



# Impact of COVID-19 on anxiety levels among patients with cancer actively treated with systemic therapy



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## ABSTRACT

**Background** Life-threatening diseases have a negative impact on emotional well-being and psychosocial functioning. This study aimed to assess the relationship between the level of anxiety caused by a neoplasm and the threat of coronavirus infection among patients with cancer actively treated with systemic therapy during the COVID-19 pandemic. Additionally, we searched for clinical factors associated with a higher level of anxiety.

**Methods** In this multicentre, prospective, non-interventional study conducted in Poland, we enrolled 306 actively treated patients with cancer and collected their clinical data, including age, gender, cancer type and treatment intention. The fear/anxiety of SARS-CoV-2 were rated in Fear of COVID-19 Scale (SRA-FCV-19S) and Numerical Anxiety Scale (SRA-NAS). The fear and anxiety associated with cancer (CRA) were rated with the NAS (CRA-NAS).

**Results** The mean level of SRA-FCV-19S was  $18.5 \pm 7.44$ , which was correlated with the SRA-NAS ( $r=0.741$ ,  $p<0.001$ ). SRA-FCV-19S was significantly higher in women versus men ( $20.18 \pm 7.56$  vs  $16.54 \pm 6.83$ ;  $p<0.001$ ) and was tumour type-dependent ( $p=0.037$ ), with the highest anxiety observed in patients with breast cancer ( $17.63 \pm 8.75$ ). In the multivariate analysis, only the female gender was significantly associated with higher SRA. CRA-NAS was higher in women versus men ( $7.07 \pm 2.99$  vs  $5.47 \pm 3.01$ ;  $p<0.001$ ), in patients treated with curative versus palliative intention ( $7.14 \pm 3.06$  vs  $5.99 \pm 3.06$ ;  $p=0.01$ ) and in individuals aged  $\leq 65$  years versus  $>65$  years ( $6.73 \pm 2.96$  vs  $5.66 \pm 3.24$ ;  $p=0.007$ ).

**Conclusions** For an actively treated patient with cancer, cancer remains the main life-threatening disease during the COVID-19 pandemic. The need for more attentive psychological care should be provided especially to female patients, patients with breast cancer, those under 65 years of age and treated with curative intention, as these factors are associated with a higher level of anxiety.

## INTRODUCTION

On 11 March 2020, the WHO declared the coronavirus disease caused by the SARS-CoV-2 virus as a pandemic.<sup>1</sup> By the end of June 2020, over 10 million people had been infected and 500 000 people died. Fear and anxiety associated with the coronavirus have changed our perceptions and social functioning in every

## Key questions

### What is already known about this subject?

► Treatment of patients with cancer during the COVID-19 pandemic is a significant challenge. Due to the high mortality among patients with cancer, many do not wish to begin the systemic treatment or return to the clinical path. They are concerned that SARS-CoV-2 infection, which can be acquired during frequent contact with the health service, is a more life-threatening condition than cancer itself. It is known that fear of the coronavirus in cancer survivors is greater when compared with the population without cancer. No studies have evaluated the anxiety level of COVID-19 among patients with cancer actively receiving systemic treatment.

### What does this study add?

► This is the first study to assess and compare fear and anxiety associated with the novel coronavirus and cancer itself in actively treated patients with cancer. From a clinical perspective, the disease of cancer is considered as more life-threatening than COVID-19 infection. Populations that express a higher level of SARS-CoV-2 anxiety are women, patients with breast cancer and those under the age of 65 years.

### How might this impact on clinical practice?

► The results of our study indicate which group of patients require intensive psychological care during the new coronavirus pandemic. This study also draws attention to the need for developing specific psychological support programmes focused on improving coping styles among individuals who are at high risk of SARS-CoV-2-related fear and anxiety. This is now of particular importance as many countries are currently encountering a recurrence of the COVID-19 pandemic.

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aspect of life. The growing morbidity and mortality of COVID-19 have led to changes in the organisation and functioning of the oncological healthcare system. Many new recommendations proposed by scientific associations concerning cancer care have

been adopted during the pandemic. Moreover, social limitations have included the mandatory confinement of citizens, wearing face masks, banning gatherings, limiting the number of people in public transportation and stores, and shutting down restaurants. Further restrictions were incorporated in hospitals such as limiting elective surgical procedures, prohibiting visitors during hospital stays, reducing systemic treatment intensity (especially among palliative patients) and implementing teleconsultations. Regarding systemic treatment, changes consisted of delaying treatment, modifying chemotherapy regimens, prolonging intervals between treatment cycles or even terminating therapy.<sup>2-6</sup> One of the most important changes was the transformation of some hospitals into locales dedicated only to patients infected with SARS-CoV-2. As a result, many patients with cancer were forced to change their location of receiving systemic treatment. Fear and anxiety are observed in 17%–46% of patients with cancer.<sup>7</sup> Anxiety reduces the quality of life in patients and negatively impacts compliance with medical treatment.<sup>8</sup> Moreover, it affects feelings of pain and incidence of nausea and vomiting, and even the side effects of drugs.<sup>9-11</sup> The SARS-CoV-2 pandemic is a reason for several mental alterations like stress, depressive symptoms, insomnia, denial, anger and fear.<sup>12</sup> Nevertheless, data on this topic for oncological patients are scarce.

We are presenting a multicentre study that was performed during the SARS-CoV-2 pandemic in Poland. The study aimed to assess the relationship between the level of cancer-related anxiety (CRA) and SARS-CoV-2-related anxiety (SRA) among patients with cancer receiving anticancer systemic therapy. Additionally, we have tried to distinguish subgroups of patients with the highest levels of anxiety and to assess the relationship between the strategy of coping with cancer and the perceived epidemiological threat caused by the COVID-19 disease.

## MATERIAL AND METHODS

This prospective, observational, non-interventional study was performed in five Polish Centers for Oncology between 11 May and 15 May 2020, during the period of serious restrictions introduced in relation to the epidemic in Poland. During the period of study, on average, 404 new COVID-19 cases were diagnosed daily in Poland, and the total number of patients infected with SARS-CoV-2 increased from 16 326 to 18 016. The first case of COVID-19 was diagnosed in Poland on 4 March 2020. The study was approved by the local bioethics committee in Olsztyn (11/2020/VII). Eligible patients were adults of 18 years and older with histopathological confirmation of malignant neoplasm, who were receiving systemic oncological therapy (chemotherapy, immunotherapy or targeted therapy) and received at least one cycle of the treatment at the time of the study. Patients who were unable to complete the questionnaires by themselves were excluded from the study. Patients with known

psychiatric disorders were not excluded. Every patient who was admitted to the hospital for the administration of systemic treatment was asked by a treating physician to participate in the study. Patients who agreed to participate signed the written informed consent and received the study questionnaire. The estimated enrolment rate was 40%.

Demographic and clinical data such as age, gender, type of cancer and type of treatment (curative or palliative) were collected from the patients' medical histories. Patients were asked to rate their fear/anxiety of SARS-CoV-2 coronavirus (SRA) and cancer (CRA) in the Numerical Anxiety Scale (NAS) from 0 (no fear/anxiety) to 10 (very high fear/anxiety) and the Fear of COVID-19 scale (FCV-19S).

The FCV-19S was designed in Iran by Ahorsu *et al.*<sup>13</sup> Subsequently, it has been validated in numerous countries becoming one of the most prevalent tools for the assessment of COVID-19 anxiety.<sup>14-18</sup> It is composed of seven statements scored from 1 to 5 points. Patients assess the level of agreement or disagreement with each statement, with the total score ranging from 7 to 35 points. The higher the score, the stronger the fear.

The NAS was developed to be easily implemented with even a limited amount of time per patient during consultation or teleconsultation. It has been used for the assessment of fear or anxiety in clinical settings.<sup>19-23</sup> Additionally, patients are familiar with similar scales that are used, for example, to assess pain intensity.

The State-Trait Anxiety Inventory (STAI) questionnaire was used to measure the presence and severity of current anxiety and a general propensity to be anxious by means of self-report. The STAI is among the most widely researched and used measure of general anxiety. There are two subscales within STAI that measure components of anxiety: state and trait. The State Anxiety Scale (S-Anxiety, STAI1) evaluates a transitory emotional state of anxiety, characterised by current, subjective feelings of apprehension, tension, nervousness, worry and activation/arousal of the autonomic nervous system that may vary in intensity over time. The Trait Anxiety Scale (T-Anxiety, STAI2) evaluates relatively stable aspects of 'anxiety proneness' that includes general states of calmness, confidence and security. Trait anxiety refers to a relatively stable response to stress with a tendency to perceive a wider range of situations as threatening. The STAI scale has 40 items, with 20 items allocated to each subscale. Item scores are added to obtain subtest total scores. The range of scores for each subtest is 20–80, where higher scores indicate greater anxiety.<sup>24-27</sup>

The Mini-Mental Adjustment to Cancer (mini-MAC) questionnaire was used to evaluate a mental adjustment to cancer. The mini-MAC scale consists of 29 statements that enable the identification and evaluation of four types of the following coping strategies:

- ▶ Anxious preoccupation—expresses anxiety resulting from the diagnosis. The disease is perceived as a source of anxiety uncontrollable by the patient.

Every change in the patient's well-being is perceived as a symptom of deterioration of the patient's condition.

- ▶ Fighting spirit—motivates the patient to undertake multiple actions aimed to overcome a disease that is perceived as a personal challenge.
- ▶ Helplessness-hopelessness—an indication of being lost, a sense of impotence, the feeling of being overwhelmed by the disease.
- ▶ Positive redefinition—problems related to the presence of disease are re-evaluated to find hope and derive satisfaction from all the years the patient has lived so far while remaining aware of the gravity of the situation.

Results are calculated for each of the examined strategies. Each strategy includes seven relevant statements. The result range of each analysed subscale result may be from 7 to 28 points—the higher the score, the stronger the behaviour typical for a given strategy of coping with cancer. The recorded intercorrelation patterns indicate that there are two styles of coping with the disease: constructive (including the fighting spirit and positive redefinition strategies) and destructive (including helplessness-hopelessness and anxious preoccupation strategies).<sup>28</sup> Constructive and destructive strategies were divided into low (1–4), medium (5–6) and high (7–10) scores according to the questionnaire manual.<sup>29</sup>

The Kolmogorov-Smirnow test, skewness and visual interpretation of histograms were used to assess normality. The  $\chi^2$  test for categorical variables, the Mann-Whitney U and Kruskal-Wallis tests with pairwise comparisons for non-normally distributed variables were used for comparisons between the groups. The Spearman correlation was used for assessing the association between variables. Differences were considered significant with a p value of  $\leq 0.05$ . The statistical analyses have been performed with IBM SPSS Statistics V.25.

## RESULTS

### Characteristics of the study group

A total of 306 patients were enrolled in the study. The study group consisted of 167 women (54.58%) and 139 men (45.42%). The median age was 63 years (range 25–87), 194 (58.50%) patients were under 65 years of age and 112 (41.50%) patients were over 65 years of age. Two hundred nine patients (68.30%) were treated with palliative intention and 97 (31.70%) with curative intention. Patients were divided into six groups based on the location of the primary tumours: gastrointestinal cancer (99; 32.35%), lung cancer (22; 7.19%), melanoma and sarcoma (47; 15.36%), breast cancer (86; 28.10%), urogenital cancers (38; 12.42%) and other (14; 4.58%) (table 1).

### The SRA and CRA on the NAS and the FCV-19S

The mean level of SRA on the FCV-19S (SRA-FCV-19S) was  $18.5 \pm 7.44$ . The analysis of the clinical parameters revealed that SRA-FCV-19S was significantly higher in women than in men ( $20.18 \pm 7.56$  vs  $16.54 \pm 6.83$ ;  $p < 0.001$ ) and depended on the tumour type ( $p = 0.037$ , table 2). The highest SRA-FCV-19S was present in patients with breast cancer ( $20.67 \pm 7.78$ ), in contrast to patients with lung cancer who had the lowest level ( $15.75 \pm 5.92$ ). There were no statistically significant differences in SRA-FCV-19S between younger and older patients, or between those treated with palliative or curative intention. Tumour type, gender, age and intention of treatment were included in a multivariate linear regression model. Only gender remained significantly associated with SRA-FCV-19S ( $B = -1.7$ , 95% CI  $-2.61$  to  $-0.79$ ,  $p < 0.001$ ), with higher levels in female individuals.

The mean level of SRA on the NAS (SRA-NAS) was  $5.40 \pm 3.27$ . Detailed results of SRA-NAS stratified by clinical and demographic factors are presented in table 2. Results from both scales, SRA-FCV-19S and SRA-NAS, were significantly correlated ( $r = 0.741$ ,  $p < 0.001$ ). In the

**Table 1** Characteristics of the study group according to the tumour type

Type of cancer, N (%)	Subtype, N (%)	Gender female, N (%)	Curative intent, N (%)
Gastrointestinal cancers, 99 (32.35)	Colorectal cancer, 55 (55.56) Pancreatic cancer, 17 (17.17) Gastric cancer, 11 (11.11) Others, 16 (16.16)	37 (37.4)	21 (21.2)
Lung cancer, 22 (7.19)		5 (22.7)	1 (4.5)
Melanoma and sarcoma, 47 (15.36)	Melanoma, 26 (55.32) Sarcoma, 21 (44.68)	29 (61.7)	10 (21.3)
Breast cancer, 86 (28.10)		82 (95.3)	52 (60.5)
Urogenital cancers, 38 (12.42)	Prostate cancer, 17 (44.74) Bladder cancer, 10 (26.32) Kidney cancer, 8 (21.05) Testicular cancer, 3 (7.89)	3 (7.9)	6 (15.8)
Other, 14 (4.58)	Ovarian cancer, 10 (71.43) Other, 4 (28.57)	11 (78.6)	4 (28.6)

**Table 2** Values of CRA and SRA in the study group

	CRA (mean±SD)		SRA (mean±SD)			
	NAS	P value	NAS	P value	FCV-19S	P value
Tumour type		0.001*		0.025†		0.037‡
All	6.34±3.10		5.40±3.27		18.50±7.44	
Gastrointestinal cancers	6.32±2.81		5.13±3.15		17.99±6.79	
Lungs cancer	5.00±2.37		4.23±2.97		15.75±5.92	
Melanoma and sarcoma	6.06±3.31		5.28±3.00		17.37±7.32	
Breast cancer	7.32±3.14		6.27±3.26		20.67±7.78	
Genitourinary cancers	5.26±3.20		4.68±3.50		17.63±8.75	
Other	6.43±3.44		6.14±3.76		19.50±6.36	
Intention of treatment		0.001		0.076		0.148
Curative	7.14±3.06		5.93±3.34		19.32±7.20	
Palliative	5.99±3.06		5.17±3.22		18.14±7.54	
Gender		<0.001		<0.001		<0.001
Women	7.07±2.99		6.23±3.11		20.18±7.56	
Men	5.47±3.01		4.40±3.19		16.54±6.83	
Age, years		0.007		0.483		0.763
≤65	6.73±2.96		5.28±3.23		18.30±7.05	
>65	5.66±3.24		5.60±3.33		18.84±8.10	

\*Significant differences in pairwise comparisons (Mann-Whitney U test): gastrointestinal vs lung ( $p=0.043$ ), gastrointestinal vs breast ( $p=0.008$ ), lung vs breast ( $p<0.001$ ), melanoma and sarcoma vs breast ( $p=0.02$ ), genitourinary vs breast ( $p=0.001$ ).

†Significant differences in pairwise comparisons (Mann-Whitney U test): gastrointestinal vs breast ( $p=0.011$ ), lung vs breast ( $p=0.006$ ), genitourinary vs breast ( $p=0.019$ ).

‡Significant differences in pairwise comparisons (Mann-Whitney U test): gastrointestinal vs breast ( $p=0.019$ ), lung vs breast ( $p=0.012$ ), melanoma and sarcoma vs breast ( $p=0.014$ ).

CRA, cancer-related anxiety; FCV-19S, the Fear of COVID-19 Scale; NAS, Numerical Anxiety Scale; SRA, SARS-CoV-2-related anxiety.

multivariate linear regression model, similarly to SRA-FCV-19S, only gender was significantly associated with SRA-NAS ( $B=-1.7$ , 95% CI  $-2.61$  to  $-0.79$ ,  $p<0.001$ ).

The mean level of CRA on the NAS (CRA-NAS) was  $6.34\pm 3.10$ . Analysis of the clinical parameters revealed that CRA-NAS was higher in women than in men ( $7.07\pm 2.99$  vs  $5.47\pm 3.01$ ;  $p<0.001$ ), higher in patients treated with curative than palliative intention ( $7.14\pm 3.06$  vs  $5.99\pm 3.06$ ;  $p=0.01$ ) and higher for those aged 65 years and under than for those older than 65 years ( $6.73\pm 2.96$  vs  $5.66\pm 3.24$ ;  $p=0.007$ ). The highest level of CRA-NAS was present in patients with breast cancer ( $7.32$ ;  $\pm 3.14$ ), whereas patients with lung cancer had the lowest level of CRA-NAS ( $5.00$ ;  $\pm 3.14$ ) (table 2). In a multivariate linear regression model, which included tumour type, gender, age and intention of treatment, significant association with CRA-NAS was found for gender ( $B=-1.7$ , 95% CI  $-2.61$  to  $-0.79$ ,  $p<0.001$ ) and age ( $B=-1.7$ , 95% CI  $-2.61$  to  $-0.79$ ,  $p<0.001$ ).

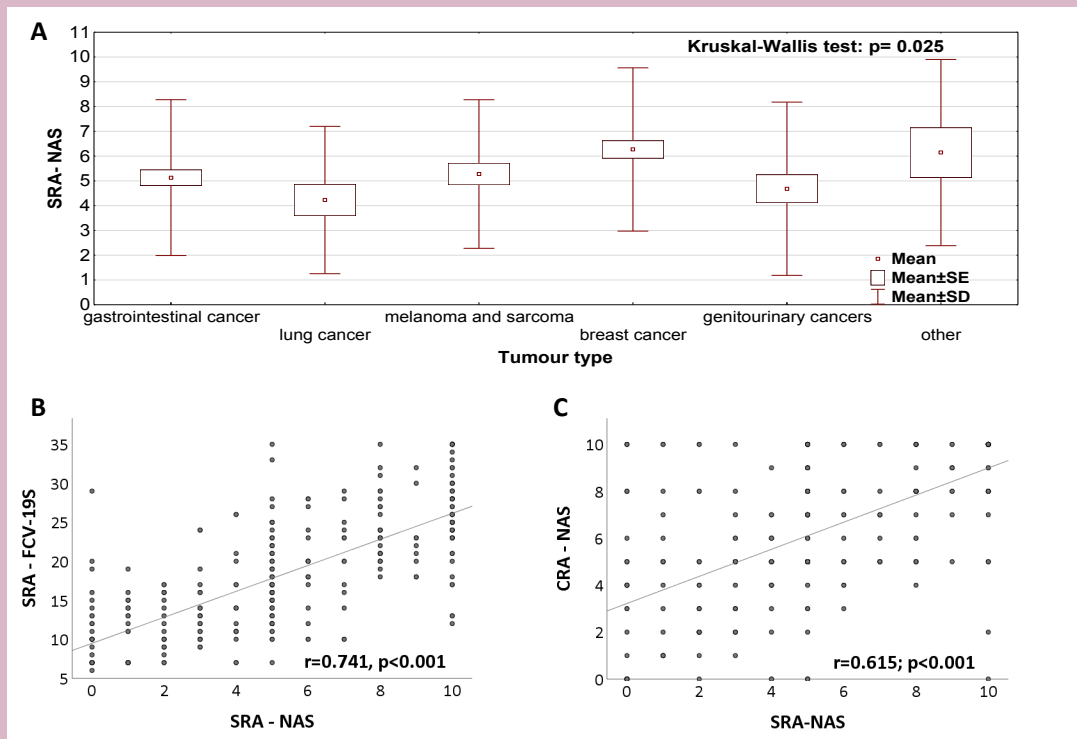
The level of CRA-NAS was significantly higher than SRA-NAS ( $6.34\pm 3.10$  vs  $5.40\pm 3.27$ ,  $p=0.025$ ). The CRA-NAS was significantly correlated with SRA-NAS ( $r=0.615$ ;  $p<0.001$ ) and SRA-FCV-19S ( $r=0.445$ ;  $p<0.01$ ) (figure 1).

### Levels of state and trait anxiety and its correlation with the SRA

The mean state anxiety in STAI1 was  $41.65\pm 9.73$  and trait anxiety in STAI2 was  $41.91\pm 8.02$ . There were no significant differences between those two components of anxiety. In the next step, we analysed whether the SRA-FCV-19S, SRA-NAS and CRA-NAS correlates with state and trait anxiety and STAI1 and STAI2 scales. There were positive correlations ( $p<0.05$ ) between SRA-FCV-19S and STAI1 ( $r=0.334$ ) and STAI2 ( $r=0.303$ ). Moreover, there were significant correlation of SRA-NAS and STAI1 ( $r=0.371$ ) and STAI2 ( $r=0.329$ ) as well as CRA-NAS with STAI1 ( $r=0.335$ ) and STAI2 ( $r=0.297$ ).

### Coping styles with cancer stress and level of anxiety and its correlation with the SRA

In 249 patients (81%), we were able to assess the style of coping with cancer stress. The rest of the data were incomplete or inconclusive ( $n=57$ ; 19%). Our study shows that the most common style of coping with cancer was a fighting spirit ( $n=169$ ; 67.87%) and positive redefinition ( $n=72$ ; 28.92%). The anxious preoccupations ( $n=7$ ; 2.81%) and helplessness–hopelessness ( $n=1$ ; 0.4%) were less common. The most common coping pattern was constructive with high standard ten in 65.02% of



**Figure 1** (A) SRA assessed on NAS depending on tumour type. (B) Correlation between SRA assessed on NAS and on FCV-19S. (C) Correlation between SRA and CRA. CRA, cancer-related anxiety; FCV-19S, Fear of COVID-19 Scale; NAS, Numerical Anxiety Scale; SRA, SARS-CoV-2-related anxiety.

patients and low standard ten for destructive in 64.24% of patients.

Patients prone to anxiety are more likely to adopt destructive styles of coping with cancer. Patients with stronger destructive styles according to standard tens have

significantly higher scores of CRA-NAS ( $p < 0.001$ ), SRA-NAS ( $p < 0.001$ ), SRA-FCV-19S ( $p < 0.001$ ), STAI1 ( $p < 0.001$ ) and STAI2 ( $p < 0.001$ ) (table 3). There were no differences between CRA-NAS, SRA-NAS, SRA-FCV-10S, STAI1, STAI2 and a constructive style of coping with cancer.

**Table 3** The mean scores in CRA-NAS, SRA-NAS, FCV-19S, STAI1 and STAI2 in the general study population, and destructive coping style with cancer

Scale	All (mean $\pm$ SD)	Standard ten (mean $\pm$ SD)			P value	Pairwise comparison
		Low (L)	Medium (M)	High (H)		
CRA-NAS	6.34 $\pm$ 3.10	5.64 $\pm$ 3.08	7.38 $\pm$ 2.83	8.77 $\pm$ 2.05	<0.001	L vs M $p < 0.001$ L vs H $p < 0.001$ M vs H $p = 0.086$
SRA-NAS	5.40 $\pm$ 3.27	4.71 $\pm$ 3.08	6.49 $\pm$ 3.30	7.62 $\pm$ 2.73	<0.001	L vs M $p < 0.001$ L vs H $p = 0.002$ M vs H $p = 0.330$
SRA-FCV-19S	18.50 $\pm$ 7.44	16.59 $\pm$ 6.34	21.28 $\pm$ 7.64	27.54 $\pm$ 9.69	<0.001	L vs M $p < 0.001$ L vs H $p < 0.001$ M vs H $p = 0.008$
STAI1	41.65 $\pm$ 9.73	38.12 $\pm$ 8.67	46.89 $\pm$ 7.42	54.77 $\pm$ 11.97	<0.001	L vs M $p < 0.001$ L vs H $p < 0.001$ M vs H $p = 0.022$
STAI2	41.91 $\pm$ 8.02	39.21 $\pm$ 6.87	46.26 $\pm$ 7.16	48.83 $\pm$ 12.29	<0.001	L vs M $p < 0.001$ L vs H $p = 0.009$ M vs H $p = 0.467$

CRA-NAS, Cancer-Related Anxiety on the Numerical Anxiety Scale; H, high standard ten; L, low standard ten; M, medium standard ten; SRA-FCV-19S, SARS-CoV-2-Related Anxiety on the Fear of COVID-19 Scale; SRA-NAS, SARS-CoV-2-Related Anxiety on the Numerical Anxiety Scale; STAI1, State Anxiety Scale; STAI2, Trait Anxiety Scale.

## DISCUSSION

Data regarding anxiety and fear associated with COVID-19 among patients with cancer are very limited. As already known, oncological patients are a very vulnerable population and mortality among patients with cancer with COVID-19 infection is around 10 times higher than in a general population.<sup>30</sup> This may cause greater fear of coronavirus and further affect patients' attitudes towards cancer treatment. In our study, we showed that SARS-CoV-2 fear and anxiety are significantly lower than cancer-associated anxiety (CRA-NAS;  $5.40 \pm 3.27$  vs  $6.24 \pm 3.10$ ,  $p=0.025$ ). Cancer is commonly perceived as a life-threatening condition with a high risk of death, which can explain that patients are more afraid of its consequences than the risk of SARS-CoV-2 infection. Moreover, we have found that SRA was higher in women and varied significantly depending on the tumour type. The highest anxiety level was in patients with breast cancer and the lowest was reported by patients with lung cancer. It should be noted that most of the patients with breast cancer were female individuals and patients with lung cancer were male individuals. In general, anxiety level is higher in female individuals than in male individuals according to the literature. We have not found any significant differences in coronavirus-related anxiety regarding patients' age or intention of treatment, contrary to CRA.

Different scales and questionnaires were proposed to evaluate the anxiety of patients. The first validated scale to access the level of anxiety was FVC-19S.<sup>13</sup> In our study, the mean level of SRA-FCS-19S was  $18.50 \pm 7.44$ . The reported mean level of the SRA-FCV-19S varies between 16.86 and 27.39, but the direct comparison of scale is difficult due to differences in study population and time of assessment.<sup>13 16</sup> Our study was performed between 11 May and 15 May 2020, 2 months after the beginning of the pandemic confinement in Poland. Despite the 2 months long adaptation to the new situation, the level of fear and anxiety was still high, but lower than in previous studies from Iran or Italy that were conducted at the time of the peak incidence and mortality of COVID-19. Lower anxiety in our study could result from baseline anxiety related to cancer diagnosis and adaptation to the pandemic reality. We have observed that SRA and CRA significantly correlated ( $r=0.445$ ,  $p<0.01$ ).

We have also used the simple numerical scale, from 0 to 10 points, to assess the anxiety. We observed a high correlation between SRA assessed on a numerical scale and anxiety on the FCV-19S ( $r=0.741$ ,  $p<0.001$ ), which suggests that both scales can be used in further studies after validation. Results from other studies show that the FCV-19S significantly correlated with the Hospital Anxiety and Depression and Severity Measure for Specific Phobia-Adult Scales.<sup>16</sup>

In the present study, CRA and SRA were significantly higher in female individuals what was confirmed in a multivariate model. Specifically, fear and anxiety were the highest in young women undergoing curative treatment for breast cancer. These results are consistent with previous studies, as it has been shown that this group of patients suffers extensively due to anxiety.<sup>31</sup> This observation stays in line with the fear

of COVID-19 in the general population, where anxiety was observed to be higher in women.<sup>15 16 18</sup>

There are many anxiety triggers for oncological patients. Nevertheless, cancer itself seems to be the most important one. Patients are also anxious about COVID-19 and its impact on the course of their treatment. One of the most significant worries was the concern about the effectiveness of delayed treatment. In contrast, anxiety and fear of getting infected with coronavirus is one of the most common reasons leading to treatment delay.<sup>32</sup>

COVID-19 has strikingly high mortality of around 30% in patients with lung cancer so high fear and anxiety could be expected in this group, but our study revealed that patients with lung cancer were affected by anxiety the least.<sup>33</sup> Also, patients with genitourinary cancers had a low fear of COVID-19. It is important to underline that majority of patients with lung or urogenital cancers were male individuals, who according to the multivariate model have significantly lower anxiety levels. Some studies show, however, that the majority of patients with lung cancer use effective strategies of coping with the disease, which correlates with a better quality of life, while a compromised quality of life is associated with a destructive coping style.<sup>34</sup> A constructive style of coping might efficiently decrease anxiety but this issue requires further investigation. Also, the study revealed a significant correlation between the score in the STAI questionnaire, CRA-NAS, SRA-NAS and SRA-FCV-19S with a destructive style of coping with cancer. As prior research has shown, emotional coping may accompany symptoms of post-traumatic stress disorder and increase their severity.<sup>35</sup> The fact of being ill provokes death-related thinking. Attempts to detach from unwanted thoughts increase their availability in people who tend to react emotionally, which may induce fear and anxiety. With oncological patients, thoughts of death and dying are inevitably present, which translates to the worsening of emotional and mental performance. It differs from the constructive coping style, which has a weak negative correlation with post-traumatic stress disorder.<sup>36</sup> No correlation was found between the questionnaires used and a constructive coping style but patients adapting the destructive style had significantly higher levels of anxiety. These results showed that the tendency to develop depressive symptoms and higher anxiety levels may also extend to other areas of the patient's life, as indicated by the SRA scales. It is especially important to recognise the group of patients with destructive coping styles, as this may result in serious mental issues especially while facing another life-threatening disease like COVID-19. These patients may require additional psychologic support at every stage of cancer diagnosis treatment and surveillance after completion of the treatment.

The correlation between SRA-FCV-19S, SRA-NAS CRA-NAS and the STAI questionnaire calls to attention the generally high level of anxiety in patients treated for cancer. It is common for patients with cancer to feel emotionally distressed. Holland *et al*<sup>37</sup> reported that patients undergoing treatment for cancer face major physical and emotional challenges and anxiety especially at the initiation of treatment when they worry about the potential side effects of

the agents and fear of recurrence after completion of treatment.<sup>37,38</sup> Usually, we experience anxiety as a result of fear and uncertainty. With daily changes in the status of the pandemic, anxiety levels are rising rapidly. The fear associated with COVID-19 is also connected with the disruptions of the healthcare system and changes in treatment routines that were previously well-established in the patients' lives.

Some limitations of the current study should be noted. In addition to the small sample size, the patients differed in terms of duration and type of anticancer treatment. The level of anxiety of cancer is not constant, so the time from diagnosis to the moment of enrolment in our study may affect the results. Moreover, levels of anxiety could vary at different times of the pandemic, in our study it was measured only once. Additionally, we did not collect data on concomitant medications, such as antidepressants, and anxiolytics that could have a substantial impact on the emotional perception of the patient's reported anxiety.

Many more factors like time from the cancer diagnosis, the duration of therapy and patients' personal information like place of residence, socioeconomic status, social media, news watching habits may potentially affect the level of anxiety.<sup>39,40</sup> There is some evidence that living in urban can be a protective factor against anxiety.<sup>41</sup> Moreover, the anxiety among residents of Wuhan, where the COVID-19 pandemics have begun, was associated with their place of residence, marital status, monthly income, exercise and frequency of video communication.<sup>42</sup> There are also data suggesting that the frequency, duration and diversity of media exposure were positively correlated with COVID-19-related fear and unspecific anxiety.<sup>43</sup> Contrarily, correlations between anxiety and place of residence, level of education or having relatives infected with SARS-CoV-2 were not observed in some studies.<sup>44</sup> In our study, media habits were indirectly studied in the FCV-19S, however, it is difficult to measure the media habits in an objective manner.<sup>43</sup> Not assessing the above-mentioned factors has to be considered as a limitation of our study.

To the best of our knowledge, this is the first multicentre study on anxiety in a population of patients with cancer during the SARS-CoV-2 pandemic. It is important to address the issues connected to COVID-19 that impact the process of cancer treatment. Most patients still perceive cancer as the main threat to their life and do not consider the pandemic as a real-life threatening situation. Also, our results revealed the relations between anxiety and the style of coping in patients with cancer. All patients should be provided with access to psychological and psychiatric care during the whole process of treatment and recovery, but stronger support should be offered during challenging times, like the COVID-19 pandemic. Moreover, patients diagnosed with breast cancer, patients below 65 years of age, patients treated with curative intent and patients with a destructive style of coping with cancer should receive special psychological care. New modes of support like teleconsultations with psycho-oncologists or virtual support groups could help patients deal with anxiety associated not only with cancer but also other unexpected, circumstances like the COVID-19 pandemic.

The findings of our study support the need for further research on this topic. A better understanding of clinical factors that may account for individual differences between the perception of cancer and COVID-19 anxiety would help to create personalised psycho-oncological supportive-care programmes during the actual pandemic. The knowledge about what generates a higher level of anxiety (cancer or SARS-CoV-2 pandemic) can help in better tailoring the treatment to the patient's expectations: oncological treatment can be modified as little as possible for those who are more afraid of cancer while for others, the treatment can be adapted to an acceptable balance between anticancer effectiveness and the patient's emotional comfort.

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