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EXPERT REVIEWS

# The reliability and validity of the Iranian version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for patients with Bone Metastases: the EORTC QLQ-BM22

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The aim of the present study was to evaluate the psychometric properties of the measure among a sample of Iranian patients with bone metastases. One hundred and seventy-seven patients with bone metastases undergoing various treatments were recruited from Imam Khomeini Hospital in Tehran to participate in the study. The coefficient alpha affirmed internal consistency reliability of the Quality of Life Questionnaire for patients with Bone Metastases (QLQ-BM22). This measure discriminated well between subgroups of the patients based on performance status and responding to treatment. Confirmatory factor analysis confirmed the factorial validity of the four hypothesized QLQ-BM22 scales. Patients in this study had a similar interpretation of the items on the QLQ-BM22 regardless of gender. All scales of the QLQ-BM22 were sensitive to change after treatment over a month's follow-up, with the exception of psychosocial aspects. The Persian version of the EORTC QLQ-BM22 was highly reliable and is valid for use among patients with bone metastases who are undergoing various treatment regimes.

**Keywords:** bone metastases • European Organisation for Research and Treatment of Cancer (EORTC) QLQ-BM22 • factor structure • health-related quality of life • multigroup confirmatory factor analysis

## Background & objectives

Bone is the most prevalent site of metastases in cancer patients [1]. According to the data, breast and prostate cancer are among the more common types of cancer that can result in bone metastasis (BM) with a prevalence rate of up to 70% [2,3]. Other types of cancer like lung and thyroid may lead to bone metastases in about 15–30% of patients [4]. In general, the risk of BM in people with all types of cancer with a survival time of 10 years was reported to be 7–9% [5]. It is estimated that 65–75% of patients with advanced stages of cancer may be affected by it [6]. Therefore, BM may be considered a frequent and predominant consequence of cancer [7]. Although the precise rate of incidence of cases of BM is unclear, it is suggested that more than 350,000 people die due to it in the USA annually [8]. BM can cause many skeletal-related disorders such as pathological fractures, osteolytic lesions, spinal injury and instability, spinal



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compression and other morbidities like pain and hypercalcemia [5,9].

All of these conditions can affect quality of life (QoL) in the patients. QoL is a subjective multidimensional concept, which shows the psychological and functional status of patients as well as disease-related symptoms and treatment progress among them [10]. This can help health professionals to assess the effects of interventions and treatments on different dimensions of a patient's life [9]. Given the medical advances in the treatment of cancer, today the survival times of such patients are longer, so QoL should be given more consideration [7] Recently, many studies were conducted to enhance patients' QoL along with better traditional endpoints like pain relief, symptom control and survival [6,11,12].

Management of the BM and its complications during the remaining years of life in patients will maximize their QoL [7]. It is indicated that the QoL is a powerful prognostic index that should be considered when making decisions about treatment approaches [13]. Indeed, patients are the best evaluators of their QoL and patients' perspectives in this regard should be extracted carefully [9]. In other words, these patients experience their specific and individual symptoms related to the disease and they have exclusive physical and emotional states with regard to cancer and therapeutic procedures [14]. Thus, these states should be presented by the patients themselves as health care providers may not be able to detect them.

Despite the importance of patients' views about their own QoL, there are few well-developed measures to assess disease-specific QOL among cancer patients [13]. However, there has been an increasing emphasis on developing such measures in the past decade. One of these measures, developed as a valid and reliable scale by the European Organisation for Research and Treatment of Cancer, is the EORTC Quality of Life Questionnaire for patients with Bone Metastases (QLQ-BM22) [7]. The EORTC QLQ-BM22 is a disease-specific measure designed to assess QoL among patients with bone metastases. Moreover, the EORTC QLQ-BM22 was designed to be used as a supplemental scale in conjunction with the core measure, the EORTC Quality of Life Questionnaire C30 (EORTC QLQ-C30) [15]. In validation studies, the EORTC QLQ-BM22 has been reported to have good psychometric properties [4,7,15]. However, the validity and reliability of the scale in cross-cultural investigations have not yet been fully evaluated [7]. Therefore, the aim of the present study was to evaluate the psychometric properties of the measure among a sample of Iranian patients with bone metastases.

## Methods

Between April 2012 and March 2013, 177 patients with bone metastases undergoing various treatments were recruited to participate in the study. All patients with bone metastases were referred to Imam Khomeini Hospital in Tehran to follow the standard treatment regimens. Patients were eligible for the study if they were over 18 years old, had confirmed histologically primary cancer, had radiologic evidence of bone metastases and read and spoke Persian/Farsi fluently. Patients were excluded if they were identified as being cognitively impaired, as assessed by the Mini-Mental State Examination. The study protocol was approved by the ethics committee of the Qazvin University of Medical Sciences. All patients gave their informed oral and written consent to participate in the study before being interviewed.

### *Measures*

#### The EORTC QLQ-C30

The EORTC QLQ-C30 is a cancer-specific questionnaire to assess QoL among patients with cancer. The QLQ-C30 consists of 30 items with five functioning scales: physical functioning (5 items), role functioning (2 items), cognitive functioning (2 items), emotional functioning (4 items), social functioning (2 items) and three symptom scales: pain (2 items), fatigue (3 items), and nausea and vomiting (2 items). Moreover, the instrument has two items, which assess patients' perception of their QOL, and six single items: dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties [16]. These items are followed by a Likert-type scale with four/seven alternative responses. The QLQ-C30 has been internationally validated throughout diverse cultures including the Persian language. The Iranian version of the EORTC QLQ-C30 had shown a good level of validity in a previous study. The QLQ-C30 is available at [17] in over 80 languages including Farsi.

#### The EORTC QLQ-BM22

The QLQ-BM22 has been developed to measure QoL in cancer patients with bone metastases. This tool contains 22 items that cover four scales including painful sites (5 items), painful characteristics (3 items), functional interference (8 items) and psychosocial aspects (6 items) [7]. The responses are based on the Likert scale and rated from 1 ('not at all') to 4 ('very much'), with a high score for the symptom scales representing a high level of symptomatology or problems, whereas a high score for the functional scales represents a high level of functioning. All scores were transformed to scores ranging from 0 to 100 [18]. The QLQ-BM22 uses the previous week as the recall period [7].

### *Procedure*

Patients with bone metastases under medical treatments including bisphosphonates, orthopedic surgery, radiation therapy, chemotherapy, hormone therapy and stable bone metastases were included in the study. At baseline, patients were asked to complete a sociodemographic questionnaire including age, gender, marital status and educational status. Clinical variables including time from primary diagnosis, primary cancer site and previous skeletal-related events were collected from patients' records. Both the EORTC QLQ-C30 and the QLQ-BM22 were administered at the time of baseline examination. Performance status (PS) was assessed by a trained physician using WHO Performance Status (WHO PS) ranging from 0 (fully active) to 5 (dead). The QLQ-BM22 was completed again by

the same patients at 1 month after baseline examination. Pain response was assessed for patients undergoing different treatments for bone metastases based on the international consensus response criteria for bone metastases trials [19]. Complete response (CR) occurs when pain is reduced by zero, and the oral morphine equivalent dose (OMED) is stable. A partial response (PR) occurs if pain is reduced by two scores or more and the OMED is stable. Furthermore, the OMED is reduced by ≥25%, and stable pain (SP) is also labeled as a PR. Pain progression (PP) is defined as an increase in pain score of 2 or more with stable analgesic (OMED) or an increase of ≥25% for the OMED, with the pain score stable or one point above baseline. SP is defined as a pain, which is not classified as CR, PR or PP. The CR and PR are considered as responders, whereas PP and SP are recognized as nonresponders. Patients were given the QoL measures in a quiet setting in the clinic before knowing the outcome of treatment or before starting treatment. Help was provided by a trained assistant in 27 cases to help read the measure. On average, it took 13 min to complete the measure.

### *Translation procedure*

Permission was obtained from the EORTC Quality of Life Department (Belgium) to translate and use the QLQ-BM22 in the study. The translation procedures were conducted in accordance with the official EORTC Translation Guidelines [20,21]. The aim of the translation project was to produce a Persian/Farsi version of the QLQ-BM22, which is conceptually equivalent to the original English version, as well as clear and easy to understand. The translation consisted of several steps:

- Forward translation – in this step, two translators independently translated the questionnaire into the Persian. Both translators were physicians, native Persian language speakers and bilingual in the English language. The translated versions were then compared by a project manager (a person responsible for coordinating the translation process). The project manager liaised with the forward translators to resolve differences between the two forward translations and generated a single reconciled version.
- Backward translation: the interim Persian version of the QLQ-BM22 was then translated into English by two translators who were native English speakers with a high level of fluency in the Persian language. The translators were not aware of the English original version and performed their translations independently of one another. The project manager compared the English translations with the original questionnaire to detect any misunderstandings, mistranslations or inaccuracies in the intermediary forward version of the questionnaire.
- Pilot testing: the Persian version of the QLQ-BM22 was then administered to 17 patients with bone metastases (9 males and 8 females, age range = 28–59 years). A structured interview was conducted with each patient individually to uncover any difficulties in understanding the questionnaire and to check the patients' interpretation of all the items. Results arising from the pilot testing showed that the second intermediary Persian version was suitable and short, with no specific item requiring change for the patients. Moreover, all of the patients found the 22 items in the questionnaire to be clear, simple and intelligible. After this phase, the final translation of the Persian version of the QLQ-BM22 was obtained and peer reviewed by the team in the EORTC Quality of Life Department and then finally approved by the EORTC Quality of Life Department. The pilot-tested version of the QLQ-BM22 was then administered to 177 patients with bone metastases.

### *Statistical analysis*

The range of measurements was computed using the percentage of patients achieving the lowest (floor) or the highest possible scores (ceiling). A high floor and ceiling effect may reduce the reliability of a tool and also impair the ability of the tool to detect changes. It is recommended that floor or ceiling effects present if more than 15% of respondents achieved the highest or lowest possible score, respectively [22].

To assess the reliability of the QLQ-BM22, internal consistency (a measure of the relatedness of items within a factor) and test–retest reliability (the stability of responses over time) were computed. Cronbach's $\alpha$ was used to assess the internal consistency of each scale. A Cronbach's $\alpha$ coefficient equal to or higher than 0.70 is considered to be acceptable [23].

The test–retest reliability of the QLQ-BM22 was determined by using the intraclass correlation coefficient (ICC) with 95% CIs. The ICCs were calculated using a two-way mixed-effect model with an agreement coefficient. The ICCs were categorized into the following: <0.40 poor to fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement and >0.80 excellent agreement [24]. Test–retest reliability was only conducted on patients with stable bone metastases with a 2-week time interval (n = 16).

Convergent and divergent validity are considered two separate types of construct validity. Convergent validity is defined as the degree to which the multiple items attempt to measure the same construct, whereas divergent validity refers to the degree to which constructs differ from each other [25]. The convergent and divergent validity of the QLQ-BM22 were assessed by computing correlation coefficients between the QLQ-BM22 and QLQ-C30. Multitrait scaling was used to examine whether each item correlated with a hypothesized dimension (convergent validity, $r \geq 0.40$, corrected for overlap). Discriminant validity is supported when an item scale correlation is higher than correlations with other scales [26].

To assess known groups or clinical validity, the subscale scores of the QLQ-BM22 were compared between patient groups according to the PS and response to treatment. It was hypothesized that patients with higher PS (WHO PS 0–1) would report higher scores on function scales and lower scores on symptoms scales of the QLQ-BM22 than those with lower


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| Table 1. Characteristics of the subjects. | |
|---|---|
| Mean age (years; standard deviation) | 50.9 (13.8) |
| *Sex (%)* | |
| Male | 95 (54.0) |
| Female | 82 (46.0) |
| *Educational status (%)* | |
| Illiterate | 54 (30.5) |
| Primary school | 42 (23.7) |
| Middle school | 29 (16.4) |
| Secondary school | 35 (20.4) |
| College | 17 (9.6) |
| *Marital status (%)* | |
| Single | 21 (11.9) |
| Married | 135 (76.2) |
| Widowed/divorced | 21 (11.9) |
| *Occupational status (%)* | |
| Employed | 45 (25.4) |
| Unemployed | 132 (74.6) |
| *WHO performance status (%)* | |
| 0 | 22 (12.4) |
| 1 | 86 (48.6) |
| 2 | 47(26.6) |
| 3 | 14 (7.9) |
| 4 | 8 (4.5) |
| *Treatment groups (%)* | |
| Radiotherapy or radiosurgery | 47 (26.6) |
| Orthopedic stabilization | 12 (6.8) |
| Chemotherapy or hormone therapy | 29 (16.4) |
| Receiving bisphosphonate | 73 (41.2) |
| Stable bone metastases not undergoing new treatment | 16 (9.0) |
| Time from primary diagnosis (months) | 23.0 (23.5) |
| *Previous skeletal-related event (%)* | |
| Yes | 70 (39.5) |
| No | 107 (60.4) |
| *Primary cancer site (%)* | |
| Breast | 66 (37.3) |
| Lung | 34 (19.2) |
| Esophagus | 7 (3.9) |
| Brain | 4(2.6) |
| Stomach | 19 (10.7) |

| Table 1. Characteristics of the subjects (cont.). | |
|---|---|
| *Primary cancer site (%) (cont.)* | |
| Prostate | 27(15.2) |
| Multiple myeloma | 6 (3.4) |
| Colorectal | 6 (3.4) |
| Renal cell/kidney | 4 (2.6) |
| Pancreas | 2 (1.1) |
| Ovarian | 1 (0.5) |
| Unknown | 1 (0.5) |

PS (WHO PS 2–4). Furthermore, it was anticipated that responders (patients with a CR and PR) would report higher scores on function and lower scores on symptoms scales of the QLQ-BM22 than nonresponders (patients with a PP and SP). Analysis of covariance (ANCOVA) was conducted to compare the subscales of the QLQ-BM22 across subgroups of patients. For the analysis, age, gender and education were adjusted. The Benjamini–Hochberg method was used to adjust for multiple comparisons and balance the amount of types I and II errors [27]. Effect sizes (Cohen's d) were computed for assessing the magnitude of differences between patient groups [28]. According to Cohen's recommendations, values of 0.2, 0.5 and 0.8 are considered to be small, medium and large effects, respectively [28].

The factor structure of the QLQ-BM22 was assessed using confirmatory factor analysis (CFA) [29]. The CFA is used to test whether the items load onto the hypothesized scales. Considering the ordinal nature of the QLQ-BM22 items, a weighted least squares using data from polychoric correlation and asymptotic covariance matrices was used as the method of estimation for the CFA. The CFA was conducted using LISREL version 8.8 [30]. Originally, a four-factor model was suggested for the structure of the QLQ-BM22 [7].The goodness of fit of the model was evaluated using a number of indices including chi-square ($\chi^2$), root mean square error of approximation (RMSEA), $\chi^2$/df, goodness-of-fit statistic (GFI), standardized root mean square residual (SRMR), the Non-Normed Fit Index (NNFI, also known as the Tucker–Lewis index), the Comparative Fit Index (CFI) and the Akaike Information Criterion (AIC) [29].

Chi-square assesses the magnitude of discrepancy between the sample and fitted covariance matrices. An insignificant Chi-square ($p > 0.05$) indicates acceptable model fit. However, Chi-square has some limitations including the sensitivity of the test to sample size. For large samples, the Chi-square statistic probably rejects a hypothesized model. Therefore, it was suggested to use other indices beside the Chi-square. The ratio $\chi^2$/df is considered as an alternative fit statistic for the Chi-square. Values between 1 and 3 are considered to be acceptable [29].

The RMSEA is relatively insensitive to sample size by incorporating a penalty function for poor model parsimony (i.e., sensitivity to the number of estimated parameters). Values of

**Table 2. Descriptive statistics of the Quality of Life Questionnaire for patients with Bone Metastases at baseline (n = 177).**

| | Forms (n) | Mean (standard deviation) | Floor (n; %) | Ceiling (n; %) | Cronbach's α | Normality |
|---|---|---|---|---|---|---|
| Painful site | 177 | 49.06 (32.40) | 12 (6.8) | 3 (1.7) | 0.730 | 0.213 |
| Painful characteristic | 177 | 38.27 (29.38) | 17 (9.6) | 15 (8.5) | 0.812 | 0.124 |
| Functional interference | 175 | 51.12 (41.19) | 16 (9.0) | 3 (1.7) | 0.931 | 0.302 |
| Psychosocial aspects | 176 | 64.85 (31.95) | 3 (1.7) | 2 (1.1) | 0.740 | 0.098 |

less than 0.08 indicate a good model fit. The GFI is an absolute fit measure and computes the proportion of variance that is accounted for by the estimated population covariance. Values equal to or higher than 0.90 reflect a good fit. The SRMR is the square root of the difference between the residuals of the sample covariance matrix and the hypothesized covariance model. A cutoff value of 0.08 was set for the SRMR. The NNFI is an incremental fit index and is less sensitive to sample size. A value of 0.90 or higher is considered to be acceptable. The CFI assumes that all latent variables are uncorrelated and compares the sample covariance matrix with this null model. A CFI value close to 0.90 is indicative of good fit. The AIC is one of the parsimony fit indice that is used when comparing non-nested or nonhierarchical models estimated with the same data. There is no definite cutoff point for the AIC, but the lowest values are considered perfect fit [29].

Studies of QoL revealed that gender differences may play a role in patients' perceptions of QoL especially in oncology [31,32]. Therefore, comparing gender differences is essential when utilizing QOL instruments. Without measurement invariance, many group differences cannot be clearly interpreted [33,34]. The aim of the measurement invariance is to check whether items of the QLQ-BM22 represent the same constructs across gender groups [34]. Therefore, in addition to the CFA, multigroup CFAs were performed to test whether the QLQ-BM22 measure has equivalent meaning across genders. A set of hierarchical levels of measurement invariance were examined based on the recommendations of Horn and McArdle [35]. Configural invariance is recognized as the most basic level of equivalence. In configural invariance, the number of factors and their loading pattern are the same across groups. It examines whether the patients in each group (i.e., male and female) use the same conceptual framework to answer the items on the scales. The next level of measurement invariance is metric invariance. In the metric model, the factor loadings are constrained to be equal across groups, but the intercepts are allowed to difer between groups [34]. According to the recommendations of Cheung and Rensvold, changes in the CFI and the NNFI equal to or lower than 0.01 are considered to be insignificant changes in model fit (i.e., invariance model) [34].

The ability of the QLQ-BM22 to detect changes in patients' health status over time can be understood as responsiveness to change. Responsiveness can be considered an aspect of the construct validity of an instrument. Patients were examined to check whether they responded to treatment (i.e., CR and PR). The responsiveness of the QLQ-BM22 to change over time was assessed using the ANCOVA adjusting for age, gender and education in all patient groups with the exception of patients with stable bone metastases. Standardized Response Mean (SRM) was used to assess the magnitude of the QLQ-BM22 change scores over time. The SRM is calculated as the score difference (follow-up baseline) divided by the standard deviation of the group's score differences [36].

## Results

The study comprised 177 patients with bone metastases (95 men and 82 women) who were a mean age ± SD of 50.93 ± 13.81 years. Twelve patients declined to be involved in the study. The mean time since primary diagnosis was 23.0 ± 23.5 months. Most patients were married, unemployed and illiterate (had no formal education). The patients' characteristics are shown in Table 1. The coefficient alpha was higher than 0.70 for all four subscales ranging from 0.73 to 0.93 (Table 2). All four subscales of the QLQ-BM22 were normally distributed ($p > 0.05$). All

**Table 3. Summary of results of multitrait/multi-item scaling tests and test–retest reliability of the Persian Quality of Life Questionnaire for Patients with Bone Metastases.**

| | Item scale correlation (range of r) | Correlations with other scales (range of r) | ICC (95% CI) n = 16 |
|---|---|---|---|
| Painful site | 0.629–0.743 | 0.140–0.515 | 0.960 (0.945–0.971)** |
| Painful characteristic | 0.691–0.925 | 0.016–0.559 | 0.991 (0.988–0.994)** |
| Functional interference | 0.690–0.870 | 0.026–0.357 | 0.979 (0.971–0.985)** |
| Psychosocial aspects | 0.530–0.812 | 0.082–0.315 | 0.932 (0.909–0.950)** |

**p < 0.01.
ICC: Intraclass correlation coefficient.


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**Table 4. Pearson's correlation coefficients between the Quality of Life Questionnaire for patients with Bone Metastases and the Quality of Life Questionnaire-C30.**

| | Painful sites | Painful characteristics | Functional interference | Psychosocial aspects |
|---|---|---|---|---|
| Physical functioning | -0.474* | -0.521* | 0.457* | 0.541* |
| Role functioning | -0.525* | -0.357* | 0.406* | 0.463* |
| Emotional functioning | -0.445* | -0.561* | 0.665* | 0.446* |
| Cognitive functioning | -0.503* | -0.486* | 0.438* | 0.593* |
| Social functioning | -0.557 | -0.424* | 0.341* | 0.577* |
| Global health status | -0.394 | -0.440* | 0.353* | 0.345* |
| Fatigue | 0.124 | 0.191 | -0.112 | -0.132 |
| Nausea/vomiting | 0.218 | 0.291 | -0.187 | -0.047 |
| Pain | 0.714* | 0.620* | -0.529* | -0.657* |
| Dyspnea | 0.294 | 0.265 | -0.122 | -0.206 |
| Insomnia | 0.148 | 0.139 | -0.372 | -0.139 |
| Appetite loss | 0.107 | 0.154 | -0.153 | -0.282 |
| Constipation | 0.172 | 0.137 | -0.136 | -0.017 |
| Diarrhea | 0.246 | 0.221 | -0.291 | -0.222 |
| Financial problems | 0.118 | 0.141 | -0.154 | -0.180 |

*$p < 0.05$.



subscales of the QLQ-BM22 demonstrated neither substantial floor nor ceiling effects (Table 2). The ICCs being used to assess the stability of the measure were higher than 0.70 and varied from 0.93 to 0.99 ($p < 0.001$). As Table 3 indicates, painful characteristics showed the highest retest reliability (ICC = 0.991).

Multitrait scaling analyses indicated that all of the item scale correlation coefficients met the standards of convergent and divergent validity. All items correlated highly with their own scale ranging from 0.53 to 0.87 (Table 3). Furthermore, item scale correlations were higher for the hypothesized scale than for competing scales (divergent validity).

To assess the construct validity of the QLQ-BM22, intercorrelations between QLQ-BM22 and QLQ-C30 were computed at baseline. The results revealed that all of the QLQ-BM22 scales were significantly correlated with the QLQ-C30 scales. As Table 4 shows, the functional scales of the QLQ-C30 were negatively correlated with the symptom scales of the QLQ-BM22 (r ranged from -0.35 to -0.56). Moreover, the functional scales of the QLQ-C30 were positively correlated with the functional scales of the QLQ-BM22 (*r* ranged from 0.34 to 0.66). There was no significant correlation between the symptom scales of the QLQ-BM22 and the symptom scales of the QLQ-C30 with the exception of pain.

Regarding known-group validity, the results indicated that patients with a higher PS, as assessed by the WHO PS, reported a significantly lower level of symptomatology or problems but a

**Table 5. Known-group validity the Quality of Life Questionnaire for patients with Bone Metastases.**

| | Performance status[†] | | | Response to treatment | | |
|---|---|---|---|---|---|---|
| | *High mean (SD) n = 108* | *Low mean (SD) n = 31* | *Effect size* | *Responder n = 41* | *Nonresponder n = 136* | *Effect size* |
| Painful site[‡,§] | 42.62 (24.04) | 52.30 (29.77) | 0.38 | 31.62 (19.35) | 54.21 (32.51) | 0.75 |
| Painful characteristic[‡,§] | 34.22 (23.28) | 48.98 (26.77) | 0.61 | 23.98 (12.00) | 50.83 (38.29) | 0.79 |
| Functional interference[‡,§] | 75.85 (34.48) | 53.12 (32.48) | 0.67 | 32.97 (22.52) | 57.88 (37.05) | 0.73 |
| Psychosocial aspects[‡] | 84.63 (26.27) | 69.03 (33.68) | 0.56 | 35.05 (24.16) | 39.64 (20.41) | 0.21 |

[†]WHO performance status: High: scores 0/1. Low: score 2, 3, 4 (baseline).
[‡]Statistically significant for WHOPS.
[§]Statistically significant for response to treatment.
SD: Standard deviation.

higher functional status compared with those with lower PS. Effect sizes were small to medium ranging from 0.38 to 0.67. Furthermore, patients who responded to treatment reported a lower level of symptomatology and a higher level of functional status compared with nonresponders. However, psychosocial aspects did not differ significantly between responders and nonresponders (Table 5). Effect sizes were small to large ranging from 0.21 to 0.79. CFA was used to measure the factorial validity of the four hypothesized QLQ-BM22 models. The results indicated that the model fit was found to be acceptable: $\chi^2$ = 334.65, degree of freedom = 203, p < 0.001, CFI = 0.96, RMSEA = 0.078, SRMR = 0.065, NNFI = 0.96, GFI = 0.90 and AIC = 446.65. The correlation between latent variables ranged from 0.40 to 0.79 with large correlations between Painful Sites and Pain Characteristics (Figure 1). As Figure 1 shows, the item loadings for the four latent variables were significant and ranged from 0.17 to 0.93.

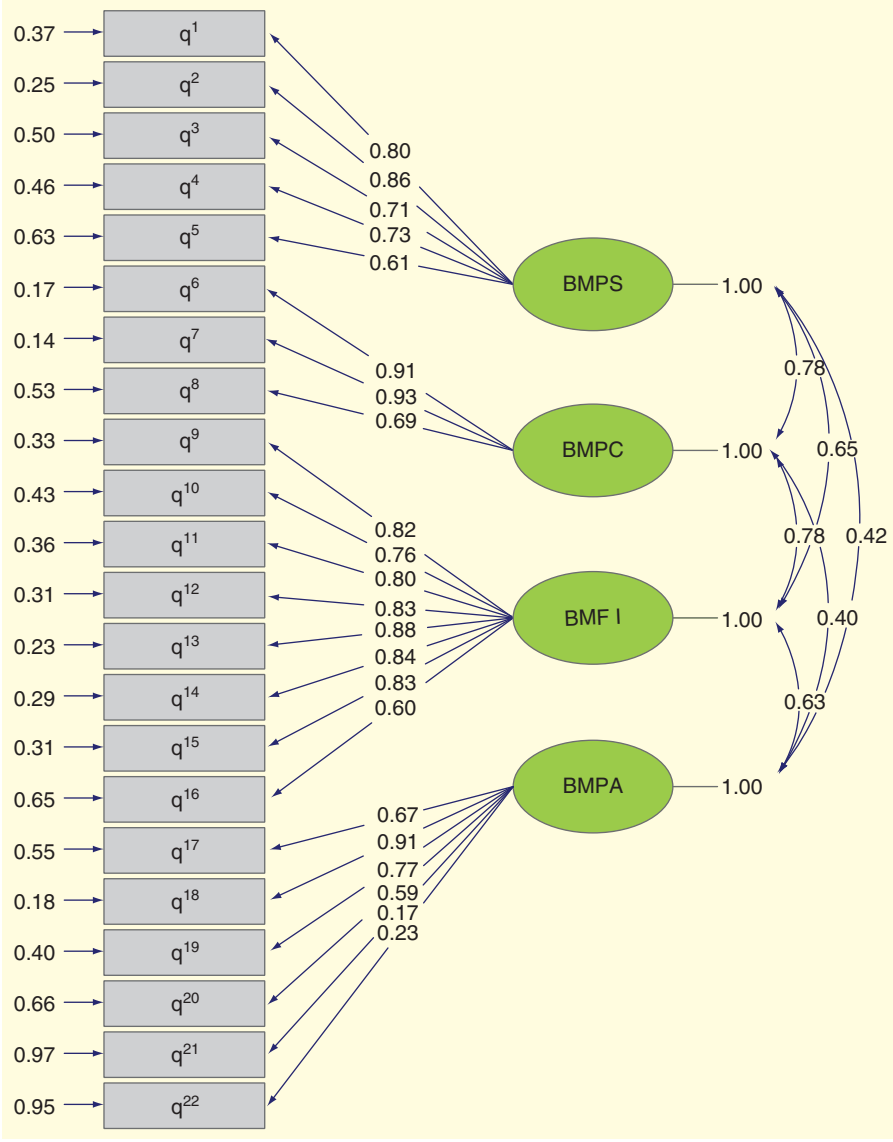


**Figure 1. Standardized estimated factor item loadings, error variances and covariance for the final model of the Quality of Life Questionnaire for patients with Bone Metastases.**

A multigroup model was used to examine whether the factor loadings were similar for males and females for each of the four measurement waves. The results indicated that configural invariance showed good fit indices: $\chi^2$ = 687.81, degree of freedom = 431, p < 0.001, CFI = 0.963, RMSEA = 0.079, SRMR = 0.077, NNFI = 0.957, GFI = 0.901 and AIC = 855.81. Goodness-of-fit statistics for the subsequent model (metric invariance) also showed acceptable fit indices: $\chi^2$ = 712.42, degree of freedom = 449, p < 0.001, CFI = 0.957, RMSEA = 0.079, SRMR = 0.078, NNFI = 0.954, GFI = 0.900 and AIC = 1128.76. According to these statistics, there were no significant differences between the two models (δCFI = 0.006, δNNFI = 0.003), stating that these models are practically equivalent in empirical fit. Therefore, factor structure of the QLQ-BM22 was invariant across gender. However, the first model (configural invariance) was partly a much more parsimonious fit compared with the second model (metric invariance).

Responsiveness to change was assessed among those patients who responded to the treatment according to the international consensus response criteria for bone metastases trials. The results are summarized in Table 6. Approximately 25.5% of the patients responded to treatment. ANCOVA revealed that symptoms scales of the QLQ-BM22 reduced significantly over time in responders while functional scales increased significantly (p < 0.05). The most responsive subscale was the Painful Characteristic with an SRM of 0.57 at 1 month and Painful Site with an SRM of 0.81 at 1 month.

## Discussion

This study aimed to assess the psychometric properties of the Iranian version of the EORTC QLQ-BM22 among patients with BM. In general, the results of this study provided some strong evidence for the reliability and validity of the QLQ-BM22. Moreover, all patients completed the questionnaire without any difficulty. There were very minor missing items for the completed questionnaires (<1.0%).

In this study, no floor or ceiling effect was seen for any of the scales of the QLQ-BM22. These results indicate that the QLQ-BM22 could measure the differences among individuals


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**Table 6. Responsiveness of the BM22 for patients who responded to the treatment based on the International Consensus Response Criteria (n = 41).**

| | Baseline mean (SD) | Follow-up | SRM 0–1 months | F (p-value)[†] |
|---|---|---|---|---|
| Painful site | 47.28 (27.87) | 27.73 (19.67) | 0.81 | 1.970 (0.030) |
| Painful characteristic | 35.63 (17.16) | 25.61 (14.30) | 0.83 | 9.981 (0.001) |
| Functional interference | 56.51 (41.79) | 70.67 (38.19) | 0.37 | 9.487 (0.001) |
| Psychosocial aspects | 66.99 (40.43) | 78.07 (39.70) | 0.29 | 24.474 (0.001) |

[†]Analysis of Covariance (ANCOVA).
SD: Standard deviation; SRM: Standardized response mean.

over a wide range. The original (English) version of the QLQ-BM22 reported similar findings [7].

In terms of internal consistency, the QLQ-BM22 questionnaire obtained acceptable results for all scales. The Persian version of the QLQ-BM22 has shown a high level of internal consistency reliability for functional interference. A level of reliability has also been reported for the functional interference of the multilanguage version of the QLQ-BM22 [37].

The test–retest reliability of the QLQ-BM22 in a subgroup of patients with stable bone metastases and not undergoing new treatment was good. Therefore, the results indicate that the QLQ-BM22 is stable over time in a stable condition. However, our study sample was relatively small (n = 16). There was an insignificant difference between two administrations of the instrument. There is less opportunity to detect significant differences in small sample sizes. To increase statistical power, a larger sample size is therefore required. Our results are in accordance with a previous study [37].

The results of the multitrait scaling analysis indicated that each item of the QLQ-BM22 within a hypothesized scale was linearly related to the total score for that scale. The multiple correlation results provide evidence of convergent validity. On the other hand, each item of the QLQ-BM22 in a given scale had the lowest correlation with other scales indicating discriminant validity. The results were similar to those found in international validation of the QLQ-BM22 [37]. Furthermore, correlations between the QLQ-BM22 and the QLQ-C30 showed that correlations existed if they cover general areas of QOL. Correlations disappeared when the times focused only on the QLQ-BM22. In this study, known-group analyses were performed to examine whether the QLQ-BM22 could differentiate between subgroups of patients based on PS and response to treatment. Similar to a previous study, the QLQ-BM22 was successfully able to discriminate between patients with high and low PS and also between responders and nonresponders [37].

This is the first study, to our knowledge, to assess factor structure and measurement invariance of the QLQ-BM22. Similar to this study's hypothesis, the factor structure of the QLQ-BM22 supposed by Chow *et al*. was successfully replicated in the Iranian sample [7]. We found evidence to confirm the four-factor solution of the QLQ-BM22 in a sample of Iranian patients. Future studies should be performed to investigate the factor structure of the QLQ-BM22 among other cultures.

Studies have been reported that gender differences may contribute as predicting factors for QoL among patients with bone metastases [38–40]; accordingly, the perceptions of males and females may affect the scale structure of the questionnaire. Therefore, a reliable and valid toll is needed to compare and assess gender differences in terms of QoL. Factorial invariance examined whether the same constructs are perceived differently across the gender groups. The present findings demonstrate that males and females who completed the QLQ-BM22 had a similar four-factor QoL model structure. Therefore, it can be concluded that patients in this study had a similar interpretation of the items on the QLQ-BM22 regardless of gender.

All scales of the QLQ-BM22 were sensitive to change after treatment over a month's follow-up, with the exception of psychosocial aspects. The finding of the study indicated that to change psychosocial aspects of patients with bone metastases, palliative treatment alone is not sufficient. The psychosocial aspects of patients with bone metastases are considered an important aspect of patients' QOL and is affected not only by pain but also by various symptoms such as fatigue, nausea, vomiting, loss of appetite, sleep disorders, dyspnea, psychological distress and social interaction difficulties [41,42]. All this is related to hope, worry and the future, and therefore, a multidisciplinary approach, including behavioral interventions, nonbehavioral counseling and therapy, informational and educational interventions, is needed to improve QoL in patients with bone metastases.

The limitations of the current study should be acknowledged. First, the patients in the study were recruited conveniently and are not representative of all Iranian patients with bone metastases. Second, the sample for performing test–retest reliability was relatively small with limited power. Third, responsiveness to change was assessed in the short term, whereas the results for the long term are unknown.

In summary, the results of this study show that the Persian version of the EORTC QLQ-BM22 is highly reliable and valid for use among patients with bone metastases who are undergoing various treatments regimes. Furthermore, the tool could be used in clinical trials for both male and female patients without any misunderstandings or gender bias.

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## Key issues

- The impact of bone metastasis (BM) on patients' quality of life (QoL) is important to consider in assessing health needs and outcomes from health care services/interventions internationally.
- The Iranian version of the QLQ-BM22 may be a useful population health level instrument for assessing health-related quality of life of BM patients among oncologists working with Persian speaking communities.
- The Iranian version of the QLQ-BM22 can serve as a screening instrument for patients with unknown performance status in primary care or clinical settings.
- The Iranian version of the QLQ-BM22 was interpreted similarly by male and female patients with BM.
- The existence of an Iranian version of the QLQ-BM22 will facilitate cross-cultural and cross-national research to enhance oncologists understanding of the impact of BM on patient's quality of life internationally.



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