Testing age as a moderator of the relationship between depression and healthy functioning in breast and gynecologic cancer patients

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This cross-sectional study aims to explore age as a moderator of the association between emotional distress and functional scales of health-related quality of life. The sample includes 106 outpatients with active breast and gynecologic cancers recruited at the Gynecology Department of the Instituto Português de Oncologia de Coimbra Francisco Gentil. Cancer patients were divided into two groups: younger women <50 years and older women ≥50 years. Participants completed a socio-demographic questionnaire and self-report measures, namely Hospital Anxiety Depression Scale (HADS) and the six functional scales of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30). Our results show that the older group reported higher depressive symptoms than younger patients. Depressive symptoms influenced healthy functioning, defined by indicators such as physical, emotional and cognitive functioning, similarly in younger and older age groups.

Key words: Age, Functioning, Depression, Gynecologic cancer, Breast cancer.

Cancer is a serious public health problem and according to GLOBOCAN 2012 breast cancer was the most frequent malignancy diagnosed among women in Europe (28.3%); corpus uteri cancer was the gynecologic cancer type presenting the highest crude rate per 100.00 (13.6), followed by cervix uteri cancer (11.2) and ovary cancer (9.4) (Ferlay et al., 2013). With scientific and technological advances in early detection and treatment improving survival time results (Sant et al., 2001), concentrating on understanding behavior outcomes associated with cancer is increasingly important (Bower, 2008).

Cancer patients are forced to change their routine and habits and worry about the progression and/or recurrence of the disease (Baker, Denniston, Smith, & West, 2005), and significant psychological adjustment is required. Emotional distress, namely depressive and anxiety symptoms (Cardoso, Graca, Klut, Trancas, & Papoila, 2015), and the loss of health-related quality of life (HRQOL) are common among female cancer patients as a reaction to diagnosis, treatment and the physical consequences (Carter, Stabile, Gunn, & Sonoda, 2013) and may endure even in

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long-term survival (Bradley, Rose, Lutgendorf, Costanzo, & Anderson, 2006). However, there is variability in these patients' emotional reaction related to exogenous variables such as age (Costanzo, Ryff, & Singer, 2009), occupational status and size of collateral effects (Gõmez-Campelo, Bragado-Álvarez, & Hernández-Lloreda, 2014).

Age has been the most explored socio-demographic characteristic in studies with cancer samples and the research by Jadoon, Munir, Shanzad and Choudhry (2010) showed that at a younger age there is a higher risk of psychological morbidity. 50 years of age is the cut-off point most used to define younger or older age groups in this setting. Specifically, female cancer patients younger than 50 seem to present more depressive symptoms than the older group (Gõmez-Campelo et al., 2014). In contrast, in other cancer samples there seems to be a tendency for depression to increase with age (Nelson et al., 2009).

In HRQOL, age-related differences are also reported, but here, Park, Lee, Lee, Lee and Hwang (2011), considering a sample of 1094 breast cancer patients, found a worse perceived quality of life in women over 50. In their recent study, Quinten et al. (2015) added that the domains of HRQOL affected vary with age, that is: older groups can present deteriorated physical functioning and better social functioning than younger groups, for example. Despite this, distress and HRQOL are not independent constructs (McMillan & Small, 2002) and the role of age in this relationship should also be tested. Consensual in the literature is the negative relationship between functional scales of HRQOL and distress, particularly depression symptoms (Montazeri, 2008; Reyes-Gibby, Anderson, Morrow, Shete, & Hassan, 2012) in oncological samples. Costa-Requena, Rodríguez and Fernández-Ortega (2013) concluded that, mainly after oncological treatment, psychological distress accounts for 62.6% of the variance in HRQOL.

Based on these findings, we examined the anxiety and depression symptoms and functionality of two groups of cancer patients: women younger and older than 50. Firstly we aimed to compare the two groups regarding depression, anxiety and physical, role, emotional, cognitive and social functioning. Second, we aimed to test the model shown in Figure 1 to evaluate the moderating effect of age in the association between emotional distress and healthy functioning of women with active cancer. Thus, we defined our hypothesis as follows:

– Younger women <50 years will present greater anxiety and depression and worse results in functional scales of the HRQOL than older cancer patients;

– Anxiety and depression symptoms will be associated with worse functioning of cancer patients;

– Age group will moderate this relationship between anxiety and depression symptoms and functioning in these patients.
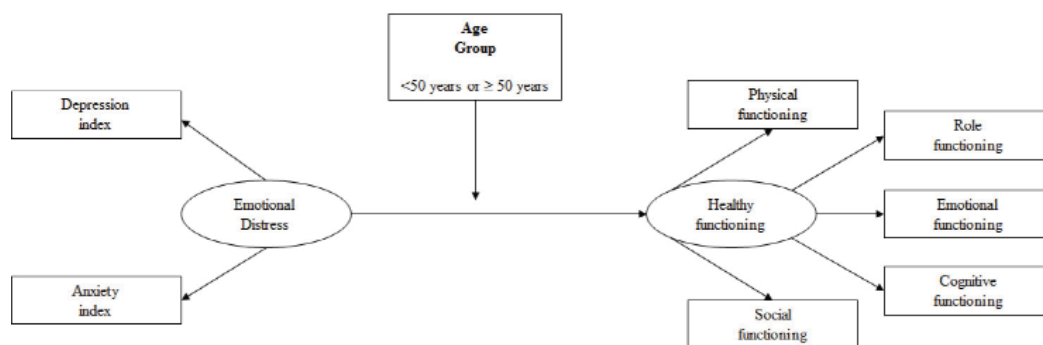

Figure 1. Proposed model

Materials and methods

Participants and procedures

The sample of this cross-sectional study was collected at the Gynecology Department of the Instituto Português de Oncologia de Coimbra Francisco Gentil. The study was first presented and approved by the Ethics Committee of the Institute. The participants were recruited, in person, at the time of external appointments in the Gynecology Unit. Informed consent was signed and self-report measures were completed. The sample included women with breast and gynecologic cancers followed up as outpatients. Among the 153 women contacted only 106 participated in our study. The inclusion criteria were: (i) active phase of the disease; (ii) 18 or older; and (iii) not having any addictive or severe psychiatric disorders. The cancer patients belonged to two age groups, <50 years (34.9%) and ≥50 years (65.1%). We found that most subjects were married (74.5%) and/or living with family (55.7%). Regarding educational status, 57.5% had completed basic education and 17.9% a college degree. Within cancer types, 64.2% were diagnosed with breast cancer and 35.8% had gynecologic cancer, that is: 14.2% cervical cancer, 8.5% endometrial cancer and 2.8% ovarian cancer. Only a small part of this sample (25.5%) had a family history of cancer. 83.1% of these patients underwent surgery and 68.9% had adjuvant therapy. Among the participants, 13.2% had, at some stage of their life, psychological counseling motivated by depressive symptoms (6.6%) and/or anxiety (22.6%). The socio-demographic and clinical characteristics were balanced between the two age groups, except for the level of education. Women younger than 50 tended to be educated up to college degrees ($p<.001$).

Measures

A socio-demographic and clinical questionnaire was used. The measurements were composed of eight items related to socio-demographic characteristics (e.g., age, civil status, nationality, education, household, etc.) and seven items with questions about clinical variables (e.g., type of cancer, family history, treatment type, previous psychological counseling, etc.).

Levels of emotional distress in breast and gynecologic cancer were assessed using the *Portuguese version of the Hospital Anxiety Depression Scale* (HADS; Zigmond & Snaith, 1983; Portuguese version by Pais-Ribeiro et al., 2007). It is a 14-item scale consisting of two sub-scales for the assessment of anxiety (HADS-A) and depression (HADS-D), both with seven items. The cancer patients were instructed to self-report their symptoms on a 4-point scale (0-3). Total scores range from 0 to 21 for each sub-scale. High scores in these sub-scales relate to more severe symptoms. In this sample, satisfactory internal consistence was obtained. The Cronbach's alpha coefficient was .72 for anxiety and .84 for depression.

Healthy functioning in the cancer patients was assessed using the five functional scales of the *Portuguese version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30* (EORTC QLQ-C30, Aaronson et al., 1993; Portuguese version by Pais-Ribeiro, Pinto, & Santos, 2008), namely physical functioning, role functioning, emotional functioning, cognitive functioning and social functioning. Participants were asked to rate the items on a 4-point scale (1-4), ranging from "not at all" to "very much". High scores for functional scales of HRQOL represent healthier functioning. The Cronbach alpha value in our sample ranged between .92 for the role functioning sub-scale and .70 for the social functioning sub-scale.

Statistical analysis

The Statistical Package for the Social Sciences, version 20 (SPSS Inc., Chicago) was used to perform descriptive and inferential statistics. The t-student test for independent samples was

conducted to determine whether there were age-related differences in depression and anxiety symptoms and functional scales. As a preliminary analysis, bivariate correlations were obtained to examine the associations between anxiety, depression and functional scales of HRQOL within each age group. Based on these results, a structural equation modeling (SEM) with maximum likelihood estimation method using AMOS, version 24, was implemented to test the moderation model. This technique allowed structuring the model with latent and single-indicator variables, that is: functional scales of HRQOL were specified as a single latent variable named for healthy functioning; and the depression index (HADS-D scores) was introduced as a single-indicator. The direct effect between depression and healthy functioning was tested. To determine whether the overall model presented a good fit, the following criteria were used: (i) chi-square (χ^2) value close to zero and non-significant; (ii) the comparative fit index (CFI) value equal to or greater than .95; and (iii) the Root Mean Square Error of Approximation (RMSEA) value of .06 or less (Hu & Bentler, 1999). In addition, for a mediocre fit, RMSEA in the range of .08 to 0.1 was accepted (MacCallum, Browne, & Sugawara, 1996). Multi-group modeling was used to evaluate the role of age-groups as moderators. Separate models for <50 years and ≥50 years groups were specified simultaneously, and unconstrained and equality constrained models were compared. More specifically, differences between χ^2 indicated whether the models were non-invariant for the two age groups.

Results

Descriptive results

Results indicate that the ≥50 years group presented higher scores in HADS-D than the younger group as shown in Table 1. Bivariate analysis for the two age groups showed that in both groups, depression was associated with functional scales such as physical functioning, emotional functioning and cognitive functioning. In the ≥50 years group, but not in the younger group, a strong association was found between depression and the role functioning scale. In the <50 years group, anxiety was only associated with emotional functioning. Regarding the older age group, this variable was associated with physical functioning, role functioning, emotional functioning and cognitive functioning. All functional scales were inter-correlated in both groups (r>.40, p<.01), with the exception of the social functioning scale, which was not associated with physical functioning in the ≥50 years group (see Table 1).

Table 1

Summary of the descriptive results

Variable	<50 years M(DP)	≥50 years M(DP)	t-value	1.	2.	3.	4.	5.	6.	7.
1. Depression	4.19(4.19)	6.68(4.15)	-2.94**	-	.551***	-.489***	-.577***	-.623***	-.399**	-.132
2. Anxiety	8.54(3.85)	8.48(3.91)	.079	.721***	-	-.265*	-.350**	-.669***	-.254*	-.057
3. Physical functioning	79.01(16.8)	74.40(18.35)	1.30	-.387*	-.190	-	.559***	.470***	.478***	.029
4. Role functioning	79.73(23.94)	70.53(30.00)	1.61	-2.47	-.109	.729***	-	.674***	.542***	.247*
5. Emotional functioning	61.26(27.37)	61.96(25.98)	-.13	-.548***	-.479**	.469**	.446**	-	.627***	.301*
6. Cognitive functioning	66.67(27.78)	68.60(25.65)	-.36	-.370*	-.182	.622***	.661***	.715***	-	.411**
7. Social functioning	71.62(28.56)	81.64(25.11)	-1.87	-.441*	-.261	.344*	.354*	.741***	.729***	-

Note. <50 years below of the diagonal and ≥50 years above of the diagonal. *p<.05; ** p<.01; ***p<.001.

Testing moderating effect of age group

Based on preliminary analysis, a path model, shown in Figure 2, was elaborated. In this model, the anxiety index was not included as a single-indicator because these symptoms were not associated with all functional scales in the <50 years group. Nor were social and role functioning considered in the tested model because these variables did not show a direct association with depression in either group. As there were differences between the age groups regarding level of education, the effect of this variable was controlled. Thus, the depression index was represented by a single indicator (HADS-D total score) and physical, emotional and cognitive functioning were specified as indicators of the single latent variable designated by healthy functioning, as referred to in the statistical analysis section. The direct effect between depression and healthy functioning was tested and multi-group modeling was used to evaluate age group differences. The chi-square was not significant [$\chi^2_{(8)}$=14.96, p=.06] and additional fit indexes (CFI=.95, RMSEA=.09) showed an acceptable fit of the baseline model (unconstrained). Standardized parameters by age groups are presented in Figure 3. A significant direct effect was found between depression and the healthy functioning latent variable for the two groups. Thus, depression was shown to be a significant predictor of less healthy functioning.
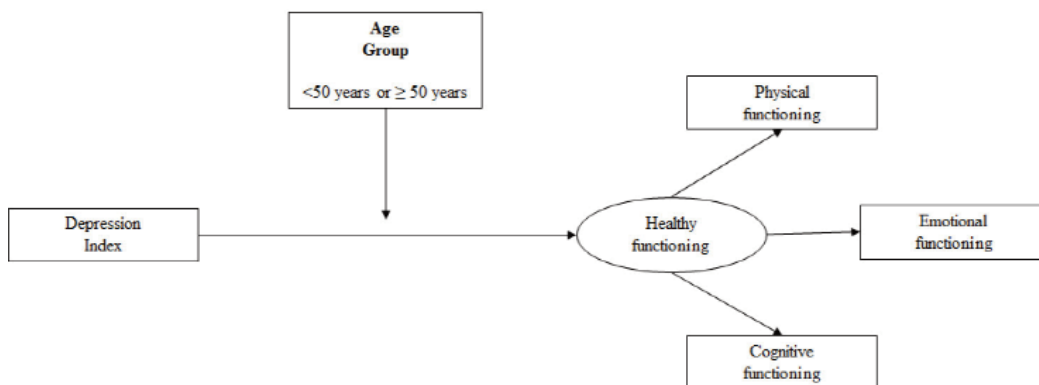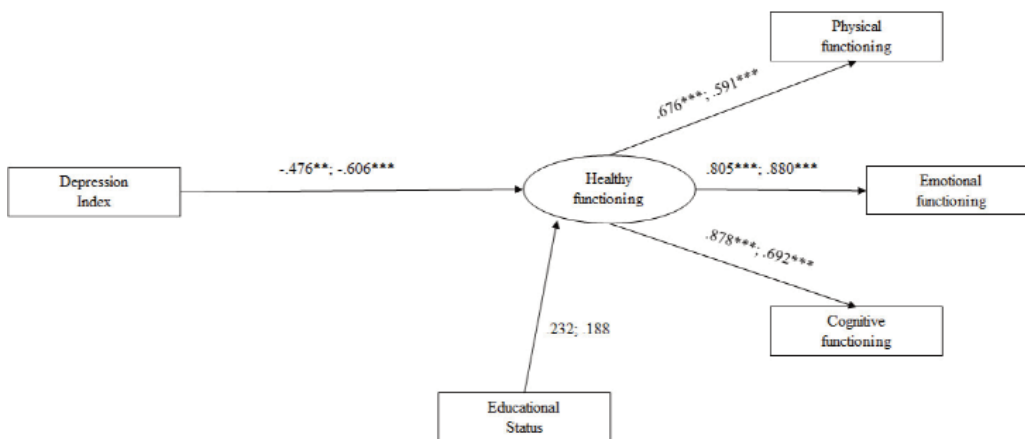

Figure 2. Testing model

Figure 3. Standardized parameters for younger or older women
Note. Values for <50 years group are presented first. ***p<.001; ** p<.01.

Considering the equally constrained model on the paths from depression symptoms to healthy functioning, the model fit was invariant for women <50 years and ≥50 years. The fit indexes were slightly better [$\chi^2_{(12)}$=16.97, p=.151; CFI=.97; RMSEA=.06] in the equality constrained model, but the difference between models was not significant [$\chi^2_{(4)}$=2.01, p>.05] indicating that age group did not moderate this relationship. However, for women <50 years, the model accounted for 32% (.324) of variance in healthy functioning and for women ≥50 years 51% (.513) of variance of this predictive variable.

Discussion

In this cross-sectional study, one path model using SEM was proposed. Our main objective was to examine the direct effect of emotional distress on the functioning of cancer patients in an active phase of the disease and the moderator role of age in this relationship. An empirical model including only depression symptoms provided a good fit with the data, suggesting that this contextual approach was valid.

More specifically, our study presented three hypotheses that were only partially confirmed:

Our first hypothesis focused on age-related differences in the distress and functional scales of HRQOL was not supported. Globally, younger cancer patients presented similar psychosocial outcomes to the women ≥50 years. However, contradicting other research (Costanzo et al., 2009; Gomez-Campelo et al., 2014; Jaddon et al., 2010), the older age group ≥50 years, and not the younger women, reported higher scores on the depression index.

Considering that depressive symptoms are relatively common in aging (Fiske, Wetherell, & Gatz, 2009) the above results are not a surprise. A recent study by Leach, Bellizzi, Hurria and Reeve (2016) shows that having cancer increased the risk of depression in a sample of older adults. The diagnosis, by itself, is emotionally demanding (Hong, Zhang, Song, Xie, & Wang, 2015) combining at this stage of the life cycle with physical vulnerabilities (Leach, Bellizzi, Hurria, & Reeve, 2016), reduced life-expectancy and poor support (Schapmire & Faul, in press) frequent in the aging process. These patients are exposed to a double risk of suffering from depressive symptoms presenting specific concerns namely with the loss of autonomy (Hurria et al., 2009). All these factors may overload the coping mechanisms of older cancer patients resulting in significant depressive symptoms. Thus, although younger patients appear in the literature as more distressed (Krok, Baker, & MacMillan, 2013), there may be a unique tendency for the increase of depressive symptoms in response to the disease in older patients, as suggested by Nelson et al. (2009).

At the same time, the menopause as a natural process occurs in the 50s. The associated hormonal imbalance may contribute to the presence of more depressive symptoms in older adults. A longitudinal study by Bromberger et al. (2007), using a sample of 3302 women, illustrates this even when reporting the increased risk of high depressive symptoms with the start of the transition to the menopause and their association with the menopausal condition over time. Nevertheless, as shown in the review by Rosenberg and Partridge (2013), some younger women also face physical and emotional challenges of the menopause earlier than would otherwise be expected as a result of cancer and its treatment and this question cannot be disregarded when evaluating this group.

To test our second and third hypotheses, we conducted a preliminary correlational analysis and it was necessary to adjust the hypothesized overall model. When we analyze the relationship between emotional distress and functional scales of HRQOL, we found that anxiety was not associated with most of the scales in the <50 years group and was therefore not included in the

model. This is in line with the literature that reports, more recurrently, associations between depression and quality of life (Montazeri, 2008) within this setting.

We also verified that not all functional scales showed a significant association with depression in both groups, for example: depression was negatively associated with role functioning in the older group, but not for the <50 years group; and a negative relationship between depression and social functioning was found in the younger group, but not in the ≥50 years group. This result seemed to point to some age-specific variations in the relationship between depression and HRQOL, which should be explored later. However, the association between depression and functional indicators such as cognitive, emotional and physical functioning was consensual in both groups. Based on the result of this analysis, the tested model explored the unique effect of depression on a latent variable integrating the three functional scales.

With the framework tested, our most important finding was that healthy functioning was impacted by depression, partially confirming our second hypothesis. However, age group did not moderate this relationship as predicted in our third hypothesis. The strongest associations between depression and functioning for the ≥50 years group were not retained in SEM. The comparison between unconstrained and equality constrained models did not confirm a significant improvement or deterioration in model fit. Thus, the direct effect of depression on the latent variable shown in other studies (Costa-Requena et al., 2013; McMillan & Small, 2002) seems to endure independently of age groups.

Lastly, the overall model shows a higher percentage of variance in healthy functioning encompassing cognitive, emotional and physical functioning (51%) in breast and gynecological cancer patients ≥50 years in comparison with the younger group. This fact reinforces the disabling role of depressive symptoms in this age group.

It should not be forgotten that the manifestation of depressive symptoms in older adults differs from younger ages. Older people are more likely to show somatic and cognitive symptoms of depression (Fiske et al., 2009) that may explain its greater predictive effect on perceived impairment of healthy functioning in our cancer patients. It remains to be seen whether other variables influence the functional scales of the HRQOL, especially in the younger group in which 68% of the variance is yet to be explained. In particular, concerns about reproductive issues and parental projects are additional factors of wear that have been shown to undermine the dimensions of quality of life (Wenzel et al., 2005) and may be an element to be explored in future studies with this age group.

Our research should be interpreted with caution since we conducted a cross-sectional study with a small sample. Thus, it is not possible to determine causal relationships between variables, and generalization of the results to other samples with different characteristics is limited. In addition, the effect of differences in the level of education between the age groups was not controlled for the test of the first hypothesis proposed. For this reason, the results regarding depressive symptoms may have been influenced by this factor. In the tested model, we considered a single effect of age, but controlling for the level of education. However, other age-related aspects and clinical characteristics may also lie at the basis of variations in the reaction to cancer, including cancer type and stage, previous treatment and the collateral effects of cancer, namely reproductive consequences (Gorman, Malcarne, Roesch, Madlensky, & Pierce, 2010).

Further research should be concerned with testing other contextual approaches that explain impairment in overall quality of life, but this time, within each age group during the active phase of the disease and long-term survival. Depression should be an element to consider in future approaches, which in our study was shown to affect the functioning of both age groups, as well as specific concerns for each chronological age. Summarizing, we also emphasize the need to develop and adjust intervention programs focused on decreasing depressive symptoms for breast

and gynecologic cancer patients in order to enhance their quality of life and this is common to women <50 years and ≥50 years.

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Será a idade um moderador da relação entre depressão e funcionamento saudável em pacientes com cancro da mama e ginecológico?

Este estudo transversal objetivou explorar o efeito moderador da idade na relação entre o *distress* emocional e domínios da qualidade de vida relacionada com a saúde. A amostra incluiu 106 mulheres, com diagnóstico de cancro da mama ou ginecológico em fase ativa, recrutadas no Serviço de Ginecologia do Instituto Português de Oncologia de Coimbra Francisco Gentil. Foram incluídos dois grupos: mulheres com menos de 50 anos de idade e mulheres com 50 anos ou mais. As participantes completaram um questionário sociodemográfico e medidas de auto-relato, nomeadamente a Escala de Ansiedade e Depressão Hospitalar (EADH) e as seis escalas funcionais do *European Organization for Research and Treatment of Cancer Quality of Life Questionnaire* Core-30 (EORTC QLQ-C30). Os nossos resultados mostraram que o grupo de mulheres com idade igual ou superior a 50 anos reportou mais sintomas depressivos do que o grupo de pacientes mais jovem. Os sintomas depressivos reportados influenciaram o funcionamento saudável, definido por indicadores como o funcionamento físico, emocional e cognitivo, similarmente dentro dos dois grupos.

Palavras-chave: Idade, Funcionamento, Depressão, Cancro ginecológico, Cancro da mama.