

Cultural Adaptation and Validation of the EORTC QLQ-BR45 to Assess Health-Related Quality of Life of Breast Cancer Patients

Original Paper

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Abstract **Background:** The European Organization for Research and Treatment of Cancer (EORTC) QLQ-BR23 is considered a premier module for breast cancer patients that is utilised synchronously with the core questionnaire. However, new and scalable treatments on breast cancer patients' quality of life (QoL) need a more accurate and comprehensive tool to be assessed. Therefore, the EORTC introduced the newly updated module EORTC QLQ-BR45. Hence, the current study aims to perform cultural adaptation, pilot testing and assessment of the psychometric properties of the Egyptian Arabic translation of the EORTC QLQ-BR45 module on Egyptian breast cancer patients.

Patients and Methods: First, a review of the existing Arabic translation and the modified preliminary translation was sent to a professional proofreader. Then, comprehensibility of the Egyptian Arabic translation was pilot tested on a sample of 13 breast cancer patients. Afterwards, 74 patients with proven locally advanced breast cancer receiving neoadjuvant chemotherapy at Beni-Suef University Hospital, Beni-Suef, Egypt were interviewed. A second interview was conducted post-surgery for patients receiving target therapy, endocrine therapy or radiotherapy. The psychometric properties of the EORTC QLQ-BR45 were assessed in terms of reliability, convergent and divergent validity.

Results: Adequate internal consistency reliability (Cronbach's α coefficients >0.7) was demonstrated for the questionnaire, except for body image scale ($\alpha = 0.51$) and systemic therapy side effects scale ($\alpha = 0.63$). Multi-trait scaling analysis exhibited acceptable convergent and divergent validity, and scaling success was observed for all questionnaire items.

Conclusion: The Egyptian Arabic version of the EORTC QLQ-BR45 module is valid and adequately reliable. These results support using the EORTC QLQ-BR45 in future breast cancer clinical trials.

Keywords Breast cancer – Quality of life – Module development – EORTC QLQ-BR45 – Validation – Reliability

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer in women and the most prevalent cause of cancer mortality in females [1, 2]. Since the past decades, health-related quality of life (HRQoL) has been considered a main clinical outcome of cancer research reflecting patient-reported outcomes (PROs) [3]. The vital importance of PROs is the expression of patient satisfaction and endurance to the disease or treatment impacts on the patients' daily life. The HRQoL is a

multidimensional structure that covers several major aspects such as disease-related and treatment-related symptoms, physical, psychological and social functioning [4]. Therefore, one of the main objectives in the treatment of breast cancer patients is to maintain their quality of life (QoL).

The European Organization for Research and Treatment of Cancer (EORTC) established an integrated framework for assessing the QoL among cancer patients. The EORTC

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QLQ-C30 version 1.0 module was introduced in 1993 as a core questionnaire used to assess the QoL among any type of cancer patients. Then, this core questionnaire was updated to version 2.0 and version 3.0 in 1997 and 2000, respectively. Version 3.0 is currently the standard version of QLQ-C30 [5]. Besides, EORTC QLQ-BR23 was developed in 1996 as a premier module to be used in conjunction with the core questionnaire for breast cancer patients [6]. Over the course of the last decade, newer therapeutic options were introduced for breast cancer. Whereas tamoxifen treatment was the gold standard in postmenopausal women for hormonal breast cancer therapy, aromatase inhibitors have become the first option in patients, although they suffer from new toxicities including arthralgia, bone loss and cognitive impairment [7, 8]. In addition, chemotherapeutic treatments have expanded to include taxanes and anthracyclines that have become standard treatments for breast cancer patients. Moreover, targeted agents represent a novel class of anticancer treatments for breast cancer patients. These anticancer therapies have a substantial effect on the QoL of patients with breast cancer due to their toxicity profile [9, 10]. Furthermore, new surgical techniques can exhibit new consequences for the QoL of the patients [11]. Consequently, due to the impact of newer treatment alternatives, it became apparent that the initial 23-item QLQ-BR23 might be ineffective for solving a variety of crucial QoL problems and possible side effects. Therefore, in 2020, the EORTC quality of life group (QLG) updated this module into the EORTC QLQ-BR45. This module can assess more accurately and comprehensively the impact of new and scalable treatments on breast cancer patients' QoL [12].

Extensive literature research is thus needed to assess the reliability and validity of the EORTC QLQ-BR45. Accordingly, the main objectives of the current study are to:

- 1) adapt and pilot test the available Arabic translation of the EORTC QLQ-BR45 module into an Egyptian Arabic version, which is currently available as the first native Arabic version and
- 2) evaluate the internal consistency reliability and validity of the Egyptian Arabic translation of the EORTC QLQ-BR45 module for determining the QoL of Egyptian breast cancer patients.

PATIENTS AND METHODS

Trial design and participants

Between June 2019 and November 2020, subjects were recruited from Beni-Suef University Hospital, Beni-Suef, Egypt. Subjects were eligible if they were female patients of age between 18 and 65 years, spoke Egyptian Arabic, had proven locally advanced breast cancer and would receive first-line neoadjuvant chemotherapy regimen (four cycles of doxorubicin/cyclophosphamide, followed by 12 cycles of weekly paclitaxel). Patients were excluded if they had a

previous history of breast cancer treatment or suffered any psychiatric disorders, physical disabilities or severe medical condition.

In the current study, sample size was calculated using Raosoft sample size calculator [13], with 0.95 confidence level and 0.1 margin error. Hence, 80 non-diabetic breast cancer patients were enrolled in the study. Six patients were excluded from the study because of protocol deviation, early withdrawal or loss to follow-up. Thus, 74 patients were interviewed on day 1 of receiving the first cycle of neoadjuvant chemotherapy treatment. After the last chemotherapy cycle, all patients underwent breast surgery, either mastectomy or breast conservative surgery. Eventually, a second interview was conducted 3–4 weeks post-surgery for 19 patients receiving targeted therapy, 34 patients receiving endocrine treatment and six patients receiving radiotherapy.

The translated Arabic EORTC QLQ-BR45 version was permitted for use in the current study by the EORTC-QLG. The EORTC-QLG provided us with the existing Arabic version for review and adaptation to the Egyptian culture. Then, the reviewed version was proofread by a professional translator who was arranged by the EORTC-QLG. Afterwards, the results of the proofreading were sent to us for review. Thus, the new version was pilot tested on 13 patients. The results of pilot testing were reviewed by the EORTC-QLG, and an approval for the use of the EORTC QLQ-BR45 was provided to the current study by the EORTC.

The study was approved by the Institutional Review Board (IRB) of the Faculty of Pharmacy, Beni-Suef University (REC-H-PhBSU-20012). The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice norms and local and national regulatory requirements. The respondent's right to confidentiality was always respected, and any legal requirements on data protection were adhered to. Approval of the written informed consent was acquired by all the patients before enrolment in the study. The consent form to the patients included a statement explaining the aim of the study, the potential length of time for participation and a description of all the procedures that would be completed during enrolment in the clinical trial. In addition, it included their right to cease their participation in the clinical trial at any time and the contact information of the researchers.

In the current study, most of our patients had received less education and could not read the consent form. Therefore, an oral presentation of the consent document, stating the requisite aspects of informed consent, was given, wherein it was thoroughly explained to the patients or the patient's legally authorised representative and a witness to the oral presentation. The witness can be a family member or someone independent of the research team. The consent document must be signed by both the patient (or the patient's representative) and the witness. The IRB approved a written summary of what should be said in the oral presentation to the patient or the representative to ensure all the required aspects are presented.

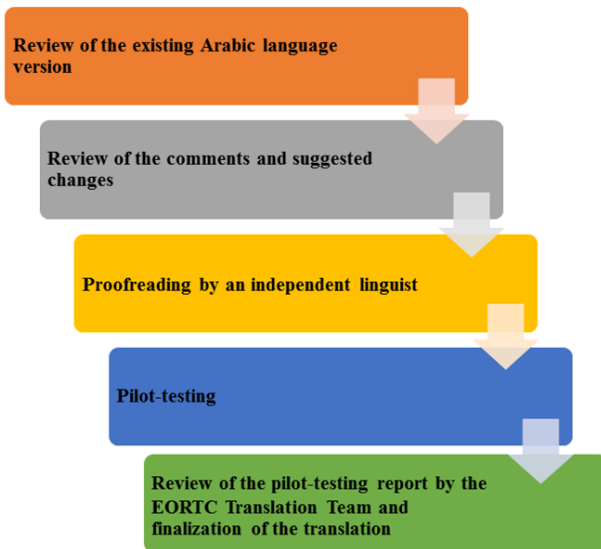


Figure 1. Flowchart of the developmental sequences of the Egyptian Arabic version of the QLQ-BR45 module.

Instrument, procedure and scoring

The breast cancer module, EORTC QLQ-BR45 questionnaire, is a supplementary questionnaire module to be used in conjunction with QLQ-C30. The EORTC QLQ-BR45 is composed of 45 items related to breast cancer or its treatment [6]. The numbering of the items in the module starts from item 31 till item 75. The module consists of three multi-item functional scales (body image, sexual functioning and breast satisfaction), two single-item functional scales (sexual enjoyment and future perspective), three multi-item symptom scales (systemic side effects, breast symptoms and arm symptoms), one single-item symptom scale (upset by hair loss) and three multi-item target therapy scales (endocrine therapy symptoms, skin mucositis symptoms and endocrine sexual symptoms). The time frame of the QLQ-BR45 module is 'during the past week' in item numbers 31–43, 47–69 and 74–75. The time frame is 'during the past 4 weeks' in item numbers 44–46 and 70–73. All the items of the questionnaire are scored on a four-point Likert scale as follows: 'not at all' (1), 'a little' (2), 'quite a bit' (3), 'very much' (4).

An appointment was arranged with all eligible patients who visited the breast cancer oncology clinic, agreed to participate in the trial and signed the informed consent to perform a face-to-face interview on day 1 of the first dose of neoadjuvant chemotherapy. Then, the patients were followed up to determine the day of the second interview after the first dose of their indicated adjuvant treatment. Finally, the second face-to-face interview was conducted. The interviews were conducted in a private room by a female trained clinical pharmacist using the structured interview questions. Then, scoring of the EORTC QLQ-BR45 was conducted following the EORTC scoring manual [14]. Afterwards, linear transformation to a 0–100 scale was done for all the responses to Likert scale items. Higher scores

for functional scales indicate a better QoL. On the other side, higher scores for symptom scales and single items indicate higher severity of the symptoms and worse QoL.

Cultural adaptation and pilot testing

Cross-cultural adaptation and pilot testing of the EORTC QLQ-BR45 were performed according to the EORTC guidelines and the international guidelines for cross-cultural adaptation of HRQOL as shown in Figure 1 [15, 16]. Some terminologies in several questionnaire items were substituted to adapt to the local culture in Egypt. Then, pilot testing was conducted on 13 breast cancer patients to check its comprehensibility in Arabic (Egypt) and debriefing. The content was assessed for items that were difficult to understand or answer and confusing or offensive items, and the questionnaire was amended accordingly. Finally, the release of an elaborated version of the EORTC QLQ-BR45 in Egyptian Arabic was done. The approval of the EORTC team was obtained at each step.

Statistical analysis

Socio-demographic data of the patients was analysed with frequencies and percentages. Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 26.0) was used to perform the statistical analysis. The psychometric properties of the EORTC QLQ-BR45 were evaluated in terms of reliability, convergent and divergent validity tests. Cronbach's α was used to evaluate the internal consistency reliability, whereas Pearson's correlation was used to evaluate the convergent and divergent validity.

Reliability Test

Cronbach's α coefficient was used to evaluate the questionnaire's internal consistency reliability, with the acceptable value being ≥ 0.70 [17, 18].

Validity

Evaluation of the convergent and divergent validity was performed using multi-trait scaling analysis. Convergent validity was anticipated in case the correlation of each item and its own scale was ≥ 0.40 , while divergent validity was anticipated in case the correlation of each item with its own scale exceeded its correlation with other scales. Scaling success was predicted in case the correlation of each item with its own scale exceeded that with other scales [17, 19].

RESULTS

Socio-demographic characteristics of the patients

Table 1 summarises the socio-demographic characteristics and the tumour characteristics of the patients at baseline.

Table 1. Socio-demographic data and tumour characteristics of the patients in the study at baseline (n = 74).

Variable	Frequency	Percentage
Age, years		
<35	8	10.81%
35–45	26	35.13%
46–55	21	28.38%
56–65	19	25.68%
Marital status		
Married	58	78.37%
Single	5	6.77%
Widow	11	14.86%
Body mass index		
Normal weight	17	22.97%
Overweight	26	35.17%
Obese	31	41.89%
Menopausal state		
Pre-menopause	38	51.35%
Post-menopause	36	48.65%
Family history of breast cancer		
Yes	15	20.27%
No	59	79.73%
Comorbidity		
Yes	16	21.62%
No	58	78.38%
Educational level		
Low level	47	63.51%
Intermediate level	18	24.32%
High level	9	12.16%
ECOG performance status		
0	19	25.68%
1	47	63.51%
2	8	10.81%
3	0	0.00%
4	0	0.00%
Histological type		
IDC	67	90.54%
ILC/mixed IDC/ILC	7	9.46%
Clinical stage		
IIB	10	13.52%
IIIA	31	41.89%
IIIB	33	44.59%
Hormone receptor status		
ER and/or PR positive	63	85.14%
ER and PR negative	11	14.86%
HER2 status		
Positive	30	40.54%
Negative	44	59.46%

ECOG: Eastern Cooperative Oncology Group, ER: estrogen receptor, PR: progesterone receptor HER2: human epidermal growth factor receptor-2, IDC: invasive ductal carcinoma, ILC: invasive lobular carcinoma.

The mean age of the patients was 48 ± 10.83 years, and the mean body mass index (BMI) was 30.32 ± 5.62 . Also, 78.37% of the patients were married and 63.51% had received low education level. The Eastern Cooperative Oncology Group (ECOG) performance status of the patients ranged from 0 to 2.

Cultural adaptation and pilot testing

In the process of adaptation of the questionnaire, several terminologies were substituted to adapt to the local culture in Egypt. The reviewed version was proofread by a professional translator. The new version was pilot tested on 13 patients. Accordingly, the patients' comments were summarised and sent to the EORTC translation team. Most of the patients refused to answer questions related to their sexual behaviour, with numbers 44, 45, 46, 72 and 73. Patients had neither understanding problems nor linguistic issues; however, they felt unwilling to answer these questions. In addition, there was an inquiry by the interviewer about question numbers 74 and 75 and if the QLQ-BR45 module should be conducted only after breast surgery. The EORTC commented that there are no specific guidelines for a specific time for the BR45 module. Furthermore, the patients who did not undergo surgical operation could answer 'not at all' to the surgery items or could skip them, and then these scales would not be scored.

Reliability test

Table 2 shows that the internal consistency reliability of most scales demonstrated an acceptable level (Cronbach's α coefficients above 0.70), except for body image ($\alpha = 0.54$) and systemic therapy side effects ($\alpha = 0.63$).

Validity test

As shown in Table 3, the magnitude of the correlation coefficient of almost all items–scale was >0.40 , showing convergent validity of the items of each scale, except for systemic therapy side effects and endocrine therapy symptoms. Furthermore, the correlation coefficient of each item with its own scale exceeded its correlation with the other scales. Thus, scaling success criteria were met and the item–scales correlation revealed divergent validity.

DISCUSSION

The development of QoL questionnaires is mainly conducted in English-speaking countries. A main objective of HRQoL studies is to measure the applicability of the QoL questionnaires to other languages and traditions. Another objective is to demonstrate the degree of implementation of acceptable intercultural validity. The current study contributes to the cross-cultural adaptation and validation of the EORTC QLQ-BR45 questionnaire in the Egyptian breast cancer population.

Table 2. Reliability of EORTC QLQ-BR45 Arabic version in female breast cancer patients in Egypt (n = 74).

Scale	Cronbach's α value ^a
Body image	0.54
Sexual functioning	0.85
Breast satisfaction	0.95
Systemic therapy side effects	0.63
Arm symptoms	0.77
Breast symptoms	0.74
Endocrine therapy symptoms	0.76
Skin mucosis symptoms	0.75
Endocrine sexual symptoms	0.88
Future perspective	Single item
Sexual enjoyment	Single item
Upset by hair loss	Single item

^aFor single items, reliability test is not applicable
EORTC: European Organization for Research and Treatment of Cancer

The EORTC procedures and the international guidelines for cross-cultural adaptation of HRQoL were rigorously followed to culturally adapt and validate the EORTC QLQ-BR45 instruments into local Egyptian Arabic [15, 16]. The available Arabic version provided by the EORTC-QLG was not for a native Arabic country. This could be justified because this version was developed in a non-Arabic-speaking country in the Middle East. Therefore, certain expressions in the available Arabic version of the EORTC QLQ-BR45 necessitate modifications to be suitable for the Egyptian culture. Furthermore, the questionnaire items may require adaptation when used in different languages and cultural settings in order to achieve equivalence between the original and the new versions. Therefore, if questionnaires are to be utilised across cultures, they must not only be adequately translated linguistically, but also culturally altered to maintain the instrument's content validity on a conceptual level [16]. Hence, it is necessary to adapt the Arabic version among different countries to ensure the validity of the instrument. Pilot testing was supplemented for Egyptian breast cancer patients to identify problematic wording and sentence structures for the target population. The mean time required for interviewing the patients was 25 min. Then, the psychometric properties of the adapted questionnaire were evaluated. Target therapy scale was used for patients receiving targeted therapy (n = 19) or endocrine therapy (n = 34), and breast satisfaction scale was used for patients post-surgery (n = 74).

In the current study, the internal consistency reliability of the majority of scales in the EORTC QLQ-BR45 was found to be satisfactory. This conclusion was drawn from Cronbach's α values exceeding 0.70 for all scales, except body image and systemic therapy side effects. The results of the current study

Table 3. Multi-trait scaling analysis for convergent and divergent validity of EORTC-QLQ-BR45 Arabic version in female breast cancer patients in Egypt (n = 74).

Scale	Subscale	Item–own scale correlation ^a	Item–other scale correlation ^a	Scaling success
Functional scales				
	Body image	0.487–0.798	0.032–0.638	4/4
	Sexual functioning	0.902–0.924	0.001–0.027	2/2
	Breast satisfaction	0.977–0.978	–0.041–0.03	2/2
Symptoms scales				
	Systemic therapy side effects ^b	0.308–0.743	0.002–0.507	7/7
	Arm symptoms	0.765–0.872	0.022–0.480	3/3
	Breast symptoms	0.649–0.827	0.016–0.308	4/4
Target therapy scales				
	Endocrine therapy symptoms ^b	0.397–0.879	0.003–0.773	10/10
	Skin mucosis symptoms	0.425–0.796	0.055–0.541	6/6
	Endocrine sexual symptoms	0.940–0.959	0.004–0.635	4/4

^aPearson's correlation coefficient^bSystemic therapy side effects and Endocrine therapy symptoms are below 0.4
EORTC: European Organization for Research and Treatment of Cancer

are in agreement with the Amharic version of EORTC QLQ-BR23 that showed internal consistency reliability value of the body image scale $\alpha = 0.51$, which was below the required Cronbach's α values [15, 20]. Also, the Iranian version of the EORTC QLQ-BR23 showed minimum internal consistency for the systemic therapy side effects with Cronbach's $\alpha = 0.63$ [21]. In the current study, other scales showed adequate internal consistency, and their Cronbach's α values ranged from 0.74 to 0.95.

On the other hand, it was observed that in the Mexican-Spanish version of the EORTC QLQ-BR23 questionnaire, all multi-item scales presented an internal reliability of Cronbach's $\alpha > 0.7$, except for the breast symptoms scale ($\alpha = 0.65$) [22]. In addition, the validation of the Turkish version of the QLQ-BR23 showed an internal reliability of Cronbach's $\alpha > 0.7$, except for the breast and arm symptoms scale, which presented with Cronbach's α values of 0.65 and 0.61, respectively [23]. In addition, the Taiwan-Chinese version of BR23 showed an internal reliability of Cronbach's $\alpha > 0.7$, except for the arm symptoms $\alpha = 0.59$ [24]. Moreover, the validation of the BR23 for women in the United Arab Emirates showed an internal reliability of Cronbach's $\alpha > 0.7$, except for the breast symptoms scale ($\alpha = 0.51$) [25].

Consequently, construct validity was assessed by the evaluation of convergent and divergent validity of items. The multi-trait scaling analysis showed a sufficient convergent validity of the instruments, indicating good correlations of most items with their respective subscale ($r \geq 0.4$) [17]. However, systemic therapy side effects and endocrine therapy symptoms did not show adequate convergent validity ($r < 0.4$). Furthermore, there were no scaling errors observed,

since the correlation of each item with its own scale exceeded its correlation with other scales demonstrating divergent validity.

In the current study, the sexual functioning and endocrine sexual functioning scales exhibited strong psychometric properties that yielded adequate convergent and divergent validity. However, the results should be cautiously considered as the sexuality items were calculated from a small number of patients (11 patients for the sexual functioning scale and 13 patients for the endocrine sexual functioning scale) because most of the patients refused to answer these questions and felt that sexuality items were upsetting and intrusive. A trial on Iranian patients found that both the patients and the therapist were reluctant to talk about sexual health, although it was deteriorated tremendously in breast cancer patients compared to healthy women [26]. This trial proposed the requirement of valid clinical guidelines to provide suitable evidence-based care for sexual health in breast cancer cohorts.

In agreement with the current study, the construct validity of the Moroccan Arabic QLQ-BR23 determined by evaluating the items' convergent and discriminant validity showed that the sexual functioning scores had strong psychometric characteristics and satisfactory multi-trait scaling findings [19]. Furthermore, the multi-trait scaling analysis of validation of the EORTC QLQ-BR45 among the Ethiopian breast cancer patients showed a strong convergent and divergent validity in most items. However, item number 38 on the endocrine therapy scale had a low correlation ($r < 0.4$) with its own scale. Additionally, the most obvious scaling failure was observed for systemic therapy side effect [27]. Furthermore, the Amharic version of the EORTC QLQ-BR23 showed that almost

all the items had strong correlations with their corresponding scale ($r \geq 0.6$), indicating a strong convergent validity of the questionnaire, except for hair loss [20].

The aforementioned results of the current study for multi-trait scaling could justify that the hypothesised scale structure of the EORTC QLQ-BR45 is relevant including both item translation and response choices. In addition, the scores of the scales derived from the Egyptian Arabic version can be involved in cross-cultural comparisons.

Even though the EORTC QLQ-BR45 is a more comprehensive module for breast cancer patients, the following points were observed in the questionnaire that need more clarification or amendment in the module's final version. The hypothesised target therapy scale, which considers evaluation of the QoL of breast cancer patients receiving target therapies, includes some side effects that could be experienced by patients receiving some classes of chemotherapeutic agents, such as tingling, numbness, mucositis and vaginal dryness. Hence, the EORTC-QLG should illustrate the items included in the target therapy scale that could be used for interviewing patients receiving chemotherapeutic agents. Also, according to 'the international update of the EORTC questionnaire for assessing the QoL in breast cancer patients using EORTC QLQ-BR45'; more clarification is required for the cases in which the new target scale could be used as one scale or three separate scales [12].

One of the limitations of the current study is that most of the patients had a low education level. This leads to the difficulty of self-administration of the questionnaires, and all the participants were interviewed. Interviewing the patients leads to the refusal of most patients to answer sexual-related questions. On the other side, interviewing the patients provided some points of strength, which included that the interviewer conducted direct verbal and non-verbal communication with the patients. Therefore, all the questions

were interpreted carefully to the patients and the missing responses were almost negligible. In addition, this data collection approach enables spontaneous reporting of in-depth assessments of patients' experiences with their diagnosis and/or treatment. Hence, this approach provides evidence that the collected PROs followed a robust validation process [28].

CONCLUSION

The Egyptian Arabic translation of the EORTC QLQ-BR45 is an adequately reliable and valid tool to measure the QoL in Egyptian breast cancer patients. Hence, clinical trials concerned with evaluating the HRQoL of breast cancer patients could effectively use this tool.

DISCLOSURE

The authors declare that they have no conflicts of interest.

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AUTHOR CONTRIBUTIONS

All authors have agreed on the submitted version of the manuscript and meet the **International Committee of Medical Journal Editors** (ICMJE) recommendations for authorship.

References

- [1] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A: **Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries**. *CA: a cancer journal for clinicians* 2018, **68**(6):394-424.
- [2] Mokhatri-Hesari P, Montazeri A: **Health-related quality of life in breast cancer patients: review of reviews from 2008 to 2018**. *Health Qual Life Outcomes* 2020, **18**(1):338.
- [3] Bonnetain F, Borg C, Adams RR, Ajani JA, Benson A, Bleiberg H, Chibaudel B, Diaz-Rubio E, Douillard JY, Fuchs CS et al: **How health-related quality of life assessment should be used in advanced colorectal cancer clinical trials**. *Annals of oncology : official journal of the European Society for Medical Oncology* 2017, **28**(9):2077-2085.
- [4] Velikova G, Coens C, Efficace F, Greimel E, Groenvold M, Johnson C, Singer S, van de Poll-Franse L, Young T, Bottomley A: **Health-Related Quality of Life in EORTC clinical trials — 30 years of progress from methodological developments to making a real impact on oncology practice**. *European Journal of Cancer Supplements* 2012, **10**(1):141-149.
- [5] EORTC. **EORTC QLQ-C30 (Version 3)**. EORTC Study Group on Quality of Life. 1995 [https://qol.eortc.org/]
- [6] EORTC. **EORTC QLQ-BR23. (version 1)**. EORTC Study Group on Quality of Life. 1994 [https://qol.eortc.org/]
- [7] Perez EA: **Safety profiles of tamoxifen and the aromatase inhibitors in adjuvant therapy of hormone-responsive early breast cancer**. *Annals of Oncology* 2007, **18**:viii26-viii35.
- [8] van Nes JGH, Fontein DBY, Hille ETM, Voskuil DW, van Leeuwen FE, de Haes JCJM, Putter H, Seynaeve C, Nortier JWR, van de Velde CJH: **Quality of life in relation to tamoxifen or exemestane treatment in postmenopausal breast cancer patients: a Tamoxifen Exemestane Adjuvant Multinational (TEAM) Trial side study**. *Breast Cancer Research and Treatment* 2012, **134**(1):267-276.
- [9] Gianni L, Dafni U, Gelber RD, Azambuja E, Muehlbauer S, Goldhirsch A, Untch M, Smith I, Baselga J, Jackisch C et al:

- Treatment with trastuzumab for 1 year after adjuvant chemotherapy in patients with HER2-positive early breast cancer: a 4-year follow-up of a randomised controlled trial.** *The Lancet Oncology* 2011, **12**(3):236–244.
- [10] Harbeck N, Iyer S, Turner N, Cristofanilli M, Ro J, André F, Loi S, Verma S, Iwata H, Bhattacharyya H et al: **Quality of life with palbociclib plus fulvestrant in previously treated hormone receptor-positive, HER2-negative metastatic breast cancer: patient-reported outcomes from the PALOMA-3 trial.** *Annals of Oncology* 2016, **27**(6):1047–1054.
- [11] Winters ZE, Afzal M, Rutherford C, Holzner B, Rumpold G, da Costa Vieira RA, Hartup S, Flitcroft K, Bjelic-Radicic V, Oberguggenberger A et al: **International validation of the European Organisation for Research and Treatment of Cancer QLQ-BRECON23 quality-of-life questionnaire for women undergoing breast reconstruction.** *British Journal of Surgery* 2018, **105**(3):209–222.
- [12] Bjelic-Radicic V, Cardoso F, Cameron D, Brain E, Kuljanic K, da Costa RA, Conroy T, Inwald EC, Serpentine S, Pinto M et al: **An international update of the EORTC questionnaire for assessing quality of life in breast cancer patients: EORTC QLQ-BR45.** *Annals of oncology : official journal of the European Society for Medical Oncology* 2020, **31**(2):283–288.
- [13] Raosoft sample size calculator [<http://www.raosoft.com/samplesize.html>]
- [14] **EORTC. EORTC Scoring Manual (Third Edition). 2001** [<https://www.eortc.org/>]
- [15] **Eortc Quality Of Life Group Translation Procedure, Fourth edition** [https://www.eortc.org/app/uploads/sites/2/2018/02/translation_manual_2017.pdf]
- [16] Beaton DE, Bombardier C, Guillemin F, Ferraz MB: **Guidelines for the process of cross-cultural adaptation of self-report measures.** *Spine* 2000, **25**(24):3186–3191.
- [17] Sprangers MA, Groenvold M, Arraras JL, Franklin J, te Velde A, Muller M, Franzini L, Williams A, de Haes HC, Hopwood P et al: **The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: first results from a three-country field study.** *J Clin Oncol* 1996, **14**(10):2756–2768.
- [18] Cronbach LJP: **Coefficient alpha and the internal structure of tests.** 1951, **16**(3):297–334.
- [19] El Fakir S, Abda N, Bendahhou K, Zidouh A, Bennani M, Errihani H, Benider A, Bekkali R, Nejari C: **The European Organization for Research and Treatment of Cancer quality of life questionnaire-BR23 Breast Cancer-Specific Quality of Life Questionnaire: psychometric properties in a Moroccan sample of breast cancer patients.** *BMC research notes* 2014, **7**:53.
- [20] Gadisa DA, Gebremariam ET, Ali GY: **Reliability and validity of Amharic version of EORTC QLQ-C30 and QLQ-BR23 modules for assessing health-related quality of life among breast cancer patients in Ethiopia.** *Health Qual Life Outcomes* 2019, **17**(1):182.
- [21] Montazeri A, Harirchi I, Vahdani M, Khaleghi F, Jarvandi S, Ebrahimi M, Haji-Mahmoodi M: **The EORTC breast cancer-specific quality of life questionnaire (EORTC QLQ-BR23): translation and validation study of the Iranian version.** *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2000, **9**(2):177–184.
- [22] Cerezo O, Oñate-Ocaña LF, Arrieta-Joffe P, González-Lara F, García-Pasquel MJ, Bargalló-Rocha E, Vilar-Compte D: **Validation of the Mexican-Spanish version of the EORTC QLQ-C30 and BR23 questionnaires to assess health-related quality of life in Mexican women with breast cancer.** *European journal of cancer care* 2012, **21**(5):684–691.
- [23] Demirci S, Eser E, Ozsaran Z, Tankisi D, Aras AB, Ozaydemir G, Anacak Y: **Validation of the Turkish versions of EORTC QLQ-C30 and BR23 modules in breast cancer patients.** *Asian Pac J Cancer Prev* 2011, **12**(5):1283–1287.
- [24] Chie WC, Chang KJ, Huang CS, Kuo WH: **Quality of life of breast cancer patients in Taiwan: validation of the Taiwan Chinese version of the EORTC QLQ-C30 and EORTC QLQ-BR23.** *Psychooncology* 2003, **12**(7):729–735.
- [25] Awad MA, Denic S, El Taji H: **Validation of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaires for Arabic-speaking Populations.** *Annals of the New York Academy of Sciences* 2008, **1138**:146–154.
- [26] Roshandel S, Lamyian M, Azin SA, Haghighat S, Mohammadi E: **Development and validation of a guideline on sexual and reproductive health of breast cancer survivors in Iran: a mixed methods study protocol.** *Health Research Policy and Systems* 2021, **19**(1):87.
- [27] Mikiyas Amare G, Panpan W, Eva Johanna K, Edom S, Changying C, Adamu A: *Health Qual Life Outcomes* 2021.
- [28] Brédart A, Marrel A, Abetz-Webb L, Lasch K, Acquadro C: **Interviewing to develop Patient-Reported Outcome (PRO) measures for clinical research: eliciting patients' experience.** *Health Qual Life Outcomes* 2014, **12**:15–15.