



Determinants of satisfaction with life and self-esteem in women with breast cancer

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Abstract

Purpose To determine satisfaction with life (LISAT) and self-esteem in women with breast cancer and the relation between sociodemographic and clinical variables with LISAT and self-esteem.

Methods Cross-sectional study with 514 Spanish women with breast cancer. Data were collected using an online questionnaire that included the Satisfaction with Life Questionnaire (LISAT-8) and the Rosenberg self-esteem scale. Variables are age, education, occupation, marital status, surgical treatment, breast reconstruction, adjuvant treatment, time since diagnosis, the self-esteem scale, and the LISAT. A multinomial logistic regression was performed to identify possible factors associated with the LISAT and self-esteem after breast cancer.

Results The average age was 46.34 (SD ± 8.28), average age at diagnosis was 42.26 (SD ± 8.56), and average time since diagnosis was 4.05 years (SD ± 5.23). Reports showed the following: good general LISAT (61.7%), economic LISAT (44.7%), and social life LISAT (75.9%) and medium sexual LISAT (41.2%). Of the respondents, 39% had lower self-esteem ($p < 0.001$). Those who were working ($p = 0.002$) and those with breast reconstruction ($p < 0.037$) had a good LISAT. Women with mastectomies had a worse LISAT ($p < 0.001$). Self-esteem was associated with the general LISAT (Pearson = 0.536, $p < 0.001$), social LISAT (Pearson = 0.502, $p < 0.001$), and sexual LISAT (Pearson = 0.329, $p < 0.001$).

Conclusions Women with breast cancer had a good LISAT overall; the sexual aspect was evaluated as the lowest in terms of life satisfaction. Marital status, occupation, surgical treatment and self-esteem are associated with the LISAT. Health professionals should know the variables that influence life satisfaction of women with breast cancer to plan and conduct appropriate nursing care.

Keywords Breast cancer · Quality of life · Self-esteem · Chemotherapy

Introduction

Breast cancer has a high incidence worldwide [1–5]. In the United States, it is the second most common cause of death, with approximately 61,000 new cases in 2016 [1]. In Spain,

during 2014, the occurrences of breast cancer were 27,747 [3]. It is estimated that 80% of women survive 5 years after diagnosis [3, 4]. However, due to the early diagnosis of cancer [2] and new treatments, life expectancy after a breast cancer diagnosis has increased.

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Women diagnosed with breast cancer are subject to different treatments, both surgical and adjuvant (chemotherapy, radiotherapy, hormonal, and others). Although these treatments help reduce mortality, they have side effects that lead to a poorer quality of life (QOL) [5] and changes in self-esteem [6, 7].

QOL is the perception of an individual's position in life. The state of one's health affects QOL. Health-related quality of life (HRQOL) measures are generally the most appropriate measures of self-perception of health status [8]. HRQOL is used to evaluate the impact of illness on people. This is a multidimensional construct (physical, psychological, social, and sexual) that assesses how people evaluate their wellbeing and the subjective management of their health situation [9]. The inclusion of cultural and ethnic factors can facilitate a more complete valuation of HRQOL [8]. Satisfaction with life (LISAT) in the various areas has been utilized as a measure of adaptation concerning outcomes and recuperation from illness to adjust to different conditions of life.

In women with cancer, this depends on the type and degree of cancer, type of intervention, treatment received, and complications encountered [10, 11].

Given that the HRQOL is a subjective dimension in which values and culture intervene, transcultural differences influence the perception of QOL [8, 12, 13]. Studying the factors that influence HRQOL in different cultures can help health professionals plan interventions [8, 13] so that women with breast cancer can be more satisfied with their lives. Although there have been several studies in Spain on QOL in women with breast cancer [14], a recent literature review [14] concluded that a need remains to increase QOL research in this group.

Three recent studies were conducted in two regions of Spain: Navarra and Valencia [11, 15, 16]. In Navarra, one study assessed HRQOL in older women with breast cancer who received radiotherapy [15], and another assessed the HRQOL in premenopausal women diagnosed with breast cancer more than 5 years previously [16]. In Valencia, the evolution of the HRQOL of women in the first year of diagnosis has been studied [11]. To the best of our knowledge, the variables that influence the satisfaction with life of women with breast cancer at different ages (young, perimenopausal, and older) have not been studied when considering the time from the diagnosis of cancer to more than 20 years after diagnosis.

The objectives of the present study were to determine the degree of satisfaction with life (general, social, sexual, and economic) and levels of self-esteem in women with breast cancer and to identify the relations among the sociodemographic and clinical variables of satisfaction with life and self-esteem.

Methodology

Design and study population

This is a cross-sectional descriptive study of women with breast cancer belonging to associations and support groups in eastern Spain. These associations are grouped in the Spanish Federation of Breast Cancer (Federación Española de Cáncer de mama, FECMA). Data were collected from June 2016 to June 2017.

The inclusion criteria were women with breast cancer for whom at least 3 months had passed since their surgery and chemotherapy treatment.

The exclusion criteria were women with other types of cancer or with metastatic or advanced stage breast cancer.

Calculation of sample size

The sample size was calculated using the Granmo program (version 7.12) (Barcelona, Spain, 2012) with an estimated population from the Arraras study (2016) [16], in which 74.5% of women with cancer had good HRQOL.

In addition, the data provided by the Spanish Society of Medical Oncology [4] were used as the reference population, indicating that 25,215 women had breast cancer in Spain in 2016.

Therefore, for an expected prevalence of 74.5% with a precision of 5%, a 95% confidence level and a 10% replacement rate, a sample of 281 women was sufficient.

Instruments

An online questionnaire was constructed that incorporated the measuring instruments of the mentioned variables:

- a. The Spanish version of the Satisfaction with Life, Questionnaire (LISAT-8) [17] is a self-administered questionnaire comprising 8 items, rated on a Likert scale. The items measure satisfaction with 8 different aspects of the patient's life (i.e., life in general, sexual life, relationship with spouse/significant other, family life, relationships with friends and acquaintances, leisure, work situation, and economic situation). The final score is calculated by adding the scores of all of the items (the total score ranges from 8 to 48). LISAT may be low, medium, or good, depending on the scores obtained. Three dimensions are evaluated: satisfaction with social life (Items 1, 4, 5 and 6), satisfaction with affective life (Items 2 and 3), and satisfaction with economic life (Items 7 and 8). The cut-points for the score range classifications are as follows: for the general LISAT, good (36–48),

medium (21–35), and low (20–8); for the social LISAT good (18–24), medium (11–17), and low (4–10); and for the Sexual and Financial LISAT good (10–12), medium (4–9), and low (4–8). The instrument has a sensitivity of 81.7% (CI 80.5–82.9) and a reliability of 79.2% (CI 77.5–80.8) [17].

- b. The Rosenberg self-esteem scale, validated in Spanish [18], comprises ten items with a Likert scale of four options. According to the sum of their items, the scale is divided into three ranges: normal or high self-esteem (between 30 and 40 points), medium self-esteem (26–29 points), and low self-esteem (<26 points). It has a Cronbach's alpha of 0.87 and a reliability of 0.74 [18].
- c. The ad hoc independent variables questionnaire measures sociodemographic variables (age, level of education, occupation, marital status), and clinical variables (surgical treatment, reconstruction of the breast, adjuvant treatment, hormonal treatment, age at diagnosis, and time since diagnosis).

Procedure

Previously, the research team contacted different associations in eastern Spain belonging to the Spanish Federation of Breast Cancer (Federación Española de Cáncer de mama, FECMA), requesting their participation in the study. From June of 2016 to June of 2017, the associations sent emails to female members diagnosed with breast cancer (988 women). The e-mail informed them about the research, invited them to participate, and included a shortcut link to the online interview; the link was available on Google Forms. Once the link was accessed, the women were required to read the information and give informed consent before filling out the questionnaire. The response rate was 53.3%.

Variables

The independent variables included sociodemographic and clinical variables. The sociodemographic variables were age, level of education, occupation, and marital status. The clinical variables included surgical treatment, (bilateral mastectomy, mastectomy, lumpectomy, and lymphadenectomy), reconstruction of the breast (yes/no), adjuvant treatment (radiotherapy, chemotherapy, and hormonal treatment), hormonal treatment (yes/no), age at diagnosis, and time since diagnosis.

Dependent variables

The dependent variables were the LISAT (satisfaction with social life, satisfaction with sexual-affective life, and satisfaction with economic life) and self-esteem (high, medium, or low).

Statistical analyses

The statistical program SPSS version 22.0, licensed to the University of Castilla La Mancha (Spain), was used for the data analysis. A descriptive analysis of the variables was conducted by calculating counts (n) and proportions (%) of the qualitative variables and the calculation of means (m) and standard deviations (SD) for the quantitative variables. Proportions of categorical variables were compared using χ -square tests for contingency tables, and when there was a frequency ≤ 5 , Fisher's test was used. A multivariable analysis was conducted to identify possible factors associated with QOL and self-esteem after breast cancer through multinomial logistic regression analysis. The variables with $p \geq 0.15$ were eliminated one-by-one from the model. The odds ratios (OR) were calculated with their confidence intervals. The internal consistency Cronbach's alpha coefficient was calculated for the Rosenberg and LISAT 8 questionnaires. For quantitative variables, a Pearson's correlation analysis (r) was performed. All hypothesis contrasts were bilateral, and in all statistical tests, "significant" values were considered, which were those whose confidence values of 95% ($p < 0.05$).

Ethics approval

The investigation respected the fundamental principles of the Declaration of Helsinki, the Universal Declaration of UNESCO, The Spanish Organic Law 15/1999 of 13 December on the Protection of Personal Data, and the Royal Decree 994/99 of the Spanish State, Information Sheet, and Informed Consent. This study was approved by the institutional ethics committee (dossier number_ Comité de Ética del Complejo hospitalario de Toledo CEITO 138).

Results

Of the 527 women who answered the questionnaires, 13 did not complete the questionnaires appropriately. The final sample comprised 514 women with a mean age of 46.34 (SD \pm 8.276). Of the women, 66.3% were between 40 and 55 years old, 57.6% had been diagnosed with cancer in the perimenopausal period (40–54 years), the mean age at diagnosis was 42.26 (SD \pm 8.563), and 48.1% had been diagnosed with breast cancer 2–5 years before the start of the present study. Most (63.7%) were married or cohabitating, 43.8% had secondary education or higher (43.8%), and 50% were working. The surgical treatments they had received were lumpectomy (37.8%), bilateral mastectomy (16.7%), or mastectomy (41.6%); of these, 40.5% had received breast reconstruction. Additional treatments included adjuvant treatment radiotherapy, chemotherapy and hormone treatment (49.4%),

hormonal treatment (75.5%), and chemotherapy only (80%). Table 1 shows the sociodemographic variables.

Satisfaction with life and self-esteem

Of the women, 61.7% reported having a good general LISAT, good economic LISAT (4.7%), good social life LISAT (75.9%), and medium sexual LISAT (41.2%). A total of 38.9% of the women in the sample had medium self-esteem (Table 2).

The relations between sociodemographic variables and the different types of LISAT of participants after cancer were studied (Table 3). Women who were married or cohabiting ($p < 0.001$), those who were working ($p = 0.002$), and those with breast reconstruction ($p < 0.037$) perceived their satisfaction with life to be good. Those who underwent mastectomy as a surgical treatment had a lower satisfaction with life ($p < 0.001$).

A multiple logistic regression model was constructed to determine which variables influenced LISAT (Table 4), with

Table 1 Sociodemographic variables of the participants ($N = 514$)

Variables	Frequency (<i>n</i>)	Percentage
Age		
< 40 years old	106	20.6
40–55 years	341	66.4
> 55 years	67	13
Age at diagnostic		
< 40 years old	186	36.2
40–55 years	296	57.6
> 55 years	32	6.2
Time since diagnostic		
First year	157	30.5
2nd to 5th years	247	48.1
6th to 10th years	68	13.2
More to 10 years	42	8.2
Marital status		
Married or cohabitating	346	67.3
Single/separated/divorced/widowed with partner	78	15.1
Single/separated/divorced/widowed without partner	90	17.6
Education level		
Elementary	64	12.5
High school	225	43.8
University	225	43.8
Occupation		
Unemployed	106	20.6
Employed	257	50
Sick leave	94	18.3
Retired	57	11.1

Table 2 Satisfaction with life and self-esteem of the participants ($N = 514$)

	Frequency (<i>n</i>)	Percentage
General LISAT		
Low	16	3.1
Medium	121	35.2
Good	317	61.7
Economic LISAT		
Low	69	13.4
Medium	215	41.8
Good	230	44.7
Social LISAT		
Low	9	1.8
Medium	115	22.4
Good	390	75.9
Sexual LISAT		
Low	114	22.2
Medium	212	41.2
Good	188	36.6
Self-esteem level		
Low	180	35
Medium	200	38.9
High	134	26.1

good general LISAT serving as the reference category. The researchers observed the following:

Regarding marital status, women without a partner were 12.03 times as likely to have a lower QOL as married women or women with partners ($p < 0.001$).

- Regarding occupations, working women were 0.35 times less likely to have a medium QOL than retired women ($p = 0.004$).
- Regarding age at diagnosis, women between 40 and 55 years old were 4.89 times as likely to have a medium QOL as women over 55 ($p = 0.009$).

When analyzing the different variables by age group (Table 5), it was determined that there was a higher percentage of married women among postmenopausal women (> 55 years) ($p < 0.001$). In addition, more premenopausal women worked, and a greater proportion of postmenopausal women (> 55 years) were retired ($p < 0.001$). Postmenopausal women had the highest percentage of lumpectomies ($p < 0.001$). Premenopausal women (< 40 years) presented the highest percentage of breast reconstructions ($p = 0.021$).

The relation between sociodemographic and clinical variables and the level of self-esteem of postcancer participants indicated that significant differences were observed only when compared with occupation ($p = 0.006$) and hormonal treatment ($p = 0.02$). Conversely, women who were working

Table 3 Sociodemographic and clinical variables of participants according to general LISAT^a (N=514)

Variables	General LISAT			p
	Low (n=16) n (%)	Medium (n=121) n (%)	Good (n=317) n (%)	
Marital status				
Married or cohabitating	7 (43.8)	105 (58)	234 (73.8)	<0.001
Single/separated/divorced/ widowed with partner	1 (6.3)	27 (14.9)	50 (15.8)	
Single/separated/divorced/ widowed without partner	8 (50)	49 (27.1)	33 (10.4)	
Occupation				
Unemployed	5 (31.3)	47 (26)	54 (17)	0.002
Employed	4 (25)	72 (39.8)	181 (57.1)	
Sick leave	3 (18.7)	42 (23.2)	49 (15.5)	
Retired	4 (25)	20 (11)	33 (10.4)	
Surgical treatment				
Lumpectomy	3 (18.8)	61 (33.7)	131 (41.3)	<0.001
Mastectomy	10 (62.5)	62 (34.3)	142 (44.8)	
Bilateral Mastectomy	2 (12.5)	46 (25.4)	38 (12)	
Lymphadenectomy	1 (6.2)	12 (6.6)	6 (1.9)	
Reconstruction				
Yes	7 (43.7)	66 (36.5)	135 (42.6)	0.037
No	8 (50)	78 (43.1)	99 (31.2)	
Not necessary	1 (6.3)	37 (20.4)	83 (26.2)	

^aLISAT: satisfaction with of life. Age, Age at diagnostic, and time since diagnostic were not statistically significant

had the highest self-esteem, and women who had hormonal treatment had the lowest levels of self-esteem.

Finally, significant correlations were observed when comparing the values obtained by the self-esteem questionnaire and the LISAT-8, with moderate correlations between self-esteem and general satisfaction (Pearson = 0.536, $p < 0.001$) and social satisfaction (Pearson = 0.502, $p < 0.001$) and low correlations between self-esteem and sexual satisfaction (Pearson = 0.329, $p < 0.001$) and economic satisfaction (Pearson = 0.393, $p < 0.001$).

The analysis of the internal consistency of the questionnaires showed a Cronbach's alpha index of 0.826 for LISAT-8. Similarly, for the LISAT-8 subscales, the Cronbach's alpha index values were 0.827 for the social subscale, 0.751 for the sexual subscale, and 0.675 for the economic subscale. For Rosenberg's self-esteem scale, the Cronbach's alpha was 0.496.

Discussion

As mentioned above, HRQOL is a subjective perception that people have about different areas of life [8]. Treatments for breast cancer, while leading to greater survival, produce numerous side effects [5, 11]; among them are alopecia, diarrhea, fatigue, nausea, and neuropathies [11].

Other adjuvant treatments, such as hormone therapy, can cause vaginal dryness, weight gain, sexual dysfunction, hot flashes, and other side effects [5, 11]. In the current study, women received breast cancer treatment.

Of the women in the sample studied, 61.7%, perceived their general LISAT to be very good, consistent with other studies [19] reporting that 1–5 years after treatment, the LISAT of women with breast cancer was similar to that of women without breast cancer in the general population [10, 11, 16, 20].

As in other studies, satisfaction with their sexual life was valued the worst: 22% rated it as poor and 41% as medium [16, 19, 21, 22]. The origin of sexual discomfort (physical, psychological, emotional, and other factors) [23] in the women studied may be due to changes in self-image and to hormonal treatments [19, 24], which were administered to 75.5% of the patients, and the sequelae of surgical treatment. Hormonal treatment is associated with loss of desire, vaginal dryness, and other related side effects [19, 24, 25].

The women who had the highest levels of satisfaction with life were those who underwent a lumpectomy [22, 26]. Women with mastectomies had the worst levels of general satisfaction with life, regardless of age [26, 27]. Women who had had reconstructions also had better general LISAT than those who had not had reconstructions [26, 27].

Table 4 Factors affecting LISAT after cancer ($N=514$)

	Low		Medium	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Marital status				
Single/separated/divorced/ widowed without partner	12.03 (3.72–38.87)	<0.001	4.43 (2.57–7.64)	<0.001
Single/separated/divorced/ widowed with partner	1.09 (0.1–9.79)	0.941	1.35 (0.76–2.41)	0.302
Married or cohabitating	Reference		Reference	
Occupation				
Unemployed	0.79 (0.17–3.78)	0.769	1.12 (0.51–2.43)	0.778
Employed	0.12 (0.02–0.63)	0.012	0.35 (0.17–0.71)	0.004
Sick leave	0.49 (0.08–3.0)	0.444	1.03 (0.46–2.31)	0.946
Retired	Reference		Reference	
Surgical treatment				
Lumpectomy	0.06 (0.005–0.81)	0.034	0.18 (0.06–0.54)	0.002
Mastectomy	0.19 (0.02–1.99)	0.166	0.15 (0.05–0.45)	0.001
Bilateral mastectomy	0.2 (0.01–3.01)	0.244	0.57 (0.18–1.79)	0.339
Lymphadenectomy	Reference		Reference	
Age at diagnosis				
<40 years old	2.69 (0.22–32.67)	0.438	3.89 (1.16–13.10)	0.028
40–55 years	1.88 (0.17–20.99)	0.607	4.84 (1.48–15.76)	0.009
>55 years	Reference		Reference	
Time since diagnosis				
First year	1.161 (0.184–7.313)	0.873	1.241 (0.562–2.739)	0.593
2nd to 5th years	0.537 (0.061–4.759)	0.577	1.608 (0.715–3.612)	0.251
6th to 10th years	3.652 (0.495–26.923)	0.204	2.089 (0.844–5.172)	0.111
More to 10 years	Reference		Reference	

The reference category is good general satisfaction with life (LISAT); introduced variables = marital status, occupation, surgical treatment, self-esteem level, time since diagnosis, age at diagnosis

OR odds ratio, CI confidence interval

In the present study, women aged between 40 and 54 had the lowest levels of sexual satisfaction compared with women of other ages although this difference was not significant. This finding may be because ovarian function may be more affected over the longer term by chemotherapy and hormonal therapy in perimenopausal women than in younger women whose ovaries return to their proper functioning levels at the end of treatment [25].

By contrast, in this study, marital status (married or cohabiting with a partner) was related to better satisfaction with life, which is consistent with other investigations [27]. Having both company and a greater satisfaction with life suggests that women with partners may have greater social and family support, with being part of a couple an important support during the breast cancer recovery phase [28].

There were not differences in the general LISAT between the different ages and the age at diagnosis, a relationship that was not clear in other studies [24]. However, while some authors [10, 20] observed that older women had lower levels of satisfaction with life because of age-related problems and

because they had less social support, in other studies, young women reported having a poorer QOL [22, 24].

As previously mentioned, in the present study, more older women were married or cohabiting, indicating greater family support [28], which could explain why they had a good LISAT despite their more advanced age.

There were also no differences in satisfaction with general life based on the time since they were diagnosed with breast cancer, possibly because one of the inclusion criteria was that at least 3 months had passed since their treatment (i.e., surgery, chemotherapy, or radiotherapy). The acute effects of those treatments (nausea, alopecia, etc.) would have already been reported, as seen in other studies [11].

Consistent with other investigations, only 25% of the sample had high self-esteem [6, 7, 29] not related to either age or surgical treatment, but to occupation and hormonal treatment. Women who worked had high self-esteem, and women who had hormonal treatments reported having poor self-esteem, possibly because of the changes that occurred with such treatments, including the possibility of more

Table 5 Relationship between independent variables and age groups ($N=514$)

Variables	<40 years ($n=106$) n (%)	40–55 years ($n=341$) n (%)	>55 years ($n=67$) n (%)	p
Marital status				
Married or cohabitating	56 (52.8)	240 (70.4)	50 (74.6)	<0.001
Single/separated/ divorced/widowed with partner	34 (32.13)	39 (11.4)	5 (7.5)	
Single/separated/ divorced/widowed without partner	16 (15.1)	62 (18.2)	12 (17.9)	
Occupation				
Unemployed	20 (18.9)	76 (22.4)	10 (14.9)	<0.001
Employed	56 (52.8)	174 (51)	27 (40.3)	
Sick leave	24 (22.6)	65 (19)	5 (7.5)	
Retired	6 (5.7)	26 (7.6)	25 (37.3)	
Surgical treatment				
Lumpectomy	32 (30.2)	129 (37.8)	34 (50.7)	<0.001
Mastectomy	37 (34.9)	154 (45.2)	23 (34.3)	
Bilateral mastectomy	33 (31.1)	45 (13.2)	8 (12)	
Lymphadenectomy	4 (3.8)	13 (3.8)	2 (3)	
Breast reconstruction				
Yes	55 (51.9)	131 (38.4)	22 (32.8)	0.021
No	30 (28.3)	133 (39)	22 (32.8)	
Not necessary	21 (19.8)	77 (22.6)	23 (34.4)	

Age at diagnostic, time since diagnostic were not statistically significant

symptoms (hot flashes, atrophic vaginitis, vaginal dryness, and decreased libido) [18] and the early onset of menopause.

Higher levels of self-esteem were related to better general and social LISAT and to a lower sexual LISAT, aspects that are consistent with the results of other studies [29, 30].

The data obtained can be useful for multidisciplinary teams to generate proposals for comprehensive interventions that improve the satisfaction with life of women with breast cancer [31]. Within multidisciplinary teams, nursing professionals have an important responsibility; oncology nursing generally focuses on helping women with cancer meet their basic needs [13]. Nurses must know what variables influence the satisfaction with life of women with cancer and help women decide on interventions that will improve their satisfaction with life. To reach consensus on the best care, communication skills are required, as indicated in other studies [32].

This study has some limitations. First, because a cross-sectional design was used, it is not possible to establish causal relations. Another limitation is related to cultural beliefs that restrict women from answering particular questions. Another limitation is that we did not include the “stage of cancer” variable, which can also be an important predictor of LISAT. Finally, the online questionnaire prevented women from asking about any doubts, and the analyzed data were self-reported information.

Conclusions

Women with breast cancer in Spain reported having a high level of satisfaction with life in general although less in terms of their sexual life. However, general satisfaction improved if they had emotional support or employment, and satisfaction with sexual life decreased with physical deformity after mastectomy.

Contributions of this article

This study was the first conducted in Spain with a sample of more than 500 women who have had breast cancer that considered different age groups (young, <40 years; perimenopausal, 40–55 years old; and older than 55 years) and time since diagnosis (1–20 years).

This study demonstrates that despite the clinical and personal circumstances of women with breast cancer, they return to having being satisfied with their general lives although the area in which they are least satisfied is their sexual lives. Overall, health centers are planning and administering adequate care, although sexuality should be addressed more effectively because this aspect of life satisfaction does not improve, even after the patient has recovered.

Author contributions All the authors have contributed intellectually to its production and are thus to be regarded as material authors. Study design: AICC, JMCT, MARB, NME. Data collection: AICC, JMCT. Data analysis: AICC, JMCT, NME. Study supervision: AICC, JMCT, MARB. Manuscript writing: AICC, JMCT, MARB, NME. Critical revisions for important intellectual content: AICC, JMCT, MARB, NME.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

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