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Quality of Life in Long-Term Elderly Early-Stage Breast Cancer Survivors from Spain

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Abstract: Background; Maintaining good Quality of Life (QOL) in elderly long-term breast cancer survivors (LTBCS) is a major challenge today. Identifying particularly affected areas and associated factors can help to optimally organise the health care provided. **Methods:** A total of 316 elderly ($\geq$70 years) stage I-IIIA LTBCS subjected to breast surgery $\geq$5 years earlier completed EORTC QLQ-C30, QLQ-BR42 and QLQ-ELD14 on two occasions in the same year. QOL scores and their one-year evolution were described and their relation to demographic and clinical characteristics was assessed using non-parametric tests. Determinants of elderly-specific key aspects of QOL were also explored with linear regression models. **Results:** QOL scores were high (>80/100 points) in most areas. Limitations were moderate (>30 points) in sexual functioning/enjoyment, skeletal symptoms and three elderly-specific scales. QOL differences between the two assessments were few and trivial. The >75 years group showed lower QOL than the $\leq$75 years group in nine QLQ-C30 and four QLQ-ELD14 areas. Patients younger at treatment, living with a partner and without limiting comorbidity showed better QOL. Combinations of lower symptoms and higher functioning with cohabitation and clinical variables were related to the two QLQ-ELD14 scales. **Conclusions:** High QOL in elderly early-stage LTBCS indicated that patients adapted well to their situation. These results, relevant due to the high age of our participants, indicate areas for improvement.

Keywords:. Quality of life; elderly; long-term survivors; breast cancer; EORTC

1. Introduction

The The prevalence of elderly breast cancer survivors is increasing: for example, in 2022 in the USA, this prevalence was estimated at over 2,200,000 elderly ($\geq$70 years) breast cancer survivors [1]. Many of these elderly breast cancer patients become long-term breast cancer survivors (LTBCS) ($\geq$5 years after diagnosis) thanks to earlier detection through screening programmes, improved treatments, and the quality of survivor care. A growing population within this group are very long-term breast cancer survivors (VLTBCS) ($\geq$10 years' post-diagnosis) [2,3].

Quality of life (QOL) in LTBCS has become a major area of study in clinical work and research [3,4]. It is helpful to study the QOL of LTBCS in order to identify symptoms, address impairments in functioning, improve survivorship care and determine whether certain symptoms and limitations relate more to age than to cancer [5].

QOL is a main treatment aim for elderly breast cancer patients [6], i.e., those aged over seventy years old [7]. Clinicians must understand the specific values and QOL priorities of these patients [8] in order to deliver personalised cancer care [9].

Several QOL studies of elderly LTBCS have been performed. However, more are needed that evaluate elderly-specific QOL areas and have a high participation rate of VLTBCS (since the risk of low participation among elderly survivors is high and more questionnaires are usually completed by those with a better QOL) [2,5,10–12]. These LTBCS studies suggest that overall QOL may be comparable to QOL in a control population, though restrictions persist in functional performance and symptoms such as cognitive and emotional impairments, pain and fatigue.

Although a small percentage of breast cancer patients (5-10%) are diagnosed with **metastatic cancer**, 30% of those diagnosed at initial stages develop metastatic breast cancer [13]. These patients differ from those at initial disease stages since they may have different disease-related characteristics (e.g., metastases) and treatments (e.g., prolonged treatments that may bring long-term toxicity but do not usually aim to cure the disease) that exert a wider psychosocial impact on them and their families owing to the uncertainty due to living with an incurable disease. These characteristics and treatments may have a great impact on their QOL [14].

The aims of this study were to characterise QOL in a sample of elderly early stage LTBCS (>5 years after diagnoses, including a group >20 years after diagnosis) and assess how key demographic and clinical characteristics, together with some general QOL aspects, may affect elderly-specific QOL areas. We expected relatively high QOL scores, with moderate or light limitations in symptoms and emotional and functioning areas. We also expected few differences between groups based on current age, as well as higher QOL in elderly-specific areas in patients that have no limiting comorbidity, do not live alone, and have lower symptoms and higher functioning.

2. Materials and Methods

A consecutive sample of breast cancer patients treated at the Oncology Departments of Hospital Universitario de Navarra were invited by their treating oncologist to participate in this study between June 2021 and November 2023 during their follow-up consultations at the Oncology Departments.

Inclusion criteria were age $\geq$ 70 years at study entry, primary breast cancer, and stage I-IIIA at diagnoses. They had undergone breast surgery with axillary evaluation by clinical discretion (SLNB, ALND, no surgery) ≥ 5 years earlier (LTBCS) and may have received adjuvant treatments (radiotherapy, chemotherapy and/or endocrine treatment). Exclusion criteria were a second line of treatment, a second tumour during follow-up, relapse during follow-up, a cognitive state that precluded QOL assessment, and a life expectancy of less than three months.

Measures

All patients completed EORTC (European Organisation for Research and Treatment of Cancer) Quality of Life questionnaires QLQ-C30 (Quality of Life core questionnaire) [15] and QLQ-BR42 (Breast cancer module) [16], the latter of which is an updated version of QLQ-B23, and QLQ-ELD14 (elderly cancer patients' module) [17]. Our group validated QLQ-C30, QLQ-BR23 and QLQ-ELD14[18–20] for use in our country. Questionnaires with under 70% of items answered were excluded. Table S1 in the supplementary material shows the main features of these questionnaires. QLQ-C30 evaluates areas common to various tumour sites and their treatment; QLQ-BR42 evaluates aspects specifically related to breast cancer; and QLQ-ELD14 evaluates important age-specific issues for elderly cancer patients (any tumour site).

The treating oncologist assessed toxicity using selected items from version 5.0 of the NCI Common Toxicity Criteria scale [21], limiting comorbidity using the Charlson questionnaire [22], and performance status using the Karnofsky scale [23]. These assessments were conducted at longer sessions on days scheduled for habitual consultations in the oncology departments. QOL assessments were also conducted at these sessions to avoid the burden of extra sessions for patients.

Data collection procedures

Patients were invited to complete the QOL questionnaires twice: once at study entry and again one year later to assess changes in QOL scores after one year. Questionnaires were completed at consultations (rather than by telephone or mail to decrease the risk of missing data). This study was approved by the Regional Ethics Committee for Biomedical Research of Navarra and followed the recommendations of the Declaration of Helsinki (project number 2019/57). All patients provided signed written informed consent.

Statistical analysis

Descriptive statistics were used to summarise the demographic and clinical characteristics and the QOL scores in the three questionnaires at the two assessments. Comparisons between two groups based on age at assessment ($\leq$75 years and >75 years) were performed using χ^2 for categorical variables and Kruskal-Wallis for continuous variables ($p<0.05$). Comparisons in the three QOL questionnaires (first assessment) were adjusted by *time since surgery* using linear regression models.

Differences in the QOL scores (first assessment) between groups based on demographic and clinical variables (age at treatment, cohabitation, radiotherapy (yes/no) and limiting comorbidity) were studied. All analyses were conducted in bivariate analysis (Kruskal-Wallis) and complemented by adjusting for time since surgery (linear regression models). Cocks et al.'s criteria [24] were used to interpret differences between groups in the QLQ-C30.

Changes between the two within-patient QOL assessments were estimated (Wilcoxon test). Differences in the QLQ-C30 were interpreted with Cocks et al. criteria [25] (which could be trivial, small, medium, or large in both comparisons).

Multivariate analyses (linear regression models, backward regression method) were then performed at the first assessment with the QLQ-ELD14 scales of 'mobility limitations' and 'maintaining purpose' (having a positive outlook in life, being motivated to continue with activities) as dependent variables and, as determinants, the demographic (cohabitation) and clinical (breast and axillary surgery, chemotherapy, radiotherapy, endocrine treatment, comorbidity) variables studied in the previous group comparisons, the six QLQ-ELD14 scales (since these showed more limitations than the other two QOL questionnaires), and selected QLQ-C30 scales, i.e., emotional functioning, fatigue and pain (which are key determinants of QOL in breast cancer [26]). Age at evaluation and *years since beginning of treatment* were included in all three models. The QLQ-ELD14 scales for mobility limitations and maintaining purpose were studied due to their relevance for elderly patients and because they frequently showed differences in the group comparisons in our study.

3. Results

3.1. Characteristics of the sample

A total of 316 women out of 334 candidates invited to participate in this study (participation rate 94.6%) performed the first assessment. Reasons for not completing the questionnaires were administrative failure, i.e., changes to days programmed for follow-up interviews (eleven cases) and participant refusal (seven cases). The second assessment was performed by 305 patients. Reasons for not performing the second assessment were relapse (six cases), death (three cases), and administrative failure (two cases). The mean age of the total sample was 75.8 years. The mean number of years since start of treatment was 12.0 (ranging from 5 to 33). Also, 27.6% of patients had more than 16 years of follow-up and 51.6% were 60–69 years old when treatment began. Most patients (57.3%) lived with another person, 46.2% had limiting comorbidity, and 83.8% had received endocrine treatment (Table 1).

Table 1. Descriptive statistics of global sample and by age group.

	All (n = 316)	**75 Years or Less (n = 185)**	**> 75 Years (n = 131)**	**p-Value**
Age, mean (SD)	75.8 (5.2)			
range	70-93			
Age at treatment, mean (SD)	63.8 (8.2)	60.5 (6.6)	68.5 (8.0)	< 0.001
Range	41-88			
< 55 years	41 (13,0%)	35 (18.9%)	6 (4.6%)	< 0.001
55–59	45 (14,2%)	31 (16.8%)	14 (10.7%)	
60–69	163 (51,6%)	113 (61.1%)	50 (38.2%)	
70 or more	67 (21,2%)	6 (3.2%)	61 (46.6%)	
Years since beginning of treatment, mean (SD)	12.0 (6.6)	11.8 (6.5)	12.3 (6.7)	0.474
5 years	51 (16.1%)	34 (18.4%)	17 (13.0%)	0.192
6–10 years	113 (35.8%)	64 (34.6%)	49 (37.4%)	
11–15 years	68 (21.5%)	43 (23.2%)	25 (19.1%)	
16–20 years	47 (14.9%)	21 (11.4%)	26 (19.8%)	
More than 20 years	37 (11.7%)	23 (12.4%)	14 (10.7%)	
Civil status				
Single	41 (13.0%)	18 (9.7%)	23 (17.6%)	< 0.001
Married	187 (59.2%)	134 (72.4%)	53 (40.5%)	
Separate	10 (3.2%)	8 (4.3%)	2 (1.5%)	
Widow	78 (24.7%)	25 (13.5%)	53 (40.5%)	
Cohabitation				
Alone	85 (31.0%)	34 (21.9%)	51 (42.9%)	< 0.001
With a partner	157 (57.3%)	114 (73.5%)	43 (36.1%)	
Children over 18 years old	11 (4.0%)	1 (0.6%)	10 (8.4%)	
With other people	21 (7.7%)	6 (3.9%)	15 (12.6%)	
Breast surgery				
Conservative	191 (60.6%)	115 (62.2%)	76 (58.5%)	0.508
Mastectomy	124 (39.4%)	70 (37.8%)	54 (41.5%)	
Axillary surgery				
Axillary node dissection	111 (35,4%)	58 (31.5%)	53 (40.8%)	0.045
Sentinel node biopsy	186 (59,2%)	119 (64.7%)	67 (51.5%)	
No	17 (5,4%)	7 (3.8%)	10 (7.7%)	
Karnofsky Scale, mean (SD)	80.4 (9.1)	82.4 (9.1)	77.6 (8.2)	< 0.001
≤80	229 (72.5%)	122 (65.9%)	107 (81.7%)	0.002
>90	87 (27.5%)	63 (34.1%)	24 (18.3%)	
ADJUVANT TREATMENT				
Chemotherapy				
No	197 (62.7%)	107 (58.2%)	90 (69.2%)	0.315
Taxanes	14 (4.5%)	8 (4.3%)	6 (4.6%)	
Anthracyclines	27 (8.6%)	17 (9.2%)	10 (7.7%)	
Taxanes + anthracyclines	51 (16.2%)	35 (19.0%)	16 (12.3%)	
Others	25 (8.0%)	17 (9.2%)	8 (6.2%)	
Radiotherapy				
No	47 (15.1%)	28 (15.3%)	19 (14.7%)	0.889
Yes	265 (84.9%)	155 (84.7%)	110 (85.3%)	
Endocrine treatment				
No	51 (16.2%)	34 (18.4%)	17 (13.1%)	0.153
Tamoxifen	80 (25.4%)	48 (25.9%)	32 (24.6%)	
Aromatase inhibitor	176 (55.9%)	101 (54.6%)	75 (57.7%)	
Aromatase inhibitor + Tamoxifen	8 (2.5%)	2 (1.1%)	6 (4.6%)	
COMORBIDITY				

	All (n = 316)	75 Years or Less (n = 185)	> 75 Years (n = 131)	p-Value
Limiting comorbidity				
No	170 (53.8%)	114 (61.6%)	56 (42.7%)	0.001
Yes	146 (46.2%)	71 (38.4%)	75 (57.3%)	

Descriptive statistics of global sample and by age group.

3.2. QOL Scores

QOL scores were high in most QOL areas. Moderate limitations (>30 points) occurred in the QLQ-BR42 in sexual functioning/enjoyment and musculoskeletal symptoms, and in three QLQ-ELD14 areas: worries about others, maintaining purpose, and joint stiffness. Slight limitations (20–29) occurred in the QLQ-C30 in Global QOL, emotional functioning, fatigue, pain and insomnia; in the QLQ-BR42 in future perspective and breast satisfaction; and in the QLQ-ELD14 in future worries and family support (Table 2). None of the QLQ-C30 scores were under the QLQ-C30 threshold for clinical significance [27]. QLQ-C30 scores in the general sample were in line with the reference values for women aged ≥70 in Spain[28]. Small differences[24] in favour of our sample appeared in role, social functioning and constipation (7–8 points) and medium differences appeared in Global QOL (11 points).

3.3. Group Differences and Changes Within a Year

Differences between the two age groups (≤75, >75 years) appeared in demographic and clinical variables: the >75 years group showed a higher frequency of widows, people who lived alone, axillary node dissection and comorbidity, as well as a lower mean Karnofsky. With regard to the QOL questionnaires, the >75 years group showed lower QOL than the ≤75 years group (after adjusting for years since beginning of treatment) in the QLQ-C30 in summary score, physical functioning, cognitive functioning, global QOL, fatigue, insomnia, appetite loss and constipation (differences of 5–8 points, i.e., small differences in all cases) as well as in the QLQ-ELD14 in mobility, maintaining purpose, joint stiffness and family support (differences of 8–14 points) (Tables 1 and 2).

Table 2. Quality of Life scores of the global sample and by age group. Adjusted for time since beginning of treatment.

QUALITY OF LIFE	All (n = 316)	75 Years or Less (n = 185)	> 75 Years (n = 131)	p-Value	Adjusted p-Value
QLQ-C30					
Summary Score[a]	88.1 (9.6)	89.5 (9.1)	86.1 (9.9)	0.002	0.002
Physical Functioning[a]	82.9 (17.0)	86.5 (16.5)	77.9 (16.6)	< 0.001	0.000
Role Functioning[a]	92.5 (15.2)	93.1 (15.9)	91.6 (14.1)	0.400	0.361
Emotional Functioning[a]	76.7 (20.6)	76.7 (20.9)	76.7 (20.4)	0.983	0.923
Cognitive Functioning[a]	88.8 (14.3)	91.3 (13.1)	85.4 (15.2)	< 0.001	0.000
Social Functioning[a]	96.6 (10.3)	96.8 (10.1)	96.3 (10.6)	0.704	0.633
Global Health Status[a]	75.2 (17.8)	77.4 (18.6)	72.0 (16.3)	0.008	0.011
Fatigue[b]	20.9 (20.4)	17.7 (19.8)	25.4 (20.5)	0.001	0.002
Nausea[b]	1.2 (9.2)	0.9 (6.2)	1.5 (12.3)	0.553	0.412
Pain[b]	21.6 (21.9)	20.4 (22.5)	23.3 (20.9)	0.242	0.282
Dyspnoea[b]	8.2 (17.7)	7.2 (16.2)	9.7 (19.6)	0.224	0.235
Insomnia[b]	24.1 (28.8)	21.4 (29.1)	27.7 (28.1)	0.056	0.046
Appetite loss[b]	5.1 (15.6)	3.6 (13.0)	7.1 (18.5)	0.047	0.035
Constipation[b]	8.6 (19.9)	6.3 (18.2)	11.7 (21.8)	0.018	0.015
Diarrhoea[b]	2.3 (11.0)	2.3 (11.5)	2.3 (10.3)	0.967	0.926
Financial impact[b]	2.4 (14.5)	2.5 (14.1)	2.3 (15.0)	0.888	0.984
QLQ-BR42					

Body Image	95.7 (13.6)	95.0 (14.6)	96.6 (12.0)	0.296	0.263
Sexual Functioning[a]	12.1 (15.6)	13.5 (16.0)	8.5 (14.1)	0.047	0.063
missing	126	48	78		
Sexual Enjoyment[a]	40.1 (24.1)	42.7 (21.8)	31.7 (29.6)	0.074	0.866
missing	232	121	111		
Future Perspective[a]	75.8 (26.2)	73.9 (27.1)	78.4 (24.8)	0.137	0.488
Breast Satisfaction[a]	76.6 (25.6)	78.1 (26.1)	74.6 (25.0)	0.311	0.371
Arm Symptoms[b]	9.7 (14.9)	8.3 (14.4)	11.8 (15.5)	0.040	0.056
Breast Symptoms[b]	4.9 (9.4)	5.0 (9.0)	4.6 (10.0)	0.741	0.773
Systemic Chemotherapy Side Effects [b]	14.9 (12.2)	14.1 (12.5)	16.1 (11.8)	0.144	0.121
Vaginal Symptoms[b]	10.8 (21.5)	11.8 (23.0)	6.1 (11.5)	0.429	0.395
Endocrine-Symptoms[b]	8.2 (11.2)	8.7 (12.4)	7.5 (9.6)	0.442	0.342
Skin Toxicity/Neuropathy[b]	15.1 (16.4)	8.7 (12.4)	7.5 (9.6)	0.442	0.503
Weight gain[b]	18.2 (27.7)	19.7 (27.3)	16.2 (28.1)	0.345	0.243
Musculoskeletal Symptoms[b]	32.9 (25.9)	30.2 (25.7)	36.4 (25.8)	0.074	0.174
QLQ-ELD					
Mobility[b]	17.4 (21.2)	13.7 (20.7)	22.6 (20.8)	< 0.001	0.000
Worries about others[b]	33.2 (22.3)	33.0 (22.6)	33.6 (21.9)	0.809	0.956
Future worries[b]	25.4 (22.9)	24.2 (23.4)	27.1 (22.3)	0.265	0.340
Maintaining purpose[a]	66.7 (29.5)	72.7 (29.2)	58.1 (27.8)	< 0.001	0.000
Burden of illness[b]	8.9 (17.1)	7.6 (15.8)	10.7 (18.8)	0.116	0.114
Joint stiffness[b]	37.9 (29.8)	34.1 (29.1)	43.3 (30.0)	0.007	0.007
Family support[a]	77.2 (32.6)	81.3 (30.5)	71.5 (34.6)	0.008	0.015

Quality of life scores of global sample and by age group. a The scores range from 0 to 100, where a higher score represents a higher functional level. b The scores range from 0 to 100, where a higher score represents more severe symptoms. *Adjusted p-value*: level of significance in the QOL questionnaires adjusting for years since beginning of treatment.

Differences between groups based on age at treatment appeared in physical and cognitive functioning (QLQ-C30; small differences), sexual functioning and breast satisfaction (QLQ-BR42), and mobility, maintaining purpose and family support (QLQ-ELD14), with better QOL in patients who were younger at time of treatment (Table S2 to S4 in supplementary material). Differences between groups based on cohabitation appeared in dyspnoea (QLQ-C30; small difference), sexual functioning (QLQ-BR42), and maintaining purpose (QLQ-ELD14), with better QOL in those living with a partner. Differences between groups based on radiotherapy (yes/no) and limiting comorbidity appeared in dyspnoea (QLQ-C30; small difference), sexual functioning (QLQ-BR42), and maintaining purpose and family support (QLQ-ELD14), with better QOL in those who had not received radiotherapy and had no limiting comorbidity (Tables S2–S4).

Regarding the assessment of changes within a year of life, significant differences were observed in six QLQ-C30 areas (0.7–3.8 points, i.e., trivial differences)[25], in two QLQ-BR42 areas (0.7–2.0 points), and in one QLQ-ELD14 area (0.9 points). Scores were higher in the first assessment in all areas except for sexual functioning (Supplementary Table 5).

3.4. Multivairiate Analyses

The multivariate model fitted to assess factors associated with mobility limitations showed that the presence of limiting comorbidity, fatigue and joint stiffness are risk factors of reporting higher scores in mobility limitations, whereas maintaining purpose had a protective effect. Similarly, the model assessing factors associated with maintaining purpose showed that living with a partner, having high scores in emotional functioning and having pain and family support are related to higher scores, whereas not having axillary surgery and having mobility limitations and future worriers are related to lower scores (Table 3).

Table 3. Multivariate analyses: QLQ-ELD14 scales.

	Mobility limitations		**Maintaining Purpose**	
	B (SE)	**p-Value**	**B (SE)**	**p-Value**
Intercept	8.53 (4.52)	0.852	43.6 (9.2)	< 0.001
Age at evaluation				
70-75 years	Ref.		Ref.	
> 75 years	6.92 (2.82)	0.208	1.8 (7.3)	0.806
Years since beginning of treatment				
5 or less	Ref.		Ref.	
6 - 10	-4.14 (2.86)	0.276	-5.6 (4.6)	0.220
11-15	2.52 (3.13)	0.246	-17.6 (5.3)	0.001
16-20	-2.88 (3.46)	0.845	-12.2 (6.5)	0.063
>20	0.34 (3.66)	0.693	-0.4 (6.7)	0.952
Cohabitation				
Alone			Ref.	
With partner			12.6 (4.3)	0.003
Children older than 18 years			-12.1 (21.0)	0.565
With others			9.4 (9.8)	0.336
Breast surgery				
Breast-conserving			Ref.	
Radical mastectomy			3.5 (3.7)	0.338
Axillary surgery			Ref.	
Axillary node dissection				
Sentinel node biopsy			-0.6 (3.3)	0.856
No			-20.4 (8.7)	0.019
Limiting comorbidity				
No	Ref.			
Yes	5.35 (2.67)	0.039		
QLQ-C30 - Emotional Functioning			0.3 (0.1)	< 0.001
QLQ-C30 - Pain			0.3 (0.1)	< 0.001
QLQ-C30 - Fatigue	0.32 (0.06)	< 0.001		
QLQ-ELD14 – Mobility limitations			-0.2 (0.1)	0.011
QLQ-ELD14 - Future worries			-0.4 (0.1)	< 0.001
QLQ-ELD14 - Maintaining purpose	-0.11 (0.04)	0.021		
QLQ-ELD14 - Burden of illness				
QLQ-ELD14 - Joint stiffness	0.19 (0.04)	< 0.001	-0.2 (0.1)	0.002
QLQ-ELD14 - Family support			0.2 (0.1)	< 0.001
R^2	39.9%		55.8%	

Variables that have a significant relation with the two QLQ-ELD14 scales were included in the multivariate analysis. R2 of the multivariable model

4. Discussion

QOL scores in a sample of Spanish elderly early stage LTBCS were high in most QOL areas. The main limitations appeared in sexuality areas, skeletal symptoms, and three elderly-specific scales. QLQ-30 scores were in line with Spanish general population reference values [28]. Differences between age groups (≤75, >75 years) showed few QOL differences. These mainly involved lower QOL in the >75 years group. Combinations of lower symptoms and higher functioning with cohabitation and clinical variables were related to higher mobility limitations and higher maintaining purpose.

Levels of compliance were high since 94.6% of the candidates agreed to participate, 91.4% filled in the second assessment, and all QOL questionnaires had over 70% of their items answered. This indicates that the study was well accepted, especially considering that lower levels of compliance were expected in elderly patients [29]. The large number of VLTBCS patients should be highlighted (48.1%, including 27.6% of patients with >16 years' follow up). Levels of comorbidity were in line with expectations for the age of this population [11].

QOL scores in the **global sample** were high. Patients with relapse in the follow-up period and those with a new tumour were excluded. This may have influenced these high QOL scores. Low scores in sexual functioning and enjoyment were also observed in elderly LTBCS from our institution [20]. Limitations in sexual functioning and enjoyment were higher (20 points higher in both sexuality scales) than those found in LTBCS (5–20 years after diagnosis) who had been diagnosed in adolescence or young adulthood [30]. Differences may be related to the patients' ages. The fact that limitations in key areas such as fatigue, pain, emotional functioning, family support and insomnia are slight (20-29 points) is positive since high long-lasting limitations in these areas could heavily affect the QOL of elderly LTBCS [31]. Also encouraging is the fact that future perspective and future worries showed only slight limitations since worry of recurrence is considered to play a key role in the QOL of breast cancer survivors [32]. It is important that cognitive functioning showed high scores. This is because the patients' high age might have favoured lower functioning and because any cancer-related cognitive impairment (CRCI) is reported to potentially have a significant impact on the QOL of survivors [33].

QLQ-C30 scores were in line with ≥73 years early-stage breast cancer survivors (who had received treatment three years earlier). These patients showed higher emotional functioning (14 points, i.e., medium difference), an area in which our patients also showed rather high QOL [34]. QLQ-C30 scores were in line with VLTBCS (10 years after surgery) who had received radiotherapy (no CT) [3]. Medium differences appeared in favour of our study in dyspnoea (13 points) and insomnia (21 points) [24]. Patients had a lower mean age, and younger survivors tend to consider cancer as a bigger threat [3]. QLQ-C30 and QLQ-BR42 scores were in line with ≥68 years early-stage breast cancer survivors from our institution (who had finished treatment three years earlier) [35]. Scores in the breast module were higher (10-20 points) than those in a study of 70–99 year-old LTBCS (5-15 years) whose disease may have been active [11]. Scores in the QLQ-30 were in line with Spanish general population reference values, which indicates that the patients adapted well to their situation [28]. Similar comparisons with the general population were found in other studies: e.g., in >65 years LTBCS (10 years after diagnoses) [4] and in disease-free 70-99 years LTBCS (5–16 years after diagnosis) [9].

Comparisons between age-based groups showed differences in few QOL areas. These mainly involved lower QOL in the >75 years group. Like the differences in demographic and clinical variables (cohabitation and performance status), these may be related to the ageing process. Interestingly, the size of these QOL differences is not high (and are small in the QLQ-C30 areas), which indicates that the patients in the eldest group in our sample adapted well to their situation. In line with our study, Gao et al. [3] found lower physical functioning, cognitive functioning and global QOL in the ≥76 years group of LTBCS (10 years after treatment) and higher fatigue, insomnia and constipation than in the 65–75 years group. The better QOL in those living with a partner highlights the role of social support in elderly patients [36]. The few differences between patients who had and had not received radiotherapy were mainly found in areas not related to the treatment. These results are in line with studies that found that RT does not seem to compromise the overall QOL of elderly breast cancer patients [37]. The few differences between the two assessments confirm the high QOL scores and suggest the stability of the patients' clinical status.

Related to determinants of the two QLQ-ELD14 areas, comorbidity has also been found to be a QOL determinant in elderly breast cancer survivors [39]. Comorbidity is more prevalent and is considered to have a more important role with ageing [2,40]. Elderly-specific QOL areas have been found to be frequent determinants in our study and to show QOL limitations, which suggests that specific supportive interventions are needed for these areas in this age group [41]. Other areas, such as cohabitation, support, emotional functioning, fatigue and pain, have also been found to be QOL determinants in LTBCS (5 years [40,42] and 10 years [3] after diagnosis).

Our study has several strengths that may add relevant information to previous studies. One of these is the patients' age (mean 75.8 years) as more information in this age group could be useful. Another strength is the large number of QOL areas we assessed. In this study we administered a general cancer questionnaire and a breast cancer questionnaire as well as an elderly-specific questionnaire whereas other studies have assessed just general QOL areas. Note also that the patients came from a "real-world" setting: unlike clinical trials, studies in the real world tend to provide more QOL information because the proportion of patients who assess QOL is higher and more QOL areas are evaluated [43]. Finally, the participation rate was very high, which limits the possibility of selection bias. However, this study also has limitations. For example, we did not have a baseline (pre-treatment) assessment with which to compare our results. Also, patients with relapse during follow-up were excluded, which may have favoured higher QOL scores (health survivors bias) [11]. Finally, the sample came from just one cultural area.

5. Conclusions

QOL in these elderly LTBCS was high in both the whole sample and the two age groups after controlling for years since beginning of treatment, which indicates that the patients offered a positive balance of their situation and expectations. These results are highly relevant owing to the sample's high mean age and the fact that intense, long-lasting limitations that could permanently inhibit the patients' ability to return to a pre-cancer lifestyle [44] were not found.

Our results support previous reports that, for most elderly early-stage breast cancer survivors, cancer-specific well-being and general emotional health do not change substantially after breast cancer diagnosis [29]. Our results can provide professionals and patients with more information about potential general and elderly-specific late effects and chronic long-term sequalae that could be treated in a comprehensive survivorship care setting [9,41,45].

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. Supplementary tables S1 to S5.

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References

1. Tonorezos, E.; Devasia, T.; Mariotto, A.B.; et al . Prevalence of cancer survivors in the United States. *J. Natl. Cancer Inst.* **2024**,*116*, 1784-1790. doi: 10.1093/jnci/djae135.
2. Arndt, V.; Koch-Gallenkamp, L.; Jansen, L.; et al. Quality of life in long-term and very long-term cancer survivors versus population controls in Germany. *Acta. Oncol.* **2017**, *56*,190-197. doi: 10.1080/0284186X.2016.1266089.
3. Gao, Y.; Rosas, J.C.; Fink, H.; Behrens, S.; Chang-Claude, J.; Seibold, P. Longitudinal changes of health-related quality of life over 10 years in breast cancer patients treated with radiotherapy following breast-conserving surgery. *Qual. Life. Res.* **2023**, *32*, 2639-2652. doi: 10.1007/s11136-023-03408-y.
4. Koch, L.; Jansen, L.; Herrmann, A. et al. Quality of life in long-term breast cancer survivors - a 10-year longitudinal population-based study. *Acta Oncol*. **2013**, *52*, 1119-1128. doi: 10.3109/0284186X.2013.774461.
5. Doege, D.; Thong, M.S.Y.; Weißer, L. et al. Health-Related Quality of Life in Very Long-Term Cancer Survivors 14-24 Years Post-Diagnosis Compared to Population Controls: A Population-Based Study. *Cancers (Basel)* **2021**, *13*, 2754. doi: 10.3390/cancers13112754.
6. Vetter, M.; Huang, D.J.; Bosshard, G.; Güth, U. Breast cancer in women 80 years of age and older: a comprehensive analysis of an underreported entity. *Acta. Oncol*. **2013**, *52*, 57-65.
7. Biganzoli, L.; Goldhirsch, A.; Straehle, C.; et al. Adjuvant chemotherapy in elderly patients with breast cancer: a survey of the Breast International Group (BIG). *Ann. Oncol*. **2004**, *15*, 207-210
8. Depboylu, B. Treatment and patient related quality of life issues in elderly and very elderly breast cancer patients. *Transl. Cancer. Res*. **2020**, *9(Suppl 1)*, S146-S153. doi: 10.21037/tcr.2019.07.08.
9. Gosain, R.; Pollock, Y.; Jain, D. Age-related Disparity: Breast Cancer in the Elderly. *Curr. Oncol. Rep*. **2016**, *18*, 69. doi: 10.1007/s11912-016-0551-8.
10. Doege, D.; Thong, M.S.; Koch-Gallenkamp, L. et al. Health-related quality of life in long-term disease-free breast cancer survivors versus female population controls in Germany. *Breast Cancer Res. Treat.* **2019**, *175*, 499-510. doi: 10.1007/s10549-019-05188-x.
11. Doege, D.; Thong, M.S.Y.; Koch-Gallenkamp, L.; et al. Clinical and sociodemographic determinants of disease-specific health-related quality of life in long-term breast cancer survivors. J. *Cancer Res. Clin. Oncol*. **2022**, *148*, 3461-3473. doi: 10.1007/s00432-022-04204-w.
12. Nilsen, M.; Stalsberg, R.; Sand, K.; Haugan, G.; Reidunsdatter, R.J. Meaning Making for Psychological Adjustment and Quality of Life in Older Long-Term Breast Cancer Survivors. *Front. Psychol*. **2021**, *28*, *12*, 734198. doi: 10.3389/fpsyg.2021.734198.
13. ABC Global Charter.http://www.abcglobalalliance.org/abc-global-alliance-charter.
14. Lee Mortensen, G.; Madsen, I.B.; Krogsgaard, R.; Ejlertsen, B. Quality of life and care needs in women with estrogen positive metastatic breast cancer: a qualitative study. *Acta Oncol.* **2018**, *57*, 146-151. doi: 10.1080/0284186X.2017.1406141.
15. Aaronson, N.K.; Ahmedzai, S.; Bergman, B.; et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Natl. Cancer Inst.* **1993**, *85*, 365–376. https://doi: 10.1093/jnci/85.5.365.
16. Bjelic-Radisic, V.; Cardoso, F.; Weis, J.; et al. An international Phase IV field study -psychometric properties of the updated module on assessing quality of life of patients with breast cancer EORTC QLQ-BR42. *Breast* **2025**, *80*, 103890. doi: 10.1016/j.breast.2025.103890.
17. Wheelwright, S.; Darlington, A.S.; Fitzsimmons, D. et al. International validation of the EORTC QLQ-ELD14 questionnaire for assessment of health-related quality of life elderly patients with cancer. *Br. J. Cancer*. **2013**, *109*, 852-858. doi: 10.1038/bjc.2013.407.

18. Arraras, J.I.; Arias, F.; Tejedor, M. et al. The EORTC QLQ-C30 (version 3.0) Quality of Life questionnaire: validation study for Spain with head and neck cancer patients. *Psychooncology* **2002**, *11*, 249-256. doi: 10.1002/pon.555.
19. Arraras, J.I.; Tejedor, M.; Illarramendi, J.J.; et al. El cuestionario de calidad de vida para cáncer de mama de la EORTC, QLQ-BR23. Estudio psicométrico con una muestra española. *Psic. Conduc*. **2001**, *9*, 81–98.
20. Arraras, J.I.; Asin, G.; Illarramendi, J.J.; Manterola, A.; Salgado, E.; Dominguez, M.A. The EORTC QLQ-ELD14 questionnaire for elderly cancer patients. Validation study for elderly Spanish breast cancer patients. *Rev. Esp. Geriatr. Gerontol*. **2019**, *54*, 321-328. doi: 10.1016/j.regg.2019.05.001.
21. National Cancer Institute. *Common terminology criteria for adverse events (CTCAE). (Version 5.0)*. National Institutes of Health. U.S. Department of Health and Human Services: Bethesda (Maryland), 2017.
22. Charlson, M.E.; Pompei, P.; Ales, K.L.; Mackenzie, C.R. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J. Chronic Dis.* **1987**, *40*, 373–383. https://doi: 10.1016/0021-9681(87)90171-8.
23. Karnofsky, D.A.; Burchenal, J.H. The evaluation of chemotherapeutic agents in cancer. In *Evaluation of chemotherapeutic agents*; McLeod, C.M. Ed.; University Press: New York, 1949; pp. 191-205.
24. Cocks, K.; King, M.T.; Velikova, G.; Martyn St-James, M.; Fayers, P.M.; Brown, J.M. Evidence-based guidelines for determination of sample size and interpretation of the European Organisation for the Research and Treatment of Cancer quality of life questionnaire core 30. *J. Clin. Oncol*. **2011**, *29*, 89–96. doi:10.1200/JCO.2010.28.0107.
25. Cocks, K.; King, M.T.; Velikova, G.; et al. Evidence-based guidelines for interpreting change scores for the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30. *Eur. J. Cancer* **2012**, *48*, 1713-1721. doi:10.1016/j.ejca.2012.02.059.
26. Kim, S.H.; Jo, H.Y. Factors Associated with Poor Quality of Life in Breast Cancer Survivors: A 3-Year Follow-Up Study. *Cancers (Basel)* **2023**, *12*, 15:5809.doi: 10.3390/cancers15245809.
27. Giesinger, J.M.; Loth, F.L.C.; Aaronson, N.K.; et al. Thresholds for clinical importance were established to improve interpretation of the EORTC QLQ-C30 in clinical practice and research. J. *Clin. Epidemiol*. **2020**, *118*, 1-8. doi:10.1016/j.jclinepi.2019.10.003.
28. Arraras, J.I.; Nolte, S.; Liegl, G.; et al; EORTC Quality of Life Group. General Spanish population normative data analysis for the EORTC QLQ-C30 by sex, age, and health condition. *Health Qual. Life Outcomes* **2021**, *19*, 208. https://doi: 10.1186/s12955-021-01820-x.
29. Reimer, T.; Gerber, B. Quality-of-life considerations in the treatment of early stage breast cancer in the elderly. *Drugs Aging* **2010**, *27*: 791-800. doi: 10.2165/11584700-000000000-00000.
30. Vrancken Peeters. N.J.M.C.; Vlooswijk, C.; Bijlsma, R.M.; et al. Sexual quality of life of adolescents and young adult breast cancer survivors. *ESMO Open* **2024**, *9*,102234. doi: 10.1016/j.esmoop.2024.102234.
31. Haidinger, R.; Bauerfeind, I. Long-Term Side Effects of Adjuvant Therapy in Primary Breast Cancer Patients: Results of a Web-Based Survey. *Breast Care (Basel)* **2019**, *14*, 111-116. doi: 10.1159/000497233.
32. Tewari, A.; Chagpar. A,B. Worry about breast cancer recurrence: a population-based analysis. *Am. Surg*. **2014**, *80*, 640-645.
33. Országhová, Z.; Mego, M.; Chovanec, M. Long-Term Cognitive Dysfunction in Cancer Survivors. *Front. Mol. Biosci*. **2021**, *8*, 770413. doi: 10.3389/fmolb.2021.770413.
34. Bantema-Joppe, E.J.; de Bock, G.H.; Woltman-van Iersel, M.; Busz, D.M. Ranchor AV, Langendijk JA, et al. The impact of age on changes in quality of life among breast cancer survivors treated with breast-conserving surgery and radiotherapy. *Br. J. Cancer* **2015,** *112*, 636-43.
35. Arraras, J.I.; Illarramendi, J.J.; Manterola, A.; et al. Quality of life in Spanish postmenopausal breast cancer patients with localized disease who finish endocrine treatment: a prospective study. *Menopause* **2023**, *30*, 613-620. doi: 10.1097/GME.0000000000002178.
36. Utley, M.; Adeyanju, T.; Bernardo, B.; Paskett, E.D.; Krok-Schoen, J.L. The association between mental health, social support and physical health outcomes among older female cancer survivors. *J. Geriatr Oncol*. **2022**, *13*, 834-838. doi:10.1016/j.jgo.2022.04.001.
37. Kunkler, I.H.; Williams, L.J.; King, C.C.; Jack, W. Breast radiotherapy: considerations in older patients. *Clin. Oncol. (R Coll Radiol)*. **2009**, *21*, 111-117. doi: 10.1016/j.clon.2008.11.012.

38. Ganz, P.A.; Desmond, K.A.; Leedham, B.; Rowland, J.H.; Meyerowitz, B.E.; Belin, T.R. Quality of life in long-term, disease-free survivors of breast cancer: a follow-up study. *J. Natl. Cancer Inst*. **2002**, *94*, 39-49. doi: 10.1093/jnci/94.1.39.
39. Jacobs, D.H.M.; Horeweg, N.; Straver, M.; et al. Health-related quality of life of breast cancer patients after accelerated partial breast irradiation using intraoperative or external beam radiotherapy technique. *Breast* **2019**, *46*, 32-39. doi: 10.1016/j.breast.2019.04.006.
40. Chu, W.O.; Dialla, P.O.; Roignot, P.; et al. Determinants of quality of life among long-term breast cancer survivors. *Qual. Life Res*. **2016**, *25*, 1981-1990. doi: 10.1007/s11136-016-1248-z.
41. Kaufmann, A.; Schmidt, H.; Ostheimer, C.; Ullrich, J.; Landenberger, M.; Vordermark, D. Quality of life in very elderly radiotherapy patients: a prospective pilot study using the EORTC QLQ-ELD14 module. *Support. Care Cancer* **2015**, *23*, 1883-92.doi: 10.1007/s00520-014-2546-z.
42. Schmidt, M.E.; Wiskemann, J.; Steindorf, K. Quality of life, problems, and needs of disease-free breast cancer survivors 5 years after diagnosis. *Qual. Life Res*. **2018**, *27*, 2077-2086. doi: 10.1007/s11136-018-1866-8.
43. Criscitiello, C.; Spurden, D.; Piercy, J.; et al. Health-related quality of life among patients With HR+/HER2- early breast cancer. *Clin. Ther*. **2021**, *43*, 1228-1244.e4. https://doi.org/10.1016/j.clinthera.2021.04.020.
44. Maurer, T.; Thöne, K.; Obi, N.; et al. Health-Related Quality of Life in a Cohort of Breast Cancer Survivors over More Than 10 Years Post-Diagnosis and in Comparison to a Control Cohort. *Cancers (Basel)* **2021**, *13*, 1854. doi: 10.3390/cancers13081854.
45. Cheung, K.L. A Continuing Mission to Optimize the Care of Older Women with Breast Cancer. *Geriatrics (Basel)* **2017**, *20*, 37. doi: 10.3390/geriatrics2040037.