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Quality of Life in Patients with Non-metastatic Breast Cancer: Evolution during Follow-up and Vulnerability Factors

Running head: Vulnerability Factors in Non-metastatic breast cancer and quality of life

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*Declarations

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ABSTRACT : (1) Objective In women with breast cancer, many disease-related psychosocial factors directly affect quality of life (QoL) during and after treatment. The aims of this prospective study were to evaluate the psychosocial factors affecting QoL and its dimensions, to study their evolution over time, and to determine the factors associated with this evolution. **(2) Methods** Thirty women with non-metastatic breast cancer were asked to complete a number of questionnaires evaluating QoL and its dimensions, symptoms of anxiety and depression, body image, social support, and coping strategies immediately after their diagnosis of breast cancer (T1), at the end of treatment (T2) and 6 months after the end of treatment (T3). **(3) Results** Level of education, mastectomy, and hormonotherapy all had an impact on QoL. QoL and its dimensions changed over time. Coping strategies, social support, body image, and symptoms of anxiety and depression were predictive factors for QoL. **(4) Conclusion** The identification of these predictive factors should help medical teams to identify the patients who are most vulnerable and susceptible to poor QoL. In women with breast cancer, it is essential to identify and treat any changes in patients' need for support in an appropriate manner, both during the course of therapy and particularly during remission.

Keywords: Anxiety; Body image; Breast cancer; Depression; Quality of life; Social support

BACKGROUND

The diagnosis of breast cancer is destabilising for women, who are faced with the fear of death, questions about their femininity, and changes in their quality of life (QoL) [1-2]. QoL has been defined as "*an aggregate of representations based on the state of health, physiological state, well-being and satisfaction with life*" [3]. Psychological readjustment (acceptance of new body image, fear of relapse, etc.), along with changes in relationships with others (becoming closer, keeping one's distance, professional adaptation, etc.) should be implemented as needed in each individual case to assure a good QoL [4]. Great variability in these readjustments is observed, which is linked to disease-related psychosocial factors which appear to directly influence the QoL of patients both during and after treatment. Some authors have demonstrated the importance of sociodemographic factors (e.g., age, residential environment, familial or professional situation) [5-7]; treatment-related factors (e.g., type of surgery, use of chemotherapy, hormonotherapy) [8]; time-related factors [9]; factors linked to psychological adaptation (e.g., coping strategies and social support) [10]; and psychological or psychiatric issues (e.g., body image, anxiety, and depression) [11]. An understanding of all these factors is necessary in order to improve the tailored psychosocial support offered to individual patients.

The aim of the current study was to develop a predictive model of QoL in patients with breast cancer, drawn from the transactional, integrative, and multifactorial model proposed by Bruchon-Schweitzer and Dantzer [12] (**Figure 1**). The model posits that two types of elements should be distinguished: (i) predictive factors (i.e., personal and environmental factors that increase vulnerability or promote resilience); and (ii) transactional processes (that is, factors such as perceived stress, control, or even adjustment strategies, accounting for the cognitive, emotional, and behavioural activity of the individual with the disease). These transactional processes have been assumed both to impact differently on QoL, and play a role in mediating or moderating variables. In other words, they have been shown to modify the impact of predictive factors on the variable that we seek to explain. Additionally, we also evaluated the psychosocial determinants of QoL in our patients, studied the changes in QoL over time,

and investigated the factors associated with these changes. We propose specific support adapted to patients with breast cancer which accounts for the above-mentioned vulnerability factors.

This study is original in its investigation of the psychosocial variables contributing to a QoL in a prospective manner. Data on the factors influencing QoL have rarely been collected prospectively in these patients [2]. A better understanding of QoL and its predictive factors is crucial, because while attention and emotional support can be put in place for the most vulnerable women, it is first necessary to identify them as early as possible [11,13-14].

METHODS

Study population

Thirty patients, aged 30-78 years (mean ± SD: 52.1 ± 11.7 years), with early non-metastatic breast cancer, were recruited voluntarily for this study. There were only three exclusion criteria: presence of recognised psychosis, patients in relapse, and presence of metastases.

Tools and procedure

The study was carried out according to the principles and rules laid down in Caverni's code of conduct for investigators and the Declaration of Helsinki [15-16]. The study was started before the Loi Jardé changes (art. L. 1121-1 and R. 1121-1 of the CSP). The study did not seek to develop biological or medical knowledge. All the participants received an information letter and gave their written informed consent before taking part.

The study was longitudinal and prospective. Data were collected at the following three distinct time points. *Time 1* (T1): between the announcement of the diagnosis and the first treatment for breast cancer; *time 2* (T2): at the end of anti-cancer treatments (i.e., surgery, chemotherapy and/or radiotherapy); and *time 3* (T3): 6 months after the end of treatments (T2 + 6 months).

Several scales were used to measure the following variables:

Quality of life (QoL)

To measure QoL, we used FACT-B (Functional Assessment of Cancer Therapy-Breast) [17], based on an initial 27 items derived from FACT-G (General) [18], and 10 breast cancer-specific items. An overall

score for QoL, as well as four partial scores (physical well-being (PWB), familial and social well-being (FSWB), emotional well-being (EWB), and functional well-being (FWB) were obtained. The higher the score, the better the patient's well-being.

Symptoms of anxiety and depression

Symptoms of anxiety and depression were measured using the HADS (Hospital and Depression Scale) [19]. The HADS is composed of 14 items. For the three scores (depression, anxiety, and overall), we used the following threshold values: (i) a score of ≤7 suggested the absence of an anxious or depressive state or of symptoms of anxiety and depression; (ii) a score of between 8 and 10 suggested a possible anxious or depressive state or possible symptoms of anxiety and depression; and (iii) a score of ≥11 suggested a definite anxious or depressive state or definite symptoms of anxiety and depression.

Body image

Body image was measured using the BIQ questionnaire (Body Image Questionnaire) [20]. A total score for satisfaction with body image ranging from 95 (favourable body image) to 19 (unfavourable body image) was obtained by adding up the responses.

Social support

Social support specific to cancer was measured using the QSSS-c (cancer-Specific Social Support Questionnaire) [21]. Four scores were evaluated: (i) emotional social support (ESS), with scores ranging from 9 to 45; (ii) material and distractive social support (MDSS), with scores ranging from 5 to 25; (iii) informative social support (ISS), with scores ranging from 2 to 10; and (iv) negative social support (NSS), with scores ranging from 4 to 20. A high score in each of these dimensions indicated that the individual receives a high level of support from others.

Coping strategies

Coping strategies were measured using the 27-item WCC scale (Ways of Coping Checklist) [22]. Three scores were obtained, relating to: problem-focused coping strategies, emotion-focused coping strategies, and social support-focused coping. A high score indicated a strong use of coping strategies.

Statistical analyses

ANOVA (analysis of variance), Student's *t* test and Linear regression analyses were used.

In all the statistical tests, the threshold of significance was $p<0.05$, but marginally significant effects ($p \leq 0.07$) were also noted. All statistical analyses were carried out using SPSS.22$^{©}$.

RESULTS

Characteristics of the study population

The sociodemographic and clinical characteristics of the study population are shown in **Tables 1a and 1b**. Half of the participants lived in rural areas, and over half have obtained a secondary school certificate. The majority of women were married or in a civil partnership. Half of the patients received adjuvant chemotherapy as treatment.

The QoL of the patients appeared to be relatively good at inclusion (mean ± SD score: 89.3 ± 23.9 out of 148).

Role of sociodemographic factors, clinical variables, and time

The complete results relative to this section are summarised in **Figures 2a to 2d** and **Table 2**. Here, we only offer the main details of our analyses.

Level of education was observed to have a significant impact on QoL. Indeed, patients with a secondary school certificate had a global QoL that increased in the period from diagnosis to 6 months after the end of the treatments. FSWB decreased after treatment in patients who had undergone a mastectomy. Patients receiving hormonotherapy had a lower PWB than those who were not taking hormones. However, in patients who were not taking hormonotherapy, FWB decreased after treatment. Finally, in the period from the diagnosis to 6 months after the end of the treatments, global QoL, EWB and FWB increased; in contrast, FSWB decreased.

Role of transactional variables

The complete results relative to this section are summarised in **Table 3**. Here, we only offer the main details of our analyses.

Emotion-focused coping was a predictive factor for a poorer QoL and low EWB at diagnosis. It also tended to predict a poorer QoL and lower EWB after the end of the treatments, and QoL and EWB

appeared again as reliable predictors at 6 months after the end of the treatments. The same was true for FSWB and FWB at diagnosis, in that the more the patients used emotion-focused coping strategies, the less their FSWB scores increased. Seeking social support-focused coping appeared to be a predictive factor for high FSWB at diagnosis. At 6 months after the end of the treatments, this was marginal for FSWB and FWB. Problem-focused coping appeared to be a predictive factor for high EWB at diagnosis and good QoL, high FSWB, and high FWB after the end of the treatments.

NSS was a predictive factor for poor QoL at T3 and low FSWB after the end of the treatments, and the results persisted at 6 months after the end of the treatments. Emotional social support was a predictive factor for good QoL 6 months after the end of the treatments.

From the diagnosis to 6 months after the end of the treatments, depression was a predictive factor for a poor QoL, low PWB, and low FSWB as well as low EWB and low FWB at diagnosis; and low FWB at 6 months after the end of the treatments. Anxiety was a predictive factor for low EWB at diagnosis and 6 months after the end of the treatments. Body image was, or tended to be, a predictive factor for good QoL and high FWB at the end of the treatments as well as for high FWB at 6 months after the end of the treatments.

DISCUSSION

The aims of this study, which was carried out in a sample of women with non-metastatic breast cancer, were threefold: to evaluate the psychosocial factors relating to QoL; to study the changes in these factors over time; and to investigate the factors associated with these changes.

Our results showed a significant effect of level of education on QoL over time. Patients in our study who had a secondary school certificate reported a QoL which improved between diagnosis and 6 months after the end of treatments. These results concur with those in the literature that level of education is protective of QoL represents a variable of psychological adjustment [23] and is associated with the development of a new way of looking at life [24]. It also suggests that individuals with a higher level of education are more able to question their doctor and to better understand the information given, and also to look for additional information themselves. As a result, they have a more realistic view of the

treatments and their long-term side-effects, and consequently have fewer disappointments or surprises [23].

We also found that the FSWB of patients who underwent a mastectomy decreased between the end of treatment and the 6-month follow-up. This was independent of the presence (or otherwise) of breast reconstruction. Mastectomy is associated with a poorer body image [7] and therefore individuals consider themselves less physically attractive. These results concur with those in the literature [25-26]. Particular attention should be paid to couples in whom a woman undergoes a mastectomy.

In our study, patients receiving hormonotherapy had a lower PWB than patients without hormonotherapy. Hormonotherapy can lead to early menopause, or to more severe symptoms associated with the menopause (hot flushes, sweating, fatigue, loss of libido, etc.) [27]. It can be hypothesised that the emergence of these symptoms may negatively affect the PWB of patients. The literature has shown that there was no significant correlation between hormonotherapy and the physical, social, emotional, and functional domains of QoL [7-8]. However, the impact of hormonotherapy on QoL was related to the type of treatment received [27]. Patients treated with aromatase inhibitors will present with fewer symptoms and better functioning than patients treated with tamoxifen. Another surprising result in our study was that the PWB of patients without hormonotherapy decreased immediately after treatment and 6 months after. No study in the prior literature has explained this effect. It is possible that taking hormonotherapy reduces the functional consequences of the disease and its treatments by justifying fatigue, for example. Patients on hormonotherapy receive more help in the house because they are still considered to be receiving treatment, in contrast to patients who are not receiving hormonotherapy [8].

Our results showed a moderate evolution of QoL, EWB, and FWB between the diagnosis and the post-treatment 6-month follow-up, as well as a decrease in FSWB. Several previous studies have reported contradictory results [2,13-14]. This variation can be explained by the persistence, in some patients, of physical and psychological problems for several months after the end of treatment (persistent side-effects, poor body image). It could also be linked to the way in which QoL has been measured [28]. The decrease in FSWB over time found in the present study supports previous studies demonstrating the difficulties encountered by patients within their social and family circles (in relation to the pursuit of

satisfaction of individual needs, adaptation to a change in role and way of life, the management of uncertainty, etc.) [29]. When fear of the disease becomes more distant and life returns to normal, the focus of the family on the disease changes to distancing. It is also possible that awareness following the diagnosis and experience of the disease leads patients to question a number of factors, notably their relationship with their partner and the place in their life of certain friends [29]. Support is necessary to help women and their partners resume their activities and roles [30].

Concerning the coping strategies used by the patients in our study, we found that emotion-focused coping appeared to be a predictive factor for low FSWB and FWB at diagnosis. These strategies also resulted in a poorer overall QoL and low EWB from diagnosis through to 6 months after the end of treatment. Emotion-focused coping may take diverse forms of expression (repression/avoidance of emotions, helplessness/hopelessness, denial, fatalism, etc.). The literature has shown that avoidance after diagnosis was accompanied by a decrease in physical, mental, and social QoL, and that avoidance decreased the meaning of a patient's life [10]. In individuals with cancer, the belief that one's life has meaning is strongly correlated with QoL [31]. Conversely, problem-focused coping appeared to be a predictive factor for high EWB at diagnosis, along with good QoL and high FSWB and FWB after treatment. These results are in line with those in the literature, which have shown that problem-focused coping is salutogenic in relation to overall QoL [32]. Finally, seeking social support-focused coping appeared to be predictive of high FSWB both at diagnosis and 6 months after the end of treatment, as well as high FWB 6 months after the end of treatment. The salutogenic side of seeking social support-focused coping will to a great extent depend on the environment of the individual patient [33]; in other words, the search for social support will only be beneficial if the environment of the patient is receptive and tuned in. Emotion-focused coping interacts with the receptivity of the patient's entourage. Thus, in women who can count on their close ones to talk freely about their cancer, emotion-focused coping will increase QoL, whereas in women whose entourage is not receptive, emotional expression is not linked to QoL [33].

The literature demonstrates that the type of support given (emotional, material, etc.) should be appropriate to the nature of the stress (controllable or not), the source of support (medical, familial, etc.),

the time of the intervention (in the acute phase of stress or after) [34], and also with the expectations of the patient [35]. Alignment between the nature of support wished for and that which is received is important [34-35]. In our study, NSS was predictive of low FSWB after treatment and poor QoL both after treatment and 6 months later. NSS represents all unwanted supporting behaviours (e.g., support that invites the person to be optimistic is often badly received by patients, particularly at the time of diagnosis and cancer treatments). NSS may generate feelings of vulnerability, helplessness, incompetence, and loss of freedom, autonomy and control, and may also affect the individual's ability to face up to the situation [36]. After treatment or the start of remission can be a particularly difficult period for patients [4]. Their entourage often associates the end of treatment with the end of the disease, at which point they distance themselves from the patient. This distancing may be perceived as negative support which could act directly and negatively on the FSWB of patients (communication problems, changes in interpersonal relationships, distancing/over protection, etc.) and on FWB (decrease in daily physical and material help, etc.). The results of our study also demonstrate that ESS is a predictive factor for good QoL 6 months after the end of treatment. This type of social support will be more beneficial and more comforting during an uncontrollable event and during an acute phase of illness [17]. Emotional support (e.g., the presence and daily attentions of the patient's close family and friends via telephone calls, visits, invitations, etc., encouragement, sharing information on the history of the disease and the changes induced, and so on) attenuates the effects of stress to which patients are subjected, and improves mental well-being [37]. In order to facilitate the adaptation of patients during the post-treatment period, efforts should be made to understand and respond to their support needs during the entire cancer experience, particularly when the treatments are finished.

The results of our study demonstrate that depression is a predictive factor for a poorer QoL, low PWB, and low FSWB, both at diagnosis and 6 months after the end of treatment. It is also a predictive factor for low EWB at the time of diagnosis, as well as low FWB both at the time of diagnosis and 6 months after the end of treatment. These results support those in the literature [11]. Anxiety also appeared to be a predictive factor for low EWB both at the time of diagnosis and 6 months after the end of treatment. These two periods are times of waiting and uncertainty (expectations of treatment, of the

first check-up mammogram, fear of relapse, etc.) which can prove to be as testing for the patient as diagnosis of the disease itself [1,4,38]. The evaluation of symptoms of anxiety and depression is necessary throughout the entirety of the care pathway, particularly during the post-treatment period. Finally, body image appears to be a predictor of good QoL after treatment, and high FWB both after treatment and 6 months later. Body image is an important component of QoL in women with breast cancer [6,39]. The ability to be able to carry out some tasks (work, enjoying life in general, appreciating hobbies, etc.) appears to depend on how patients perceive their body image, and may explain the impact on FWB of patients in our study. Specific support to work on body image (e.g., socio-aesthetics [40]) should therefore be implemented as early as possible.

Study Limitations

Our study has several limitations. First, the generalisability of our results is limited since our sample was relatively small and recruitment was limited to a single centre. A multicentre study could be proposed to control for the bias attributed to inter-establishment differences in management, in case these differences directly influence the QoL of patients. It also would be interesting to explore the evolution of variables over a longer follow-up period of 2–5 years, particularly as we showed an effect of time elapsed since diagnosis on QoL. The study sample is not representative of the usual breast cancer population. Indeed, the study is composed the half of patient with mastectomy. Therefore, some caution is needed when interpreting our results. Finally, while the use of mixed methodology has many positive aspects, carrying out a longitudinal study takes time and limits the number of recruited patients. This was a pilot study; the results we have obtained encourage us to continue the initial study, taking into account its present limitations.

Clinical Implications and recommendations

With regard to the clinical implications of this study, the results lead us to propose a number of recommendations, which are as follows. (i) The most vulnerable patients should be identified by assessing their level of education and level of anxiety and depression, both during treatment and up to 6 months after the end of treatment. These patients could, for example, receive closer paramedical follow-up by a coordinating nurse; (ii) support should be adapted to each couple (in sexology, for example),

particularly when women with breast cancer have had a mastectomy; (iii) psychological consultations should be offered in the months following the end of treatment in order to assure ESS in this post-cancer phase; and (iv) the services of a socio-aesthetician should be integrated as early as possible after the diagnosis to overcome the problems of body image.

CONCLUSION

This study investigated the variability in QoL of women with non-metastatic breast cancer using an integrative and multifactorial model [12]. The demonstration of the direct effects of some factors on QoL and its dimensions should help teams to identify vulnerable patients who are at the greatest risk of poor QoL. It is essential to identify, propose, and address their changes in needs in order to support patients with breast cancer in an appropriate manner during the course of their disease, particularly after treatment has ended and during remission.

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Table 1a. Sociodemographic and clinical characteristics of the study population

Characteristic	N (%)
Residential environment	
Rural	15 (50.0)
Urban	15 (50.0)
Level of education	
< Secondary school certificate	13 (43.4)
≥ Secondary school certificate	17 (56.7)
Familial situation	
Married or civil partnership	19 (63.3)
Widowed	2 (6.7)
Cohabiting	5 (16.7)
Divorced	4 (13.3)
First treatment received	
Surgery	28 (93.3)
Chemotherapy neo adjuvant	2 (6.7)
Nature of surgery	
Lumpectomy	14 (46.7)

Mastectomy	16 (53.3)
Second treatment received	
None	5 (16.7)
Chemotherapy	15 (50.0)
Radiotherapy	9 (30.0)
Hormonotherapy	1 (3.3)
Third treatment received	
None	8 (26.7)
Radiotherapy	15 (50.0)
Hormonotherapy	7 (23.3)
Breast reconstruction	
Yes	11 (36.7)
No	19 (63.3)
Sequelae after treatment	
None	4 (13.3)
Pain	14 (46.6)
Fatigue	8 (26.7)
Physical limitations	1 (3.3)
Other	3 (10.0)

Table 1b. Type of adjuvant treatment after lumpectomy or mastectomy

	Chimiotherapy and radiotherapy and hormonotherapy N (%)	Radiotherapy and hormonotherapy N (%)	Hormonotherapy only N (%)	Chimiotherapy and radiotherapy N (%)	Radiotherapy only N (%)	No additional treatment N (%)
Lumpectomy	4 (28.6)	6 (42.8)	1 (7.1)	7 (50.0)	0 (0.0)	0 (0.0)
Mastectomy	7 (43.7)	1 (6.2)	11 (6.2)	0 (0.0)	3 (18.7)	5 (31.2)

Table 2. Effect of time on quality of life (QoL) and its dimensions

	T1 (mean ± SD)	T2 (mean ± SD)	T3 (mean ± SD)	F	p	η^2
QoL	89.3 ± 23.9	94.3 ± 17.7	99.7 ± 17.5	5.64	**	0.16
FSWB	19.2 ± 5.8	17.9 ± 6.4	17.3 ± 5.8	3.18	*	0.10
FWB	15.2 ± 6.7	16.6 ± 5.5	17.1 ± 5.1	5.06	**	0.15
EWB	13.9 ± 6.3	16.2 ± 4.9	17.7 ± 4.0	10.23	***	0.26

Legend. QoL: quality of life; FSWB: familial and social well-being; FWB: functional well-being; EWB: emotional well-being; T1: post-diagnosis; T2: after treatment; T3: T2 + 6 months; F: Fisher's ANOVA; η^2 = eta² or correlation relationship: a value between 0.010 and 0.059 corresponds to a weak effect, a value between 0.06 and 0.138 to a moderate effect, and a value >0.138 means that the effect is strong; $*p \leq 0.05$; $**p \leq 0.01$; $***p \leq 0.001$.

Table 3. Effects of coping strategies, social support, and psychological factors (depression, anxiety, body image) on quality of life (QoL) and its dimensions

Predicted construct	Set of variables	Individual predictors	T1 R^2	T1 β	T2 R^2	T2 β	T3 R^2	T3 β
QoL	Coping s.	Problem-focused		--		.52 **		--
		Emotion-focused	.46 ***	-.72 ***	.45 ***	-.31 *	.41 ***	-.51 *
		SS-focused		--		--		--
	Social s.	ESS						--
		MDSS	ns.		ns.		.20 *	--
		ISS						--
		NSS						-.52 **
	Psychol. factors	Anxiety		--		--		--
		Depression	.68 ***	-.59 **	.45 ***	-.50 **	.54 ***	-.71 **
		Body image		--		.32 #		--

Predicted construct	Set of variables	Individual predictors	T1 R^2	T1 β	T2 R^2	T2 β	T3 R^2	T3 β
PWB	Coping s.		ns.		ns.		ns.	
	Social s.		ns.		ns.		ns.	
	Psychol. factors	Anxiety		--		--		--
		Depression	.23 *	-.59 **	.19 *	-.62 **	.22 *	-.67 **
		Body image		--		--		--

Predicted construct	Set of variables	Individual predictors	T1 R^2	T1 β	T2 R^2	T2 β	T3 R^2	T3 β
FSWB	Coping s.	Problem-focused		--		.64 ***		--
		Emotion-focused	.18 *	-.34 #	.45 ***	--	.17 #	--
		SS-focused		--		--		.45 #
	Social s.	ESS				.52 **		.53 **
		MDSS	ns.		.41 ***	--	.42 ***	--
		ISS				--		--
		NSS				-.39 *		-.36 *
	Psychol. factors	Anxiety		--		--		--
		Depression	.16 *	-.52 *	.24 *	-.48 *	.30 **	-.63 **
		Body image		--		--		--

Predicted construct	Set of variables	Individual predictors	T1 R^2	T1 β	T2 R^2	T2 β	T3 R^2	T3 β
EWB	Coping s.	Problem-focused		.38 ***		--		--
		Emotion-focused	.77 ***	-.69 ***	.32 **	-.37 *	.39 ***	-.49 **
		SS-focused		--		--		--
	Social s.		ns.		ns.		ns.	
	Psychol. factors	Anxiety		-.51 ***				-.54 **
		Depression	.68 ***	-.40 **	ns.		.36 **	--
		Body image		--				--

Predicted construct	Set of variables	Individual predictors	T1 R^2	T1 β	T2 R^2	T2 β	T3 R^2	T3 β
FWB	Coping s.	Problem-focused		--		.40 *		--
		Emotion-focused	.16 #	-.49 **	.22 *	--	.27 **	--
		SS-focused		--		--		.40 #
	Social s.		ns.		ns.		ns.	
	Psychol. factors	Anxiety		--		--		--
		Depression	.40 ***	-.71 ***	.32 **	--	.60 ***	-.47 **
		Body image		--		.48 *		.51 **

*Legend. Coping s: coping strategies; Social s: social support; Psychol factors: psychological factors; SS-focused: social support focused-coping; ESS: emotional social support; MDSS: material and distractive social support; ISS: informative social support; NSS: negative social support; "R²" - adjusted R²; "beta" - standardized coefficients; # - p < .10; * - p < .05; ** - p < .01; *** - p < .001.*