Received: 29 January 2018 | Revised: 8 June 2018 | Accepted: 14 June 2018

DOI: 10.1002/pon.4824

PAPER

WILEY

Relationship of demoralization with anxiety, depression, and quality of life: A Southern European study of Italian and Portuguese cancer patients

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Funding information
Fondazione Alazio, Palermo, Italy and Università degli Studi di Ferrara, Grant/Award Number: Fondazione Alazio Project on Demoralization; University Research Funds, Università degli Studi di Ferrara

Abstract

Background: Demoralization syndrome is a significant condition that has not been greatly studied in Southern European countries.

Aims: To extend the knowledge of demoralization in Southern Europe by examining its prevalence according to different methods of assessment, its relationship with anxiety and depression, and its impact on quality of life (QoL) among cancer patients.

Methods: A convenience sample of 195 cancer outpatients from two oncology centers (102 from Lisbon, Portugal, and 93 from Ferrara, Italy) participated in an observational, cross-sectional study using the Diagnostic Criteria of Psychosomatic Research-Demoralization interview (DCPR/D) and psychometric tools (Demoralization scale-DS; Patient Health Questionnaire–9/PHQ-9; Hospital Anxiety Depression Scale-HADS; and European Quality of Life-5-EQ-5D).

Results: A 25.1% prevalence (CI 95%, 0.19-0.31) of clinically relevant demoralization was reported on the DCPR/D interview. A total demoralization score cutoff score ≥ 25 maximized sensitivity (81.6%), and specificity (72.6%) in identifying DCPR/D demoralized patients. The DCPR/D and DS were associated with poorer levels of QoL. About half of the patients who were demoralized were not clinically depressed (PHQ-9). Self-reported suicidal ideation (PHQ-9 item 9) was found in a minority of patients (8.2%), most of whom (77%) were cases of depression (PHQ-9), but one-quarter (23%) were not depressed, yet moderately/severely demoralized (DCPR/D and DS).

Conclusions: This Southern European study confirms the importance of demoralization in cancer patients as a different condition with respect to depression and its relationship with poor QoL and suicidal ideation.

KEYWORDS

cancer, demoralization, depression, oncology, psychiatry, psycho-oncology, quality of life

1 | BACKGROUND

Demoralization, as introduced by Frank, is a syndrome of existential distress denoting a persistent failure of coping, with internally or externally induced stress, and typically occurring in patients with severe conditions that threaten life or integrity of being.[1] Demoralization has been more specifically described as a mental state of subjective incompetence,[2] and, in agreement with Kissane et al[3] and Clarke and Kissane,[4]

it is a syndrome, with a 15% to 30% prevalence,[5-7] a duration of more than 2 weeks, encompassing several existential and psychological dimensions (eg, hopelessness or loss of meaning and purpose in life; pessimism, helplessness, sense of being trapped or personal failure).

In medical settings, especially in oncology and palliative care, a diagnosis of demoralization has been found to be distinct from major depression,[8-10] yet to have negative consequences on patients' quality of life (QoL),[11] coping styles, and dignity.[12] Very importantly, it is also associated with higher demand for a hastened death[13] and frank suicidal ideation, after controlling for other mental disorders, including self-reported depression.[14,15] Existential and meaning-centered psychotherapy approaches are gradually emerging as specific for demoralization and its symptoms, rather than for major depression.[16,17]

Relatively few data have been available from Southern Europe. Two Italian studies showed a 28% prevalence of demoralization in breast cancer patients[18] and a relationship between demoralization and poor QoL, maladaptive coping, and worries about cancer.[19] A cross-sectional Portuguese study showed a higher prevalence of demoralization (52.5%) in a sample of 80 terminally ill cancer patients, with comorbidity of demoralization and depression[20] in 30%. In 226 palliative care patients in Spain, high anxiety was associated with greater demoralization.[21]

Given this background, the aims of the present study were to extend the knowledge of demoralization in two Southern European countries, Italy and Portugal, by examining (1) its prevalence comparing a categorical structured clinical interview with a dimensional self-report measure and (2) its relationship with QoL and psychological variables, among cancer patients in two countries, Italy and Portugal, within a larger European psychosocial oncology study.[22]

2 | SUBJECTS AND METHODS

2.1 | Subjects

A convenience sample of cancer outpatients participated in a cross-sectional, observational study that was conducted in two centers, the Unit of Clinical Oncology, University Hospital S. Anna, Ferrara (Italy), and the Oncology Department of the Centro Hospitalar de Lisboa Central, Lisbon (Portugal), during a period of 6 months. Criteria for inclusion were ages between 18 and 70 years, cancer diagnosis in all stages of disease, and good knowledge of their native language. Exclusion criteria were presence of severe cognitive impairment (MMSE score $\leq$ 24) and Karnofsky Performance Rating Scale score $\leq$ 50. Attention was paid to having patients fulfil the same criteria at the two centers. The study was approved by the ethical committee or related boards of each hospital. Each patient was informed about the aims of the study, gave his/her written consent to participate, and was individually met by research clinicians in the two units trained in psycho-oncology, who administered a semi-structured interview and a psychometric battery during a single session.

2.2 | Assessment

Demoralization was examined by means of two different instruments, the Diagnostic Criteria for Psychosomatic Research-Demoralization interview (DCPR/D) and a self-report scale that is the Demoralization Scale (DS). The categorical diagnosis of demoralization by the DCPR/D enables calculation of clinically relevant threshold scores on the DS, which no study has yet done.

Quality of life was measured through the European Quality of Life-5 (EQ-5D), psychological variables consisted of depression and anxiety, as assessed by the Patient Health Questionnaire-9 (PHQ-9), and the Hospital Anxiety Depression Scale (HADS).

The DCPR/D is part of a larger semi-structured clinical interview,[23] with a diagnosis made if the following criteria are met: (1) failure to meet one's own expectations and/or those of others; (2) inability to cope with some pressing problems; (3) helplessness/hopelessness, or giving up; and (4) duration of the condition $\geq$1 month. The DCPR/D has been used in large samples of medically ill and cancer patients, and it has been proposed as a "gold standard" for the assessment of demoralization.[8,15,16,24]

The DS[25] is a 24-item self-report tool on 5-point Likert scale ("never" = 0; "all the time"=4), based on the original criteria developed by Kissane (Table S1). The scale, used in its validated Italian and Portuguese versions,[20,26] had four subscales (disheartenment; loss of meaning/purpose; dysphoria; sense of failure) in factorial analysis, with good (DS-Disheartenment, IT: α = 0.9, PT: α = 0.89; DS-Loss of meaning, IT: α = 0.81, PT: α = 0.80; total demoralization score (DS-Total), IT: α = 0.89, DS-Total PT: α = 0.89) or acceptable (DS-Dysphoria, IT: α = 0.72; PT: α = 0.75; DS-Sense of failure, IT: α = 0.71, PT: α = 0.79) levels of internal consistency (Cronbach α). A DS-Total is obtained by summing item scores.

The EQ-5D[27] is a measure of health outcomes through five questions covering mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each scored on a 3-point scale (1 = no problems; 3 = extreme problems). A Visual Analogue Scale (VAS) measures overall health (0 = worst imaginable health; 100 = best imaginable health). Responses to these questions were both used as raw scores and, as recommended, converted through a standardized scoring system, to a single Health State Index (HSI) (range score 0-1, higher score = better QoL). The scale had been used in a European project involving the countries participating in this study.[28,29]

The PHQ-9[30] is derived from the PRIME-MD and it is based on the nine Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for major depressive disorder. Each item is rated on a 4-point Likert scale (from 0 = not at all to 3 = nearly every day) over the past 2 weeks. A threshold of $\geq$10 was used to identify cases of depression. Cronbach α in this study had good (IT: α = 0.82, PT: α = 0.89) levels of internal consistency. The scale had been used in a previous Southern European psycho-oncology study.[31]

The HADS[32] is a 14-item self-reported instrument divided into two subscales: HADS-Anxiety (seven items) and HADS-Depression (seven items) (item responses on 0-3 Likert scale, score range = 0-21 each), and a HADS-Total score yielded by summing the two subscales. Cronbach α showed good levels of internal consistency (HADS-Anxiety, IT: α = 0.81, PT: α = 0.86; HADS-Depression, IT: α = 0.80, PT: α = 0.82; HADS-Total, IT: α = 0.86; PT: α = 0.87). The scale had been used in a previous Southern European psycho-oncology study.[33,34]

The patients' socio-demographic and medical information were gathered from each patients' clinical chart.

2.3 | Statistical analysis

Distribution and frequency analyses were used to describe the sample. Student *t* test, analysis of variance, and χ^2 test where used to analyze the differences between samples. Spearman's rho test was used to test the correlation between the variables. The sensitivity, specificity, positive predictive, and negative predictive values of different scores on the DS in discriminating between demoralized cases and noncases were examined by using the DCPR/D as a "gold standard." Receiver operating characteristic analysis was used to explore the optimal DS cutoff score in detecting cases in our sample,[35] with an area under the curve value >0.80 considered as indicative of good discrimination. Statistical analysis was carried out using the Statistical System Statistical Package for Social Sciences (SPSS) in its version 17.

3 | RESULTS

3.1 | Socio-demographic and clinical characteristics of the sample

Of 224 patients meeting the recruitment criteria and approached for the study, 199 (88.4%) accepted and 25 declined to participate (13 from PT and 12 from IT: 17 reported that they were not interested in the study, 5 did not have time to wait; 3 had other problems). No difference was found between those who accepted and those who declined participation. Of the former group, complete data were available for 195, 93 (47.7%) from Italy and 102 (52.3%) from Portugal, with no significant differences between the two countries (Table 1). The mean age was 53.44 (± 10.51) years. Most patients were female (n = 152, 77.9%), married (n = 147, 75.4%), and employed (n = 105, 53.84%). Mean education was for 10.82 (±4.2) years. The majority of patients (n = 113, 57.94%) had breast cancer, and local/loco-regional disease (n = 123, 63.1%).

TABLE 1 Socio-demographic and clinical variables for Italian, Portuguese, and total samples of participants

	Italy (n = 93)	Portugal (n = 102)	Total (n = 195)
Socio-demographic			
Age, mean (SD) in yrs	54.34 (9.9)	52.82 (11.03)	53.55 (10.51)
Education (yrs)	10.59 (3.78)	9.95 (4.49)	10.2 (4.2)
Sex			
Male	29 (31.2%)	24 (23.5%)	43 (22.1%)
Female	64 (68.8%)	78 (76.5%)	152 (77.9%)
Marital status			
• single	9 (9.7%)	13 (12.7%)	22 (11.3%)
• married	73 (78.5%)	74 (72.5%)	147 (75.4%)
• widowed	2 (2.2%)	3 (2.9%)	5 (2.6%)
• divorced	8 (8.6%)	12 (11.8%)	20 (10.3%)
• unknown	1 (1.1%)	0 (0)	1 (0.5%)
Occupation			
• employed	47 (50.5%)	58 (56.8%)	105 (53.84%)
• retired	32 (34.4%)	30 (29.4%)	62 (31.8%)
• unemployed	7 (7.5%)	5 (4.9%)	12 (6.15%)
• housewife	6 (6.4%)	7 (6.8%)	13 (6.6%)
• unknown	1 (0.1%)	---	1 (0.1%)
Clinical Site			
• breast	46 (49.4%)	67 (65.8%)	113 (57.9%)
• gastrointestinal	25 (26.9%)	26 (25.5%)	51 (26.2%)
• genitourinary	9 (9.7%)	10 (9.8%)	19 (9.7%)
• respiratory	9 (9.7%)	7 (6.8%)	16 (8.2%)
• other	4 (4.3%)	2 (1.9%)	6 (3.1%)
Stage			
• local	32 (34.4%)	43 (42.15%)	75 (38.5%)
• loco-regional	20 (21.5%)	28 (27.4%)	48 (24.6%)
• metastatic	41 (44.8%)	31 (30.4%)	72 (36.9%)
Treatment			
• surgery	81 (87%)	91 (89.2%)	172 (88.2%)
• chemotherapy	81 (87%)	86 (84.3%)	167 (85.6%)
• radiotherapy	41 (44%)	61 (59.8%)	102 (52.3%)
• hormone-therapy	49 (56.7%)	53 (51.9%)	102 (52.3%)

3.2 | Demoralization according to the DCPR and DS

The mean DS-Total was 24.74 (±13.38), with no difference between the IT and PT cohorts (t = 0.3, P = ns). With respect to Italians, Portuguese patients reported lower scores on the subscale DS-Dysphoria (t = 3.1, P = .002), and higher scores on DS-Failure (t = 2.89, P < .01) and DS-Loss of meaning/purpose (t = 3.5, P = .001) (Table S2).

Forty-nine patients (25.1%; 24 IT, 25.8%; 25 PT, 24.5%) (CI 95%, 0.19-0.31) met the DCPR/D criteria for demoralization, with no difference between countries (χ^2 = 0.043, *df*, 1; P = ns). DCPR/D cases showed higher scores on all the DS subscales (all P < .001) (Table 2). Further analyses were done following the procedure suggested by Mullane et al[36] and Robinson et al[37] on the DS-Total score, with 13.9% to 26.3% patients resulting no/low, 68.6% to 51.5% moderately, and 18% to 22.2% severely demoralized, respectively (Appendix S1).

Although some differences between the DCPR/D interview criteria and the DS exist (eg, DCPR/D time frame = 1 month; DS = 2 weeks), we conducted a receiver operating characteristic analysis, considering the interview as the gold standard. A DS-Total cutoff score ≥ 25 maximized the sensitivity and specificity in identifying DCPR/D demoralized patients (40/49 = sensitivity 81.6%, CI, 70.8%-92.5%; 106/146 = specificity 72.6%, CI, 65.4%-79.8%) (χ^2 = 43.4; *df*, 1; P = .001). The positive predictive and negative predictive values were 50% (40/80) and 92% (106/115), respectively (misclassification rate = 25.1%, n = 49) (Figure 1).

3.3 | Association between demoralization and QoL

DCPR/D+ patients had higher scores on EQ-5D dimensions (raw scores), the HSI, and the EQ-5D/VAS (all P < .001) (Table 3). Correlation analyses showed significant associations of all the DS subscales and DS-Total with EQ-5 D-Mobility and Anxiety/Depression, EQ-5D-VAS, and HSI (rho between .19 and .55, P from <.01 to <.001). EQ-5D-Pain/Discomfort was associated with DS-Disheartenment (rho = .31, P < .01) and DS-Total (rho = .23, P < .01). EQ-5D-Usual

TABLE 2 Differences on the DS scale between DCPR/D cases and noncases

	DCPR	
	DCPR/D noncases (n = 146)	DCPR/D cases (n = 49)
Demoralization scale (DS)		
Mean (SD) scores		
• Disheartenment	6.32 (5.95)*	11.95 (4.87)
• Loss of meaning	3.64 (4.32)**	5.81 (3.94)
• Failure	6.1 (3.9)***	8.18 (3.2)
• Dysphoria	4.37 (3.24)****	7.89 (3.47)
• Total	20.41 (12.52)*****	33.85 (10.63)

*t = 5.98, F = 35.74, P < .001;
**t = 3.22, F = 9.44, P = .02;
***t = 3.75, F = 11.53, P = .001;
****t = 6.23, F = 41.63, P < .001;
*****t = 7.25, F = 44.59, P < .001

Activities was associated with DS-Disheartenment (rho = .33, P < .001), DS-Loss of meaning/purpose (rho = .21, P < .01), and DS-Total (rho = .31, P < .001) (Table S3).

3.4 | Association between demoralization and other psychological variables

DCPR/D+ or DS-demoralized patients showed higher scores on HADS-Anxiety, HADS-Depression, HADS-Total, and PHQ-9, with increasing scores according to increasing levels of demoralization (all P < .001) (Tables 3 and S4). These scales were also significantly correlated with all the DS-subscales (rho from .42 to .78, P < .001) (Table S3).

On the PHQ-9, 41 patients (21%) were classified as cases of depression. Among this group, 26 (63.4%) were also DCPR/D+. Twenty-three (out of 49, 46.9%) were DCPR/D+ but not depressed, and 15 (out of 146 DCPR/D-, 10.3%) were depressed but not demoralized (χ^2=37.94, df, 1; P = .001). Self-reported suicidal ideation (score 2/3 on PHQ-9 item 9) was reported by 16 patients (8.2%), of whom 13 (77%) were PHQ-9+, and 3 (23%) were PHQ-9- but DCPR/D+ or moderately/severely demoralized on the DS. Suicidal ideation was associated with DS-Disheartenment (rho = .30, P < .001) and DS-Loss of meaning/purpose (rho = .33, P < .001) more than DS-Failure (rho = .23, P < .01) and DS-Dysphoria (rho = .15, P < .05).

3.5 | Association of demoralization with clinical variables

No difference was found between males and females on any DS subscale or DS-Total. Patients with metastatic disease had higher scores on the DS-Disheartenment (F = 8.53, df, 2; P = .01) and DS-Total (F = 4.35, df, 2; P = .01). Age was slightly correlated with DS-Dysphoria (rho = −.15, P = .03).

4 | DISCUSSION

In the present study, we examined demoralization among cancer patients in two Southern European countries, Italy and Portugal.

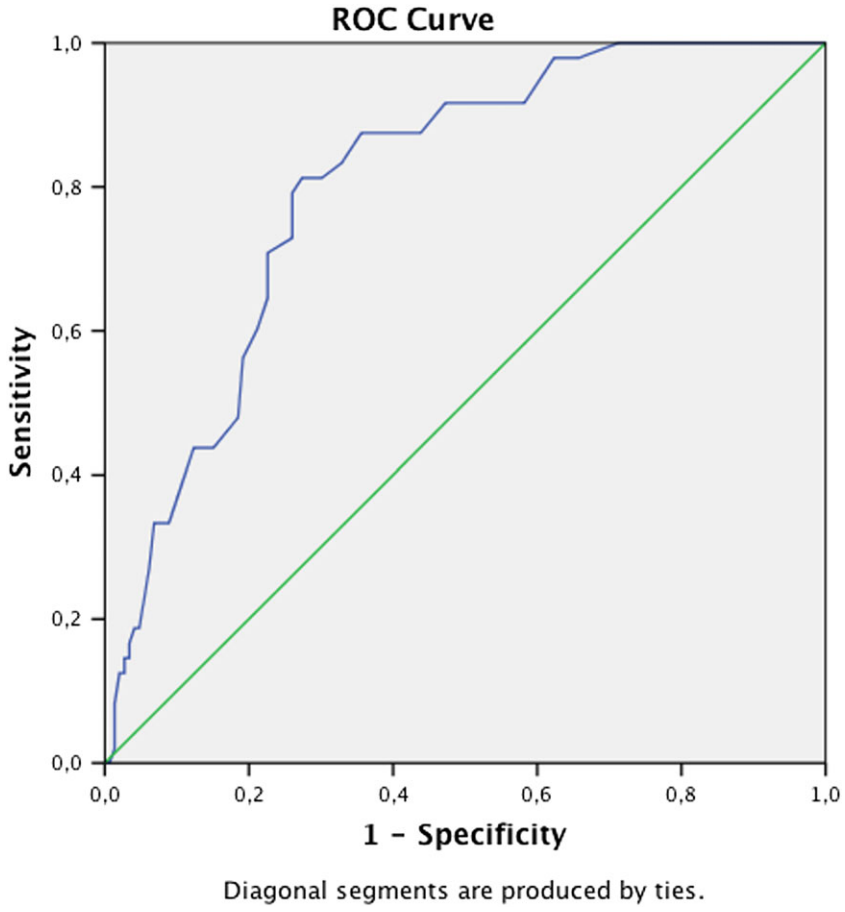

FIGURE 1 Receiver operating characteristic (ROC) analysis comparing the Diagnostic Criteria of Psychosomatic Research-Demoralization ("gold standard") versus the Demoralization Scale

TABLE 3 Differences on the quality of life and psychosocial variables between demoralized and nondemoralized patients (DCPR/D)

	DCPR	
	DCPR/D noncases (n = 146)	DCPR/D cases (n = 49)
HADS-Anxiety	6.14 (3.27)	10.6 (3.1)**
HADS-Depression	4.39 (3.7)	8.2 (4.12)**
HADS-Total	10.53 (6.1)	18.83 (5.6)**
PHQ-9	5.2 (4.12)	9.61 (4.13)**
EQ-5D		
• Mobility item	1.26 (0.44)	1.53 (0.58)**
• Self-care item	1.1 (0.33)	1.24 (0.56)*
• Usual activities item	1.43 (0.6)	1.89 (0.65)**
• Pain/discomfort item	1.68 (0.53)	1.97 (0.52)**
• Anxiety/depression item	1.63 (0.53)	2.1 (0.47)**
EQ-5D Health State Index (HSI)	0.6 (0.34)	0.26 (0.44)**
EQ-5D VAS	66.73 (10.6)	53.54 (15.1)**

Abbreviations: DCPR/D, Diagnostic Criteria for Psychosomatic Research, Demoralization module; EQ-5D, European Quality of Life-5; HADS, Hospital Anxiety Depression Scale; PHQ-9, Patient Health Questionnaire for DSM-IV depression.

* $F = 4.14$, $P < .05$.

** $F = 9.18\text{-}71.32$, $P < .01$.

Our first main finding, in general agreement with most studies, was that demoralization as assessed by the DCPR/D clinical interview was diagnosable in one out of four patients. By using the DS-Total score, the percentage of patients with severe and moderate demoralization (18%-22% and 68.6%-51.5%, respectively, according to two different scoring systems[36,37]) was similar to that reported in palliative care settings in other studies (eg, Germany: 15.7%, 73.1%[10]; Ireland: 14%, 68%[36]).

A further related finding was that DCPR/D+ patients had higher scores on all the DS subscales measuring the several components of these conditions, with only a few differences on some DS-subscales between Portuguese and Italian patients.

With the DCPR/D clinical interview as a "gold standard," a cutoff score ≥ 25 maximized the sensitivity (81.6%), and the specificity (72.6%) of the DS in identifying DCPR/D+ patients. This cutoff is lower than the cutoff ≥30 proposed by Kissane et al[25] and used in some other cross-cultural studies in palliative settings.[38] However, no other authors have compared the DS with another demoralization instrument, like the DCPR/D. A clear limitation was that the DCPR/D uses a longer time framework (1 month vs 2 weeks in the DS) and it does not examine phenomena like loss of meaning or dysphoria, which is examined through five items in the DS.

A second significant main finding is that demoralization was associated with poorer QoL. Physical (such as pain), functional, and psychological symptoms, as measured by the EQ-D5, were associated with demoralization. This confirms the few other studies from Northern Europe reporting that demoralized cancer patients have poorer levels of QoL,[10,12,39] as already demonstrated also in patients diagnosed with major depression.[28,29]

The difference between the constructs of demoralization and anhedonic depression, as reported in English-speaking countries,[12] was confirmed in our study. It is evident that some level of comorbidity between demoralization and depression should be expected, just as frequent comorbidity exists between anxiety and depression and between demoralization and anxiety. In fact, we found significant correlations between the DS and both the PHQ-9 and the HADS-Depression and Anxiety subscales. However, in line with previous studies conducted both in medically ill patients[9] and cancer patients,[18] there were also clear differences, as shown by the finding that almost half of patients who were DCPR/D+ were shown to be not clinically depressed.

We finally examined the association between demoralization and self-reported suicidal ideation (item 9 on the PHQ-9). Although a minority of patients reported having thoughts to commit suicide (8.3%), one-quarter of them were not clinically depressed on the PHQ-9 but were demoralized. This result is in general agreement with a few studies that investigated this aspect,[14,15] indicating that this subgroup of patients with poor coping yet no major depression needs an alternative diagnostic category to capture the phenomenology that represents such serious symptomatology.

4.1 | Study limitations

There are a number of limitations to our study. First, the large number of patients with breast cancer in comparison with other types of cancer and the low number of male cancer patients indicates the need for replication in samples of patients with more representative cancer sites. Also, the characteristics of the sample (convenience sample of outpatients with a good performance status) prevent us from generalizing our results to other contexts, such as patients admitted to the hospital and those with more advanced disease. A further issue regards the fact that we should have explored a series of important cultural factors (eg, religious affiliation, spirituality, socioeconomic status, household income, living in suburb, or rural area or city) to more precisely infer the possible role of cultural factors on demoralization when comparing the data of Northern versus Southern European countries. The association between demoralization and other dimensions, such personality traits, existential and spiritual variables, and dignity is also necessary to have a more specific characterization of the syndrome and the possible variables influencing or predisposing to it.

Future research should explore possible expansion of the DCPR/D semi-structured interview to include some aspects that are part of the demoralization syndrome, as defined by Kissane et al[3] (eg, meaninglessness and dysphoric mood). Recently, Julião et al[20] used Kissane's criteria in a categorical way to make the diagnosis of demoralization in palliative care in Portugal, although caution is called for regarding this interview, as it had not been specifically validated. Alternatively, the development of a DCPR/D-based psychometric tool could be interesting to favor the assessment of psychological conditions that are not part of the standard psychiatric nosology (such as both demoralization and the other constructs measured by the DCPR). Also, a new shorter version of the DS (DS-II) that was not available at the time of our study has been recently validated in Australia[37,40]

measuring demoralization through two parameters, Meaning/Purpose and Distress/Coping Ability, and showing good psychometric properties. Studies comparing this new version could enlarge the interpretation of demoralization both from the clinical and the intervention point of view.

4.2 | Clinical implications

The strength of this study is that it is the first examining a possible correlation between the DS and a structured clinical interview for demoralization, the DCPR/D, extending the knowledge of this syndrome and the need for a correct assessment. This reinforces the significance of demoralization given its impact on several aspects of the patients' QoL, including mental and physical health care. Taking into account the negative consequences that demoralization brings and the role of the cultural variables in the context of psychological responses to a diagnosis of cancer, the results obtained in the present study are helpful in deepening our understanding of this issue in Mediterranean countries.

ACKNOWLEDGEMENTS

The authors wish to thank all the patients participating in the study. The Fondazione Alazio (Palermo, Italy) and the University of Ferrara (Ferrara, Italy) are acknowledged for funding the project. The authors are also indebted to the Board of Physicians, Surgeons and Orthodontists—Section of Ferrara (Ferrara. Italy), the UNITALSI Triveneta—Sezione di Adria (Adria, Italy), the Istituto Oncologico Romagnolo—IOR (Forlì, Italy), and the Associazione per Supporto Psico-Oncologico—ASPO (Ferrara, Italy) for their unconditional support.

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(Further reading can be found in Appendix S2).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Nanni MG, Caruso R, Travado L, et al. Relationship of demoralization with anxiety, depression, and quality of life: A Southern European study of Italian and Portuguese cancer patients. *Psycho-Oncology*. 2018;27:2616–2622. https://doi.org/10.1002/pon.4824