress ( $\chi^2(1)=5.719$ ,  $p<0.05$ ;  $\chi^2(1)=6.594$ ,  $p<0.05$ ;  $\chi^2(1)=10.212$ ,  $p<0.01$ , respectively). Interestingly, all the emotional problems listed (depression:  $\chi^2(1)=8.652$ ,  $p<0.01$ ; fear:  $\chi^2(1)=33.587$ ,  $p<0.01$ ; nervousness:  $\chi^2(1)=27.621$ ,  $p<0.01$ ; sadness:  $\chi^2(1)=8.526$ ,  $p<0.01$ ; worry:  $\chi^2(1)=29.944$ ,  $p<0.01$ ; and loss of interest for usual activities:  $\chi^2(1)=12.034$ ,  $p<0.01$ ) corresponded to

the level of distress. Family problems and spiritual concerns were not related to the level of distress. Taking into account physical problems, although those symptoms are more related to disease and treatments, two problems (sleep and getting around) were related to distress levels ( $\chi^2(1)=12.277$ ,  $p<0.01$  and  $\chi^2(1)=20.261$ ,  $p<0.01$ , respectively).

Results of the bivariate analysis of the risk factors linked to high distress levels are listed in Table 3. Socio-demographic characteristics, such as age, partnership status, educational degree, and household income level, were not linked to the level of distress. Moreover, disease characteristics, such as disease stage, type of treatment, duration of disease, distance from the hospital facility where the patient was treated, and type of facility where the patient was treated, did not correlate with the level of distress.

The most commonly marked problems from the problem list are shown in Table 4. More than half of the participants reported worry (57.7%), followed by fatigue, sleep, nervousness, and child care (35.3%, 33.3%, 31.8%, and 31.3% respectively). In the high-level distress group, worry, fatigue, and nervousness were the most commonly reported problems, while every fourth patient in that group felt fear.

**Table 3.** Bivariate analysis of the risk factors linked to high degree of distress (N=201)

Variables	Distress 0-3 (N=92 (45.8%)) n (%)	Distress 4-10 (N=109 (54.2%)) n (%)	p-value
Age			
Single	28 (13.9)	31 (15.4)	
Educational degree			0.086
Elementary	13 (6.5)	9 (4.5)	
Secondary	56 (27.9)	58 (28.9)	
University and postgraduate	23 (11.4)	42 (20.9)	
Household income			0.723
Low	37 (18.4)	38 (18.9)	
Medium	35 (17.4)	44 (21.9)	
High	20 (10.0)	27 (13.4)	
Tumor stage			0.672
Early breast cancer	59 (29.4)	73 (36.3)	
Advanced breast cancer	33 (16.4)	36 (17.9)	
Types of treatment			0.667
Chemotherapy	45 (22.4)	50 (24.9)	
Other therapies	47 (23.4)	59 (29.4)	
Duration of disease			0.258
<6 months	34 (16.9)	30 (14.9)	
6–12 months	16 (8.0)	27 (13.4)	
>12 months	42 (20.9)	52 (25.9)	
Hospital			0.183
University hospital	64 (31.8)	66 (32.8)	
General hospital	28 (13.9)	43 (21.4)	
Distance to the hospital			0.240
<50 km	76 (37.8)	95 (47.3)	
50–100 km	5 (2.5)	8 (4.0)	
>100 km	11 (5.5)	6 (3.0)	

**Table 4.** Number and percentage of all patients (N=201) and those with high level of distress (N=109) for problem variables

Problem	Overall patients n (%)	High level distress patients n (%)
Worry	116 (57.7)	82 (40.8)
Fatigue	71 (35.3)	56 (27.9)
Sleep	67 (33.3)	48 (23.9)
Nervousness	64 (31.8)	52 (25.9)
Child care	63 (31.3)	42 (20.9)
Housing	62 (30.8)	42 (20.9)
Family health issue	59 (29.4)	39 (19.4)
Fear	58 (28.9)	50 (24.9)
Getting around	55 (27.4)	44 (21.9)
Dry/itchy skin	54 (26.9)	38 (18.9)
Insurance/financial	53 (26.4)	34 (16.9)
Tingling in hands and feet	49 (24.4)	37 (18.4)
Sadness	45 (22.4)	33 (16.4)
Memory/concentration	42 (20.9)	33 (16.4)
Transportation	39 (19.4)	25 (12.4)
Dry/congested nose	37 (18.4)	21 (10.4)
Feeling swollen	31 (15.4)	22 (10.9)
Loss of interest in usual activities	30 (14.9)	25 (12.4)
Work/school	28 (13.9)	23 (11.4)
Dealing with children	26 (12.9)	17 (8.5)
Treatment decision	24 (11.9)	18 (9.0)
Diarrhea	22 (10.9)	17 (8.5)
Indigestion	22 (10.9)	17 (8.5)
Nausea	22 (10.9)	16 (8.0)
Pain	22 (10.9)	20 (9.9)
Eating	21 (10.4)	18 (9.0)
Appearance	19 (9.5)	16 (8.0)
Mouth sore	18 (9.0)	14 (7.0)
Depression	17 (8.5)	15 (7.5)
Constipation	17 (8.5)	10 (5.0)
Change in urination	16 (8.0)	12 (6.0)
Spiritual/religious concern	14 (7.0)	11 (5.5)
Dealing with partner	10 (5.0)	8 (4.0)
Breathing	9 (4.5)	7 (3.5)
Sexual	6 (3.0)	5 (2.5)
Ability to have children	5 (2.5)	3 (1.5)
Bathing/dressing	5 (2.5)	3 (1.5)
Fever	2 (1.0)	1 (0.5)

Data are presented as N (%), unless noted otherwise

Furthermore, we analyzed the relationship between some of the problems in problem list and socio-demographic factors. We found a significant correlation between the child care problem and education level ( $\chi^2(2)=6.622$ ,  $p<0.05$ ), as well as the type of treatment ( $\chi^2(1)=4.259$ ,  $p<0.05$ ). Patients with secondary education and those who received other types of therapy than chemotherapy experienced more problems with child care.

## DISCUSSION

The COVID-19 pandemic became, in a very short time, a great threat worldwide in terms of health, as well as social and economic aspects. From the beginning of the pandemic, patients with cancer were considered a high-risk population (European Society for Medical Oncology 2020, Dai et al. 2020, Lee et al. 2020, Miyashita et al. 2020, Lang et al. 2020).

Epidemiological measures imposed during the pandemic, such as social distancing and lockdown, additionally burdened patients with cancer. Under these new circumstances, according to the present findings, more than half of patients with breast cancer, who were actively treated at the time of the research, had a high level of distress. Previous reports addressing the level of distress in patients with breast cancer estimated that approximately 20–40% suffer from a high level of distress (Mehnert et al. 2018, Carlson et al. 2019, Hewit et al. 2004). Patients who were unable to attend regular visits, due to the lack of transportation or other limitations caused by the epidemiological measures, were not included in the study; this criterion may have influenced the results. Additionally, the study did not include newly diagnosed patients that had not initiated their oncological treatments (i.e., the group of patients associated with higher levels of distress) (Hewit et al. 2004). Comparatively, recent studies reported a significantly lower percentage of highly stressed individuals among the general population during the COVID-19 outbreak (Qiu et al. 2020, Wang et al. 2020, Mazza et al. 2020) though it is difficult to compare results obtained through different assessments.

In this study, socio-demographic and disease characteristics, as predictive factors of distress, were not linked to higher levels of distress. Notably, previous studies conducted in the pre-epidemic era emphasized that age, type of treatment, income level, and living alone were predictors of high distress in patients with cancer (Carlson et al. 2019, Kaiser et al. 2010, Mergenthaler et al. 2011, Syrowatka et al. 2017, Cimprich 1999).

Regarding distress in patients with breast cancer, worry, fatigue, sleep, nervousness, fear, and child care were some of the most prominent problems experienced during the COVID-19 pandemic. These data are also markedly different from those of previous studies, which reported fatigue, sleep, and getting around as the most prevalent problems among patients with cancer (Mehnert et al. 2018, Mergenthaler et al. 2011, Van Hoose et al. 2015, Cimprich 1999).

Taking into account problems in the highly distressed group, we identified emotional problems (worry, sadness, depression, nervousness, fears, and losing interest) and practical problems (child care, housing, and work/school) to be strongly associated with a high level of distress. These findings differ significantly from those of previous reports, in which emotional problems were not strongly expressed (Van Hoose et al. 2015).

Participants receiving chemotherapy experienced fewer childcare problems compared with the group receiving other types to treatment. This could be explained by the fact that chemotherapy is perceived as a more complex therapy by family caregivers or

individuals who offer social support to those patients, and are therefore willing to offer more help (Slevin et al. 1990, Berry et al. 2017).

### Study limitations and strengths

The strengths of our study include its multicentric design and nationwide character. To the best of our knowledge, this is the first research study to address the level of distress and problems in patients with breast cancer during the COVID-19 pandemic in Croatia. Therefore, apart from providing directions for future studies, these findings also have practical value (i.e., highlighting the unmet needs of these patients and indicating the importance of psychosocial support).

A limitation of this study arises from the fact that patients with breast cancer, who were not able to attend previously arranged appointments due to the lack of transportation or fear of COVID-19 infection, were not included in the study. We also did not include patients who were in the course of radiotherapy or newly diagnosed waiting for surgery, etc.

This was a cross-sectional study; hence, another limitation is the lack of data on the level of distress in patients with breast cancer in Croatia prior to the pandemic. This study emphasizes the need to determine the level of distress among patients with cancer in Croatia. Prospective, longitudinal studies are warranted to examine possible positive interventions and problem-solving approaches in the future.

Furthermore, it should be taken into consideration that measures implemented by the Croatian Government regarding the COVID-19 pandemic were prompt, firm, and transparent. These measures included financial measures easing the loss of household income, which created a feeling of comfort among the general population, as well as patients (Government of the Republic of Croatia 2020). This was accompanied by a comparatively low number of infections and mortality caused by the pandemic in Croatia. On May 24, 2020 (date of completion of data acquisition for our study) the COVID-19-related mortality rate in Croatia was 24 deaths per million. Of note, this rate in Italy, Spain, and the UK was 541, 640, and 540 deaths per million, respectively (Our World in Data 2020, John Hopkins Coronavirus Resource 2020). Therefore, the results of our study may significantly differ from those obtained in countries which are highly burdened by the pandemic.

### CONCLUSION

Even in a country with a favorable epidemiological situation at the beginning of the COVID-19 pandemic and under strict epidemiological measures (e.g., lockdown and strict social distancing), 54% of patients

with breast cancer reported a high level of distress. Interestingly, in previous reports, the percentage of patients with breast cancer experiencing a high level of distress was approximately 20-40% (Mehnert et al. 2018, Carlson et al. 2019, Hewit et al. 2004). The most significant problems reported by the participants of our study affected emotions, causing worry, sadness, depression, fear, and nervousness. Additionally, specific practical problems emerged (e.g., child care, housing, and work/school), most probably partly due to the lockdowns and social distancing. During the COVID-19 pandemic, distress should be promptly assessed, and additional psychological and social support targeting specific practical and emotional problems should be provided to ease the burden and reduce the perceived level of distress in patients with breast cancer. Further longitudinal, prospective studies addressing the impact of the pandemic on the level of distress among patients with breast cancer are needed.

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### **Contribution of individual authors:**

Anuska Budisavljević, Renata Kelemenić Dražin & Natalija Dedić Plavetić conceived and designed the study;

Iva Kardum Fucak, Tatjana Silovski, Anuska Budisavljević, Renata Kelemenić Dražin, Vesna Telesmanić Dobrić, Mario Nalbani, Zvonko Curić, Zvezdana Boric-Mikez & Tatjana Ladenhauser collected the data; created the original dataset and contributed to the interpretation of data;

Iva Kardum Fucak & Anuska Budisavljević performed the statistical analysis;

Anuska Budisavljević wrote the first draft of the manuscript;

Renata Kelemenić Dražin, Natalija Dedić Plavetić & Tajana Silovski revised the first draft of the manuscript;

Stjepko Pleština supervised all phases of the study design and writing of the manuscript.

### **References**

1. Adler NE & Page AEK: *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs*, Chapter 2. National Academies Press, Washington, 2008
2. Berry LL, Dalwadi SM & Jacobson JO: *Supporting the supporters: what family caregivers need to care for a loved one with cancer*. *J Oncol Pract* 2017; 13:35-41
3. Carlson LE, Zelinski EL, Toivonen KI, Sundstrom L, Jobin CT, Damaskos P et al: *Prevalence of psychosocial distress in cancer patients across 55 North American cancer centers*. *J Psychosoc Oncol* 2019; 37:5-21
4. Cimprich B: *Pretreatment symptom distress in women newly diagnosed with breast cancer*. *Cancer Nurs* 1999; 22:185-194
5. Croatian Institute for Public Health. *Coronavirus - latest recommendations*. Available online at: <https://www.hzjz.hr/sluzba-epidemiologija-zarazne-bolesti/koronavirus-najnovije-preporuke/>; 2020 [accessed 30 December 2020]
6. Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z, et al: *Patients with cancer appear more vulnerable to SARS-CoV-2: A multicenter study during the COVID-19 outbreak*. *Cancer Discov* 2020; 10:783-791
7. Donovan KA, Grassi L, McGinty HL, Jacobsen PB: *Validation of the distress thermometer worldwide: state of the science*. *Psychooncology*. 2014; 23:241-50
8. European Society for Medical Oncology. *Covid-19 and cancer*. Available online at: <https://www.esmo.org/covid-19-and-cancer>; 2020 [accessed 30 December 2020]
9. Government of the Republic of Croatia. *Set of measures adopted to prop up economy during COVID-19 epidemic*. Available online at: <https://vlada.gov.hr/news/set-of-measures-adopted-to-prop-up-economy-during-covid-19-epidemic/29024> [accessed 30 December 2020]
10. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al: *China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China*. *N Engl J Med*. 2020; 382:1708-1720
11. Herschbach P, Keller M, Knight L, Brandt T, Huber B, Henrich G, et al: *Psychological problems of cancer patients: a cancer distress screening with a cancer-specific questionnaire*. *Br J Cancer*. 2004; 91:504-511
12. Hewit M, Herdman R & Holland J: *Meeting Psychosocial Needs of Women with Breast Cancer*, 31-32, 62. National Academies Press, Washington 2004.
13. Jakovljevic M, Bjedov S, Jaksic N & Jakovljevic I: *COVID-19 pandemic and public and global mental health from the perspective of global health security*. *Psychiatr Danub* 2020; 32:6-14
14. Johns Hopkins Coronavirus Resource Center. *COVID-19 Map*. Available online at: <https://coronavirus.jhu.edu/map.html> [accessed 30 December 2020]
15. Kaiser NC, Hartoonian N & Owen JE: *Toward a cancer-specific model of psychological distress: population data from the 2003-2005 National Health Interview Surveys*. *J Cancer Surviv*. 2010; 4:291-302
16. Lee LY, Cazier JB, Starkey T, Turnbull CD, Kerr R, Middleton G: *UK Coronavirus Cancer Monitoring Project Team. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study*. *Lancet*. 2020; 395:1919-1926
17. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al: *J. Cancer patients in SARS-CoV infection: a nationwide analysis in China*. *Lancet Oncol*. 2020; 21:335-337
18. Lipsitch M, Swerdlow DL & Finelli L: *Defining the epidemiology of Covid-19 - Studies needed*. *N Engl J Med*. 2020; 382:1194-1196
19. Marcinko D, Jakovljevic M, Jaksic N, Bjedov S & Minoljevic Drakulic A: *The importance of psychodynamic approach during COVID-19 pandemic*. *Psychiatr Danub* 2020; 32:15-21
20. Ma X, Zhang J, Zhong W, Shu C, Wang F, Wen J, et al: *The diagnostic role of a short screening tool - the distress*



- thermometer: a meta-analysis. *Support Care Cancer*. 2014; 22:1741–1755
21. Mazza C, Ricci E, Biondi S, Colasanti M, Ferracuti S, Napoli C, et al: A Nationwide survey of psychological distress among Italian people during the COVID-19 pandemic: immediate psychological responses and associated factors. *Int J Environ Res Public Health* 2020; 17:3165
  22. Mehnert A, Hartung TJ, Friedrich M, Vehling S, Brähler E, Härter M, et al: One in two cancer patients is significantly distressed: prevalence and indicators of distress. *Psychooncology*. 2018; 27:75–82
  23. Mergenthaler U, Heymanns J, Köppler H, Thomalla J, van Roye C, Schenk J, et al: Evaluation of psychosocial distress in patients treated in a community-based oncology group practice in Germany. *Ann Oncol* 2011; 22:931–938
  24. Miyashita H, Mikami T, Chopra N, Yamada T, Chernyavsky S, Rizk D, et al: Do patients with cancer have a poorer prognosis of COVID-19? An experience in New York City. *Ann Oncol*. 2020; 31:1088–1089
  25. National Comprehensive Cancer Network, National Comprehensive Cancer Network Guidelines, Distress Management, Version 2.2020, Available on line at: [https://www.nccn.org/professionals/physician\\_gls/pdf/distress.pdf](https://www.nccn.org/professionals/physician_gls/pdf/distress.pdf) [accessed 30 December 2020]
  26. Ng CG, Mohamed S, Kaur K, Sulaiman AH, Zainal NZ, Taib NA: My BCC Study group. Perceived distress and its association with depression and anxiety in breast cancer patients. *PLoS One*. 2017; 12:e0172975
  27. Our World in Data: Total confirmed COVID-19 deaths per million people. Available online at: <https://ourworldindata.org/grapher/total-covid-deaths-per-million?year=2020-05-24> [accessed 30 December 2020]
  28. Qiu J, Shen B, Zhao M, Wang Z, Xie B, Xu Y: A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: implications and policy recommendations. *Gen Psychiatr* 2020; 33:e100213
  29. Slevin ML, Stubbs L, Plant HJ, Wilson P, Gregory WM, Armes PJ, et al: Attitudes to chemotherapy: comparing views of patients with cancer with those of doctors, nurses, and general public. *BMJ* 1990; 300:1458–146
  30. Syrowatka A, Motulsky A, Kurteva S, Hanley JA, Dixon WG, Meguerditchian AN, et al: Predictors of distress in female breast cancer survivors: a systematic review. *Breast Cancer Res Treat*. 2017; 165:229–245
  31. Van Hoose L, Black LL, Doty K, Sabata D, Twumasi-Ankrah P, Taylor S, et al: An analysis of the distress thermometer problem list and distress in patients with cancer. *Support Care Cancer*. 2015; 23:1225–1232
  32. Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, et al: Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) Epidemic among the general population in China. *Int J Environ Res Public Health*. 2020; 17:1729
  33. World Health Organization. Media briefing on Covid-19. Available online at: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020> [accessed 3 August 2020]

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