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Describing quality of life trajectories in young Hispanic women with breast cancer: 5-year results from a large prospective cohort

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ABSTRACT

Introduction: Cancer treatments have a detrimental impact on the quality of life (QoL) of young women with breast cancer (YWBC). Research exploring QoL trajectories has been mostly centered on postmenopausal women. Here we report longitudinal changes across all QoL domains and associated factors in YWBC.
Methods: In this prospective longitudinal cohort study, women aged ≤40 with stage I-III BC completed the European Organization for the Research and Treatment of Cancer Core QoL questionnaire at diagnosis and during 4 follow-up visits over 5 years, alongside demographic and clinical data collection. Group-based multivariate trajectory modeling was used to identify patient groups based on their functional and symptom scores, finding 3 groups (best, good, and poor). Factors associated with each trajectory pattern were identified with multinomial logistic models.
Results: A total of 477 women (median age: 36; IQR: 32–38) were clustered into the best (n = 259, 54 %), good (n = 79, 17 %), or poor trajectory groups (n = 139, 29 %). Throughout the disease, patients with a poor QoL experienced clinically significant impairment in emotional functioning, nausea and vomiting, and pain. They also had significant cognitive impairment, dyspnea, and diarrhea. Patients with a good QoL had clinically meaningful diarrhea for the first 7 months, while those with the best QoL had clinically important nausea and vomiting during the first 2 months since diagnosis. Noteworthy, all groups experienced significant financial difficulties throughout their follow-up. Regular alcohol consumption at diagnosis (aOR [adjusted odds ratio] 1.64; 95 % CI [confidence interval] 1.02–2.65) and HER2-positive BC (aOR 2.53; 95 % CI 1.35–4.73) were independent factors associated with classification to the poor and good groups, respectively.
Conclusion: This study underscores the variability in QoL among YWBC and the importance of ongoing monitoring. Strategies to improve access to economic resources, manage treatment-related adverse effects, and support patients in discontinuing modifiable risk factors are needed.

1. Introduction

Breast cancer (BC) is one of the leading causes of cancer mortality worldwide and continues to represent a significant threat to global public health and a burden to the economy. The incidence of BC has shown a steady increase over the last decades. According to estimates, the number of new BC cases worldwide in 2022 was 2.3 million, while in 2050, it is expected to increase by a staggering 57 % to reach 3.6 million [1,2]. Noteworthy, young women exhibit a higher incidence of aggressive BC phenotypes, and less favorable outcomes than their older

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counterparts [3–5].

In recent years, researchers and clinicians have dedicated significant efforts to optimizing available therapeutic resources and adding new treatment options, resulting in accelerated drug approval, lower recurrence-risk, and improved survival outcomes for patients with BC [6,7]. While this may seem a significant milestone in the oncology field, it is paramount to consider that many of these treatments cause major adverse events and can have a long-lasting impact on patients' quality of life (QoL).

QoL involves a multidimensional evaluation of the 3 fundamental pillars of health: physical, mental, and social well-being [8]. Studies have documented that patients experiencing low QoL are at a higher risk of treatment non-adherence and tend to have worse survival rates [9, 10]. Recently, there has been a growing interest in studying the QoL and its determinants in patients with BC. Certain cross-sectional studies have explored the QoL during specific treatment phases, without accounting its temporal evolution, whereas others have conducted longitudinal analyses to assess its evolution considering the entire population as a unique group [11–13]. However, it is crucial to acknowledge that, within any population, some patients may exhibit diverse behaviors and have unique variations in their QoL.

To overcome these challenges, some authors have used group-based trajectory modeling, identifying groups with similar QoL patterns over time within a study population [14–19]. Nonetheless, many of these studies have focused only on specific QoL domains to determine the ideal number of groups, thereby overlooking other crucial components that evaluate the multidimensionality of QoL. Additionally, most studies investigating QoL trajectories in patients with BC have primarily centered on postmenopausal women [14,16,18].

Thus, the current understanding of QoL in young women with BC (YWBC) is limited despite the unique challenges this population faces related to age-specific concerns such as sexuality, fertility, career development, and family planning. Here, we aimed to assess how the QoL of YWBC changes from diagnosis through long-term follow-up and to identify the most affected QoL domains and the factors influencing these changes.

2. Methods

2.1. Data source

The design, inclusion criteria, and recruitment process employed in the Joven & Fuerte cohort have been previously outlined [20]. Briefly, women aged ≤40 recently diagnosed with BC were recruited from 2014 to 2020 from three referral cancer centers across two cities in Mexico. Patients were prospectively followed, completing questionnaires at various intervals: at diagnosis (baseline) and four subsequent follow-up visits (approximately at month 6, and years 1, 2–3, and 4–5 post-enrollment). Primary BC treatment modalities were typically completed within 8 months of diagnosis. The study protocol was approved by the Research Ethics Committee of the Instituto Nacional de Cancerologia and the School of Medicine of the Instituto Tecnologico y de Estudios Superiores de Monterrey.

2.2. Variables of interest and instruments

Sociodemographic, clinical, and treatment characteristics were collected through self-reported patient questionnaires and medical records. These variables included age, education level, marital status, number of children, employment status, monthly household income, type of insurance, alcohol and smoking habits, physical activity, body mass index, cancer stage and subtype, as well as details on breast and axillary surgery, radiotherapy, chemotherapy, and hormone therapy regimens. Sociodemographic and clinical variables were collected at baseline, while treatment characteristics were completed during the first year of follow-up. QoL was assessed using the validated European Organization for the Research and Treatment of Cancer Core QoL questionnaire (EORTC QLQ-C30), which consists of 30 items including multi-item scales and single-item measures [21]. Most items (28 out of 30) are rated on a 4-point Likert scale, while the remaining 2 on a 7-point Likert scale. The questionnaire includes a global health status, 5 functional scales (physical, role, emotional, cognitive, and social functioning), 3 symptom scales (fatigue, nausea and vomiting, and pain), and 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). Following the QLQ-C30 manual [22], we calculated raw scores and applied a linear transformation to standardize them, resulting in scores ranging from 0 to 100 for all scales and items. Higher scores represent a higher response level, with functional scales indicating better functioning while symptom scales and other items indicating more pronounced symptomatology [22].

2.3. Study population

In the present study, we included patients with stage I-III BC who had completed at least 1 QLQ-C30 questionnaire. If patients experienced disease recurrence or were diagnosed with a second primary malignancy, we used the questionnaires they completed before these events occurred.

2.4. Statistical analysis

We used a descriptive analysis to summarize patient characteristics. To comprehensively evaluate the variations in the QoL of YWBC over 5 years post-diagnosis, we used group-based multivariate trajectory modeling. This approach extends the principles of traditional group-based trajectory modeling, which uses finite mixture modeling to categorize patients into clusters exhibiting similar QoL trends [23]. With group-based multivariate trajectory modeling, patients are clustered into groups based on various indicators of the outcome of interest, with trajectories being defined by polynomial regressions on time within each group [24,25]. Hence, this method enables the use of all available scales and items within the QLQ-C30 questionnaire rather than focusing only on a specific scale or score.

Determining the optimal number of groups with group-based multivariate trajectory modeling holds a greater significance than identifying the polynomial degree [23]. Therefore, we consecutively tested 1 to 5 trajectories using a high polynomial degree (cubic functional forms), deemed adequate for capturing complex patterns within the data. We relied on a combination of fit statistics and clinically relevant data to determine the final number of trajectories. Our criteria included the Akaike-, Bayesian-, Consistent Akaike-, sample size-adjusted Bayesian-, Hannan-Quinn information criterion (lower values indicate a better balance between goodness of fit and complexity), an average posterior probability of assignment exceeding 70 %, sufficient sample sizes per group (each group consisting of over 10 % of the overall sample), and visual inspection of trajectory plots. No normalization methods were employed to maintain a constant sample mean vector, as the score ranges are consistent across all QLQ-C30 scales and items.

The model selection metrics we used to determine the appropriate number of trajectory groups are shown in the eTable 1 in the Supplement. First, we ruled out the models with 4 and 5 trajectory groups, as they contained groups with less than 10 % of the overall number of patients. All the models had an average posterior probability of group classification close to 1 for all groups, indicating strong confidence in group assignment. Among the remaining 3 models, the one with the lowest average rank across criteria had 3 trajectory groups (average rank: 2.4). It had the second lowest Akaike-, sample size-adjusted Bayesian-, and Hannan-Quinn information criterion.

2.5. Factors associated with trajectory group classification

After determining the appropriate number of groups, we used Chi-squared, Fisher's Exact, and Kruskal-Wallis tests to examine associations between variables. Also, we employed multinomial logistic models to explore the relationships between variables and trajectory group classification. The reference group was selected based on the trajectory showing the most favorable outcomes, as we were interested in the factors associated with groups with worse outcomes. All statistical analyses were performed using R Statistical Software version 4.2.2 [26]. We conducted trajectory analyses with the *GBMT* package [27]. The statistical significance was defined as $P < 0.05$.

3. Results

Of the 590 women in the Joven & Fuerte cohort, 477 were included in this analysis after excluding those with stage IV BC, those who did not complete any QLQ questionnaires, and those who only completed questionnaires after disease recurrence, as detailed in the eFig. 1 in the Supplement. Table 1 shows that patients had a median age of 36 years (interquartile range 32–38), had an education level of high school or lower (50 %), had a partner (62 %), were unemployed (60 %), and covered by public insurance (87 %). Regarding baseline habits, most did not regularly consume alcohol (67 %), did not smoke (71 %), or did not regularly exercise (51 %). A large proportion were diagnosed with stages II (49 %) or III (39 %), and had hormone receptor-positive human epidermal growth factor receptor two (HER2)-negative (52 %), HER2-positive (22 %), or triple-negative BC (26 %). Most patients underwent mastectomy (74 %), received chemotherapy with anthracycline regimens (82 %), and were treated with tamoxifen or an aromatase inhibitor (42 %).

3.1. QoL trajectories

Over half of the patients (n = 259, 54 %) were clustered to the trajectory group that we labeled 'best' based on the better average functioning and lower symptom scores. The remainder were assigned to trajectory groups that we labeled 'good' (n = 79, 17 %) and 'poor' (n = 139, 29 %). Fig. 1 shows the behavior of each group across functional and symptom scales and items.

Throughout the disease, patients in the poor trajectory group reported mean values that crossed the thresholds for clinically significant impairment [28], in emotional functioning, nausea and vomiting, pain, and financial difficulties. Starting at month 6, they experienced clinically relevant cognitive impairment and began to feel clinically meaningful dyspnea by month 22, on average. Additionally, they experienced clinically relevant diarrhea from diagnosis until month 9. Patients' appetite loss improved gradually over time compared to baseline values. Regarding fatigue, insomnia, and constipation, baseline values initially worsened but improved slightly by year 5. Their global health status, role and social functioning fluctuated over time, with values worsening below initial scores by year 5.

Women in the good and best trajectory groups had similar mean scores across most QoL domains. The good trajectory group experienced clinically significant diarrhea during the first 7 months of treatment, while the best trajectory group experienced clinically relevant nausea and vomiting during the first 2 months after diagnosis. Both groups faced clinically relevant financial difficulties throughout follow-up. Cognitive functioning deteriorated over time in both groups, with women in the good trajectory group failing to recover to initial values by year 5, while those in the best group did. At year 5, mean scores for global health status, physical, role, emotional, and social functioning were better than initial scores for both groups. A detailed description of the mean scores across trajectory groups over time is provided in the eTable 2.1-2.15 in the Supplement.

3.2. Predictors of trajectory group classification

As shown in Table 1, although differences were not statistically significant, patients in the poor trajectory group were the youngest, had the highest proportion of employed individuals (40 % vs 28 % vs 37 %), and the highest percentage of baseline regular alcohol consumption (34 % vs 25 % vs 23 %) compared to women with good and best QoL, respectively. They had the lowest proportion of women with a partner (53 % vs 73 % vs 63 %, P = 0.018). Additionally, this group exhibited a numerically lower percentage of patients receiving anthracycline-free regimens (4 % vs 8 % vs 7 %) and a higher percentage of hormone schemes containing luteinizing hormone releasing hormone analogues (24 % vs 23 % vs 20).

Despite no statistical differences between groups, patients in the best trajectory had the lowest education level (53 % vs 46 % vs 46 %), the smallest percentage of regular smokers (21 % vs 25 % vs 22 %), the highest proportion of individuals with a monthly household income exceeding MXN $6800 (USD $408) (34 % vs 32 % vs 29 %), and were more likely to engage in regular exercise (43 % vs 39 % vs 41 %) compared to those in the good and poor groups, respectively. Additionally, they had the lowest proportion of stage III BC (36 % vs 43 % vs 43 %), a reduced need for neoadjuvant chemotherapy (48 % vs 57 % vs 51 %), and a decreased likelihood to receive radiotherapy (71 % vs 76 % vs 73 %). They were also most likely to undergo mastectomy (76 % vs 70 % vs 73 %) or sentinel node biopsy procedures (41 % vs 33 % vs 37 %).

In a univariate multinomial logistic analysis (Table 2), compared to women with the best QoL trajectory, patients who regularly consumed alcohol were more likely to belong to the poor trajectory group (odds ratio [OR] 1.74; 95 % confidence interval [CI] 1.10–2.77; $P = 0.019$) and those with HER2-positive were more likely to belong to the good trajectory group (OR 2.58; 95 % CI 1.41–4.73; $P = 0.002$). Both predictors remained significant in a multivariate model, as displayed in Table 3.

4. Discussion

In this study, we conducted a longitudinal assessment of the QoL using group-based multivariate trajectory modeling. We found that most YWBC maintain a good QoL over time. However, it is paramount to closely monitor patients, especially during active treatment phases, to identify and promptly address any areas of QoL impairment. Clinicians should be aware of the QoL deterioration young women could experience, with particular attention to cognitive decline, financial difficulties, diarrhea, nausea, and vomiting, so they can offer patients effective strategies to manage symptoms and tailor interventions to improve their overall QoL.

Previous research has shown that when exploring QoL subscales individually, distinct trajectory groups emerged for each domain, with less than 1/3 of patients being assigned to the same group [16]. Moreover, different factors were associated with each trajectory group depending on the specific subscale analyzed. Group-based multivariate trajectory modeling allows to analyze all available subdomains of a QoL questionnaire, thus comprehensively evaluating the multidimensional nature of QoL. Here, we employed this approach to analyze the QLQ-C30 questionnaire.

Based on this approach, this study identified 3 distinct trajectory groups. This aligns with a study showing that adults from the general population can experience 4 patterns of disruption in normal functioning after interpersonal loss or traumatic events [29]. In that investigation, the author described that individuals may experience a stably good adjustment, a gradual return to pre-event levels following notable impairment, gradual increasing distress affecting functioning, or stably poor adjustment with no recovery [29]. Fortunately, 71 % of our patients had the best or good QoL. However, our 29 % rate of patients experiencing poor QoL is higher than in other studies, where

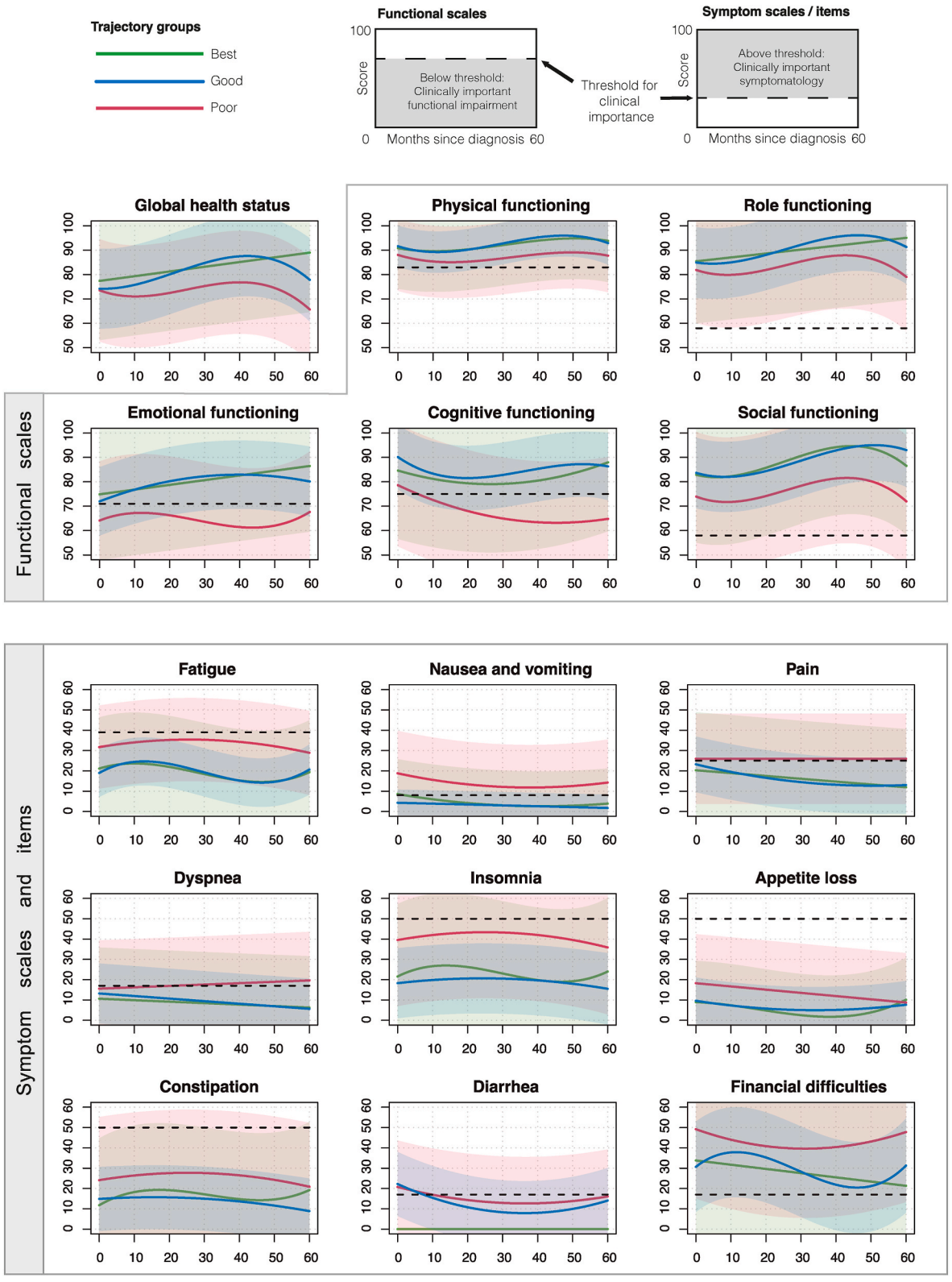

Fig. 1. EORTC QLQ-C30 scores across trajectory groups and months since breast cancer diagnosis.
The solid lines represent the predicted mean trajectories, with shaded regions indicating 95 % pointwise prediction intervals. Higher scores represent a greater response, either greater functionality or symptomatology. Dotted horizontal black lines represent the thresholds for clinical importance, as established by Giesinger JM et al. in *J Clin Epidemiol* 2020. Scores below or above these thresholds represent clinically significant impairment in functional or symptom domains, respectively. EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Core Quality of Life Questionnaire.

Table 1
Sociodemographic and clinical characteristics according to QoL trajectory groups.

	Overall n = 477 (100 %)	Best n = 259 (54 %)	Good n = 79 (17 %)	Poor n = 139 (29 %)	P-value
Age					
Median [Q1,Q3]	36.0 [32.0,38.0]	36.0 [32.0,38.0]	36.0 [33.0,38.0]	35.0 [31.5,38.0]	0.311
Education level					
>High school	223 (47 %)	112 (43 %)	42 (53 %)	69 (50 %)	0.255
≤High school	237 (50 %)	137 (53 %)	36 (46 %)	64 (46 %)	
Missing	17 (4 %)	10 (4 %)	1 (1 %)	6 (4 %)	
Marital status					
Not partnered	164 (34 %)	85 (33 %)	20 (25 %)	59 (42 %)	**0.018**
Partnered	296 (62 %)	164 (63 %)	58 (73 %)	74 (53 %)	
Missing	17 (4 %)	10 (4 %)	1 (1 %)	6 (4 %)	
Number of children					
Median [Q1,Q3]	2.00 [1.00,2.00]	2.00 [1.00,3.00]	2.00 [1.00,2.00]	2.00 [0,2.00]	0.209
Missing	18 (4 %)	11 (4 %)	1 (1 %)	6 (4 %)	
Employment status					
Not employed	287 (60 %)	154 (59 %)	56 (71 %)	77 (55 %)	0.128
Employed	173 (36 %)	95 (37 %)	22 (28 %)	56 (40 %)	
Missing	17 (4 %)	10 (4 %)	1 (1 %)	6 (4 %)	
Monthly household income (MXN $)					
<6800	279 (58 %)	148 (57 %)	47 (59 %)	84 (60 %)	0.664
≥6800	152 (32 %)	87 (34 %)	25 (32 %)	40 (29 %)	
Missing	46 (10 %)	24 (9 %)	7 (9 %)	15 (11 %)	
Type of insurance					
Private	34 (7 %)	23 (9 %)	5 (6 %)	6 (4 %)	0.212
Public	416 (87 %)	219 (85 %)	72 (91 %)	125 (90 %)	
Missing	27 (6 %)	17 (7 %)	2 (3 %)	8 (6 %)	
Regular exercise					
No	243 (51 %)	127 (49 %)	46 (58 %)	70 (50 %)	0.598
Yes	200 (42 %)	112 (43 %)	31 (39 %)	57 (41 %)	
Missing	34 (7 %)	20 (8 %)	2 (3 %)	12 (9 %)	
Regular smoking					
No	339 (71 %)	185 (71 %)	57 (72 %)	97 (70 %)	0.854
Yes	106 (22 %)	55 (21 %)	20 (25 %)	31 (22 %)	
Missing	32 (7 %)	19 (7 %)	2 (3 %)	11 (8 %)	
Regular alcohol consumption					
No	318 (67 %)	180 (69 %)	57 (72 %)	81 (58 %)	0.052
Yes	127 (27 %)	60 (23 %)	20 (25 %)	47 (34 %)	
Missing	32 (7 %)	19 (7 %)	2 (3 %)	11 (8 %)	
Body mass index					
Overweight or Obese	280 (59 %)	152 (59 %)	46 (58 %)	82 (59 %)	0.976
Underweight or Normal	192 (40 %)	103 (40 %)	33 (42 %)	56 (40 %)	
Missing	5 (1 %)	4 (2 %)	0 (0 %)	1 (1 %)	
Stage					
0	11 (2 %)	7 (3 %)	2 (3 %)	2 (1 %)	0.775
I	47 (10 %)	27 (10 %)	7 (9 %)	13 (9 %)	
II	233 (49 %)	133 (51 %)	36 (46 %)	64 (46 %)	
III	186 (39 %)	92 (36 %)	34 (43 %)	60 (43 %)	
Subtype					
HR-HER2+	33 (7 %)	16 (6 %)	9 (11 %)	8 (6 %)	0.063
HR + HER2-	250 (52 %)	140 (54 %)	31 (39 %)	79 (57 %)	
HR + HER2+	70 (15 %)	33 (13 %)	19 (24 %)	18 (13 %)	
TNBC	124 (26 %)	70 (27 %)	20 (25 %)	34 (24 %)	
Breast surgery					
Mastectomy	354 (74 %)	198 (76 %)	55 (70 %)	101 (73 %)	0.654
Breast conserving surgery	114 (24 %)	56 (22 %)	22 (28 %)	36 (26 %)	
None	6 (1 %)	4 (2 %)	1 (1 %)	1 (1 %)	
Missing	3 (1 %)	1 (0 %)	1 (1 %)	1 (1 %)	
Axillary surgery					
Axillary dissection	283 (59 %)	147 (57 %)	51 (65 %)	85 (61 %)	0.631
Sentinel node biopsy	184 (39 %)	106 (41 %)	26 (33 %)	52 (37 %)	
None	7 (1 %)	5 (2 %)	1 (1 %)	1 (1 %)	
Missing	3 (1 %)	1 (0 %)	1 (1 %)	1 (1 %)	
Chemotherapy schemes					
Anthracycline-based	390 (82 %)	210 (81 %)	65 (82 %)	115 (83 %)	0.676
No chemotherapy	53 (11 %)	30 (12 %)	6 (8 %)	17 (12 %)	
Non-containing anthracycline	30 (6 %)	18 (7 %)	6 (8 %)	6 (4 %)	
Missing	4 (1 %)	1 (0 %)	2 (3 %)	1 (1 %)	
Chemotherapy timing					
Neoadjuvant chemotherapy	240 (50 %)	124 (48 %)	45 (57 %)	71 (51 %)	0.540
Adyuvant chemotherapy	180 (38 %)	104 (40 %)	26 (33 %)	50 (36 %)	
No chemotherapy	53 (11 %)	30 (12 %)	6 (8 %)	17 (12 %)	
Missing	4 (1 %)	1 (0 %)	2 (3 %)	1 (1 %)	
Hormone therapy schemes					
Tamoxifen and/or aromatase inhibitor	199 (42 %)	114 (44 %)	29 (37 %)	56 (40 %)	0.788
Containing LHRHa	105 (22 %)	53 (20 %)	18 (23 %)	34 (24 %)	

(*continued on next page*)

Table 1 (*continued*)

	Overall n = 477 (100 %)	Best n = 259 (54 %)	Good n = 79 (17 %)	Poor n = 139 (29 %)	P-value
No hormone therapy	169 (35 %)	91 (35 %)	30 (38 %)	48 (35 %)	
Missing	4 (1 %)	1 (0 %)	2 (3 %)	1 (1 %)	
Radiotherapy					
No	129 (27 %)	75 (29 %)	17 (22 %)	37 (27 %)	0.477
Yes	344 (72 %)	183 (71 %)	60 (76 %)	101 (73 %)	
Missing	4 (1 %)	1 (0 %)	2 (3 %)	1 (1 %)	

QoL, Quality of life; HR, Hormone receptor; HER2, Human epidermal growth factor receptor two; TNBC, Triple negative breast cancer, LHRHa, Luteinizing hormone releasing hormone analogue, MXN $, Mexican peso.

Table 2
Univariate multinomial logistic regression of factors associated with trajectory group classification (v reference "Best", n = 259; 54 %).

Factor	Good n = 79 (17 %)		Poor n = 139 (29 %)		*P*-global
	OR (95 % CI)	*P*	OR (95 % CI)	*P*	
Age, ≤35 *v* > 35	1.02 (0.62–1.70)	0.924	1.15 (0.76–1.74)	0.495	0.788
Education level, ≤High school *v* > High school	0.70 (0.42–1.17)	0.172	0.76 (0.50–1.16)	0.199	0.254
Marital status, Partnered v Not	1.50 (0.85–2.66)	0.162	0.65 (0.42–1.00)	0.050	**0.017**
Number of children, ≥1 v No	0.93 (0.51–1.70)	0.809	0.75 (0.46–1.22)	0.247	0.513
Employed, Yes v No	0.64 (0.37–1.11)	0.111	1.18 (0.77–1.81)	0.452	0.121
Household income MXN $, ≥6800 v < 6800	0.90 (0.52–1.57)	0.723	0.81 (0.51–1.28)	0.370	0.663
Type of insurance, Public v Private	1.51 (0.55–4.12)	0.419	2.19 (0.87–5.52)	0.097	0.195
Regular exercise, Yes v No	0.76 (0.45–1.29)	0.312	0.92 (0.60–1.42)	0.718	0.596
Regular smoking, Yes v No	1.18 (0.65–2.13)	0.583	1.07 (0.65–1.78)	0.779	0.855
Regular alcohol consumption, Yes v No	1.05 (0.59–1.89)	0.864	1.74 (1.10–2.77)	**0.019**	0.056
Body mass index, Underweight or Normal v Overweight or Obese	1.06 (0.63–1.77)	0.827	1.01 (0.66–1.54)	0.971	0.976
Stage, III v 0-I-II	1.37 (0.82–2.29)	0.227	1.38 (0.90–2.10)	0.135	0.238
Subtype, HER2+ v HR + HER2-	2.58 (1.41–4.73)	**0.002**	0.94 (0.54–1.63)	0.826	**0.026**
Subtype, TNBC v HR + HER2-	1.29 (0.69–2.43)	0.429	0.86 (0.53–1.41)	0.552	
Surgery, Breast conserving surgery v Mastectomy	1.41 (0.79–2.52)	0.239	1.26 (0.78–2.04)	0.347	0.685
Surgery, None v Mastectomy	0.90 (0.10–8.22)	0.926	0.49 (0.05–4.44)	0.526	
Axillary surgery, Sentinel node biopsy v Axillary dissection	0.71 (0.41–1.21)	0.203	0.85 (0.55–1.30)	0.449	0.584
Axillary surgery, None v Axillary dissection	0.58 (0.07–5.05)	0.619	0.35 (0.04–3.01)	0.336	
No CT v Anthracycline-based CT	0.65 (0.26–1.62)	0.352	1.03 (0.55–1.96)	0.916	0.638
Non-containing anthracycline CT v Anthracycline-based CT	1.08 (0.41–2.83)	0.880	0.61 (0.24–1.58)	0.307	
No CT v Neoadjuvant CT	0.55 (0.22–1.41)	0.214	0.99 (0.51–1.92)	0.975	0.529
Adyuvant CT v Neoadjuvant CT	0.69 (0.40–1.19)	0.183	0.84 (0.54–1.31)	0.442	
No hormone therapy v Tamoxifen and/or Aromatase inhibitor	1.30 (0.73–2.31)	0.381	1.07 (0.67–1.72)	0.768	0.788
Containing LHRHa v Tamoxifen and/or Aromatase inhibitor	1.34 (0.68–2.62)	0.400	1.31 (0.76–2.23)	0.329	
Radiotherapy Yes v No	1.45 (0.79–2.64)	0.229	1.12 (0.70–1.78)	0.635	0.467

HR, Hormone receptor; HER2, Human epidermal growth factor receptor two; TNBC, Triple negative breast cancer; CT, chemotherapy; LHRHa, Luteinizing hormone releasing hormone analogue; MXN $, Mexican peso.

Table 3
Multivariate multinomial logistic regression of factors associated with trajectory group classification (v reference "Best", n = 259; 54 %).

Factor	Good n = 79 (17 %)		Poor n = 139 (29 %)		*P*-global
	aOR (95 % CI)	*P*	aOR (95 % CI)	*P*	
Marital status, Partnered v Not	1.53 (0.83–2.81)	0.168	0.77 (0.49–1.21)	0.256	0.105
Regular alcohol consumption, Yes v No	1.07 (0.58–1.97)	0.837	1.64 (1.02–2.65)	**0.042**	0.120
Stage, III v 0-I-II	1.38 (0.81–2.35)	0.242	1.52 (0.98–2.38)	0.063	0.143
Subtype, HER2+ v HR + HER2-	2.53 (1.35–4.73)	**0.004**	0.81 (0.45–1.47)	0.493	**0.023**
Subtype, TNBC v HR + HER2-	1.25 (0.65–2.39)	0.498	0.85 (0.51–1.43)	0.546	

HR, Hormone receptor; HER2, Human epidermal growth factor receptor two; TNBC, Triple negative breast cancer.

deteriorating or poor trajectory groups accounted for 17 %–21 % of patients [14,17,19]. This difference may derive from prior studies focusing on older patients without family planning or career development concerns, who typically undergo less aggressive treatments than younger women. A recent study among American YWBC found that 6 %, 4 %, and 11 % of patients had poor trajectories in physical, psychological, and sexual domains, respectively [30]. This underscores the variability in the percentage of women clustered into a poor trajectory when estimating trajectories based on individual scales. Moreover, it highlights the importance of considering factors such as socioeconomic status, demographics, and lifestyle behaviors in studies exploring QoL. Our study is focused on Mexican women, making it the largest study to date focused on QoL aspects in young Hispanic breast cancer patients.

As summarized in Fig. 2, even patients categorized in the best or good trajectory groups experienced clinically significant symptoms that warrant attention and could benefit from discussion during clinical encounters. Clinicians should actively assess patients' emotional and cognitive health while addressing symptoms like nausea, vomiting, diarrhea, or pain with targeted therapeutics. Moreover, it is essential to closely monitor patients from diagnosis, especially during active treatment phases. Regular evaluations can help promptly identify patients at risk of QoL deterioration.

Despite causing severe adverse events, chemotherapy remains a cornerstone of BC treatment. Common cytotoxic agents, such as anthracyclines, alkylating agents, and capecitabine, are associated with acute toxicities like nausea, vomiting, and diarrhea [31]. The clinically

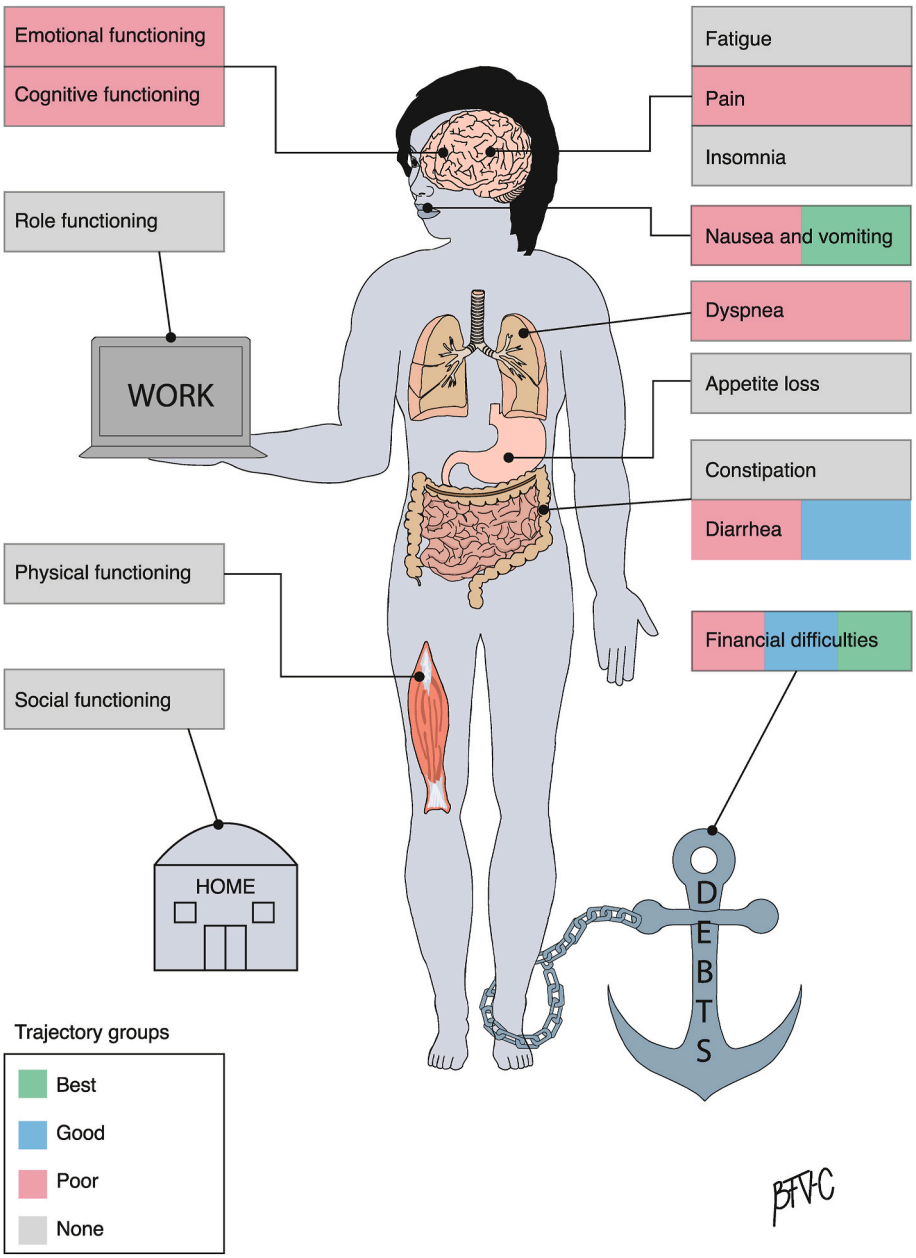

Fig. 2. Summary of trajectory groups experiencing clinically significant impairment in the EORTC QLQ-C30 questionnaire.
Color-coded boxes indicate trajectory groups whose mean trajectory crossed the threshold for clinically significant impairment in functional or symptom domains. EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Core Quality of Life Questionnaire.

significant nausea and vomiting experienced by our patients coincide with the intravenous administration of anthracycline/cyclophosphamide combinations, which have a high risk (>90 %) of causing emetogenicity [32]. Additionally, certain hormone therapies and cytotoxic agents have been linked to cognitive impairment [33,34], potentially explaining the cognitive deterioration observed in all of our groups, as most patients in this cohort received these treatments. Oncologists must understand the multifactorial etiologies, pathophysiology, and management recommendations for treatment-related adverse events to provide patients with available strategies to manage these symptoms and improve their QoL [31,33].

Alarmingly, all our groups faced financial difficulties throughout the disease. Most patients had public health insurance and scarce economic resources, highlighting the constrained setting of our population. Furthermore, Mexico's lack of universal healthcare coverage and shortage of oncologic drugs force patients to pay out-of-pocket for unavailable medicines [35,36]. YWBC in such settings are especially vulnerable due to a lack of access to therapies, potential treatment interruptions, and unmet supportive care needs. Moreover, a study has documented that the high costs of treatments and expenses for transportation and accommodation when seeking treatment at cancer-referral centers affect a patient's economy [37]. Additionally, we have previously shown that, at 2 years of follow-up, 26 % of our patients experienced a reduction in their work activity [38]. Thus, governments must prioritize access to therapies, and institutions should ensure access to oncology social workers who can assist patients to overcome financial barriers whenever needed [37,39]. Moreover, policymakers and employers must develop plans to facilitate a prompt return to work, provide adequate sick leave coverage, and create adaptable work environments that meet the needs of patients with cancer [37].

Our findings are consistent with prior research, showing that non-smoking and regular physical activity are more prevalent among

patients with a good QoL [14,17]. Additionally, we identified that baseline regular alcohol consumption is an independent predictor for having a poor QoL. Although we found no statistical association for the type of surgery, hormone therapy, or chemotherapy regimens, we believe further exploring using a specific BC QoL questionnaire is needed and will be pursued in future studies. Additionally, it is important to acknowledge that certain factors may uniquely impact various QoL domains. Exploring each domain individually through additional statistical analyses could yield more tailored results. However, given the multidimensional nature of QoL, it is paramount to acknowledge that an interrelation of factors may contribute to a poor QoL rather than focusing on a specific characteristic. For instance, compared to older patients, YWBC have a poorer body image and overall QoL [40], which could further decline due to the aggressive treatment strategies they receive. Moreover, the gonadotoxic effects of chemotherapy and the contraindication of pregnancy during adjuvant endocrine therapy negatively impact young women's QoL by affecting their fertility and hindering their plans of having children.

This study has limitations that must be considered when interpreting the results. We relied on patient-reported outcomes with inherent patient and health provider barriers [41]. Attrition bias cannot be ruled out, particularly at later time points as shown in the eFig. 1 in the Supplement. We did not use standardized scales to assess behavioral factors which limits the interpretability of specific results. Furthermore, psychosocial factors such as coping strategies and personality type, which could impact patients' QoL, were not evaluated [42].

5. Conclusions

Our results underscore the variability in the QoL among YWBC, emphasizing the importance of identifying patients at risk of QoL impairment and addressing their specific needs. It is paramount to entrust patients with early behavioral changes, such as practicing regular exercise and quitting alcohol and smoking, and thoroughly explaining how these changes can improve their QoL [43]. While most women with BC have a good QoL, even those with the best trajectory have specific needs and experience clinically relevant symptoms. Thus, health professionals must avoid assuming that all patients require the same psychosocial interventions and should closely monitor patients throughout their BC journey. Oncologists should carefully balance survival outcomes, adverse events, and health-related costs when recommending treatments and interventions to ensure patients benefit from life-saving therapies throughout their BC path. Lastly, patients should have timely access to economic resources and effective strategies for managing treatment-related adverse effects.

CRediT authorship contribution statement

Bryan F. Vaca-Cartagena: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Ana S. Ferrigno Guajardo:** Writing – review & editing, Data curation. **Hatem A. Azim Jr:** Writing – review & editing, Supervision, Data curation, Conceptualization. **Federico Rotolo:** Writing – review & editing, Formal analysis, Data curation. **Antonio Olivas-Martinez:** Writing – review & editing, Formal analysis, Data curation. **Alejandra Platas:** Writing – review & editing, Data curation. **Alan Fonseca:** Writing – review & editing, Data curation. **Fernanda Mesa-Chavez:** Writing – review & editing, Data curation. **Marlid Cruz-Ramos:** Writing – review & editing, Data curation. **Ana Rodriguez:** Writing – review & editing, Data curation. **Alejandro Mohar:** Writing – review & editing, Data curation. **Cynthia Villarreal-Garza:** Writing – review & editing, Supervision, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: **Hatem A. Azim Jr**: Consulting: Evexta Bio, Pep Therapy, Linkinvax, **Federico Rotolo**: Financial**:** Sanofi, Stock and Other Ownership Interests: Innate Pharma, **Cynthia Villarreal-Garza**: Grants: Pfizer, AstraZeneca, and Gilead, Honoraria: MSD, AstraZeneca, Eli Lilly, and Novartis, Support for attending meetings and travel: Novartis, MSD, and AstraZeneca.

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Appendix A. Supplementary data

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