Depression and Health-Related Quality of Life Among Young Adult Breast Cancer Patients: The Mediating Role of Reproductive Concerns

Ana Bártoło, MSc,¹ Isabel M. Santos, PhD,² Elisabete Valério, MSc,³ and Sara Monteiro, PhD¹

Biological motherhood plays an important role in the lives of many young women facing breast cancer and threats to reproduction may be disruptive. In this study, we explored the indirect effects of the importance of parenthood and childlessness on depression and health-related quality of life (HRQoL) among cancer patients 18–40 years of age ($n = 104$) through reported reproductive concerns. These specific concerns fully mediated the relationship between the importance of parenthood in women's lives and HRQoL. Greater importance of parenthood was directly associated with higher depression symptoms. Interventions should address the reproductive needs and concerns of patients to improve their HRQoL.

Keywords: parenthood, women, childless, distress, oncology, younger

Introduction

CURRENT ESTIMATES INDICATE that breast cancer in young adult women (20–39 years) has incidence rates in European countries ranging from 12.6/100,000 to 41.0/100,000, for Moldova and Italy, respectively.¹ This malignancy is known to influence the reproductive ability through cytotoxic effects of chemotherapy and radiotherapy treatments. Most chemotherapeutic regimes used in breast cancer treatments can induce the damage of germinal tissue in the gonads and lead to premature ovarian failure.² The aging of the reproductive system is another factor affecting the ovarian reserve of those who are nearer to the latter end of young adulthood, when anticancer treatments are completed (e.g., prolonged adjuvant hormonal therapy³). Therefore, the desire for biological motherhood and potential lack of choice in family building projects may represent additional challenges in the course of the disease.

Specific guidelines have been developed to improve fertility counseling, but some women still report limited conversations, which only focused on warnings not to become pregnant during chemotherapy,⁴ and report a lack of information regarding the early menopause and infertility risk and options to assess and preserve their fertility.⁵ Previous research has identified professional and organizational barriers to discussion of oncofertility care with cancer patients. Most professionals point to lack of time, awareness, and knowledge

as barriers to dealing with fertility issues and report disagreement between departments on who is responsible for discussing this topic.⁶ Nevertheless, some patients have not yet completed their families at the time of diagnosis and desire to have children after treatment.⁷

An unfulfilled desire for parenthood seemed to be associated with impaired mental health.⁸ Distress caused by an interrupted desire for childbearing can persist even 5–10 years post-treatment.⁹ Moreover, the wish for children in the future has been identified as a significant positive predictor of the reproductive concerns among women with breast cancer.^{9,10} Menstrual changes, potential treatment-related fertility loss, and fertility options have been consistently indicated as major concerns among younger women.^{11,12} However, other issues related to their own health after a potential pregnancy and the genetic risk to their offspring also worry cancer patients.¹³ These unique concerns reflect a serious problem, since they have been shown to increase the risk of depression^{14,15} and a poorer QoL.¹⁶

Our aim was to provide a better understanding of the mechanisms involved in the maladjustment of young adult women faced with a reproduction-threatening disease. In general, although the desire for children and childlessness are a burden and a worrying factor, it is unclear how much the meaning of motherhood influences psychosocial outcomes among cancer patients. Thus, we explored the association between the representation of the importance of parenthood,

¹Center for Health Technology and Services Research (CINTESIS), Department of Education and Psychology, University of Aveiro, Aveiro, Portugal.

²William James Center for Research, Department of Education and Psychology, University of Aveiro, Aveiro, Portugal.

³Breast Clinic, Instituto Português de Oncologia Francisco Gentil, Porto, Portugal.

fertility, and parenthood concerns and depression, and health-related quality of life (HRQoL). Furthermore, based on the emergent literature, we hypothesized that the relation between these variables is likely to be complex, that is, greater importance of parenthood in women's lives may be associated with higher depression symptoms and lower HRQoL through reproductive concerns.

Materials and Methods

Participants and procedure

This cross-sectional study included breast cancer patients who were recruited from a hospital in the North of Portugal. Women 18–40 years of age, diagnosed over the age of 18 with early stage breast cancer ($\leq$ IIIA) who received chemotherapy were eligible to participate in the study. The researcher invited 170 patients to participate on the day of the medical appointment. Of these, 104 were included in this analysis. We excluded patients for the following reasons: having undergone hysterectomy, prophylactic oophorectomy or tubal ligation procedures, or being currently pregnant. The protocol for this research was approved by the Hospital Ethics Committee and participants gave their consent before enrolment. Sociodemographic and clinical information was assessed by standard questions.

Measures

Reproductive concerns. Fertility and parenthood concerns were assessed with the 18-item Reproductive Concerns After Cancer Scale (RCACS).¹⁷ The psychometrically validated Portuguese version of the scale presents five dimensions: fertility potential, children's health risk and future life, partner disclosure, barriers to getting pregnant/having children, and acceptance of the fertility status.¹⁸ For each item, participants are asked to rate how much they agree/disagree with each statement on a 5-point Likert scale. The global index ranges from 18 to 90 with higher scores indicating higher levels of reproductive concerns. In this study, the Cronbach's alpha coefficient was 0.836.

Importance of parenthood. Representations of the importance of parenthood were measured using two subscales of the Portuguese version of the Fertility Problem Inventory. Based on the approach proposed by Moura-Ramos et al.,¹⁹ the importance of parenthood global index was obtained from the need for parenthood and rejection of a childfree lifestyle subscales, involving questions related to perceiving parenthood as a main goal in life and the negative view of life without a child. Participants respond using a 6-point Likert scale from "Strongly disagree" to "Strongly agree." A higher score represents greater importance of parenthood in women's lives. The alpha coefficient was good in this sample ($\alpha=0.859$).

Depression. Depression symptoms were assessed through the depression subscale of the 14-item Hospital Anxiety and Depression Scale (HADS).²⁰ This subscale is composed of seven items and participants are invited to respond using a 4-point Likert scale. The total score ranges

from 0 to 21, with higher scores indicating a higher level of depressive symptoms. A Cronbach's alpha of 0.847 was obtained in the present sample.

Health-related quality of life. The European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core-30 (EORTC QLQ-C30)²¹ is a thirty-item questionnaire used to measure HRQoL, including five functional scales, a global health status/QoL scale, three-symptom scales, and single-item measures. In this study, only the functional scales assessing physical, role, emotional, cognitive, and social functioning were used. Items are rated on a 4-point Likert scale ranging from "not at all" to "very much." The scores range from 0 to 100, with higher scores indicating better functioning. Cronbach's alpha coefficients were acceptable (ranging from 0.605 to 0.920 for cognitive and social functioning, respectively).

Statistical analysis

Data analysis was performed with IBM SPSS software, version 24 and IBM Amos software, version 24. Pearson's correlations were used to evaluate the bivariate relations between importance of parenthood, reproductive concerns, and psychosocial aspects. The correlations were classified as weak (0–0.3), moderate (0.3–0.7), and strong (>0.7 –1.0).²² To test the mediating effect of reproductive concerns, a path analysis was conducted using AMOS. The importance of parenthood was defined as an exogenous variable and depression and HRQoL as endogenous variables. Bootstrap procedures using 5000 samples were used to obtain the confidence intervals and significance of the indirect effects.²³ The bias-corrected 95% bootstrap confidence intervals that do not include zero determined a significant mediation effect. To assess overall model fit, the chi-square statistics (χ^2), comparative fit index (CFI), standardized root mean residual (SRMR), and root mean square error of approximation (RMSEA) were used. Nonsignificant χ^2 values and CFI equal to or greater than 0.95, SRMR value below 0.08 and RMSEA below 0.06 were required for a good-fitting model.²⁴

Results

Descriptive statistics: sociodemographic, clinical, and reproductive characteristics and concerns

Participants had an average age of 36.61 years (standard deviation [SD]=3.03). Of the 104 respondents, 71.2% were married or lived in a cohabitation relationship and more than 50% had received college education. Most participants had received radiotherapy and 67.3% were undergoing endocrine therapy. The mean length of survival was 36.14 months (SD=24.51). Forty percent of the young women did not have a biological child and 43.3% reported they wanted a (another) child. At the time of enrolment in the study, 14 (13.5%) participants had a history of miscarriage or abortion. Ninety-two women (88.5%) had received information about the implications of diagnosis/treatments for fertility, but only 19.2% reported having undergone fertility preservation before treatment. Women presented higher mean scores for concerns related to children's health risk and future life (mean [M]=3.90; SD=1.12) and to barriers to getting

pregnant/having a child ($M = 2.76$; $SD = 0.95$) compared with other concern of RCACS dimensions. Based on the cutoff criteria defined by Gorman et al.,¹⁵ 35.6% of this sample presented moderate-to-high overall reproductive concerns. In addition, there is no relation between partnership status and reproduction-related concerns ($r = -1.78$, $p = 0.071$). Socio-demographic, clinical, and reproductive characteristics are presented in Table 1.

TABLE 1. PATIENT SOCIODEMOGRAPHIC, CLINICAL, AND REPRODUCTIVE CHARACTERISTICS ($N = 104$)

Characteristics	n	%	Mean	SD
Age at enrolment, in years			36.61	3.03
Age at diagnosis, in years			33.44	4.23
Relationship status				
Married/cohabiting	74	71.2		
Single/other	30	28.8		
College educated				
Yes	54	51.9		
No	50	48.1		
Employment status				
Employed	89	85.6		
Unemployed	13	12.5		
Student	1	1.0		
Length of survival, in months			36.14	24.51
Cancer treatment				
Surgery	89	85.6		
Radiotherapy	78	75.0		
Endocrine therapy	70	67.3		
History of miscarriages/abortions				
Yes	14	13.5		
No	89	85.6		
Number of biological children				
No children	42	40.4		
One child or more	62	59.6		
Received information about fertility-related implications				
Yes	92	88.5		
No	12	11.5		
Underwent fertility care before treatment				
Yes	20	19.2		
No	83	79.8		
Wants a (or another) biological child				
Yes	45	43.3		
No	52	50.0		
Overall reproductive concerns				
Low ^a	67	64.4		
Moderate to high ^b	37	35.6		
Dimensions of concern				
Fertility potential			2.46	1.05
Children's health risk and future life			3.90	1.12
Partner disclosure			2.05	0.98
Barriers to getting pregnant/having children			2.76	0.95
Acceptance			2.31	0.90

^aMean scores in the RCACS <3.

^bMean scores in the RCACS >3 to 5.

RCACS, Reproductive Concerns After Cancer Scale; SD, standard deviation.

Relationship between importance of parenthood, reproductive concerns, and psychosocial outcomes

There was a moderate positive correlation between importance of parenthood and self-reported reproductive concerns. Reproduction-related concerns were also positively associated with depression symptoms and negatively associated with physical, emotional, and social functioning. In turn, higher importance of parenthood was associated with higher levels of depression. Moderate negative correlations were found between depression and all functional scales of HRQoL (Table 2).

Path analysis: the role of reproductive concerns

A path model examining the indirect effect of the importance of parenthood on depression and HRQoL through reproductive concerns was conducted as shown in Figure 1. The importance of parenthood, overall reproductive concerns, and depression index were represented by single indicators. In turn, physical, emotional, and social functioning were specified as indicators of a single latent variable (unobserved) designated HRQoL. Based on correlations analysis, cognitive and role functioning were not included in the model since these variables were unrelated to reproductive concerns. Direct paths were controlled and dependent errors were correlated. The fit indexes indicated the good fit of the model ($\chi^2_{(6)} = 5.83$, $p = 0.443$; CFI = 1.00, SRMR = 0.027, RMSEA = 0.000). As hypothesized, the effect of the importance of parenthood on HRQoL assessed through physical, emotional, and social functioning was fully mediated by reproductive concerns (-0.133 BC 95% CI: -0.274 to -0.034 , $p = 0.013$), that is, greater importance of parenthood in women's lives was associated with increased reproductive concerns and, consequently, they reported a poorer QoL. Additionally, there was a positive direct effect of the importance of parenthood on depression. However, no significant indirect effect was found in this relationship (0.032 BC 95% CI: -0.050 to 0.122 , $p = 0.349$).

Discussion

To our knowledge, this is the first study providing preliminary evidence about the indirect effect of the meaning of parenthood on breast cancer patients' HRQoL, through reproductive concerns. These findings demonstrate the need to improve HRQoL, namely the physical, emotional, and social functioning of women who attach great importance to motherhood in their lives, by addressing reproductive concerns during health care provision.

In line with the results of Ljungman et al.,⁹ the most common areas of concern among these young adult women were children's health risk and future life and the barriers to getting pregnant/having a child, involving issues related to their own health and future. Therefore, in addition to discussions about the effects of exposure to gonadotoxic therapy on the reproductive potential, concerns about perceptions of genetic risk and pregnancy as a trigger to recurrence should be addressed. As suggested in recent research,²⁵ it is important to clarify misconceptions and to address preimplantation genetic diagnosis as an option for patients with a heritable syndrome. More specifically, the literature has shown that women with BRCA mutation have unique concerns related to

TABLE 2. PEARSON CORRELATIONS BETWEEN IMPORTANCE OF PARENTHOOD, REPRODUCTIVE CONCERNS, AND PSYCHOSOCIAL OUTCOMES

Variables	Mean $\pm$ SD	1	2	3	4	5	6	7	8
1. Reproductive concerns	49.38 $\pm$ 11.35	1							
2. Importance of parenthood	58.36 $\pm$ 15.30	0.419***	1						
3. Depression	3.42 $\pm$ 3.42	0.207*	0.343***	1					
4. Physical functioning	82.58 $\pm$ 14.54	-0.228*	-0.043	-0.546***	1				
5. Role functioning	82.37 $\pm$ 20.88	-0.110	0.013	-0.341***	0.523***	1			
6. Emotional functioning	71.37 $\pm$ 26.34	-0.193*	-0.137	-0.486***	0.381***	0.267**	1		
7. Cognitive functioning	79.01 $\pm$ 21.66	-0.179	-0.034	-0.432***	0.508***	0.450***	0.547***	1	
8. Social functioning	78.37 $\pm$ 26.57	-0.255**	-0.176	-0.663***	0.429***	0.283**	0.513***	0.370***	1

* $p < 0.05$.** $p < 0.01$.*** $p < 0.001$.

childbearing and feel pressure to make decisions about future motherhood.²⁶ Special attention should be given to these issues, even when there is no personal history of cancer yet, but a germline mutation is present.

Our data suggested that a young adult with breast cancer who reported more need to start or complete their family and a more negative view of a childless life had a higher risk of experiencing depressive symptoms, regardless of their reproductive concerns. Although there is a gap in the literature regarding representations of the importance of parenthood and its impact on women with cancer, this direct effect is not completely surprising and similar results have been found in infertile women.²⁷ These women have to deal with the uncertainty about their reproductive capacity and potential interruption or discontinuation of their family building projects. Particularly, when biological motherhood is a major goal in life, young adult women may find it more difficult to adjust their expectations, with acceptance and reorganization of a childless future resulting in more emotional difficulties. Interrupted desired childbearing is recognized as a distress factor, and even long-term survivors⁶ and some breast cancer

patients, in the case of a hormone-sensitive disease, discontinue endocrine therapy due to their desire for future fertility.²⁸ Based on this, it is imperative to fill the gaps in counseling about options to preserve fertility and alternative family-building options,⁵ decreasing psychological morbidity, and increasing the empowerment of these young adult women in their decision-making processes.

The major contribution of this study is to show the psychosocial impact of the importance of parenthood on the life of women faced with a reproduction-threatening disease. This study provided a better understanding of the psychological mechanisms involved in responding to the challenges of an oncological disease at a reproductive age, highlighting the mediating role of reproductive concerns. Future research should include larger samples and prospective longitudinal studies replacing cross-sectional designs, which do not reveal the trajectory of the meaning of parenthood and childlessness and its direct and indirect impact on psychosocial outcomes. A mixed-methods approach incorporating the voices of young adult women may also help explain the results of our path analysis. Additionally, the

FIG. 1. Path model examining the mediating role of reproductive concerns. *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. Thick lines illustrate the mediation effect.

length of survival and the use of fertility care should be considered in more complex pathway models.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

This article was supported by National Funds through FCT—Fundação para a Ciência e a Tecnologia within CINTESIS, R&D Unit (reference UID/IC/4255/2019); and a PhD fellowship for A.B. (SFRH/BD/115855/2016).

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Address correspondence to:

Ana Bárto, MSc

Department of Education and Psychology

University of Aveiro

Campus Universitário de Santiago

Aveiro 3810-193

Portugal

E-mail: anabartolo@ua.pt