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Self-reported measure of subjective distress in response to COVID-19 pandemic in patients referred to our skin cancer unit during the first wave



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Abstract During the Italian first wave of the COVID-19 pandemic, social restrictions and bad news spread daily by mass media inevitably had a huge influence on the mental state of the population. To assess how much the COVID-19 outbreak impacted the psychologic state of patients referring to our Skin Cancer Unit from March 9 to May 31, 2020, we administered to them a self-report questionnaire, the Impact of Event Scale-Revised (IES-R). To evaluate the trend of the IES-R score over time, we set a temporal cutoff of March 27 (the day with the highest number of deaths for COVID-19 in Italy during the first wave). Three hundred fifty-five patients completed the questionnaire, reporting an average IES-R score of 25.5 (\pm 16.4); 32.4% of participants reached a total IES-R score >32. Patients who visited after March 27, 2020 reported a higher psychologic impact, since the IES-R score significantly increased from 23.6 (\pm 15.6) to 28.3 (\pm 17.2). A group reported higher scores (of participants reaching an IES-R score >32, 57.4% were women and 33.9% were men). We gathered that, at an early stage of events of this magnitude, it could be useful to submit the IES-R questionnaire in high-risk and oncologic patients: we could potentially identify individuals at risk of developing post-traumatic stress disorders, who might be tempted to postpone necessary medical consultations. This could be also the basis for increasing targeted psychologic support in selected patients.

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Introduction

From the beginning of 2020, the COVID-19 pandemic has dramatically undermined people's psychologic stability. During the first half of the year, the period of the first epidemic wave in Europe, factors such as the number of infections and deaths announced daily by mass media and the decrees of the Italian Prime Minister aimed at containing infections, resulting in social restrictions and social isolation, inevitably had a psychologic impact on people, giving rise to states of anxiety, stress, and discomfort.^{1,2}

The clinical activity of our Skin Cancer Unit, dedicated to dermatologic screening and early diagnosis of skin cancers in healthy patients and staging and follow-up of patients with a personal history of melanoma or other skin tumors, was carried out regularly during all phases of the ongoing COVID-19 pandemic. Some of our patients, due to their oncologic history, inevitably harbor an anxious state (to the point that they did not postpone the dermatologic visit scheduled during the weeks of national lockdown), which can significantly worsen as a result of the COVID-19 pandemic.

In this retrospective study, we aimed to assess how much the COVID-19 outbreak has impacted the psychologic state of patients referring to our Skin Cancer Unit from the first day of the Italian lockdown (March 9, 2020) to the first weeks of phase II, with a gradual easing of social restriction due to the progressive reduction of new infections. To do this, we distributed to patients a self-report questionnaire, the Impact of Event Scale-Revised (IES-R), one of the most widely used psychodiagnostic tests, which is commonly used to assess subjective distress caused by traumatic events.^{3,4}

Through the questionnaires, we evaluated if demographic and sociocultural factors (such as age, sex, level of education, and employment status) were related to a different level of distress in response to the COVID-19 outbreak. We also assessed whether the mean score obtained by the IES-R questionnaire, over time, has been influenced by various factors related to the pandemic (the trend in the number of infections and deaths and the resulting increase in restrictive measures).

Methods

The retrospective study involved all patients referred to the Skin Cancer Unit of the Arcispedale Santa Maria Nuova in Reggio Emilia, Italy, from March 9, 2020 (day of the Italian quarantine, lockdown, dictated by the Italian Prime Minister) to May 31, 2020, a few weeks after the gradual easing of the lockdown (with the reopening of manufacturing and restaurant and movements permitted within regional boundaries). Only adults (aged ≥ 18 years) who were able to provide verbal informed consent were recruited for the study. To all patients who came to our Unit for the first visit of dermatologic screening or a follow-up visit after the diagnosis of a skin malignancy, we administered a copy of the IES-R, a self-report questionnaire. Patients were asked to fill in the questionnaire anonymously (reporting only sex, age, level of education, and job) and return it to the medical staff at the time of the visit.

The IES-R is a standardized psychometric scale available in a validated Italian version.⁵ It is a tool commonly used by psychologists and psychotherapists to investigate the presence of post-traumatic symptoms. It includes 22 items (divided into three subcategories: intrusion, avoidance, and hyper-arousal) that patients must rate on a scale from 0 to 4 (0, not at all; 1, a little bit; 2, moderately; 3, quite a bit; and 4, extremely) based on their experience concerning the traumatic event (the ongoing COVID-19 pandemic) referring to the last 7 days. The sum of the means of each subscale instead of raw sums is recommended. The scores for each subscale range from 0 to 4, and the maximum overall score possible is 12.^{3,4} Unfortunately, there are no specific cutoff scores for the IES-R, although several studies have used a total score cutoff > 32 to identify moderate to severe psychologic impact after exposure to a stressful event.^{4,6,7} We adopted this cutoff (total IES-R score > 32) to identify patients with greater distress.

The study protocol was approved by the local Ethics Committee (protocol No. 2020/0104369). The participants' personal information including names was anonymized to maintain and protect confidentiality.

We evaluated if the mean IES-R score and total score daily obtained from questionnaires returned by patients was influenced, over time, by the most important news provided by mass media referring to the ongoing COVID-19 pandemic (the trend in the number of daily infections and deaths for COVID-19 in Italy, and progressive increase of restrictive measures). To do this, we identified a temporal cutoff, on March 27, 2020, which coincided with the highest number of deaths from COVID-19 per day in Italy,8 and we distinguished the first timepoint (T1) from the beginning of the observation period (first day of lockdown) up to March 27; from March 28 onward (T2), the curve of infections and deaths gradually began to decline, and consequently, the restrictive measures gradually relaxed. We also analyzed whether any difference in the IES-R score was influenced by demographic (age, sex) and sociocultural factors (level of education and employment status).

Statistical analysis

Sex, age, level of education, and employment status variables were compared before and after the cutoff date (March 27, 2020) and according to the IES-R score cutoff (32 points).

Mean IES-R partial and total scores were also compared according to the cutoff date.

The χ^2 test was used for categorical variables, while Student *t* test or Mann-Whitney U test was used for quantitative variables after checking for normal distribution.

To assess which factors were independently associated with the risk of manifesting symptoms of psychologic distress related to the COVID-19 pandemic, a multivariate lo
 Table 1
 Demographic and sociocultural characteristics of patients and IES-R score (mean value, total value, and subscale scores) according to the two time frames (before and after March 27, 2020) identified

	Time interval	Total	P value	
	T1(Before March 27, 2020)	T2(After March 27, 2020)		
Sex, no. (%)				0.645
- Men	98 (47.3)	63 (42.6)	161 (45.4)	
- Women	92 (44.4)	73 (49.3)	165 (46.5)	
- Unknown	17 (8.2)	12 (8.1)	29 (8.2)	
Age, median (interquartilerange)	57.8 (±17.2)	54.4 (±17.2)	56.3 (±17.3)	0.072
Level of education, no. (%)				0.039
- Primary school	31 (15.4)	16 (10.9)	47 (13.5)	
- Lower secondary school	53 (26.4)	24 (16.3)	77 (22.1)	
- Upper secondary school	78 (38.8)	67 (45.6)	145 (41.7)	
- University	39 (19.4)	40 (27.2)	79 (22.7)	
Employment status, no. (%)				0.173
- Employed	62 (31.2)	50 (33.8)	112 (32.3)	
- Self-employed	19 (9.5)	9 (6.1)	28 (8.1)	
- Retired	86 (43.2)	53 (35.8)	139 (40.1)	
- Unemployed	15 (7.5)	13 (8.8)	28 (8.1)	
- Other	17 (8.5)	23 (15.5)	40 (11.5)	
IES-R total score, mean (SD)	23.6 (±15.6)	28.3 (±17.2)	25.5 (±16.4)	0.008
IES-R mean score, mean (SD)	3.2 (±2.2)	3.8 (±2.4)	3.5 (±2.3)	0.01
IES-R score, Avoidance subscale				0.01
- Total subscale score, mean (SD)	8.9 (±5.9)	10.6 (±6.4)	9.6 (±6.1)	
- Mean subscale score, mean (SD)	1.1 (±0.7)	1.3 (±0.8)	$1.2 (\pm 0.8)$	
IES-R score, Intrusion subscale				0.009
- Total subscale score, mean (SD)	8.4 (±6.1)	$10.2 (\pm 7)$	9.1 (±6.6)	
- Mean subscale score, mean (SD)	$1(\pm 0.8)$	1.3 (±0.9)	$1.1 (\pm 0.8)$	
IES-R score, Hyperarousal subscale				0.061
- Total subscale score, mean (SD)	6.4 (±5.4)	7.5 (±5.6)	6.8 (±5.5)	
- Mean subscale score, mean (SD)	1.1 (±0.9)	1.2 (±0.9)	1.1 (±0.9)	
IES-R total score >32, no. (%)	55 (26.6)	60 (40.5)	115 (32.4)	0.006

IES-R, Impact of Event Scale-Revised; T, timepoint.

gistic regression model with backward variable selection was built up, including those variables significantly associated with an IES-R score >32 in univariate analysis.

Alpha level was set at 0.05, while an alpha level of 0.10 was used as the cutoff for variable inclusion in multivariable models. Statistical analysis was performed by Stata 15 (StataCorp, College Station, Texas).

Results

Of the 759 patients who came to our Skin Cancer Unit for a visit during the observation period, 483 (63.6%) completed the questionnaire. The remaining 276 patients did not do so, because they were minors or were not interested, or due to lack of time. One hundred twenty-eight patients did not fully complete the questionnaire, so only 355 of 483 questionnaires were considered valid and used for subsequent evaluations.

Demographic and sociocultural characteristics are presented in Table 1. The mean age of participants was 56.3 (± 17.3) , and men and women were equally represented (45.4% and 46.5%, respectively). More than half of the participants had a higher level of education (64.4% attended upper secondary school or university). In terms of employment status, 40% of respondent patients were retired and 32.3% were employed.

If we analyze the sociodemographic characteristics of patients who visited and who filled out the questionnaires during the two timepoints analyzed (T1 and T2), the only significant difference concerns the level of study: in T2 the number of patients with a high level of education increased (72.8% attended upper secondary school or university) compared with T1 (58.2%, P = .039).

The psychologic impact of the COVID-19 outbreak, measured using the IES-R scale, revealed an average mean score (the result of the mean value of the sums of the average scores obtained from the 3 subscales) of 3.5 (\pm 2.3) and an average total score (the result of the mean value of the sums of the scores obtained from the 22 questions) of 25.5 (\pm 16.4). Of the participants 32.4% reached a total IES-R score > 32 (Table 1). Avoidance and intrusion subscales achieved higher partial scores (9.6 \pm 6.1 and 9.1 \pm 6.6, respectively) than the hyperarousal subscale (6.8 \pm 5.5).

	IES-R score		Total	P value
	<u><32</u>	>32		
Sex, no. (%)				0.009
- Men	122 (50.8)	39 (33.9)	161 (45.4)	
- Women	99 (41.3)	66 (57.4)	165 (46.5)	
- Unknown	19 (7.9)	10 (8.7)	29 (8.2)	
Age, median (interquartile range)	55.8 (±17.7)	57.4 (±16.4)	56.3 (±17.3)	0.429
Level of education, no. (%)				0.632
- Primary school	30 (12.8)	17 (14.9)	47 (13.5)	
- Lower secondary school	49 (20.9)	28 (24.6)	77 (22.1)	
- Upper secondary school	103 (44)	42 (36.8)	145 (41.7)	
- University	52 (22.2)	42 (36.8)	79 (22.7)	
Employment status, no. (%)				0.891
- Employed	77 (32.6)	35 (31.5)	112 (32.3)	
- Self-employed	21 (8.9)	7 (6.3)	28 (8.1)	
- Retired	92 (39)	47 (42.3)	139 (40.1)	
- Unemployed	18 (7.6)	10 (9)	28 (8.1)	
- Other	28 (11.9)	12 (10.8)	40 (11.5)	
IES-R, Impact of Event Scale-Revised.				

 Table 2
 Questionnaires with IES-R score exceeding or not the cutoff score >32 (indicating moderate to severe psychologic impact after exposure to a stressful event) according to sociodemographic characteristics of patients

The average total score was also compared between the two time intervals identified (T1 and T2), showing that patients who visited during T2 reported a higher psychologic impact of COVID-19 than those who came to the hospital before March 27, 2020 (T1), since the IES-R score significantly increased from 23.6 (\pm 15.6) to 28.3 (\pm 17.2; *P* = .008). Accordingly, avoidance and intrusion subscale scores also significantly increased in T2.

Table 2 shows how many questionnaires exceeded the IES-R score cutoff of 32 according to sociodemographic characteristics. Female sex was significantly associated with higher scores in the IES-R (57.4% of participants reaching a score > 32 were women and 33.9% were men). Other so-ciodemographic variables including age, level of education, and employment status were not associated with statistically significant differences in IES-R scores.

With multivariate logistic regression analysis, aimed at identifying factors that are independently associated with a greater risk of reaching an IES-R score > 32, we found that male sex and having fulfilled the questionnaire during the first time interval (T1) were significantly associated with a lower risk of obtaining a score >32, and therefore with a lower risk of manifesting symptoms of psychologic distress related to the COVID-19 pandemic (OR = .488 and P = .003 for sex, and OR =1.756 and P = .021 for time interval; data not shown in tables).

Finally, we analyzed in detail which of the 22 questions received higher scores and if the answers to these changed over time (from T1 to T2). Only three questions reached mean scores higher than 1.7, that is, question 1 (intrusion subscale: "Any reminder brought back feelings about" $[1.71 \pm 1.26]$), question 11 (avoidance: "I tried not to think about it" $[1.77 \pm 1.26]$

1.29]), and question 21 (hyperarousal: "I felt watchful or on guard" [2.1 \pm 1.46]; data not shown). Table 3 shows percentages of patients who answered 0 (not at all), 1 (a little bit), 2 (moderately), 3 (quite a bit), or 4 (extremely) to each question in the two time intervals considered. This highlighted the significant differences from T1 to T2: we see how mean scores for questions 11 ("I tried not to think about it"), 2 ("I had trouble staying asleep"), and 16 ("I had waves of strong feelings about it") significantly increased at the second time-point.

Discussion

From the day after the World Health Organization declared the coronavirus epidemic in China to be a public health emergency of international concern, the Italian Government proclaimed a state of emergency and implemented the first measures to contain the contagion. The most drastic measure was taken on March 9, 2020, the date on which the government proclaimed the national lockdown (closure of all nonessential activities of all connected people's movements in national territory). On May 18, 2020, given the reduction of positive cases and related deaths, the lockdown ended and the phase II emergency began, with gradual reopenings and movements permitted within regional boundaries. In the period between these two dates, social restrictions and news spread daily by the mass media may have had a greater influence on the mental state of the people.

The original experimental idea was that in a time when people were living in lockdown, social isolation, distance from work, distance from relations (familiar, affective, and **Table 3** The trend of the partial scores obtained for single questions in the two time intervals considered (before and after March 27, 2020): percentages of patients who answered 0 (not at all), 1 (a little bit), 2 (moderately), 3 (quite a bit), or 4 (extremely) to the single questions of the IES-R questionnaire

	IES-R score				P value	
	0(not at all)	1(a little bit)	2(moderately)	3(quite a bit)	4(extremely)	
Avoidance subscale, no. (%)						
Question 5						0.141
- Before March 27, 2020	55 (26.6)	55 (26.6)	45 (21.7)	43 (20.8)	9 (4.3)	
- After March 27, 2020	33 (22.3)	27 (18.2)	35 (23.6)	42 (28.4)	11 (7.4)	
Question 7						0.305
- Before March 27, 2020	75 (36.2)	52 (25.1)	36 (17.4)	27 (13)	17 (8.2)	
- After March 27, 2020	56 (37.8)	24 (16.2)	27 (18.2)	26 (17.6)	15 (10.1)	
Question 8						0.244
- Before March 27, 2020	75 (36.2)	57 (27.5)	37 (17.9)	24 (11.6)	14 (6.8)	
- After March 27, 2020	58 (39.1)	31 (20.9)	29 (19.6)	25 (16.9)	5 (3.4)	
Question 11		. ,				0.016
- Before March 27, 2020	50 (24.2)	55 (26.6)	47 (22.7)	38 (18.4)	17 (8.2)	
- After March 27, 2020	25 (16.9)	30 (20.3)	28 (18.9)	48 (32.4)	17 (11.5)	
Ouestion 12						0.281
- Before March 27, 2020	103 (49.8)	51 (24.6)	29 (14)	15 (7.2)	9 (4.3)	
- After March 27, 2020	62 (41.9)	34 (23)	27 (18.2)	19 (12.8)	6 (4.1)	
Ouestion 13	02(110)	0.1 (20)	_, (10)	1) (12:0)	0 ()	0.076
- Before March 27, 2020	137 (66 2)	36 (17.4)	23 (11.1)	6(2.9)	5(2.4)	01070
- After March 27, 2020	88 (59 5)	24 (16 2)	18 (12.2)	15(10.5)	3(2)	
Ouestion 17	00 (0).0)	21 (10.2)	10 (12.2)	10 (10.5)	5 (2)	0.24
- Before March 27, 2020	104 (50.2)	48 (23.2)	30 (14 5)	21 (10 1)	4(19)	0.21
- After March 27, 2020	68 (45 9)	32 (21.6)	19 (12.8)	20 (13.5)	9(61)	
Ouestion 22	00 (+3.7)	52 (21.0)	1) (12.0)	20 (15.5)) (0.1)	0.079
- Before March 27, 2020	112 (54 1)	41 (19.8)	38(184)	9(43)	7 (3 4)	0.077
- After March 27, 2020	78 (52 7)	+1 (15.5) 23 (15.5)	22(14.9)	17(11.5)	8 (5 4)	
Intrusion subscale No. (%)	76 (32.7)	25 (15.5)	22 (14.9)	17 (11.5)	0 (3.4)	
Question 1						0.307
Refore March 27, 2020	54 (26.1)	44 (21.3)	17 (22 7)	18 (23.2)	14 (6.8)	0.307
- After March 27, 2020	25(16.0)	30(264)	$\frac{47}{22.7}$	$\frac{40}{25.2}$	17(0.0)	
- Alter March 27, 2020	25 (10.9)	39 (20.4)	33 (22.3)	39 (20.4)	12 (0.1)	0.043
Refere March 27, 2020	110 (57 5)	29(194)	26(12.6)	19 (9 7)	6(20)	0.045
- Before March 27, 2020	119(37.3)	30(10.4)	20(12.0)	10(0.7) 10(128)	0(2.9)	
- Alter March 27, 2020	08 (43.9)	25 (10.9)	25 (15.5)	19 (12.0)	13 (0.0)	0.674
Defere March 27, 2020	57 (07 5)	54 (26.1)	40 (22 7)	42 (20.2)	5 (2 4)	0.074
- Before March 27, 2020	37(27.3)	34(20.1)	49 (25.7)	42(20.5)	5 (2.4) 5 (2.4)	
- Alter March 27, 2020	51 (20.9)	39 (20.4)	39 (20.4)	34 (23)	5 (5.4)	0.121
Question 6	52 (25.1)	(7, (22, 4))	40 (10 2)	29 (19 4)	10 (4.9)	0.131
- Before March 27, 2020	52(25.1)	07(32.4)	40 (19.3)	38 (18.4)	10(4.8)	
- After March 27, 2020	31 (20.9)	39 (26.4)	41 (27.7)	34 (23)	3 (2)	0.405
Question 9	06 (46 4)	52 (25 ()	25 (16 0)	10 (0 7)	5 (2.4)	0.405
- Before March 27, 2020	96 (46.4)	53 (25.6)	35 (16.9)	18 (8.7)	5 (2.4)	
- After March 27, 2020	60 (40.5)	41 (27.7)	21 (14.2)	19 (12.8)	/ (4./)	0.154
Question 14	100 ((2.2))	40 (10 2)	17 (0.0)	14 (6.0)	7 (2,4)	0.154
- Before March 27, 2020	129 (62.3)	40 (19.3)	17 (8.2)	14 (6.8)	7 (3.4)	
- After March 27, 2020	78 (52.7)	33 (22.3)	20 (13.5)	15 (10.1)	2(1.4)	0.000
Question 16	0.5 (1.5.1)		21 (15)	22 (12 ()	0 (1 0)	0.028
- Before March 27, 2020	96 (46.4)	49 (23.7)	31 (15)	22 (10.6)	9 (4.3)	
- After March 27, 2020	46 (31.1)	37 (25)	30 (20.3)	21 (14.2)	14 (9.5)	0.070
Question 20	1 (0 (70 7)		14/60	5 (2.1)	1 (0.5)	0.263
- Before March 27, 2020	163 (78.7)	24 (11.6)	14 (6.8)	5 (2.4)	1 (0.5)	
- After March 27, 2020	110 (74.3)	17 (11.5)	10 (6.8)	6 (4.1)	5 (3.4)	

IES-R, Impact of Event Scale-Revised.

sexual), and levels of anxiety were going to increase more and more, and generate anxiety disorders and stress reactions mostly related to post-traumatic stress disorder. Evidence on previous viral outbreaks (H1N1 influenza, severe acute respiratory syndrome, Middle East respiratory syndrome),⁹⁻¹² and recent findings on the ongoing COVID-19 pandemic indicate that viral outbreaks and resulting quarantine measures are associated with depressive and stress- and anxiety-related symptoms in people.^{7,13-17} Several publications have even documented how personal restriction measures during the COVID-19 pandemic pose a dangerous risk factor for domestic violence and suicide.¹⁸⁻²⁰

The IES-R has been widely used for more than 30 years as a measure of stress reactions after traumatic events; it provides a low-cost short self-report measure to detect posttraumatic stress disorder and is a valuable tool for identifying individuals who would require dedicated interventions. The IES-R is a 22-item self-administered questionnaire comprised of 3 subscales representative of the major symptoms of post-traumatic stress: intrusion, avoidance, and hyperarousal.^{3-5,21} The intrusion subscale includes 8 items related to intrusive thoughts, nightmares, intrusive feelings, and imagery associated with the traumatic event. The avoidance subscale includes 8 items related to avoidance of feelings, situations, and ideas. The hyperarousal subscale includes 6 items related to difficulty concentrating, anger and irritability, psychophysiological arousal on exposure to reminders, and hypervigilance.

According to previous findings, significant genderrelated differences on perceived stress were found. Generally, women achieved higher scores on self-perceived stress.^{7,16,17,22}

The average total scores on the IES-R were compared between the two timepoints, showing that respondents reported a higher impact of COVID-19 in the second time interval (T2, from March 28 to May 31): despite the gradual easing of social restrictions of that period, patients were probably still frightened by what happened during the first weeks of the lockdown. More specifically, avoidance and intrusion subscale scores were statistically higher at T2 than at T1, whereas hyperarousal was almost stable over time.

These findings are in line with previous research,²³ which demonstrated that changes in reactions to traumatic events can be reliably assessed using the Impact of Event Scale. The IES-R is more sensitive to change during the COVID-19 pandemic as compared with the Depression Anxiety and Stress Scales-21, another self-report instrument to assess symptoms of depression, anxiety, and stress.⁷ We deduce that this instrument could be a useful for assessing intra-individual fluctuations in traumatic stress symptoms over time, because the pandemic outbreaks and restrictive measures can be long-lasting, as can their consequences. It is important to follow stress and depressive symptomatology over time, in particular for individuals who are under other stressful circumstances, such as patients affected by skin tumors with a higher risk of progression or recurrence. The magnitude of the SD

at both time intervals (range, 15.6-17.2) shows that there are large inter-individual differences in how the COVID-19 outbreak affects experienced traumatic stress symptoms.

The strength of the study is given by the heterogeneity of the sample, including patients with different sociocultural characteristics. We can hypothesize that patients not seeking medical attention during the first wave of the pandemic could have an even higher IES-R score than patients tested in this study: they missed follow-up or screening visits probably because frightened by the circumstances connected to ongoing emergency.

Conclusions

In line with previous findings, traumatization as a result of pandemic outbreaks might occur not only in health care workers and infected individuals, but also in the general population. Accordingly, it seems useful to submit the IES-R questionnaire in high-risk and vulnerable populations, such as oncologic patients.

We see several possibilities for the use of the IES-R, for instance, to identify, among our patients, individuals at risk of developing post-traumatic stress disorders or other anxietyrelated disorders, and to examine the long-term impact of the COVID-19 pandemic in dermato-oncologic patients or high-risk patients (ie, individuals with several atypical moles and/or previous melanoma) who periodically need to undergo oncologic and dermatologic visits and threaten to suspend the follow-up path. This could be the basis for increasing targeted psychologic supports to be offered to the categories of patients most at risk for psychologic breakdown and to have a one-on-one physician-patient approach (eg, call any patient who does not attend the visit).

Conflict of interest

None.

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Dr. Marco Zanoli provided the patient questionnaire and reviewed the manuscript.

Supplementary materials

Supplementary material associated with this contribution may be found in the online version, at doi:10.1016/j. clindermatol.2021.11.014.

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