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Final development and validation of the BOMET-QoL questionnaire for assessing quality of life in patients with malignant bone disease due to neoplasia

A Sureda[1], D Isla[2], JM Cózar[3], M Ruiz[4], M Domine[5], M Margelí[6], E Adrover[7], M Ramos[8], M Pastor[9], A Martín[10], A Llombart[11], B Massuti[7], M Muñoz[12], A Barnadas[1], J Fernández[13], R Colomer[14], C Allepuz[15], M Gilabert[16], X Badia[17]

Summary

This paper describes the final development and validation of the BOMET-QoL questionnaire for assessing health-related quality of life (HRQoL) in patients with malignant bone disease due to neoplasia (MBDN).

An observational prospective study was conducted of 263 patients with MBDN. Sociodemographic and clinical variables, Eastern Cooperative Oncology Group (ECOG) Performance Scale Index and Pain Management Index (PMI) were gathered. Patients completed the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and BOMET-QoL questionnaires and the perception of general health status. Both questionnaires were completed again 15 days after the baseline visit by 98 clinically stable patients (Group A), and 3 months and 6 months after the baseline visit by 165 clinically unstable patients (Group B). Prior to validation of the BOMET-QoL questionnaire, a factor analysis and psychometric selection of the original items was developed by means of Rasch analysis.

The BOMET-QoL questionnaire consisting of 25 items was reduced to an integrated version of 10 items. Scores on the BOMET-QoL-10 questionnaire were shown to be related to the presence, number and duration of irruptive pain crises, the PMI and the ECOG index ($p<0.001$), and with changes in the perception of general health status and ECOG index ($p<0.01$). The internal consistency of the questionnaire and the intraclass correlation coefficient (ICC) were high (Cronbach's $\alpha = 0.93$; ICC = 0.97). BOMET-QoL-10 is an easy to manage and valid questionnaire in clinical practice conditions.

Key words: bone metastasis, myeloma, quality of life, questionnaires

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[1] Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [2] Hospital Clínico Lozano Blesa, Zaragoza, Spain; [3] Hospital Virgen de las Nieves, Granada, Spain; [4] Hospital Virgen del Rocío, Sevilla, Spain; [5] Fundación Jiménez Díaz, Madrid, Spain; [6] Hospital Germans Trias i Pujol, Barcelona, Spain; [7] Hospital General de Alicante, Alicante, Spain; [8] Instituto Oncológico de Galicia, La Coruña, Spain; [9] Hospital Universitario La Fe, Valencia, Spain; [10] Hospital de Cabueñes, Gijón, Spain; [11] Instituto Valenciano de Oncologia, Valencia, Spain; [12] Hospital Clínic de Barcelona, Barcelona, Spain; [13] Hospital Central de Asturias, Oviedo, Spain; [14] Institut Catala d'Oncologia, Gerona, Spain; [15] Hospital Miguel Servert, Zaragoza, Spain; [16] Novartis Farmacéutica S.A., Barcelona, Spain; [17] Health Outcomes Research Europe—a unit of IMS, Barcelona, Spain

Address for correspondence: Dr Xavier Badia, Health Outcomes Research Europe—a unit of IMS, Avd. Diagonal, 618, 1ºC, 08021 Barcelona, Spain.
E-mail: xbadia@es.imshealth.com

Background

The assessment of health-related quality of life (HRQoL) in oncology has increased in recent years and has become an important outcome measure of new therapies[1]. In patients with advanced cancer whose treatment is directed mainly to relieve symptoms, especially pain, it is particularly important to have instruments that assess, in a standard manner, the impact of disease and treatment on HRQoL from the patient's point of view[2].

In oncology clinical practice, bone metastasis (BM) represents the third most common metastatic site of primary tumours and is the primary factor with regard to morbidity and impact on HRQoL[3]. Pain is the most common clinical occurrence, with malignant bone disease being the principal cause of pain in the oncological patient[4–6]. In addition to pain, malignant bone disease due to neoplasia (MBDN) frequently produces other complications that may lead to a significant deterioration in the HRQoL of patients[7], such as pathological fractures[8], medullar compression[9], hypercalcaemia and bone marrow infiltration[10,11].

In recent years, therapy for MBDN has experienced significant improvement owing to its multidisciplinary approach and new treatments, especially second- and third-generation biophosphates[12,13]. Nevertheless, the effects produced by symptoms and general cancer treatment, and particularly MBDN, on HRQoL have not been properly studied[14,15]. It is implicitly assumed that if a symptom is controlled, HRQoL must consequently be improved. Although this hypothesis is possible, it must be accompanied by empirical studies to corroborate it[16,17].

At present, a series of specific instruments are available for the assessment of HRQoL in oncology, such as the Cancer Rehabilitation Evaluation System (CARES)[18], the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 quality of life questionnaire[19], Functional Assessment of Cancer Therapy (FACT)[20] and the Rotterdam Symptom Check List (RSCL)[21]. However, they may be insufficiently sensitive to some changes exclusively associated with MBDN. According to this concept, the 25-item BOMET-QoL questionnaire was designed to assess the quality of life in patients with MBDN. A detailed description of its primary development in a prior pilot study can be found in a previously published work[22].

As well as testing the final content of the questionnaire in a large sample of patients, an essential aspect for a HRQoL questionnaire to be applied with rigor, both in the research context and in common clinical practice[23], is to assess its measurement properties.

The BOMET-QoL questionnaire was developed in three phases: item generation, item selection and reduction analysis. A preliminary questionnaire was then developed and self-administered to 92 patients with BM. A final reduction analysis was performed by conducting factorial analysis (eight dimensions) and Rasch

modelling (25 items). The BOMET-QoL-25 showed good internal consistency and it is a feasible and reliable questionnaire to assess HRQoL in patients with BM[22].

The aim of this study was to perform the final development of the BOMET-QoL questionnaire and to analyse the measurement properties of the resulting questionnaire in common clinical practice conditions.

Methods

An observational, prospective, multicentre study was designed and carried out in the oncology, urology and haematology services of 46 hospital centres in Spain. A total of 263 patients diagnosed as having breast, prostate or non-microcytic lung cancer with bone metastasis or myeloma were included.

Patients were assigned to two groups: Group A included clinically stable patients with no expected changes in disease control in a 15-day period; and Group B consisted of patients with an expected change in their health status owing to clinical progression of their disease, initiation or change of treatment, or an intervention of known efficacy.

The inclusion criteria was men and women > 18 years of age, with diagnosis of lung, breast, prostate cancer or myeloma and an expected survival of at least 6 months. Written informed consent was obtained from all patients.

A minimum sample size of 152 patients in Group B was required to detect changes in the score of the BOMET-QoL questionnaire (0.25 standard deviation (SD), 0.05 significance level and 80% statistical power). To assess the test–retest reliability and to be able to detect an intraclass correlation coefficient (ICC) of 0.70 (0.60 minimum coefficient, 0.05 significance level, 80% statistical power), a minimum sample size of 76 patients in Group A was required[24].

Patients included in Group A made two visits (baseline visit and 15 days after baseline visit) and patients in Group B made three visits (baseline visit, 3 months after and 6 months after baseline visit). At the first visit, sociodemographic and clinical variables (such as site and diagnosis date of the primary tumour; MBDN sites; presence, number and duration of irruptive pain crisis; concomitant chronic and osteoarticular diseases; and treatment for the primary tumour and MBDN) were gathered. In addition, the investigator included the Eastern Cooperative Oncology Group (ECOG) Performance Scale[25] and the Pain Management Index (PMI)[26], which relates the type of analgesic treatment received by the patient to the pain level declared by the patient. After the first visit, patients completed the Spanish version of the EORTC-QLQ-C30 questionnaire, the BOMET-QoL questionnaire and the perception of general health status. At the second and third visits, changes in treatments, ECOG index and PMI were registered. Similarly, changes in health status perceived by the patients were computed and the EORTC-QLQ-C30 and BOMET-QoL questionnaires were again administered.

The final version of the BOMET-QoL questionnaire is unidimensional and consists of 10 items that can be answered on a Likert scale with five categories scoring from 0 to 4, and the temporal frame refers to 'the last week'. The global score is computed by adding the answers obtained on the items and can range from 0 (worst HRQoL) to 40 (best HRQoL). The scores are standardised so that the final scores range from 0 (worst HRQoL) to 100 (best HRQoL).

Reduction of the BOMET-QoL questionnaire occurred in two phases. In the first phase, a factor analysis with varimax rotation of the primary BOMET-QoL questionnaire items was made. In the second phase, each of the resulting factors was computed by means of the Rasch Rating Scale Model. Rasch analysis was performed with the 2.82 version of the BIGSTEPS programme[27], obtaining the calibration of each item. To determine the contribution of each item to the global health measurement, the χ^2 statistics most commonly used in the Rasch analysis were computed: infit and outfit. Generally, an item is considered to be amenable to being eliminated if it presents infit or outfit values >1.3[28]. Rasch analysis was repeated as many times as necessary until all items in the reduced version of the BOMET-QoL questionnaire presented suitable values for both statistics.

Subsequently, a descriptive analysis of the sociodemographic and clinical variables stratified by group (Groups A and B) and by type of neoplasia were made. To compare such variables between the different groups, χ^2 test and Student's *t*-test or its non-parametric equivalent Mann–Whitney *U*-test were used.

With the information obtained at the first visit, the score of the BOMET-QoL questionnaire was correlated with the presence and duration of irruptive pain crises, the PMI and the ECOG index.

Correlation between the score on the BOMET-QoL questionnaire and the score obtained on the EORTC QLQ-C30 questionnaire was computed by means of the Pearson's correlation coefficient, expecting a mild relationship ($r = 0.4$–0.7)[29].

To assess the validity of the questionnaire, the relationships between changes observed in the score on the BOMET-QoL questionnaire, the ECOG index and health status perceived in Group B was analysed. Changes in the BOMET-QoL scores were expected in those patients with changes in the ECOG index or health status.

The reliability of the questionnaire was assessed according to internal consistency and test–retest reliability. Internal consistency was achieved by means of the Cronbach's α statistic[30], expecting a good level of internal consistency ($\alpha \geq 0.7$). In Group A, the test–retest reliability was analysed from the scores obtained on the BOMET-QoL questionnaire between the baseline visit and the second study visit by means of the ICC, expecting an ICC ≥ 0.70[31].

Results

A total of 263 patients with MBDN were included. The mean age (± SD) of the patients was 62.20 ± 12 years and 42.9% were male. Of the 263 patients, 38.8% were diagnosed as having breast cancer, 16.7% had non-

Table 1. Sociodemographic and clinical characteristics of the patients by study group.

	Group A	*Group B*	*Total*
Age (Mean (SD))*	60.82 (12.58)	63.02 (11.73)	62.20 (12.08)
Sex (N (%))*			
Male	42 (42.9)	84 (50.9)	126 (47.9)
Female	56 (57.1)	81 (49.1)	137 (52.1)
Education level (N (%))*			
College graduate	13 (13.3)	14 (8.5)	27 (10.3)
High school	31 (31.6)	53 (32.1)	84 (31.9)
Elementary school	45 (45.9)	82 (49.7)	127 (48.3)
Some school	8 (8.2)	12 (7.3)	20 (7.5)
Type of baseline neoplasia (N (%))*			
Breast	45 (45.9)	57 (34.5)	102 (38.8)
Lung	23 (23.5)	21 (12.7)	44 (16.7)
Prostate	14 (14.3)	34 (20.6)	48 (18.2)
Myeloma	16 (16.3)	53 (32.1)	69 (26.3)
Elapsed time between the baseline visit and the baseline neoplasia diagnosis (Mean (SD))*	3.20 (3.69)	2.69 (4.38)	2.88 (4.14)
Concomitant osteoarticular diseases Yes (N (%))*	15 (15.3)	29 (17.8)	44 (16.9)
Non-osteoarticular chronic diseases Yes (N (%))*	32 (32.7)	55 (33.7)	87 (33.3)

SD, standard deviation.

* $p > 0.05$

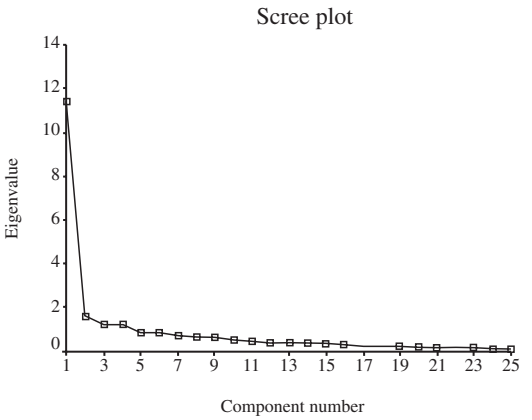
microcytic lung cancer, 18.2% had prostate cancer and 26.3% had myeloma (Table 1).

Factor analysis, including the total sample, showed the unidimensionality of the questionnaire, with only one factor explaining 61.2% of the variance (Figure 1). The subsequent Rasch analyses reduced the questionnaire to 10 items (Table 2).

A total of 98 patients were included in Group A and 165 in Group B. There were no statistically significant differences in the sociodemographic characteristics of the patients according to the study group (Table 1).

The primary site of the MBDN was the spine (79.1%), followed by the pelvis (49.8%) and ribs (46%), with no difference between study groups. As shown in Table 1, no statistically significant differences were found according to the mean time (SD) elapsed between the diagnosis of neoplasia and study initiation ($p=0.34$) and the percentage of patients that suffered from concomitant, non-osteoarticular chronic diseases.

Figure 1. Sedimentation graph obtained by factor analysis with the 25 initial items on the BOMET-QoL questionnaire.



Of the 263 patients in both groups, 31.5% were receiving or had received chemotherapy and 5% received radiation therapy for the primary tumour in the final month.

Moreover, 6.1 and 35% of patients received chemotherapy and analgesics ($p<0.01$), respectively, during the study or in the previous month for MBDN, and 76.9% of patients who received other treatments for MBDN received zoledronic acid.

At the baseline visit, 31.3% of patients in Group B and 17.3% in Group A presented irruptive pain ($p=0.019$) and the mean number (SD) of crises presented by the patients with irruptive pain was 2.12 (0.99) and 3.90 (3.96) for patients in Groups A and B, respectively ($p<0.01$). In addition, 22.3% of patients showed a negative PMI, indicating unsuitable analgesic treatment, with no difference between study groups ($p>0.05$).

In addition, 49.4% of patients were able to walk and perform mild working (ECOG 1), and 50% of patients in Group B declared having a general health status between 'slightly bad' and 'bad', whereas this percentage was significantly lower in Group A (24.4%; $p<0.001$).

Scores on the EORTC QLQ-C30 questionnaire were similar at the baseline visit and at the visit 15 days later in all dimensions in Group A. In Group B, scores for the functional and global dimensions increased, indicating an improvement in HRQoL of the patients in this group assessed according to this questionnaire.

The mean score (SD) of the BOMET-QoL-10 questionnaire at the baseline visit was lower (worse HRQoL) in Group B than in Group A (62.53 (23.53) and 46.72 (21.35), respectively) ($p<0.01$).

Validation of the BOMET-QoL-10 questionnaire

The impact on HRQoL assessed by the BOMET-QoL-10 questionnaire and the

Table 2. Content of the primary BOMET-QoL-25 questionnaire and of the final version of the reduced BOMET-QoL-10 questionnaire.

Primary BOMET-QoL-25 questionnaire		*BOMET-QoL-10*
1.	I feel tired	+
2.	I have little interest in doing things	-
3.	I find it difficult to get out of bed	+
4.	I find it very difficult to bend down	-
5.	I have difficulty getting dressed	-
6.	I'm afraid of falling in the shower	-
7.	I have difficulty doing things with my hands, for example picking up a glass or handling tools	-
8.	I have a feeling as if my bones were made of glass and are going to break at the slightest effort	-
9.	I have a feeling of general discomfort	+
10.	I feel depressed and feel like crying	+
11.	I usually think the worst	-
12.	I think that what is happening to me is never going to end	-
13.	I have little interest in going out of the house	+
14.	I avoid making plans for my life; I live from day to day	-
15.	I avoid doing activities with my family	+
16.	The medical treatment and visits due to my health problem affect my daily life	-
17.	I need someone around	-
18.	I feel pain in certain parts of my body, such as my back, legs, hips..., which affects my life	+
19.	I'm in constant pain which affects my life	+
20.	Due to the pain caused by my illness, I need to take sleeping tablets	-
21.	The pain due to my illness prevents me from walking normally	-
22.	I have an intense pain that constantly bothers me	+
23.	The pain prevents me from enjoying life like before	+
24.	I feel dissatisfied with my sex life	-
25.	Having a limited sexual activity makes me feel bad in my daily life	-

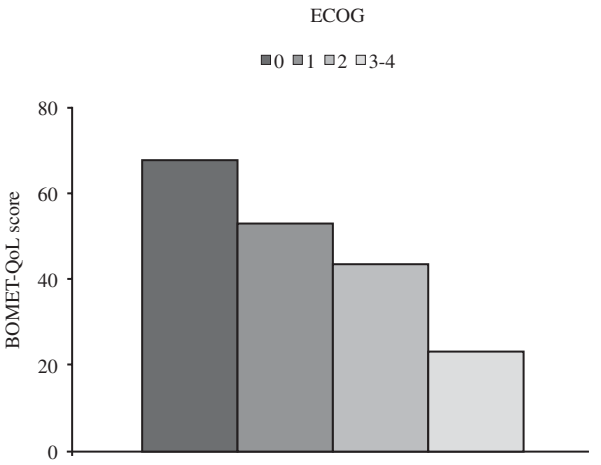
+, include item; -, exclude item.

variables of irruptive pain, PMI and ECOG index were shown to be correlated, with a higher score on the BOMET-QoL-10 questionnaire observed when the number of pain crises was lower, the PMI was 0 (good pain control) or the score of the ECOG index was between 0 and 1 ($p<0.01$) (Figure 2).

All the dimensions of the BOMET-QoL-10 are shown to be correlated in a statistically significant manner with the dimensions of the EORTC-QLQ-30 score ($p<0.01$).

The longitudinal validity and sensitivity to change of the BOMET-QoL-10 questionnaire was assessed only for patients in Group B. The valuable number of patients at 3 months was 137, and at the 6-month follow-up was 118. The main

Figure 2. Relationship between the Eastern Cooperative Oncology Group Performance Scale Index and the score obtained on the BOMET-QoL-10 questionnaire.



reason for this was the death of some patients (24 patients). In this group of patients it was observed that the scores for HRQoL increased (better HRQoL) significantly throughout the study follow-up ($p<0.01$).

Changes in the question regarding the general health status between the baseline visit and the visit 3 months later, and changes in the ECOG index were correlated with the scores observed on the BOMET-QoL-10 questionnaire ($p<0.01$).

Figure 3 shows the changes in scores on the BOMET-QoL-10 questionnaire and the ECOG index according to changes in the patient's health status. To compare the changes in the scores of both questionnaires, two axes have been used, maintaining proportionality in both scales with regard to maximum values (100 in BOMET-QoL-10 and 5 in ECOG) and minimum values (–100 in BOMET-QoL-10 and –5 in ECOG). It can be observed that the BOMET-QoL-10 questionnaire detects changes better than the ECOG index.

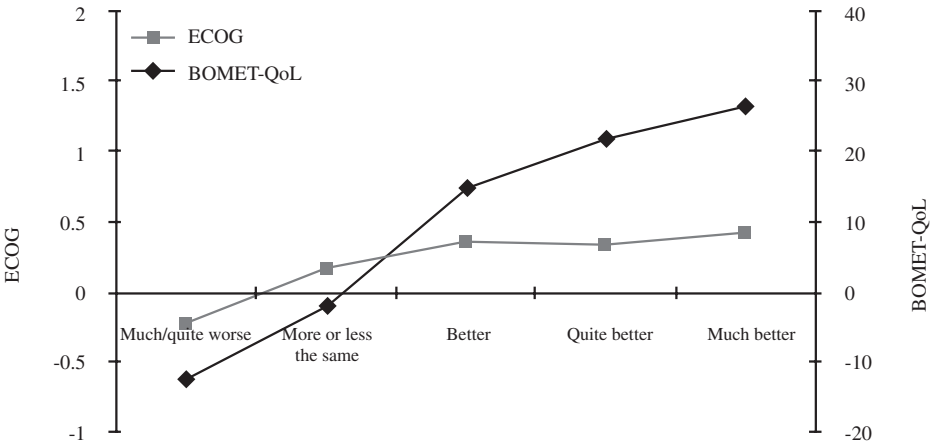
Regarding the reliability of the questionnaire, the Cronbach's α coefficient was 0.93 and the ICC was 0.94.

Table 3 shows a comparative analysis between the preliminary 25-item questionnaire and the current 10-item one.

Discussion

The aim of this project was the final development and validation of the BOMET-QoL questionnaire to assess the quality of life in patients with MBDN. As a result of the reduction process, an easy and simple to

Figure 3. Changes in scores of the BOMET-QoL-10 and Eastern Cooperative Oncology Group Performance Scale Index according to changes in the health status of the patient.



manage questionnaire was obtained with only 10 items and one dimension. Similarly, the 10-item BOMET-QoL questionnaire has shown good measurement properties with regard to reliability, validity and sensitivity to changes, very similar to the 25-item version, and is of great utility both in clinical research and in common clinical practice.

Use of HRQoL questionnaires in common clinical practice makes it possible for clinicians to obtain standardised information about the impact of disease or treatment on HRQoL of patients. However, nowadays many clinicians do not use HRQoL questionnaires owing to the difficulty in interpreting the results of the multidimensional information outcomes[32] or to the extension, a reason that on many occasions limits their use in clinical trials[33]. For this reason, it is necessary to develop short and easy to manage questionnaires that are easier to complete by the patient and to assess by the professional, but that maintain good measurement properties[34]. Nowadays, several procedures are used to reduce questionnaires: those based on the classical test theory (CTT) and those based on the item response theory such as Rasch analysis. Prieto *et al*[35] compared the reduction of the Nottingham Health Profile questionnaire according to both procedures, but failed to decide the suitability of one over the other. In this study, it was decided to reduce the BOMET-QoL-25 questionnaire by means of Rasch analysis because it has some advantages with regard to the CTT, since it considers each answer as a probabilistic function, lineal combination of the 'ability of the person' and the 'answer's difficulty', and makes it possible to build a measurement rule with the hierarchically placed items and to find people according to their competence (e.g. health status).

The outcomes of the study indicate that approximately one-quarter of the patients

Table 3. Comparison of the measurement properties of the BOMET-QoL-25 with the version of the BOMET-QoL-10 questionnaire.

Measurement properties	*Questionnaire*	*BOMET-QoL-25*	*BOMET-QoL-10*
Transversal validity	Correlation number irruptive pain crises	^{r}= -0.258‡	^{r}= -0.293‡
	Correlation mean duration irruptive pain crises	^{r}= 0.142‡	^{r}= 0.226‡
Longitudinal validity	Relationship between the change in the question "general health status" and the change in the scores*	Yes‡	Yes‡
	Relationship between the change in ECOG and the change in the scores*	Yes‡	Yes‡
Sensitivity to change	Effect size†	-0.74	-0.84
Reliability	Cronbach's	0.84	0.93
	ICC	0.92	0.94

^{r},Pearson's correlation coefficient; ECOG, Eastern Cooperative Oncology Group; ICC, intraclass correlation coefficient.
* Between baseline visit and the visit 3 months after.
† Between baseline visit and the visit 6 months after.
‡ $p<0.01$.

included in the study presented an unsuitable pain management, according to the PMI. Moreover, almost one-half of the patients presented an irruptive pain crisis within 24 h prior to the baseline visit. These data agree with other studies that show how this type of pain has a high prevalence in neoplastic patients and is described in >40% of them, with a mean of 1.5 episodes per patient per day[36]. Studies performed in the USA and France have obtained estimations of 42 and 51%, respectively, from patients who did not receive suitable analgesic treatment for their irruptive pain episodes[37].

There are several studies which conclude that measures of the HRQoL can predict survival time better than functional scales such as the ECOG index[38,39]. Although this hypothesis cannot be confirmed with the information obtained in this study, the authors can state that the BOMET-QoL-10 questionnaire is more sensitive to changes in the health status of patients with MBDN than the ECOG index, because it not only assesses the impact of the disease on a physical level but also on more subjective aspects of the patient. For this reason, the authors think that both questionnaires could be used jointly in common clinical practice to assess, more globally, the impact of this disease both on functional level and on daily life from the point of view of the clinician and the patient.

The outcomes obtained with regard to internal consistency and test–retest reliability indicate a high homogeneity and good reproducibility throughout the questionnaire. Regarding validity, just like other specific questionnaires for advanced cancer, the BOMET-QoL-10 has shown significant correlations with the ECOG and EORTC-QLQ-C30 questionnaire[40,41]. Nevertheless, because the EORTC-QLQ-C30 questionnaire does not have a global score, but a score by dimensions, the authors have failed to assess which one of these two questionnaires is more sensitive to changes in health status in patients with MBDN. The authors suspect that the BOMET-QoL-10 could possibly detect changes in health status in these patients better than the EORTC-QLQ-C30, as it has been designed specifically to be used in patients with this disease. This hypothesis is reinforced if we take into account the outcomes of other studies, which indicate that the use of the EORTC-QLQ-C30 questionnaire is not very suitable in advanced oncological pathology or in patients undergoing palliative therapy[42,43]. However, the authors do not think of the BOMET-QoL-10 as an instrument to replace the specific cancer questionnaires available today, but as a complementary questionnaire for the assessment of HRQoL in patients with MBDN in clinical trials.

A small percentage of patients have been included with ECOG 3 and 4 in this study, which could involve a shift in selection and a decrease in representativeness of the study sample. Another limitation of our study lies in the fact that although the sample size has enabled us to assess the measurement properties of our questionnaire, it is not enough to assess a cut-off score for each type of baseline neoplasia that lets us know the minimum clinically important difference according to HRQoL, or to make comparisons regarding the impact of MBDN on HRQoL measured by means of the BOMET-QoL-10 questionnaire among different types of neoplasia.

Conclusion

In summary, this study has enabled the authors to develop and assess the measurement properties of the BOMET-QoL-10, confirming its usefulness as a valid instrument for research and clinical practice. It would be desirable in the future to assess its clinical application in a wider sample of patients with each type of baseline neoplasia, including those with the highest levels of severity.

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