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Psychophysical well-being profiles in patients before hematopoietic stem cell transplantation

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Abstract

Objectives: The literature offers very few in-depth reports on the time directly before hematopoietic stem cell transplantation (HSCT). Also, researchers have focused on selected aspects of psychophysical well-being and treated the sample as homogeneous. Thus, we chose to investigate distinct multidimensional well-being profiles (including anxiety, depressive symptoms, and health-related quality of life [HRQOL] domains) among patients just before HSCT, as well as profile predictors (generalized self-efficacy) and outcomes (transplant appraisal) on the basis of the transactional stress model.

Methods: Depression (CES-D), anxiety (HADS-A), HRQOL (EORTC QOL-C30), generalized self-efficacy (GSES), and transplant appraisal (single-item scale referred to threat and challenge) were measured in 290 patients (56.9% male; mean age = 47.28, SD = 13.79) after admission for HSCT (67.2% autologous). Unconditional and conditional latent profile analyses were applied.

Results: Four latent well-being profiles were identified: well-functioning (51%, highest well-being in all aspects), dysfunctional (10%, weakest functioning in all aspects), and 2 profiles with moderate HRQOL and high (5.6%) or low (33.4%) anxiety and depressive symptoms. Generalized self-efficacy predicted profile membership, controlling for demographic and clinical variables. The highest levels were observed in the well-functioning group ($P < .01$). Appraisal was predicted by latent profile analyses classes: low threat in the well-functioning group ($P < .001$) and the highest threat and challenge in the dysfunctional group ($P < .01$).

Conclusions: The findings highlight the diverse nature of well-being in pre-HSCT patients and the manner in which transplant appraisal and generalized self-efficacy are related to different profiles of pre-HSCT multidimensional well-being, thus indicating the practical implications of the study.

KEYWORDS

anxiety, cancer, depression, hematopoietic stem cell transplantation, latent profile analysis, oncology, quality of life, self-efficacy

1 | BACKGROUND

Hematopoietic stem cell transplantation (HSCT) is potentially a highly stressful event, which may affect patient well-being at any stage of the procedure: pre-, peri-, and post-HSCT. Previous studies concentrated on post-HSCT functioning of the patients[1]; meanwhile, the pre-HSCT attitude and well-being may have consequences for their further recovery.[2] Peak levels of distress are mostly reported prior to and immediately after HSCT.[3] Approximately 4% to 55% of the patients report clinical levels of depression, anxiety, or traumatic stress symptoms at the pre-HSCT stage.[4-7]

According to the Lazarus and Folkman stress and coping model,[8] dealing with stressful conditions is preceded by an individual appraisal of an event (in terms of threat, harm, loss, or challenge), connected with the emotional response, both of which are determined by personal (eg, generalized self-efficacy) and situational factors. Several studies have supported that assumption in the oncology settings,[9,10] although outside the context of HSCT.

Cognitive appraisal, ie, evaluation of the significance of an event for personal well-being,[8] has not been widely investigated. In noncancer populations, threat appraisal was positively associated with negative outcomes, eg, anxiety and depressive symptoms, while

challenge appraisal was positively associated with positive outcomes, eg, life satisfaction or health-related quality of life (HRQOL).[11] In melanoma survivors, threat and challenge appraisals were related to well-being and distress.[9] In another study, among breast cancer survivors, the relationship between threat appraisal and fear of recurrence was moderated by self-efficacy: Women with high threat appraisal and low self-efficacy had the highest fear of cancer recurrence.[12]

Self-efficacy seems to be particularly important in coping with an illness. It refers to a person's perceived capability to manage their personal functioning.[13] Therefore, it affects patient appraisal of an event, as well as the emotional response and coping behaviors. Previous studies showed that patients with higher self-efficacy are more likely to demonstrate greater persistence in trying to achieve well-being as compared to those with lower self-efficacy.[13] A significant relationship between self-efficacy and well-being indices (ie, depression, anxiety, and HRQOL) was noted at the post-HSCT stage.[14] The beneficial effect of self-efficacy in relation to HRQOL and depressive and anxiety symptoms[15,16] was reported by various studies in cancer patients. However, none of the previous studies examined its role in the pre-HSCT period.

In addition to the lack of data on the interrelationship between key stress and coping model variables in the context of HSCT, earlier research focused on selected indices of well-being, not allowing for its multidimensional nature. Meanwhile, the indices of well-being such as depression, anxiety, and HRQOL domains are highly correlated in most HSCT samples.[5,17,18] Moreover, most studies have been based on mean results for an entire group of patients (the so-called variable-centered approach).[19] However, it is unlikely that all pre-HSCT patients experience depressive, anxiety, or distress symptoms in the same manner. Indeed, the coping process and emotional adaptation associated with HSCT vary with each individual patient. This is evidenced by high variances of well-being indices before HSCT.[6,7,20] Thus, it would be advisable to identify homogeneous subpopulations with different well-being profiles within a heterogeneous sample of pre-HSCT patients (the so-called person-centered approach)[19] and to evaluate the transactional stress model using the person-centered approach. This knowledge would help to plan for the tailored to the individual intervention.

Our study attempted to address the abovementioned issues. First, we used the transactional stress and coping model as a starting point for the analysis of the relationships between the main variables of that model and verifications of its assumptions in the context of HSCT, especially cognitive appraisal, self-efficacy, and well-being of patients at the pre-HSCT stage. That stage of the therapy, frequently marginalized by most authors, is vital for further convalescence. Secondly, while analyzing patient well-being, we considered its multidimensional nature and investigated all well-being indices (depression, anxiety, and HRQOL domains) together and the well-being profile in the entire group. Thirdly, we based the verification of the Lazarus and Folkman model on the person-centered approach, ie, we tested the assumption of group heterogeneity in terms of well-being profile and searched for subgroups of people with similar emotional and physical and social functioning. We also investigated the association between selected profiles and key variables of the coping process: self-efficacy and cognitive appraisal. We investigated whether self-efficacy was a predictor of well-being profiles and whether cognitive appraisal was determined

by these profiles. The direction of the latter relationship resulted from the following: (1) Contemporary studies have adopted the theory about an interdependence between the cognitive and the emotional processes,[21] in contrast to the cognitive-oriented stress model; (2) the key role of the cognitive appraisal in coping has been questioned as studies show that the process might in fact be reactive in nature (emotions predict appraisal and coping)[22]; and (3) we assessed patient well-being within the last 7 to 14 days, while appraisal referred to the moment of survey completion. Thus, temporal aspects of the study determined the direction of the relationship between the variables.

Summarizing, the aim of the study was to identify the distinct well-being profiles among patients before HSCT. Also, we wished to evaluate whether different well-being subgroups could be predicted by patient generalized self-efficacy, as well as demographic and clinical factors, and whether they could determine transplant appraisal. It was hypothesized that 3 to 4 different patterns of well-being, including depressive symptoms, anxiety, and HRQOL dimensions, would be found: low, medium, and high (Hypothesis 1), and that subgroup membership would be associated with patient cognitions. In particular, high well-being would be connected with higher self-efficacy and challenge appraisal and lower threat appraisal of the transplant (Hypothesis 2).

2 | METHODS

2.1 | Participants and procedure

The sample comprised 290 patients admitted for HSCT. Most participants were in a stable relationship, had at least secondary education, were professionally inactive, assessed their economic status as average, and had to undergo autologous HSCT (see Table 1).

The inclusion criteria for the study were as follows: preparation for the first autologous or allogeneic HSCT, age ≥ 18 years, no history of other major disabling medical or psychiatric conditions, and written informed consent. A total of 561 patients met the study criteria between November 2014 and July 2017. Of the eligible patients, 297 gave their written informed consent. Of them, 6 participants were deemed ineligible for HSCT, and 1 did not return the questionnaires. Recruitment occurred in a single center by a psychologist. Demographic and psychological data were self-reported, while clinical data were obtained from the medical records. The study protocol was approved by the Local Ethics Committee (decision no. 24/2014) and was in accordance with the Helsinki declaration.

2.2 | Measures

Well-being dimensions included symptoms of depression, anxiety, and indicators of HRQOL.

Depressive symptoms were assessed with a 20-item Centre for Epidemiological Studies Depression Scale (CES-D)[23] on a 4-point scale, with total scores between 0 and 60 (higher scores denote higher depressive symptoms in the past 2 wk).

Anxiety was assessed with a 7-item anxiety scale from the Hospital Anxiety and Depression Scale (HADS-A)[24] on a homogeneous 4-point scale from 0 (rarely or never) to 3 (often), with total scores between 7 and 28 (higher scores denote higher anxiety in the past 2 wk).

TABLE 1 Sample characteristics (N = 290)

Demographic Characteristics	n	(%)
Male	165	(56.9%)
Employment: yes	108	(37.2%)
Marital status: married/partnership	248	(85.5%)
Subjective economic status		
Above average	38	(13.1%)
Average	227	(78.3%)
Below average	25	(6.8%)
	M	(SD), range
Age, y	47.28	(13.79), 19-71
Education, y	14.04	(3.22), 6-28
Clinical characteristics	n	(%)
Primary diagnosis		
Leukemias and other myeloid neoplasms	66	(22.8%)
Acute leukemia (ALL, AML)	53	(18.3%)
Chronic leukemia (CML, CLL)	4	(1.3%)
Myelodysplastic syndrome (MDS)	6	(2.0%)
Myeloproliferative disorders	3	(1.0%)
Lymphomas	123	(42.4%)
Hodgkin (HL)	37	(12.8%)
Non-Hodgkin (NHL)	86	(29.7%)
Multiple myeloma (MM)	86	(29.7%)
Other cancer types (solid tumor, other)	15	(5.2%)
Medical comorbidities		
None	141	(48.6%)
1	83	(28.6%)
2	40	(13.8%)
3 or more	26	(9.0%)
Type of transplant:		
Autologous (autoHSCT)	195	(67.2%)
Allogeneic (alloHSCT)	95	(32.8%)
	M	(SD), range
Time since diagnosis (months)	21.63	(26.0), 3-180
Medical comorbidities	0.90	(1.19), 0-7

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia; CML, chronic myelogenous leukemia.

HRQOL was assessed with the EORTC QOL-C30 questionnaire.[25] The global health status (GHS; 2 items assessed on a 7-point scale; total scores between 2 and 14), functional scale (15 items concern physical, role, emotional, cognitive, and social functioning assessed on a 4-point scale; total scores between 15 and 60), and symptom scale (13 items assessed on a 4-point scale; total scores between 13 and 52) were analyzed. Raw domain scores were used (higher scores denote better GHS, worse functioning and more somatic symptoms in the past week).

Generalized self-efficacy was assessed with the validated short 5-item version of the Generalized Self-Efficacy Scale by Schwarzer and Jerusalem,[26] on a 4-point scale, with total scores between 5 and 20 (higher scores denote higher generalized self-efficacy).

Transplant appraisal was assessed on the basis of the Lazarus and Folkman theory[8] and was similar to the one used by Peacock et al.[27] A single-item scale related to threat (*To what extent do you see the*

transplant procedure as a threat?) and challenge (*To what extent do you see the transplant procedure as a challenge?*) was assessed on a 5-point scale, with total scores between 1 and 5 (higher scores indicated higher appraisal at the moment of the test).

2.3 | Statistical analysis

Descriptive statistics were computed using IBM SPSS (IBM Corp; Armonk, New York) ver. 24. The dataset contains no missing values. To identify heterogeneous classes of multidimensional well-being (including depressive symptoms, anxiety, and HRQOL dimensions) among pre-HSCT patients, latent profile analysis (LPA)[28] was conducted using Mplus statistical package ver. 8.[29] The minimum recommended sample size for this analysis is 5×2^k, where k is the number of the variables in the analysis.[30] The minimum acceptable sample size was determined to be N = 160 (5×2^5). First, the unconditional LPA was applied. The maximum likelihood with robust standard errors was used as an estimator.[29] Models fitting between 1 and 5 classes were run successively. Determination of the appropriate classification was based on the Akaike Information Criterion (AIC), the Bayesian Information Criterion (BIC), the Sample-Size Adjusted Bayesian Information Criterion (SSABIC), the Bootstrap Likelihood Ratio Test (BLRT), entropy value, and practical usefulness of the latent profile. The model with the lower AIC, BIC, and SSABIC values, greater entropy value (closer to 1), and significant BLRT test indicated good fit.[31] Next, the conditional LPA was estimated. Latent profile analysis predictors (self-efficacy and demographic and clinical variables) and outcomes (transplant appraisal) were examined using the 3-step and Lanza et al approaches,[32] respectively.

3 | RESULTS

Table 2 shows descriptive statistics and correlations between the variables. Effect sizes of these results were low to high. For all variables, the absolute values of both skewness and kurtosis were below 1.4, which allows for an assumption of normal distribution.

3.1 | Unconditional LPA

In Table 3, most indices suggest the superiority of the 5-class LPA (AIC, BIC, SSABIC, and BLRT), with the exception of entropy (supporting the 4-class model). However, in the 5-class classification, one class was represented by less than 5% of all participants[33]; the profiles were also similar impeding their practical usefulness. Thus, the parsimony principle supports the 4-class model.

In the 4-class classification, most of the sample (n = 147, 51%, class 4) belonged to the subgroup with highest well-being (well-functioning group), ie, the lowest depressive, anxiety, and somatic symptoms and highest GHS (Figure 1). Participants with the weakest functioning (dysfunctional group; high depression, anxiety, functional scale, and symptom scale, low GHS) covered 10% of the sample (n = 31, class 3). The remaining 2 subgroups have similar, moderate levels of HRQOL domain, but differ with respect to CES-D and HADS-A. Class 1 (n = 14, 5.6%) included participants with higher and class 2 (n = 98, 33.4%) with lower depressive and anxiety symptoms (see Table S1 for estimated means).

TABLE 2 Descriptive statistics and bivariate correlations (N = 290)

	M	SD	Cronbach α	2.	3.	4.	5.	6.	7.	8.
1. CES-D	14.36	8.49	.87	.78**	−.42**	.58**	.50**	−.30**	.27**	.12*
2. HADS-A	12.32	3.71	.79		−.32**	.51**	.37**	−.21**	.30**	.11
3. GHS	9.68	2.23	.85			−.59**	−.52**	.19**	−.33**	−.11
4. FS	28.74	6.99	.86				.74**	−.26**	.39**	.23**
5. SS	22.11	5.28	.82					−.09	.24**	.18**
6. GSES	15.47	2.09	.80						−.18**	−.11
7. Threat	2.89	1.08	n/a							.35**
8. Challenge	3.25	1.16	n/a							

Abbreviations: CES-D, depressive symptoms; FS, functional scale (QOL-C30); GSES, generalized self-efficacy; GHS, global health status (QOL-C30); HADS-A, anxiety symptoms; SS, symptom scale (QOL-C30).

n/a, not applicable.

*P < .05.

**P < .01.

3.2 | Conditional LPA

First, all predictors were tested separately. Only education, type of transplant, and time elapsed since the diagnosis did not predict LPA classification (Table S2). Next, a joint model for all significant predictors was calculated (Table 3). Self-efficacy significantly differentiated the well-being profiles, controlling for demographic and clinical variables. Participants in the well-functioning group showed higher general self-efficacy as compared to other patients. Besides, well-functioning participants were mostly male, cohabiting, and with fewer medical comorbidities.

Both transplant appraisals were predicted by LPA classes. Participants in the dysfunctional group reported higher (compared to classes 1 to 3), while well-functioning participants lower (compared to class 2) levels of threat. Membership in the dysfunctional group was also associated with higher challenge appraisal as compared to classes 2 and 4.

4 | DISCUSSION

The aim of the study was to test the assumption of heterogeneity of multidimensional well-being among patients before HSCT by means of searching for different well-being profiles in the pre-HSCT sample and to identify profile predictors and outcomes with respect to antecedents (ie, self-efficacy, demographic, and clinical factors) and mediators (ie, cognitive appraisal) of transactional stress and coping model. As expected, participants varied in multidimensional well-being and represented distinct well-being profiles. Subgroup membership was associated with the level of generalized self-efficacy, transplant threat, and challenge appraisal, as well as certain demographic characteristics.

Four different well-being profiles were identified in the study group, which supports our first hypothesis. Many patients (51%, class 4) were characterized by good emotional (the lowest levels of anxiety and depression), physical (the least somatic complaints), and global (the highest score of the overall health and QOL) functioning. On one hand, it confirms the relatively good adaptation to adversity: Trajectories of the well-functioning people are usually the most common, which is consistent with other studies.[34,35] On the other hand, it is important to bear in mind that even the results of the well-functioning

group exceed the cutoff for anxiety (the cutoff for HADS-A and CES-D being ≥8 and ≥16, respectively[24,36]), indicating its relatively strong manifestation during the pre-HSCT period. Considerably increased anxiety in the pre-HSCT period is consistent with the findings of earlier studies.[4-7] Notably, our study group was not homogenous in terms of clinical characteristics. It included patients with various diseases and transplants (autologous and allogeneic), which in turn influenced both, the mood and the anxiety levels in the individuals.

The second largest group (33.4%, class 2) included patients who scored within the mild range in all scales. The worst functioning patients comprised 10% of the study group (class 3) and differed from the smallest group (5.6%, class 1) by significantly hindered quality of life: physical, role, emotional, cognitive, and social functioning, as well as a number of somatic complaints and negative global self-assessment of their health. The scores for depression and anxiety in classes 1 and 3 were similar but exceeded the cutoffs in all 3 groups. The percentage share of the subgroup with the weakest functioning was consistent with other reports for cancer patients,[34,35] indicating a global rather than specific nature of the adaptation or well-being profiles.

Generalized self-efficacy was a significant predictor of profile membership, namely, patients in the well-functioning group (class 4) had significantly higher levels of this resource, as compared to other classes, which confirms our second hypothesis. Our findings support the earlier reports on the beneficial role of perceived self-efficacy in coping with cancer.[13-16] Identification of the relationship with multidimensional well-being, indicating that the effect of generalized self-efficacy is complex in nature (typical only for people who function high in numerous domains simultaneously), is a novel finding of our study. The remaining groups, characterized by poorer functioning (classes 1-3) did not demonstrate the differentiating effect of self-efficacy.

Cognitive appraisal was predicted by class membership, albeit hypothesis 2 was only partially supported. Namely, the well-functioning group (class 4) was distinguished by low threat appraisal, while the dysfunctional group (class 3) was characterized by high threat and challenge appraisal. Mixed appraisal in a dysfunctional group may indicate intensified coping efforts in that group of patients, ie, persistent efforts to improve well-being in the face of unfavorable resolution (negative mood as well as assessment of one's health), suggesting a

TABLE 3 Results of LPA: fit statistics, average class probabilities for the most likely class membership by latent class, and mean structure of class predictors and outcomes

Fit Statistics	1 Class	2 Class	3 Class	4 Class	5 Class
Unconditional LPA					
LL	−3937.45	−4094.63	−4009.58	−3972.64	−3935.84
# parameters	20	16	22	28	34
AIC	7914.97	8221.26	8063.15	8001.28	7939.68
BIC	7988.37	8279.97	8143.89	8104.04	8064.45
SSABIC	7924.95	8229.24	8074.12	8015.24	7956.63
Entropy		0.866	0.845	0.871	0.834
BLRT test		−4324.03	−4094.63	−4009.58	−3972.64
BLRT P value		.000	.000	.000	.000
2-class model	1	2			
1, n = 206, 70.3%	.970	.030			
2, n = 84, 29.7%	.049	.951			
3-class model	1	2	3		
1, n = 148, 50.6%	.944	.056	.000		
2, n = 97, 34.5%	.072	.917	.011		
3, n = 45, 14.9%	.000	.062	.938		
4-class model	1	2	3	4	
1, n = 14, 5.6%	.916	.032	.034	.019	
2, n = 98, 33.4%	.016	.904	.008	.072	
3, n = 31, 10.0%	.050	.054	.896	.000	
4, n = 147, 51.0%	.001	.042	.000	.957	
5-class model	1	2	3	4	5
1, n = 105, 36.5%	.907	.093	.000	.000	.000
2, n = 103, 34.9%	.102	.853	.006	.039	.000
3, n = 22, 8.1%	.000	.002	.957	.014	.026
4, n = 47, 15.8%	.000	.073	.033	.880	.014
5, n = 13, 4.8%	.000	.000	.019	.013	.969

Conditional LPA				
Predictor	**1 Class**	**2 Class**	**3 Class**	**4 Class**
Sex (1 = female)	2.26*	0.46	1.31*	Reference class
Age	−0.01	0.02	0.00	
Employment (1 = yes)	0.55	−0.60	0.45	
Marital status (1 = cohabiting)	−1.87*	0.08	−1.30*	
Primary diagnosis–M/LL	0.15	−0.41	−0.47	
Primary diagnosis–MM	0.39	0.62	0.35	
Medical comorbidities	0.87*	0.30	0.70**	
GSES	−0.52**	−0.23**	−0.46**	

Outcome	1 Class	2 Class	3 Class	4 Class	Overall Chi-Square Test
Threat	2.91	3.23	3.72	2.49	59.56*** 1, 2 < 3 2, 3 > 4
Challenge	3.35	3.32	3.90	3.06	1.97** 2 < 3 > 4

Abbreviations: AIC, the Akaike Information Criterion; BIC, Bayesian Information Criterion; BLRT, the Bootstrap Likelihood Ratio Test; GSES, generalized self-efficacy; LL, log likelihood; M/LL, leukemias; MM, multiple myeloma; SSABIC, the Sample-Size Adjusted Bayesian Information Criterion.

Conditional LPA: Unstandardized coefficients are shown.
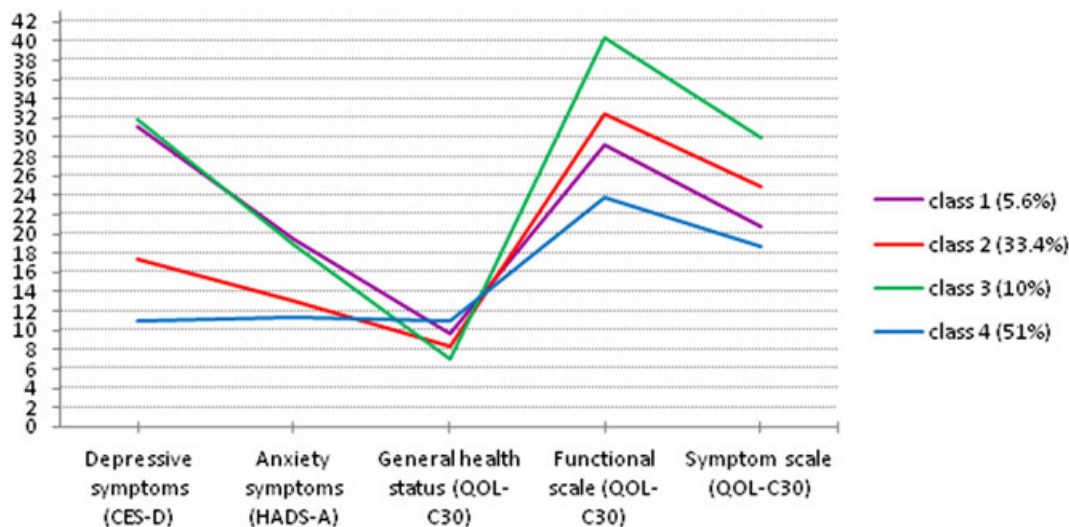
N = 290.

*P < .05.

**P < .01.

***P < .001.

FIGURE 1 Multidimensional well-being profiles in 4-class latent profile analysis

transactional model of stress.[8] Transplant appraisal or reappraisal was lower in the groups with higher well-being, particularly in the well-functioning group. The latter is characterized by the lowest levels in both scores, which supports the explanatory hypothesis. The obtained result may also indicate a motivational, ie, beneficial, function of negative affect, and the demand for it, which was also observed by other authors.[37] In light of the dynamic and reciprocal nature of the relationship between variables of a stress model, its verification should take place in longitudinal conditions.

Male sex, cohabiting, and less medical comorbidities defined the well-functioning class members. Better adaptation at the pre-HSCT stage among males was reported earlier.[7,38] The same was observed for cohabiting[14,39] and better physical health (fewer or no comorbidities),[40] also for other periods post-HSCT. Notably, other clinical factors (primary diagnosis and type of transplant) were not related to LPA membership, indicating lack of privilege for any clinical group as far as pre-HSCT well-being is concerned.

4.1 | Study limitations

Our study is not without limitations. The data were self-reported, and thus, it could be distorted. Because of the cross-sectional design of the study, we were not able to draw conclusions about the cause-and-effect relationships between the investigated variables. Prediction and effects of LPA membership are preliminary and need to be verified by longitudinal studies. Also, the sample was heterogeneous in terms of primary diagnosis, predominantly consisting of patients deemed eligible for an autologous HSCT. The dissimilarity of autologous and allogeneic HSCT, ie, longer hospital stay and a higher risk of complications and mortalities in allogeneic HSCT may affect patients pre-HSCT psychological attitudes. Although to collect a sample size of almost 300 patients before HSCT constituted a significant challenge, larger groups of patients with different types of transplant and diagnosis, as well as group comparisons, should be investigated. Further studies should also take into account the long-term outcomes of the pre-HSCT well-being profiles.

4.2 | Clinical implications

Despite the limitations, our findings cast a new light on the understanding and practical implications of pre-HSCT well-being. As far as well-being is concerned, heterogeneity of the sample indicates the necessity to modify and adjust psychological support and medical procedures to the current functioning of the affected patients, particularly those with little resources (single and medically burdened) and the poorest well-being (our dysfunctional group), as they should receive psychological care and counseling in the first place. Obviously, coping is the most intensified in the latter group at the pre-HSCT stage, which might lead to premature depletion of the resources. Enhancing self-efficacy may be a pivotal point of the interventions.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.