Original Article

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Quality of Life and Age-Related Predictor Symptoms in Breast Cancer Survivors Undergoing Hormone Therapy: A Study from the Northern Region of Morocco

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ABSTRACT

Objective: The aim of this study was to assess the health-related quality of life (HRQoL) of breast cancer (BC) survivors during adjuvant hormone therapy (AHT) as a function of age and to identify predictor symptoms.

Materials and Methods: The study was based on a cross-sectional survey of 216 BC survivors undergoing AHT, in the Northern Region of Morocco. HRQoL was assessed using a validated HRQoL questionnaire, the Functional Assessment of Cancer Treatment (FACT-ES). Multiple linear regression analysis was used to identify predictor symptoms for the subscales of the FACT-ES.

Results: Younger women (<45 years) had lower scores on the emotional well-being subscale (p = 0.021). Irritability (β: -0.786; p = 0.001) and mood swings (β: -0.835; p = 0.031) were the strongest negative predictors of emotional quality of life. In both age groups, items related to social support had a positive effect on survivors' social HRQoL (p<0.05).

Conclusion: BC survivors' HRQoL during AHT differed by age group. Emotional problems negatively influenced HRQoL in younger women. Knowledge of the symptoms that predict HRQoL in BC survivors may help clinicians develop personalized interventions.

Keywords: Age; breast cancer; hormone therapy; quality of life; predictor symptoms; survivors

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Key Points

- Young survivors are more prone to emotional distress.
- Overweight and physical problems are more prevalent among older survivors.
- Social support has a positive effect on health-related quality of life for breast cancer survivors of all ages.
- Clinicians must manage breast cancer survivors during adjuvant hormone therapy, taking account of the predominant symptoms in each age group.

Introduction

Female breast cancer (BC) is a global burden. It ranks first in terms of incidence in the vast majority of the world's countries (1). In Morocco, BC is the leading cancer in women, with an incidence rate of 38.8% of all cancers, and a death toll exceeding 4000 in 2022 (1). It is an age-related disease, most often affecting older women. However, several studies from Morocco have reported that the disease frequently affects younger women (2). These include a study of 265 female BC patients in North-East Morocco, which showed that the average age of the participants was 45 years (3).

BC is currently considered one of the most curable cancers, with a steadily improving 5-year survival rate, reaching 80.6% in Morocco (4). This is essentially due to the evolution of diagnostic methods and the development of new therapeutic techniques. With the increasing number of survivors of BC, the assessment of health-related quality of life (HRQoL) in these patients is considered a fundamental necessity, particularly in the case of long-term treatment, including adjuvant hormone therapy (AHT). HRQoL is currently considered a key determinant of treatment success in modern oncology, not only for young women who are exposed to psychological distress due to the disease or the effects of treatment (5), but also for older women, who

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represent the highest prevalence of BC (6). Indeed, several researchers have assessed HRQoL of BC survivors as a function of age in several countries (7-9). However, the relationship was not explicitly examined in most of these studies, sometimes leading to contradictory results. For example, some authors found that HRQoL was poorer in older patients than in younger women (9, 10). In contrast, other studies have reported better HRQoL in older women than in younger women, particularly in psychological terms, despite their impaired physical function and comorbidities (11, 12).

Currently, the majority of studies of BC survivors seek to explore socioeconomic and clinical predictors of HRQoL (13-15). Nevertheless, studies investigating predictors in terms of symptoms as a function of age remain very scarce, particularly during AHT. A recent study (2023) aimed at identifying the main symptoms in BC patients during AHT, showed that loss of sexual interest and joint pain were the symptoms most commonly reported by women. However, the study did not examine existing differences between younger and older women (10).

To the best of our knowledge, the present study is the first in Morocco and in the African context, to assess HRQoL of BC survivors as a function of age while identifying predictor symptoms related to AHT.

This study may have important clinical implications, as knowledge of these differences in HRQoL will enable personalized management of women according to their age. In addition, this research will provide valuable information on the symptoms that predict HRQoL in both age groups (younger and older), with a view to improving the overall health of these patients by acting on these predictors.

The primary aim of this study was to evaluate HRQoL in BC survivors based on their age, as well as to identify predictor symptoms during AHT.

Materials and Methods

Study Design

The present study was a cross-sectional study of 216 BC survivors undergoing AHT between 2015 and 2020. Those women were identified from the local cancer registry located at the focal point of each province in the northern region of Morocco. Data collection was done over two periods (8 months in total), 4 months in each province. The data was collected after authorization to collect data from the health authorities of the region, in collaboration with the archiving managers and head nurses of each oncology center. Participants were invited to participate in the study. For literate women, they individually completed the questionnaire assessing HRQoL which was the Functional Assessment of Cancer Treatment (FACT-ES) Arabic version. For illiterate women, the data collection was done via direct interviews. The compilation of data was completed using different sources: consultation of women's medical records and examination reports.

Study Population

Sample

To calculate the size of our sample, we used the following formula:

$$n = z^2 \, p \, q \, / \, e^2$$

where n = sample size; z = the confidence level (for a 95% confidence interval, $z = 1.96$); p = the total population (2023); q = 1-p; and e = the tolerated margin of error (5%). The minimum sample size found was $n = 324$.

The sampling method used for this study is proportional stratified probabilistic sampling, which makes it possible to have a representation closest to the general population. The choice of this sampling technique was imposed by the fact that the population naturally presents itself in strata, each stratum corresponding to a province. Thus, two strata were determined (Al Hoceima/Tetouan). However, since the size of each stratum is uneven, we opted for proportions corresponding to the percentage of women represented by the stratum to which they belong in relation to the minimum sample size determined beforehand ($n = 324$). Then inside each stratum, a simple random sample was carried out, after compiling the data in Excel.

The study database initially included 324 women, 216 of whom successfully completed our questionnaire, a response rate of 67%. Participants were stratified according to age (<45 years versus ≥45 years) to compare younger and older patients, based on available literature.

Women with early BC undergoing AHT [tamoxifen or aromatase inhibitors (AI)] were eligible to participate in this study.

Assessment of HRQoL

HRQoL was assessed using the FACT-ES, which is an international scale, initially developed by Fallowfield in 1999 (16) to assess HRQoL in BC patients undergoing AHT. It has been translated into several languages, including Arabic. Previous studies have demonstrated that the Arabic version of the FACT-ES is sensitive and reliable for assessing HRQoL in cancer patients in Arab populations (17). This questionnaire includes four domains: physical well-being (PWB); social well-being (SWB); emotional well-being (EWB); and functional well-being (FWB). There is also a 19-question subscale on endocrine symptoms (ES). The PWB, SWB and FWB each comprise seven items, and the EWB contains five items. FACT-ES has been translated and validated in several languages, including Arabic. Version 4 of FACT-ES Arabic was used for this study. Participants' responses to the various items were assessed using a 5-point Likert scale, with response scores ranging from 0 to 4 (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit and 4 = very much). A higher overall HRQoL score FACT-ES and higher individual domain and ES scores indicate a better HRQoL. Missing values were calculated as an average of the observed items, if more than half of the items making up the subscale were answered, as suggested by its developer.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS), version 21.0 (IBM Inc., Armonk, NY, USA). Descriptive statistics included frequencies and percentages for categorical variables (socio-demographic and clinical) and mean and standard deviation for continuous variables (FACT-ES scores). Differences between variables were obtained using chi-square tests for categorical variables and non-parametric tests (Wilcoxon-Mann-Whitney) for continuous variables. A multivariate analysis including significant variables from the univariate analysis was performed to identify predictors of the FACT-ES subscales in both age groups. Regression coefficients were used for linear regression results. In all multivariate analyses, the significance level (p) was set at 0.05. The minimum important difference for interpreting group differences in HRQoL for the FACT-ES scales is

estimated at 3 to 8 points and at two points or more for the subscales, as recommended by the developer of FACT (16).

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki, after obtaining authorization for data collection from the health authorities of the region under no. 488/00 of 05/02/2000 due to the non-existence of an ethics committee at the time of the study. Informed consent was obtained and confidentiality of participants' private information was respected.

Results

Sociodemographic and Clinical Characteristics

The basic demographic data of patients receiving AHT are presented in Table 1. About 76% (n = 117) of women aged over 45 years were illiterate. More than half of the participants in both age groups were married. The results also show that almost half (n = 77) of women aged over 45 years have three or more children. Regarding employment status, almost all (90%) of the participants in both categories were unemployed. Regarding clinical variables (Table 2), data analysis revealed that more than 60% of women in both age groups had stage II BC. In addition, almost all women under 45 years (94.4%) were taking Tamoxifen, 70% of whom had treatment-induced menopause. In women aged over 45 years, nearly 60% were on AI, of whom 70% reported being postmenopausal. Regarding the duration of AHT use, the study results showed that more than half (53%) of women aged over 45 years had used this therapy for more than 2 years.

HRQoL According to Age

Table 3 compares HRQoL between younger (≤45 years) and older (>45 years) women. The results show that older women have a significantly better overall HRQoL, as well as a lower burden from the endocrine therapy, in addition to a better emotional quality of life. Nevertheless, younger women had significantly better mean PWB scores. However, no significant differences were observed for either SWB or FWB between the two age groups.

Predictor Symptoms of HRQoL According to Age

Table 4 highlights the symptoms that predict HRQoL in both age groups. The main symptoms that negatively influenced HRQoL in young women were psychological symptoms, namely: I feel nervous (β: -1.087), I am afraid that my health will deteriorate (β: -1.306), mood swings (β: -0.835), irritability (β: -0.786). Younger women also reported that gynecological symptoms also had a negative effect on HRQoL, including vaginal irritation (β: -0.931) and vaginal dryness (β: -1.115). For older women, physical problems such as generalized pain (β: -0.697), joint pain (β: -1.206) and lack of energy (β: -0.593), in addition to vasomotor symptoms including day and night sweats (β: -0.595), hot flashes (β: -0.628) and weight gain (β: -1,105) had a negative effect on their HRQoL.

In terms of variables related to social support ("I feel close to my partner") or family support ("My family supports me morally"), these had a positive impact on the HRQoL in both age groups.

Discussion and Conclusion

The present study is the first to assess the HRQoL of BC survivors during five years of AHT as a function of age in the population of northern Morocco. Then, the predictor symptoms in the same population using the FACT-ES questionnaire were investigated. It is hoped that this will enable healthcare providers to identify survivors who may be at risk of impaired HRQoL and therefore provide targeted and appropriate care for each woman.

Most studies conducted in Western countries consider the boundary between "young" and "old" women to be 50 years (18, 19), as this is the average age at which menopause begins. However, the age of onset of menopause depends on several hormonal, hereditary and environmental factors. According to the World Health Organization the age of onset of menopause varies widely both between individuals in the same population and between different populations around the world, ranging from 45 to 55 years (20). Based on a literature review,

Table 1. Comparison of socio-demographic characteristics by age group (n = 216)

Variables	Age <45 years (n = 61)	Age ≥45 years (n = 155)
Education		
Illiterate	22 (36.1%)	117 (75.5%)*
Primary	18 (29.5%)*	15 (9.7%)
Secondary	17 (27.9%)*	18 (11.6%)
University	4 (6.6%)	5 (3.2%)
Marital status		
Single	21 (34.4%)*	40 (25.8%)
Married	36 (59%)	91(58.7%)
Divorced	4 (6.6%)	8 (5.2%)
Widow	0 (0%)	16 (10.3%)*
Number of children		
None	22 (36.1%)	52 (33.5%)
One child	6 (9.8%)	8 (33.5%)
Two children	10 (16.4%)	18 (11.6%)
Three or more children	23 (37.7%)	77 (49.7%)
Job		
Unemployed	56 (91.8%)	150 (96.8%)
Employed	5 (8.2%)	5 (3.2%)
Economic level		
Low	19 (31.1%)	46 (29.7%)
Medium	42 (68.9%)	107 (69%)
High	0 (0.0%)	2 (1.3%)
Type of insurance		
CNOPS	2 (3.3%)	16 (10.3%)*
CNSS	5 (8.2%)*	3 (1.9%)
RAMED	53 (86.9%)	136 (87.7%)
Others	1 (1.6%)	0 (0%)
Provenance		
Rural	27 (44.3%)	61 (39.4%)
Urban	34 (55.7%)	94 (60.6%)

CNOPS: National Fund for Social Security Organizations; CNSS: National Social Security Fund; RAMED: Insurance for low-income patients

*: Significant difference for chi-squared test is <0.05

the mean age of menopause used in most epidemiological and HRQoL studies of women with BC in the Moroccan and similar contexts was 45 years (2, 21). Thus, we opted to subdivide our study sample into two age groups: <45 years and ≥45 years. Several studies have examined the influence of age on HRQoL in BC patients (22). However, the majority of these studies do not directly explain this relationship, with contradictory results. For example, some authors found that the HRQoL of older patients was poorer than that of younger women (23, 24), while other studies reported the opposite, concluding that young age was an important risk factor for poor HRQoL (19, 25). Other results mentioned the influence of age only on certain dimensions of HRQoL, notably the physical role (26). Still other studies have found no significant difference between older and younger patients (27).

In the present report, younger age (<45 years) was associated with lower overall HRQoL (FACT-ES), except for PWB. This corroborates with some previous studies (28, 29), which highlighted a positive relationship between younger age and better physical functioning.

Regarding SWB, the present study found a significant age-related difference, with higher scores in older women, which is consistent with the results of some studies that found a strong association between young age and low SWB (11). Previous reports have explained this finding by suggesting that older women are likely to live in better conditions of social stabilization than younger women, who may experience divorce and problems with spouses who do not accept their illness (30). However, this result contradicts other studies that have detected a strong association between younger age and better SWB (31). Given the inconsistency of these results, further research is needed to clarify the influence of age on the SWB of BC survivors, particularly among Moroccan patients in other regions.

Table 2. Comparison of clinical characteristics by age group (*n* = 216)

Variables	Age <45 years (*n* = 61)	Age ≥45 years (*n* = 155)
Stage of cancer		
Stage I	0 (0%)	5 (3.2%)
Stage II	40 (65.6%)	107 (69%)
Stage III & IV	21 (34.4%)	43 (27.7%)
Type of hormone		
Tamoxifen	60 (94.4%)*	63 (40.6%)
Aromatase inhibitors	1 (1.6%)	92 (59.4%)*
Menopausal status		
Premenopausal	18 (29.5%)*	17 (11%)
Menopausal	0 (0%)	107 (69%)*
Menopausal induced	43 (70.5%)*	31 (20%)
Surgery type		
Mastectomy	42 (68.9%)	121 (78.1%)
Conservative	19 (31.1%)	34 (21.9%)
Pretreatments		
Chemotherapy	8 (13.1%)	29 (18.7%)
Radiotherapy	2 (3.3%)	12 (7.7%)
Both	51 (83.6%)	114 (73.5%)
Treatment time/period		
Less than 6 months	21 (34.4%)	44 (28.4%)
Between 6 to 12 months	12 (19.7%)	22 (14.2%)
Between 1 & 2 years	5 (8.2%)	7 (4.5%)
More than 2 years	23 (37.7%)	82 (52.9%)*

*: Significant difference for chi-squared test is <0.05

Linear regression analysis demonstrated a positive effect of social support on SWB in both age groups. These results corroborate those of a recent study (32) and with other previous studies, demonstrating that adequate social support from family members, husband, friends and neighbors was associated with a significant improvement in HRQoL of BC patients (33).

Concerning the psychological and emotional dimension, the present study showed that younger survivors exhibit more psychological distress than older women. The literature also presents similar results. Indeed, the results of some systematic reviews have revealed that depressive syndromes are more pronounced in younger patients (12), which can be explained by the fact that younger women have more difficulty adapting to life with BC than older women. In addition, they complain and pay more attention to adverse effects, especially those related to menopause and infertility (34).

Given the paucity of literature on age-related predictive symptoms of HRQoL in BC survivors on AHT, our analysis and discussion included some results from studies of women classified according to menopausal status, given that premenopausal women are considered young and postmenopausal women older.

The results of our study concerning ES, showed a greater weight of these symptoms in younger patients than in older women, which is contradictory to the results of a study conducted in Saudi Arabia that revealed that women over 60 years old had more ES than younger women (23). However, these results align perfectly with those reported by Borreani et al. (35), highlighting that 64% of younger (premenopausal) patients reported a clinically significant worsening of their ES.

Our results showed that the main predictors of the ES subscale having a negative impact on young women's HRQoL were both psychological and gynecologicalphysical. These findings align with those of Borreani et al. (36), which reported that items on the EWB subscale were predictive of the symptom group classified as "worse". In terms of gynecological symptoms, a previous study showed that the older (menopausal) group of women suffered less vaginal dryness than younger (premenopausal) women (37). These results contradict those of the present study.

For older women in the present study, joint pain and lack of energy were the symptoms most commonly reported. This agrees with the majority of previous studies (38), demonstrating a failure of physical function associated with joint pain in this group of women. Similarly, a further study found that lethargy, joint stiffness, shoulder and knee joint pain were significantly more frequent/severe in older BC survivors (39). This is because older women are at risk of declining physical function due to the combined effect of basic age-related symptoms and the side effects of AHT (40).

Our study also found that the sensation of hot flushes and night sweats were negatively predicted in elderly women. A study showed

Table 3. Comparison of dimensions of HRQoL as a function of age

Quality of life dimensions	Age classes	Mean	SD	*p* (Mann-Whitney U)	Total
Physical well-being (PWB)	<45 years	19.15	4.14	0.003*	18.03±4.26
	≥45years	16.98	2.32		
Social/family well-being (SWB)	<45 years	18.57	3.85	0.488	18.93±3.65
	≥45years	19.07	3.58		
Emotional well-being (EWB)	<45 years	15.67	2.49	0.021*	17.88±4.50
	≥45years	18.97	4.51		
Functional well-being (FWB)	<45 years	21.13	2.77	0.894	21.04±2.68
	≥45years	21.01	2.66		
Endocrine symptom (ES)	<45 years	39.64	2.36	0.001*	46.48±8.80
	≥45years	49.17	8.95		
FACT-ES	<45 years	117.16	4.04	0.001*	124.37±9.18
	≥45years	127.21	9.10		

SD: Standard deviation; *: The difference is significant at ≤0.05
FACT-ES score = PWB+SWB+EWB+FWB +ES; HRQoL: Health-related quality of life; FACT-ES: Functional Assessement of Cancer Treatment

Table 4. Predictor symptoms of HRQoL as a function of age

Age	Dimensions (FACT-ES)	Sub-dimensions	Coefficients β	*p*
<45 years	Social well-being	My family supports me morally	0.865	**0.005***
		I feel close to my partner	1.107	**0.014***
	Emotional well-being	I feel nervous	-1.087	**0.004***
		I'm worried about my health getting worse	-1.306	**0.002***
	Functional well-being	I sleep well	0.921	**0.042***
		I enjoy my usual hobbies	0.867	**0.038***
	Endocrine symptom	Vaginal irritation	-0.931	**0.041***
		Vaginal dryness	-1.115	**0.015***
		Mood swings	-0.835	**0.031***
		Irritability	-0.786	**0.001***
	Physical well-being	I lack energy	-0.593	**0.003***
		I have pain	-0.697	**0.045***
≥45 years	Social well-being	My family supports me morally	1.002	**0.002***
		I feel close to my partner	0.352	**0.033***
	Endocrine symptom	Hot flashes	-0.628	**0.043***
		Night and day sweats	-0.595	**0.014***
		Weight gain	-1.105	**0.048**
		Joint pain	-1.206	**0.006***

*: Significant influence at the 0.05 level; FACT-ES: Functional Assessement of Cancer Treatment; HRQoL: Health-related quality of life

similar results, highlighting that hot flushes and night sweats are less frequent in younger women and increase with age (41). Regarding weight gain, the results of a previous study demonstrated a strong relationship between weight gain and advanced age (post-menopausal) (42).

Finally, the inherent limitations of this study should not be overlooked. The most important limitations relate to the descriptive and cross-sectional nature of the study, as some factors were collected retrospectively, which may have influenced the results obtained. Another limitation is the study instrument. The FACT-ES does not include questions relating to spiritual well-being, whereas religious practice is an important daily activity for elderly patients and should be included in HRQoL surveys conducted in the Moroccan context, as suggested by a recent study (6). Despite its limitations, the conclusions drawn from this research may contribute to improving HRQoL in BC survivors on AHT. They may pave the way to identify optimal patient-centered interventions, while taking into account the HRQoL

predictors corresponding to each age group. This study may also provide valuable opportunities for further work. Thus, the results of this study may provide a basis for a subsequent study examining the influence of AHT associated symptoms on adherence and treatment compliance.

In conclusion, the present study showed that over the five years of AHT, older BC survivors had better HRQoL than younger women. The main predictors of HRQoL in the latter group were symptoms related to psychological distress and gynaecological problems. Joint pain and impaired physical function had a negative impact on HRQoL in older women. The results of our study add to previous data in the literature and suggest self-management of BC survivors on AHT, through the implementation of interventions targeting predictors relative to each age group.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki, after obtaining authorization for data collection from the health authorities of the region under no. 488/00 of 05/02/2000 due to the non-existence of an ethics committee at the time of the study.

Informed Consent: Informed consent was obtained and confidentiality of participants' private information was respected.

Footnotes

Authorship Contributions

Concept: F.E.B., A.L., Z.B.A.; Design: F.E.B., A.L., N.B., R.A., S.B.; Data Collection or Processing: F.E.B., N.B., Z.B.A.; Analysis or Interpretation: F.E.B., A.L., N.B., R.A.; Literature Search: F.E.B., A.L., Z.B.A., R.A.; Writing: F.E.B., S.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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