

Post-Traumatic Stress Symptomatology and Adjustment of Medical Oncology Practice During the COVID-19 Pandemic Among Adult Patients With Cancer in a Day Care Hospital

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BACKGROUND: The COVID-19 pandemic may induce post-traumatic stress disorder (PTSD) symptoms among patients with cancer, who also face adaptations to their treatment. The authors assessed the occurrence of PTSD symptoms, investigated pandemic-induced adjustments in medical oncology practice in patients with cancer, and explored risk factors for PTSD and the association between PTSD symptoms, insomnia, and quality of life (QoL). **METHODS:** This prospective French study was conducted in patients with solid/hematologic tumors who were receiving medical treatment in the day care departments of 2 cancer centers during the lockdown. Adjustments to medical oncology practice were collected from medical records. PTSD (measured using the Impact of Event Scale-Revised), insomnia (measured using the Insomnia Severity Index), QoL (measured using the Functional Assessment of Cancer Therapy-General instrument), and cognitive complaints (measured using the Functional Assessment of Cancer Therapy-Cognitive Function instrument) were collected through validated questionnaires. **RESULTS:** Clinical data and questionnaires were available for 734 and 576 patients, respectively. The median patient age was 64 years, and 69% of patients were women. Twenty-one percent of patients had PTSD. Twenty-seven percent (95% CI, 23%-30%) had an adjustment in their medical oncology program, including adjournments (29%), treatment interruptions (16%), modified treatment plans (27%), or adapted monitoring (27%). Women and patients experiencing an adjustment in oncology practice had a higher odds of PTSD (odds ratio= 2.10 [95% CI, 1.07-4.14] and 1.65 [95% CI, 1.03-2.63]; $P < .05$). PTSD symptoms were correlated with worse scores for QoL, cognition, and insomnia. **CONCLUSIONS:** Twenty-one percent of patients with cancer experienced PTSD symptoms associated with poor QoL during the first COVID-19-induced lockdown. Medical oncology practice was adjusted in approximately one-quarter of patients and was associated with the occurrence of PTSD symptoms. Psychosocial support should be offered in cancer centers to promote emotional resilience and avoid PTSD symptoms in patients. *Cancer* 2021;127:4636-4645. © 2021 American Cancer Society.

KEYWORDS: COVID-19, lockdown, patients with cancer, post-traumatic stress disorder (PTSD), treatment adjustments.

INTRODUCTION

COVID-19¹ was first diagnosed in France on January 24, 2020.² The pandemic rapidly spread, leading to the implementation of a nationwide lockdown from March 17, 2020, to May 11, 2020. A major disease outbreak like the COVID-19 pandemic may induce symptoms of post-traumatic stress disorder (PTSD),³ especially in people at high risk of infection. Several studies have reported a higher risk of COVID-19 infection and induced complications in patients with cancer.⁴ In response to both this higher vulnerability of patients with cancer to COVID-19 and the lockdown measures, guidelines were issued to adjust oncologic care during the COVID-19 pandemic.⁵⁻¹⁴ This led to frequent delays and disruptions in cancer health care.¹⁵ Altogether, the fear of becoming infected,^{16,17} the fear of cancer care disruption, and social isolation because of the lockdown measures¹⁸ may have added stress in an already vulnerable cancer population. Indeed, cancer diagnosis and treatment may already be experienced as traumatic in a substantial proportion of patients with cancer,

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especially those who have a history of trauma, psychiatric conditions, low socioeconomic status, young age, advanced disease, invasive treatment, reduced quality of life (QoL), and poor social support.¹⁹ Various surveys have shown that the psychological impact of the COVID-19 pandemic has led to increased levels of stress and anxiety in patients with cancer.²⁰⁻²³ To our knowledge, only 1 small study in hematologic patients used a dedicated scale to explore the frequency of PTSD symptoms in patients with cancer during the first COVID-19 lockdown.²⁰ That study identified high levels of psychological distress, especially among younger patients and women. To date, no study has focused on the association between PTSD symptoms and COVID-19-induced adjustments in terms of changes in medical oncology practice. However, adjustments may include delayed or modified treatments and cancellation or postponement of monitoring visits, all of which are likely to induce stress in patients with cancer. In addition, a relation between PTSD and QoL has been observed in patients who have cancer,²⁴ and both post-traumatic experiences and poor QoL were associated with sleep disturbances in those with advanced disease.²⁵ Moreover, previous studies have suggested that perceived cognitive dysfunction in patients with breast cancer may be mediated by post-traumatic stress.²⁶ The relations between PTSD and QoL, insomnia, and cognitive complaints have not been yet explored in patients with cancer during the COVID-19 pandemic.

We conducted a large, prospective study in patients with solid/hematologic malignancy who were receiving medical treatment during the first COVID-19 lockdown in the outpatient clinics of 2 regional French cancer centers. Our objectives were: 1) to estimate the proportion of patients with cancer who had PTSD symptomatology during the first lockdown period, 2) to assess pandemic-induced adjustments in medical oncology practice and their association with PTSD symptoms, 3) to assess demographic and clinical factors associated with PTSD symptoms, and 4) to investigate the association between PTSD symptoms and insomnia, QoL, and cognitive complaints in patients with cancer.

MATERIALS AND METHODS

Study Design and Participants

COVIPACT is a prospective study conducted in 2 French cancer centers. The study population includes adult outpatients who were receiving an oncologic treatment at the day care hospital that was initiated before or during the pandemic lockdown, from the beginning of the first

nationwide lockdown on March 17, 2020, until May 29, 2020. Patients who were at least 18 years old and were being treated for solid or hematologic cancers during the first lockdown were included.

Data Collection

Medical evaluation

Demographics and clinical information, such as patient characteristics, initial cancer treatment, and pandemic-induced adjustments in medical oncology practice, were extracted from medical records. History of psychological disorders was based on past or present consumption of psychotropic drugs or known condition, as reported in the medical records.

Enrolled patients were asked to complete validated self-report questionnaires on PTSD symptoms, insomnia, QoL, and cognition. Questionnaires were administered from April 16, 2020, to May 29, 2020, ie, during the first lockdown in France.

Post-traumatic stress evaluation

Participants completed the Impact of Event Scale-Revised (IES-R) questionnaire,²⁷ a 22-item questionnaire that assesses subjective distress caused by traumatic events. Because the authors of the IES-R allow instructions for the assessed event to be adapted, patients participating in the COVIPACT study were asked the following: "For each IES-R item, indicate how much you were troubled over the last 7 days regarding the COVID-19 pandemic." Items are rated on a 5-point scale, ranging from 0 (*not at all*) to 4 (*extremely*). The IES-R yields a total score ranging from 0 to 88, and scores can also be calculated for the intrusion, avoidance, and hyperarousal subscales. A total IES-R score ≥ 33 indicates PTSD symptomatology.²⁸

Quality-of-life evaluation

Patients answered validated self-administered questionnaires to evaluate their QoL. The Functional Assessment of Cancer Therapy-General (FACT-G) is a 27-item questionnaire designed to measure 4 domains of health-related QoL in patients with cancer: physical, social, emotional, and functional well-being (6 or 7 items each).

Cognitive complaints evaluation

The Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog) assesses cognitive complaints on 4 subscales²⁹: perceived cognitive impairments (20 items; score range, 0-72), impact on QoL (4 items; score range, 0-16), comments from others (4 items; score range, 0-16), and perceived cognitive abilities (9 items; score range, 0-28).

Insomnia evaluation

The 7-item Insomnia Severity Index (ISI) was used to assess the severity of both nighttime and daytime components of insomnia.³⁰ A 5-point Likert scale is used to rate each item from 0 (*no problem*) to 4 (*very severe problem*). The total score ranges from 0 to 28 and is interpreted as follows: absence of insomnia (0-7), subthreshold insomnia (8-14), moderate insomnia (15-21), and severe insomnia (22-28).

All questionnaires were administered to 576 patients. Only questionnaires with an overall item response rate >80% were considered valid for analyses (ie, between 560 and 567, depending on the questionnaires). The remaining missing items were imputed using the average of completed items.

Study Outcomes

The main outcomes were the proportion of patients with cancer who had PTSD symptomatology during the first lockdown period and the proportion of patients with pandemic-induced adjustments in medical oncology practice.

Adjustment of medical oncology practice referred to any change from standard practice and treatment that was made to prevent the spread of the COVID-19 during the first lockdown. The following were considered adjustments in medical oncology practice: any adaptation in type of treatment (chemotherapy, immunotherapy), in treatment plan (rhythm of administration, cycles of treatment), in method of administration (patient's home instead of day care), and in monitoring (phone or video consultation) and any treatment adjournment or interruption. Each adjustment was discussed and validated during multidisciplinary meetings. Secondary outcomes included QoL, insomnia, and cognition.

Statistical Analysis

The minimal number of participants needed to assess the proportion of patients with pandemic-induced adjustments in medical oncology practice was estimated to be 385 patients with a 95% CI and a maximal 5% margin of error.

Characteristics of patients were described using numbers and proportions for categorical variables and means and standard deviations (or medians and interquartile ranges) for continuous variables. Clinical characteristics were compared according to adjustments in medical oncology practice using χ^2 tests and Student tests.

We used logistic regression to assess the association between adjustments in medical oncology practice

and clinical factors (factors were selected based on P values < .10 in univariate analysis) with odds of PTSD symptoms. We also used linear regression to analyze IES-R total scores and subscale scores as continuous measures. Analyses were controlled for the study center.

Scales and subscales of QoL, cognitive complaints, and insomnia were described and compared according to PTSD symptoms using the Mann-Whitney-Wilcoxon test. Associations between PTSD symptoms and QoL, cognitive complaints, and insomnia were then assessed in linear models adjusted for the previously selected clinical factors. Differences >10% on QoL scales were considered clinically relevant.^{31,32}

All statistical analyses were carried out using R statistical software (4.0.3). A 2-side P value < .05 was considered statistically significant.

Ethics Approval

Approval for the study was obtained from the local ethics committee (ref. 220 C07; South Mediterranean II Committee for the Protection of Persons). The study was conducted in compliance with the French research standard (MR-003 "Research in the Field of Health Without Collection of Consent"; compliance commitment to MR-003 for the Francois Baclesse Center [no. 2146328 v.0, dated from January 26, 2018]). All patients received information and none expressed any opposition to the use of their data. The trial is registered as Regional Center for Biology identifier 2020-A00879-30 (ClinicalTrials.gov identifier trial NCT04366154).

RESULTS

In total, there were 734 patients in the study, including 576 who completed at least 1 self-administered questionnaire on stress, insomnia, QoL, and cognition (Fig. 1). Characteristics of the whole sample are presented in Table 1.

Demographic and Clinical Characteristics

Among the 734 patients included in the study, the median age was 64 years, and 29% of patients were older than 70 years; 69% were women, and 91% had an Eastern Cooperative Oncology Group score of 0 or 1 (Table 1). The median time since cancer diagnosis was 14 months. Patients were mostly treated for breast cancer (41%); lung, head, and neck cancer (22%); digestive system cancer (17%); or gynecologic cancer (11%). Chemotherapy was the most frequent therapy (49%), followed by targeted therapy (19%), a combination of chemotherapy and targeted therapy (17%), and immunotherapy alone

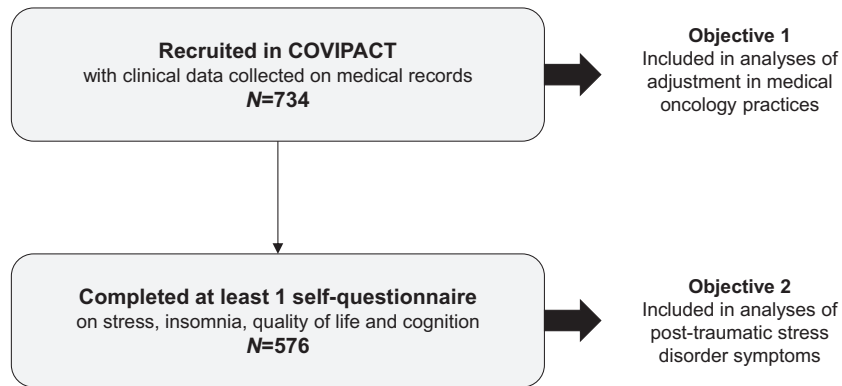


Figure 1. Flow chart of participants in the COVIPACT study (N = 734; ClinicalTrials.gov identifier NCT 04366154).

(8%). More than one-half of patients had initiated their current cancer treatment before lockdown (63%), with a median time since treatment initiation of 2.2 months.

Changes in Medical Oncology Practice

Medical oncology practice was modified in 195 patients (27%; 95% CI, 23%-30%). Changes were more frequent in patients who were treated with immunotherapy alone (which concerned mainly patients with lung, head, and neck cancer) or targeted therapy alone (mainly patients with breast cancer) (Table 1). Patients who received de novo treatment and who initiated their treatment after the beginning of the first lockdown were less likely to experience an adjustment in their medical oncologic treatment.

Among these 195 patients, adjustments in medical oncology practice included adjournments (29%), treatment interruptions (16%), adapted treatment plan (mostly adaptation in the rhythm of administration; 27%), adapted monitoring (mostly phone/video consultation; 27%), and other modifications, such as a change of treatment type or administration method (10%). Details of modifications by clinical subgroups are provided in Figure 2.

PTSD Symptoms and Associated Factors

The subgroup of 576 patients who completed at least 1 self-administered questionnaire had the same characteristics as the overall sample (Table 2; see Supporting Table 1). Approximately 21% of them had PTSD symptomatology. All IES-R subscale scores were higher in patients who had PTSD symptoms: median scores in patients with versus without PTSD were 15 versus 6 for avoidance, 18 versus 5 for intrusion, and 11 versus 2 for hyperarousal (see Supporting Table 2).

In univariate analysis, PTSD symptomatology was more frequent in patients younger than 70 years (23%),

women (24%), patients with breast cancer (24%) or gynecologic cancer (26%), those who had a history of psychological disorder (33%), and those whose medical oncology practice was adjusted (28%) (Table 2). We observed no difference in time since cancer diagnosis according to PTSD symptomatology. In multivariate models adjusted for age, study center, type of cancer, and history of psychological disorders, women and patients whose medical oncology practice was adjusted had statistically higher odds of PTSD symptoms (OR, 2.10 [95% CI, 1.07-4.14] and 1.65 [95% CI, 1.03-2.63]; $P < .05$). When considering the IES-R score as a continuous measure, only sex remained significantly associated with more symptoms on the global scale and subscales.

PTSD Symptoms: Quality of Life, Cognition, and Insomnia

Patients with PTSD symptomatology had the worst scores on all dimensions of QoL (FACT-G; except on the FACT-G social well-being subscale), cognition (FACT-Cog), and insomnia (ISI) (Fig. 3; see Supporting Table 2). Average differences in scores among patients with or without PTSD symptoms were -17.6 [95% CI, -20.5 , -14.8] for the total FACT-G score, -13.8 [95% CI, -16.1 ; -11.5] for the FACT-Cog perceived subscale score, and 6.8 [95% CI, 5.6 - 8.0] for the ISI (all $P < .001$) (Table 3). Associations remained similar and statistically significant after adjustment for age, sex, study center, type of cancer, history of psychological disorder, and adjustments in medical oncology practice during the first lockdown (Table 3).

DISCUSSION

To our knowledge, COVIPACT is the first large study to focus on both the occurrence of PTSD symptoms and adjustments in medical oncology practice in patients with

TABLE 1. Univariate Association Between Demographic and Clinical Characteristics and Cancer Treatment Modifications, N = 734

Patient Characteristic	No. of Patients (%) ^a			P ^b
	Total Sample, N = 734	Adjustment in Medical Oncology Practice, N = 195 (27%)	No Adjustment in Medical Oncology Practice, N = 539 (73%)	
Age, y				
Mean ± SD	62.3 ± 11.7	63.1 ± 10.6	62.0 ± 12.1	.29
≥70	215 (29)	56 (29)	159 (29)	.91
<70	519 (71)	139 (71)	380 (71)	
Sex				
Female	509 (69)	133 (68)	376 (70)	.76
Male	225 (31)	62 (32)	163 (30)	
BMI: Mean ± SD, kg/m ²	25.4 ± 5.1	25.0 ± 5.0	25.6 ± 5.2	.16
ECOG performance status				
0 or 1	664 (91)	168 (88)	496 (93)	.54
≥2	63 (9)	23 (12)	40 (7)	
Type of cancer				<.01 ^c
Breast cancer	304 (41)	82 (42)	222 (41)	.90
Lung, head and neck cancer	163 (22)	65 (33)	98 (18)	<.01 ^c
Digestive system cancer	123 (17)	12 (6)	111 (21)	<.01 ^c
Gynecologic cancer	78 (11)	16 (8)	62 (12)	.25
Urologic cancer	29 (4)	6 (3)	23 (4)	.61
Other solid and hematologic cancer	37 (5)	14 (7)	23 (4)	.16
Stage of solid cancer ^d				
Metastatic	435 (60)	124 (65)	311 (58)	.13
Localized	289 (40)	67 (35)	222 (42)	
De novo treatment				
Yes	360 (49)	76 (39)	284 (53)	.01 ^c
No	374 (51)	119 (61)	255 (47)	
Therapy				<.01 ^c
Chemotherapy alone	361 (49)	59 (30)	302 (56)	<.01 ^c
Targeted therapy alone	136 (19)	62 (32)	74 (14)	<.01 ^c
Chemotherapy and targeted therapy	128 (17)	31 (16)	97 (18)	.58
Immunotherapy alone	61 (8)	26 (13)	35 (6)	<.01 ^c
Other treatment ^e	48 (7)	17 (9)	31 (6)	.21
Initiation of treatment				
Before lockdown ^f	462 (63)	157 (81)	305 (57)	<.01 ^c
During lockdown	272 (37)	38 (19)	234 (43)	
History of chronic conditions				
Hypertension	248 (34)	70 (36)	178 (33)	.48
Cardiovascular disease	166 (23)	27 (14)	64 (12)	.57
Pulmonary disease	116 (16)	38 (19)	78 (14)	.10
Other cancer	105 (14)	30 (15)	75 (14)	.62
Diabetes	91 (12)	27 (14)	64 (12)	.48
Psychological disorders	58 (8)	22 (11)	36 (7)	.04 ^c
Kidney disease	28 (4)	11 (6)	17 (3)	.12
Immune disease	16 (2)	4 (2)	12 (2)	.88
Other chronic condition	174 (24)	49 (25)	144 (27)	.66

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

^aValues are or N (%) of nonmissing data, unless specified otherwise. Data were missing for <1% of patients (3 were missing BMI, 7 were missing ECOG performance status, and 1 was missing history of chronic conditions).

^bP values were derived from Student tests or χ^2 tests.

^cThis P value indicates a significant difference.

^dThe analysis excluded 10 hematologic cancers.

^eOther treatment includes any combinations of immunotherapy or hormone therapy with other therapy (all administered to <15 patients [$<2\%$]).

^fLockdown in France started on March 17, 2020.

cancer during the first COVID-19 lockdown using validated self-report questionnaires and data from medical files. A few smaller studies assessed either PTSD symptoms or treatment adjustments in patients with cancer during the COVID-19 pandemic and found results in line with ours.

The occurrence of PTSD symptoms in patients with cancer during the first COVID-19 lockdown was first investigated by Romito et al²⁰ in a study of 77 outpatients with lymphoma in Italy. Those authors found that 36% of patients had PTSD symptoms according to the IES-R. This higher proportion of PTSD compared with that

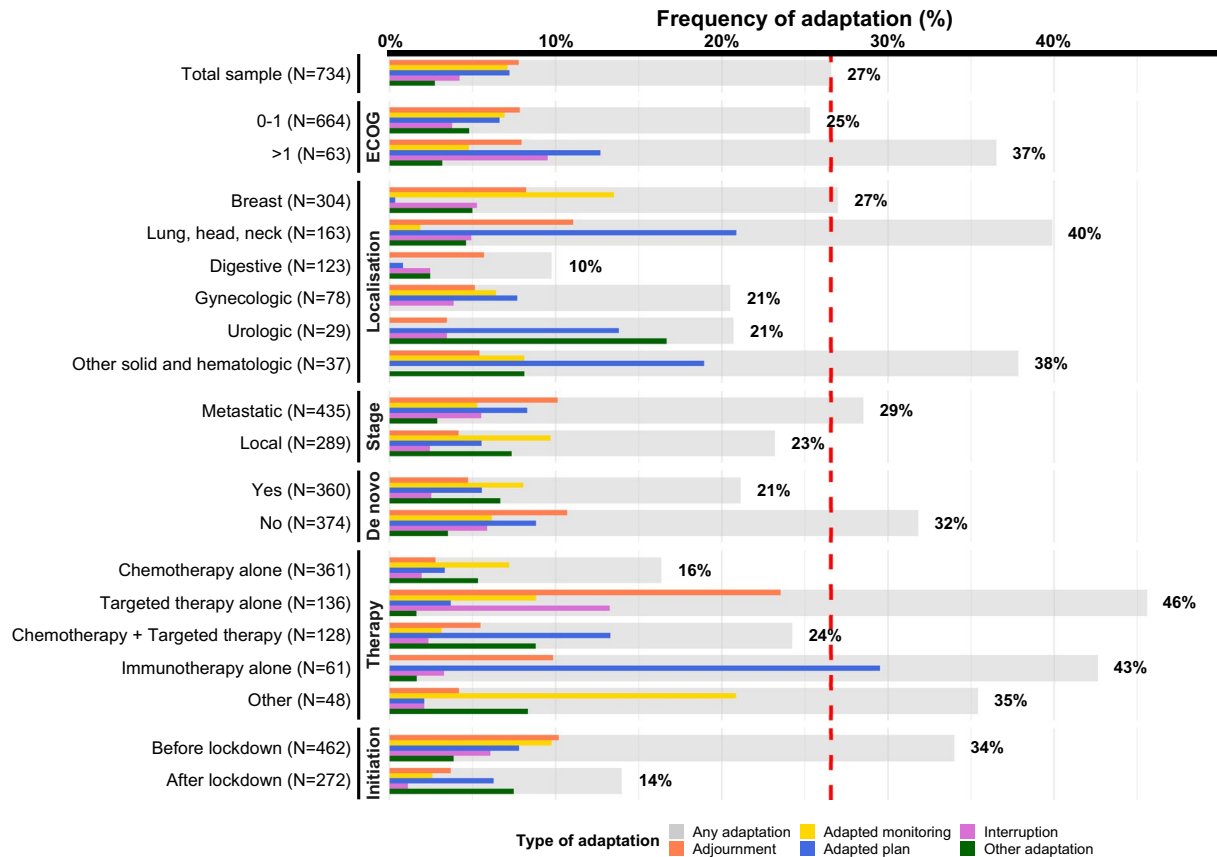


Figure 2. Adjustment in medical oncology practice by clinical characteristics. Adjustment in medical oncology practice (any adaptation or specific types of adaptations) are presented as percentages of the total sample by clinical characteristics. The red dashed line indicates the percentage of any adaptation in the total patient sample (27%). ECOG indicates Eastern Cooperative Oncology Group.

found in our patients might be caused by differences between study populations, particularly differences in the incidence of COVID-19. Romito et al also found more PTSD symptoms in younger patients and women, which is in agreement with our results. However, they did not collect adjustments in medical treatment and thus could not investigate an association with PTSD symptoms. In a Chinese cross-sectional study that included 660 patients with breast cancer, Juanjuan et al²² reported that 20.8% of patients showed severe distress symptoms during the COVID-19 pandemic according to the IES-R, which is similar to our findings. In addition, 46.2% patients self-reported that they had to discontinue or modify their treatment during the outbreak, which was associated with a higher risk of distress, as found in our study using medical records. Swainston et al²³ analyzed the psychological effect of self-reported treatment disruption in patients with breast cancer. In that study, 31.6% of participants reported a change in their medical oncology treatment,

and women who experienced a service disruption reported poorer perceived cognitive function. Altogether, these results are in line with our findings in patients with heterogeneous types of cancers.

In addition, our results confirm the strong relation between PTSD symptoms and QoL, cognition, and insomnia observed in patients with and without cancer. Indeed, insomnia is commonly associated with PTSD both in veterans³³ and in the general population.³⁴ Associations between PTSD and poorer cognition^{26,35} or lower QoL³⁶ have also been documented in patients with cancer.

PTSD symptoms during the COVID-19 pandemic should be interpreted with caution in patients with cancer because cancer diagnosis and treatment are traumatic experiences in themselves.¹⁹ In a recent meta-analysis, prevalence estimates of cancer-related PTSD ranged from 7.3% to 13.8% using screening questionnaires other than the IES-R.³⁷ Regarding the IES-R, several cutoff

TABLE 2. Multivariate Associations Between Clinical Factors and Post-Traumatic Stress Disorder Symptomatology, N = 563

Variable	No. of Patients (%)		OR [95% CI] ^a	P
	No PTSD Symptoms: IES-R Score <33	PTSD Symptoms: IES-R Score ≥33		
Total sample	443 (79)	120 (21)		
Age, y				.26
<70	322 (77)	95 (23)	1.34 [0.81-2.26]	
≥70	121 (83)	25 (17)	1.00	
Sex				.030 ^b
Male	133 (86)	21 (14)	1.00	
Female	310 (76)	99 (24)	2.10 [1.07-4.14]	
Type of cancer				.88
Digestive system cancer	80 (86)	13 (14)	1.00	
Breast cancer	191 (76)	60 (24)	1.17 [0.58-2.51]	
Lung, head and neck cancer	87 (80)	22 (20)	1.43 [0.66-3.23]	
Gynecologic cancer	46 (74)	16 (26)	1.46 [0.61-3.57]	
Urologic cancer	20 (87)	3 (13)	1.04 [0.22-3.68]	
Other solid and hematologic cancer	19 (76)	6 (24)	1.75 [0.53-5.42]	
History of psychological disorders				.13
No	412 (80)	105 (20)	1.00	
Yes	31 (67)	15 (33)	1.68 [0.85-3.23]	
Adjustment in medical oncology practice				.037 ^b
No	336 (81)	78 (19)	1.00	
Yes	107 (72)	42 (28)	1.65 [1.03-2.63]	

Abbreviations: IES-R, Impact of Event Scale-Revised; OR, odds ratio; PTSD, post-traumatic stress disorder.

^aORs (95% CIs) for PTSD symptomatology were estimated using logistic regression, and the model was adjusted for study center.

^bThis P value indicates a significant difference.

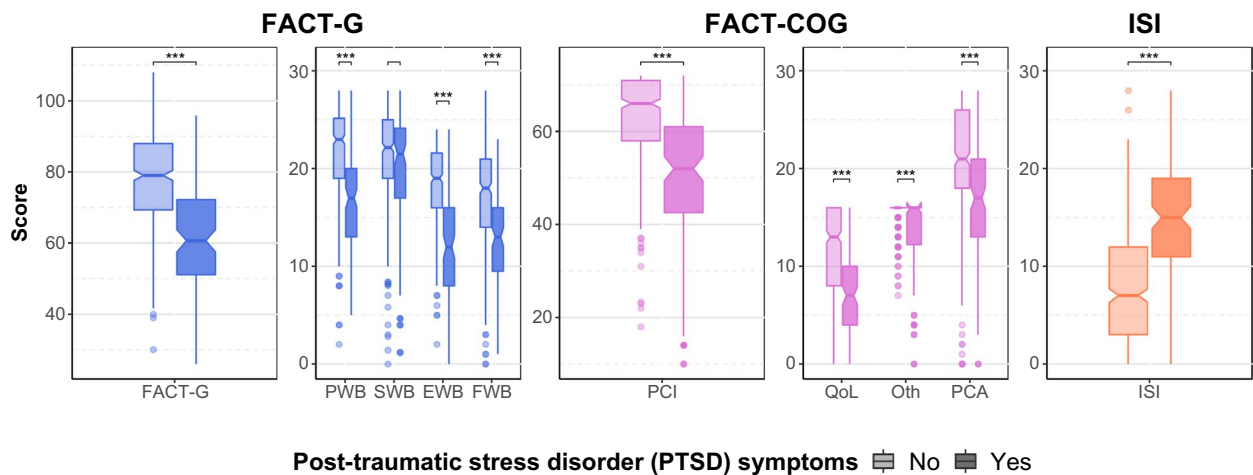


Figure 3. Scales and subscales of quality of life (QoL), cognition, and insomnia by post-traumatic stress disorder (PTSD) symptoms. For the Functional Assessment of Cancer Therapy-General (FACT-G) and the FACT-Cognitive Function (FACT-Cog), higher scores indicate better QoL and cognition, respectively. For the Insomnia Severity Index (ISI), higher scores indicate greater severity of insomnia. Pairwise comparisons are from the Mann-Whitney-Wilcoxon test. Three asterisks indicate P values < .001. EWB indicates emotional well-being; FWB, functional well-being; Oth, other; PCA, perceived cognitive abilities; PCI, perceived cognitive impairments; PWB, physical well-being; SWB, social well-being.

values for PTSD symptomatology have been suggested, ranging from 24 to 33, depending on the population.³⁸ Although these values have not been validated in patients with cancer, several studies reported proportions of approximately 6% to 29% of cancer-related PTSD using

the conservative cutoff score of 33,³⁹⁻⁴¹ which is in the same range as the proportion of 21% that we found in the COVID-19 context. However, those prior studies used cancer as the main traumatic stressor, whereas the COVID-19 pandemic was the main stressor in the

TABLE 3. Multivariate Associations Between Post-Traumatic Stress Disorder Symptoms and Indices of Quality of Life, Cognition, and Insomnia

Measure	No PTSD Symptoms: IES-R Score <33	PTSD Symptoms: IES-R Score ≥33	P
Total sample	79%	21%	
FACT-G, n = 551			
Mean score ± SD	78.7 ± 13.8	61.3 ± 14.0	
Unadjusted β [95% CI] ^a	Reference	-17.6 [-20.5, -14.8]	<.01 ^b
Adjusted β [95% CI]	Reference	-17.5 [-20.3, -14.6]	<.01 ^b
FACT-Cog PCI, n = 553			
Mean score ± SD	63.1 ± 9.8	49.3 ± 15.3	
Unadjusted β [95% CI]	Reference	-13.8 [-16.1, -11.5]	<.01 ^b
Adjusted β [95% CI]	Reference	-13.6 [-15.9, -11.3]	<.01 ^b
ISI, n = 552			
Mean score ± SD	8.2 ± 6.0	14.9 ± 5.7	
Unadjusted β [95% CI]	Reference	6.8 [5.6-8.0]	<.01 ^b
Adjusted β [95% CI]	Reference	6.4 [5.1-7.6]	<.01 ^b

Abbreviations: FACT-Cog, Functional Assessment of Cancer Therapy-Cognitive Function; FACT-G, Functional Assessment of Cancer Therapy-General; IES-R, Impact of Event Scale-Revised; ISI, Insomnia Severity Index; PCI, perceived cognitive impairments subscale; PTSD, post-traumatic stress disorder.

^aβ-coefficients (95% CIs) were calculated from linear models. Adjustment includes age of patients, sex, study center, type of cancer, history of psychological disorders, and adjustment in medical oncology practice during lockdown.

^bThis P value indicates a significant difference.

current study. In addition, we did not observe any association between PTSD symptoms and clinical oncology factors such as disease stage or time since cancer diagnosis, which are risk factors for cancer-related PTSD.³⁷ Overall, it is unlikely that we captured PTSD symptoms related to cancer only or the pandemic only; rather, we identified an exacerbation of cancer-related stress symptoms linked to lockdown-induced constraints that led to adjustments in practice and lack of social support.

Our findings on COVID-19 pandemic-induced adjustments in medical oncology practice in a large sample of patients with cancer in France are original. Other studies investigated changes in care for patients with cancer but focused on specific localizations, such as head and neck¹⁰ or gynecologic cancers.⁴² Moreover, treatment modifications were often self-reported by patients or physicians and were not collected from medical records. In France, a national study (PRATICOVID; Commission for Data Protection and Liberties reference number 2217722v0)⁴³ conducted in 9 hospitals to describe the adaptation of care for patients with cancer induced by the pandemic reported that 44% of medical cancer treatments were adapted in 268 patients receiving medical treatment, which is higher than in our study. However, one-half of those patients received an oral chemotherapy protocol, and most (70%) were followed by telemedicine. Moreover, patients were recruited in military and general hospitals versus cancer centers in the current study.

This study has some limitations. First, we did not consider all dimensions of management for patients with

cancer because we focused on medical oncology practice. Second, patients were not diagnosed with PTSD based on structured clinical diagnostic interviews: we used the IES-R, which is a validated and widely used instrument to screen for PTSD symptoms. Moreover, analyzing the IES-R score as both a continuous and a dichotomous variable led to some discrepancies in findings. Although the use of regression methods on continuous data is generally favored, the choice to dichotomize the IES-R score was based on its right-skewed distribution.⁴⁴ In addition, dichotomized measures represent distinct groups of individuals better according to the presence of PTSD symptoms; thus our analyses aimed to assess group differences rather than individual differences, which are clinically more meaningful. However, we cannot rule out the possibility that misclassification of patients may explain discrepancy. Third, the cross-sectional design of our analysis precludes any conclusions regarding causality. Finally, these results represent the early onset of PTSD symptoms, which could then worsen after a few months or, conversely, decline with adjustment over time, and deserve further investigation in longitudinal studies.

Despite these limitations, our study is the first to assess PTSD symptomatology and to report its association with adjustments in medical oncology practice during the first COVID-19-induced lockdown among many patients with cancer using validated questionnaires and data collected from medical files. This is important because the COVID-19 pandemic is ongoing and will continue to lead to major changes in oncology practice worldwide. In

a population already at high risk for psychological distress, changes in patient care may act as an additional stressor that must be considered by physicians when deciding to implement treatment adjustments. More attention should be paid to the psychological needs of patients with cancer to prevent or detect and manage PTSD symptoms in this vulnerable population. We recommend rapidly implementing psychosocial support for treated patients with cancer to promote emotional resilience and to avoid the onset of PTSD symptoms. In parallel, psychological support should be proposed to patients who have already developed PTSD during this long pandemic with its successive lockdowns.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Florence Joly: Conceptualization, writing—original draft, and supervision. **Olivier Rigal:** Resources and project administration. **Lydia Guittet:** Writing—review and editing. **Sophie Lefevre-Arbogast:** Formal analysis and writing—original draft. **Jean-Michel Grellard:** Project administration. **Giulia Binarelli:** Investigation and writing—review and editing. **Marie Lange:** Investigation and writing—review and editing. **Chantal Rieux:** Investigation. **Marie Fernet:** Investigation. **Laure Tron:** Investigation. **François Garnier:** Investigation. **Romain Travers:** Data curation. **Adeline Morel:** Resources. **Doriane Richard:** Investigation and project administration. **Bénédicte Griffon:** Supervision. **Alexandra Leconte:** Project administration. **Etienne Bastien:** Investigation. **Florian Quilan:** Investigation. **Louis-Ferdinand Pépin:** Supervision. **Fabrice Jardin:** Resources. **Marianne Leheurteur:** Resources. **Bénédicte Clarisse:** Conceptualization, methodology, funding acquisition, writing—review and editing, and supervision. **Justine Lequesne:** Methodology, formal analysis, and writing—original draft. **Audrey Faveyrial:** Resources, visualization, and writing—review and editing.

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