Validity and reliability of the Italian version of the ECOS-16 questionnaire in postmenopausal women with prevalent vertebral fractures due to osteoporosis

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Abstract

Objective

To investigate the reliability and validity of the Italian version of ECOS-16 (Assessment of health related quality of life in osteoporosis) in comparison to other questionnaires in postmenopausal women with osteoporosis.

Methods

A cross-sectional multicentre study was carried out among postmenopausal women with osteoporosis who were attending primary care centres and hospital outpatient clinics. The patient group included 234 females (mean age 69 years, range 48-89) who presented vertebral fractures due to osteoporosis. The control group consisted of 244 asymptomatic osteoporotic subjects matched for age with the patient group. The psychometric properties of the questionnaires were evaluated in terms of feasibility, validity (construct validity and discriminant validity) and internal consistency. Test-retest reliability was analysed for 196 outpatients who reported that their general health status due to osteoporosis had not changed after one week. In all patients the ECOS-16, the SF-36 (Medical Outcomes Study Short Form-36), EUROQoL (EQ-5D), mini-OQLQ (mini-Osteoporosis Quality of Life Questionnaire), and RMDQ (Roland-Morris Disability Questionnaire) were administered, and all clinical variables and sociodemographic variables were taken into account. Construct and discriminant validity were assessed by Spearman's correlations, the Wilcoxon rank sum test, the Kruskal Wallis test and by receiver operating characteristic (ROC) curves. Internal consistency was evaluated using Cronbach's alpha and the test-retest reliability was evaluated by intra-class correlation coefficients (ICCs).

Results

96.9% of the patients answered all items of the ECOS-16 questionnaires. The mean administration time was 10 minutes. Factor analysis yielded two factors that accounted for 88.4% of the explained variance in the ECOS-16 questionnaire. The first factor was the ECOS-16 Physical Component Score (PCS) (45.9% of the explained variance) and the second factor was the ECOS-16 Mental Component Score (MCS) (42.4% of the explained variance). The inter-item correlation between the two factors was 0.48. Significant correlations were found between the scores of similar domains or subscales of the ECOS-16 and SF-36, EQ-5D and mini-OQLQ, supporting the concept of convergent construct validity. The total ECOS-16 score progressively increased with the number of prevelant vertebral fractures ($p < 0.001$) and the effect of the first fracture was already statistically significant ($p < 0.01$). On ROC curve analysis the total ECOS-16 score showed the highest performance among the different questionnaires in discriminating between patients with vertebral fractures and controls with no fractures. In the reliability study, internal consistency within the domain of ECOS-16 was generally good, with Chronbach's alpha values ranging from 0.81 to 0.89. Test-retest reliability was 0.87 for the total ECOS-16 score.

Conclusions

The Italian version of the ECOS-16 questionnaire was demonstrated to have good psychometric properties and could offer a useful tool in research and routine clinical practice to evaluate HRQoL in post-menopausal women with osteoporosis. A full validation of the psychometric properties will require data on its sensitivity to change.

Key words

Osteoporosis, ECOS-16, vertebral fractures, quality of life, questionnaire.

This study was supported in part by an unrestricted educational grant from Chiesi Farmaceutici, Italy. Chiesi Farmaceutici did not provide funding to the authors for, nor did it participate in the preparation of, the manuscript.

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Received on September 4, 2006; accepted in revised form on December 15, 2006.

Competing interests: none declared.

Introduction

Osteoporosis is a chronic disease characterized by low bone mass, diminished bone strength, and increased skeletal fragility (1, 2). The most common clinical manifestation of osteoporosis is vertebral fracture (1-4). A vertebral fracture may have long-lasting consequences, but it is often difficult to specify the exact moment of onset of a fracture. Osteoporosis has frequently been referred to as a "silent thief" (5) and vertebral fractures too may be "silent". According to recent estimates, less than one-third of vertebral fractures cause sufficient symptoms to attract the immediate attention of a doctor (6-9). Other fractures may only cause vague complaints leading to a delayed diagnosis. Vertebral fractures may result in spinal deformity (kyphosis), height loss, impaired physical function, immobility, decreased pulmonary function and gastroesophageal reflux (10-18). The decline in physical function and changes in body appearance contribute to social isolation, loss of self-esteem and depression (19-23).

Assessments of fracture and bone mineral density can provide useful information on the physical effects of osteoporosis. However, these quantitative results do not provide qualitative information regarding the association of osteoporosis with daily living activities (24). Health-related quality of life (HR-QoL) is a multidimensional concept characterizing the health of individuals according to specific dimensions, namely physical, social, emotional, and functional well-being (25, 26). Generic and disease-specific instruments measure different dimensions of health experience, and both have been recommended in quality of life studies (25-27). Generic measures that have been extensively tested in osteoporosis include the Medical Outcomes Study Short Form-36 (SF-36) (14, 28-32), the Sickness Impact Profile (SIP) (25), the Nottingham Health Profile (NHP) (23, 25), and the EuroQuol-5D (EQ-5D) (22, 23).

Disease-specific instruments are useful for measuring clinically important changes in response to treatments (25, 26). The most widely used condition-specific instrument for the assessment of osteoporosis are the Osteoporosis Quality of Life Questionnaire (OQLQ) (33, 34), the Osteoporosis Assessment Questionnaire (OPAQ) (35-38), the Osteoporosis-Targeted Quality of Life Questionnaire (OPTQoL) (19, 39-41), and the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) (23, 32, 33, 42-46). However, their length and administration time have limited their use to clinical trials and highlighted the need for the development of questionnaires that are easier to administer in routine clinical practice.

For this reason specific short form questionnaires, such as the mini-OQLQ (47) and the ECOS-16 (Assessment of health-related quality of life in osteoporosis), for women with osteoporosis were developed (48, 49). We previously validated the Italian version of the mini-OQLQ (50). This questionnaire was derived from the original 30-item OQLQ (34, 47). ECOS-16 items were obtained from the Spanish versions of the OQLQ and QUALEFFO questionnaires, and were then reduced using Rasch analysis to obtain a total of 16 items – 12 from the QUALEFFO and 4 from the OQLQ (48, 49). This multidimensional self-assessment instrument has been thoroughly studied and many of its psychometric properties are known (48, 49). However, to allow comparison between assessments made in different countries, this questionnaire not only needs to be translated, but also must be adapted for use in different cultures. We report on the linguistic validation of an Italian version of ECOS-16 and present data on its metric properties.

Patients and methods

Recruitment of patients

In this cross-sectional, multicentre study the ECOS-16 questionnaire was administered to 478 postmenopausal women (mean age 68.5 years, range 48-89) with primary, clinically stable (i.e., no change in treatment and no new clinical deformities in the last 12 months) osteoporosis, who were attending primary care centres and hospital outpatient clinics. The patient

group was comprised of 234 females (mean age 69 years, range 48-89) who presented vertebral fractures due to osteoporosis, and the control group consisted of 244 asymptomatic osteoporotic subjects who were matched for age with the patient group. The women were screened in five rheumatologic centres in northern and central Italy. Diagnosis of osteoporosis was confirmed by a Bone Mineral Density (BMD) scan using Dual Energy X-Ray Absorptiometry (DEXA). Osteoporosis was defined as a T-score (the difference between the measured BMD and the mean value for young adults, expressed in standard deviations) lower than –2.5, according to the World Health Organization study group definition (51). T-scores represent the number of standard deviations (SDs) below the mean for young healthy women. All measurements at the left femoral neck and lumbar spine (L2–L4), in the anteroposterior position, were obtained by the DXA technique using a Hologic scanner (Hologic QDR 4500, Hologic, Inc, Bedford, Mass, USA). Total spine x-ray films in lateral views in various positions – neutral/flexion/extension in standing, and flexion/extension in the lateral decubitus position – were taken with a film-tube distance of 1.8 m. The anterior, central, and posterior heights of each of the vertebral bodies from T4 to L5 in a neutral standing x-ray film were measured using a caliper.

Vertebral fracture was considered to be present if at least one of three height measurements (anterior, middle, and posterior) of one vertebra had decreased by more than 20% compared with the height of the nearest uncompressed vertebral body (52). Exclusion criteria were as follows: (i) concurrent systemic inflammatory rheumatic disease or other diseases that might explain the patient's back pain (such as severe scoliosis, lumbar spondylolisthesis, or lumbar disc disease); (ii) a history of metabolic bone disease (including hyperparathyroidism, osteomalacia, or Paget's disease); (iii) a medical comorbidity that would preclude the patient's full participation in the study procedures (e.g., terminal conditions such as end-stage renal disease, heart failure, or malignancy); (iv) severe psychiatric emotional, cognitive or speech impairments that would have prevented them for answering the questionnaires; and (v) patients with documented vertebral fractures within the last 6 months. In addition, women who had recently started treatment for osteoporosis (with the exception of calcium and vitamin D supplements and/or hormonal replacement up to 6 months prior to randomization) were excluded. All subjects gave their informed consent, and the study was approved by the appropriate review committees.

Background and illness-related variables

Demographic and socio-economic information were assessed from patient interviews. Age was given in years. Educational level was separated into three categories based on the Italian school system: 1 = primary school, 2 = secondary school, and, 3 = high school/university. Marital status was recorded in 2 categories: 1 = living together, 0 = living alone. The body mass index (BMI = body weight divided by the square of the height) was used to assess obesity. In all patients the existence of comorbidities was also assessed by means of the Self-Administered Comorbidity Questionnaire (SCQ) (53). The SCQ is a modification of the widely used Charlson Index (54) and is based on patient interview or questionnaire responses rather than chart abstraction for the assessment of comorbidity and has excellent agreement with the chart-based Charlson Index (53, 55). We evaluated the rate of endorsement of each of 12 specific conditions, as well as the number of conditions endorsed. We assigned a score of one point if the condition was endorsed and additional points if the subject reported that she was currently receiving treatment for the condition, or if it limited activities. Each condition could, therefore, contribute 0 to 3 points for a possible maximum of 36 points.

Health-related quality of life questionnaires

In all patients, the ECOS-16 questionnaire (48, 49), mini-OQLQ (47, 50), Roland-Morris Disability Questionnaire (RMDQ) (56), SF-36 (57, 58), and EQ-5D (59) were administered, and all clinical variables and sociodemographic variables were taken into account.

ECOS-16 questionnaire

The ECOS-16 questionnaire was based on the combination of two disease-specific HRQoL questionnaires for women with osteoporosis: the OQLQ and the QUALEFFO (48, 49). All items have five possible responses, although the response options differ from one item to another. The 16 items are divided qualitatively into four dimensions: pain, physical functioning, fear of illness and psychosocial functioning. The score for each item ranges from 1 to 5. ECOS-16 generates a single summary score obtained by calculating the arithmetic mean of the answered items, so the total score ranges from 1 (best HRQoL) to 5 (worst HRQoL). The translation of the ECOS-16 into Italian was carried out by two bilingual researchers who were unaware of the objective of the questionnaire. It was then translated back into English by two different bilingual people who had no prior knowledge of the instrument. The initial Italian version was administered to a pilot group of 46 patients with chronic low back pain to evaluate any eventual difficulties in comprehension of the items. After some minor modifications, a definitive Italian version of the ECOS-16 was obtained (see Appendix).

Mini-Osteoporosis Quality of Life Questionnaire

The Italian version of the mini-OQLQ was used to measure the participants' HRQoL (50). The questionnaire was adapted from the original 30-item OQLQ (47) to enhance the instrument's usefulness in clinical practice. The mini-OQLQ includes the two items from the OQLQ with the highest impact in each of the five domains (symptoms, physical functioning, emotional functioning, activities of daily living, and leisure) for a total of 10 items. Each item is associated with a seven-point scale. The total score for the instrument can vary from 10 to 70, while

the domain scores can vary from 2 to 14. To standardize all the scores, the total and domain scores were divided by the number of items that were used to generate the values. A standardized rating of 1 represents the worst possible functioning (extreme difficulties, constant fear, extreme distress) and a rating of 7 represents the best possible functioning (no difficulties, no fear, no distress). The mini-OQLQ instrument has been evaluated in osteoporotic women with back pain due to vertebral fractures and has been found to be reliable and valid both for measuring differences in HRQoL between patients with osteoporosis and changes within these patients over time (47, 49, 50).

The Roland-Morris Disability Questionnaire

The RMDQ is a self-administered disability measure in which higher levels of disability are reflected by higher values on a 24-point scale (56). Patients are asked whether any of a series of statements applied to them during the last 24 hours. The RMDQ-24 score is calculated by adding up the number of "yes" items ranging from 0 (no disability) to 24 (maximum disability). The Italian version of the RMDQ has been shown to yield reliable measurements, which are valid for inferring the level of disability in patients with low back pain (60).

Medical Outcomes Study Short Form-36

The SF-36 is a generic instrument with scores that are based on responses to individual questions that are summarized in eight scales, each of which measures a specific health concept (57, 58). These eight health concepts are bodily pain, physical functioning, general health perception, role function–physical aspect, role function–emotional aspect, vitality, social functioning, and mental health (57).

The pain scale consists of two items asking patients to rate pain severity over the past week on a 5-point scale. The physical functioning scale consists of ten items that evaluate involvement in a range of activities such as running, playing, lifting heavy objects, climbing stairs, walking, and bathing or dressing oneself. Respondents are asked to rate on a 3-point scale the extent to which their health had limited their ability to engage in various activities over the past 4 weeks (1 = greatly limited, 2 = slightly limited, and 3 = not limited at all). The psychological and social function scales include five and two items, respectively.

For each of the SF-36 scales the items are scored with higher values indicating better health, and the individual scores are then added. The total scores are transformed to a 0–100 scale using a designated scoring algorithm. These eight scales, weighted according to normative data, are scored from 0 to 100, with higher scores reflecting a better quality of life (57). The SF-36 survey also includes a single-item measure of health transition, which is not used to score any of the eight multi-item scales. The SF-36 has been validated for use in Italy (58) and can be completed within 15 minutes by most subjects.

Recently, the authors of the SF-36 have developed algorithms to calculate two psychometrically based summary measures: the Physical Component Summary Scale Score (PCS) and the Mental Component Summary Scale Score (MCS) (61). The PCS and MCS provide greater precision, reduce the number of statistical comparisons needed, and eliminate the floor and ceiling effects that have been noted in several of the subscales (61).

EUROQoL-5D

The EQ-5D is a standardised, self-administered questionnaire that classifies the patient into one of 243 health states (59). It describes HRQoL in terms of five dimensions: mobility, self-care, usual activities (work, study, housework, family or leisure), pain/discomfort, and anxiety/depression. Each dimension is subdivided into three levels indicating 'no problem', 'a moderate problem' or 'an extreme problem'. Different health states can be described using a five-digit code number relating to the relevant level of each dimension. The perception of "one's own health state" on a VAS also forms part of the EQ-5D, but is scored separately. The anchors for this graduated 20 cm scale (0-100 points) are "worst imaginable health state" at 0, and "best imaginable health state" at 100. Respondents classify and rate their health on the day of the survey. Therefore, data from EQ-5D can be represented in three distinct forms; Part 1 may be presented either as a profile (EQ-$5D_{Profile}$) based on the unweighted responses indicating a patient's level of problem in each of the five domains, or as a health index (EQ-$5D_{Utility}$) by applying a suitable weighting system such as the utilities obtained from the UK national survey; and the VAS rating in Part 1 can be interpreted directly as a quantitative measure of the patient's evaluation of his or her own global health status (EQ-$5D_{VAS}$). The EQ-$5D_{Utility}$ and EQ-$5D_{VAS}$ scores were used in this study. The validity and reliability of the EQ-5D have been found acceptable in Europe among different populations and patient groups (22, 23, 62, 63).

Data processing

All data was stored in a FileMaker 7.0 relational database for Macintosh and was processed using the SPSS (version 11.0) and MedCalc (version 9.0) statistical software packages for Windows XP.

Statistical analysis

Parametric techniques may be applicable for certain ordinal level data; however, our data was generally not normally distributed (Kolmogorov-Smirnov test for normal distribution) and therefore the use of non-parametric techniques provided a more conservative estimate of statistical significance. Where appropriate, median and interquartile ranges are presented, as well as mean and standard deviations.

The differences among the groups were computed by the Wilcoxon test for independent samples, as appropriate. The floor (percentage of patients with the lowest score) and ceiling (percentage of patients with the highest score) effects were calculated for each of the ECOS-16 items and for the total score. Following standard guidelines for the evaluation of the measurement properties of quality of life instruments (64),

we tested the feasibility, validity, and reliability of the ECOS-16 questionnaire. The operational qualities (feasibility) of the ECOS-16 questionnaire were analyzed based on the percentage of patients who were able to complete the questionnaire by themselves and the amount of time required to fill it out.

Validity refers to the ability of an instrument to measure what it is intended to measure. Establishing the criterion or content validity of an instrument claiming to measure HRQoL is difficult as there are no established gold standards for comparison. Evidence for construct validity can only be accumulated by *a priori* hypothesized patterns of associations with other validated instruments. In this study, the construct validity was examined in three ways.

First, we explored the underlying component structure of the items. This was evaluated by performing principal component factor analysis, using principal axis extraction with the varimax rotation method, an approach that maximizes the independence of the factors. An eigenvalue criterion of 1.0 was used to select the factors and the results are given in terms of the percentage of variance in the scale score explained by the principal factor. Items were accepted on the final factors if they had a load of more than 0.50 on the corresponding factor.

Secondly, we examined convergent validity by correlating the scores of the index subscales with the other measures applied in the study. A particular subscale is expected to converge with the scores of those instruments targeting the same construct, and to deviate from the scores given by instruments or scales assessing a different construct (divergent validity). To quantify these relationships, Spearman's rho correlation coefficients were obtained.

Finally, to investigate the possible influence of patient characteristics such as age, level of education, comorbidities (number and score using the SCQ questionnaire) and the severity of vertebral involvement on radiographs, the associations between the ECOS-16 subscales and these characteristics were quantified by Spearman's correlation coefficients, the Wilcoxon rank sum test, and Kruskal-Wallis one-way analysis of variance. Differences were considered significant when $p < 0.05$.

Table I. Sociodemographic variables and clinical characteristics of 478 osteoporotic patients with and without vertebral fractures.

	Osteoporosis with vertebral fractures (n = 234)	Osteoporosis without vertebral fractures (n = 244)	*p*
Age (years)			
- mean (± SD)	69.0 (6.9)	68.1 (9.9)	NS
- range	48-89	50-87	
Years postmenopause			
- mean (± SD)	19.8 (10.8)	22.1 (11.9)	NS
- range	5-46	6-48	
Educational level, n (%)			
- primary school	128 (54.7)	117 (47.9)	NS
- secondary school	62 (26.5)	61 (25.0)	
- high school/university	44 (18.8)	66 (27.1)	
Marital status, n (%)			
- living together	131 (55.9)	153 (62.7)	NS
- living alone	103 (44.1)	91 (37.3)	
Body mass index			
- mean (± SD)	25.4 (3.6)	24.9 (3.5)	NS
- range	18.1-44.8	17.5-45.1	
No. of comorbid conditions, n (%)			
- None	52 (22.2)	113 (46.3)	< 0.0001
- 1-2	110 (47.0)	91 (37.3)	
- 3-4	54 (23.1)	34 (13.9)	
- 5 or more	18 (7.7)	6 (2.5)	
Comorbidity score by SCQ*			
- mean (±SD)	3.45 (2.1)	1.96 (2.4)	< 0.001
T-score L2-L4			
- mean (± SD)	-3.45 (0.79)	-3.20 (0.81)	< 0.01

*SCQ: Self-Assessment Comorbidity Questionnaire.
Note: Percentages are rounded to the nearest decimal place.

Discriminant validity was assessed by receiver operating characteristic (ROC) curve analysis to compare the ability of ECOS-16 to discriminate between patients with and without fractures in comparison to the other generic and specific questionnaires. ROC curves were plotted for each model to determine the area under the curve (AUC) and the sensitivity (i.e., the probability that a test result will be positive when the vertebral fracture is present) and specificity (the probability that a test result will be negative when the vertebral fracture is not present). The AUC was used to evaluate the diagnostic performance of the questionnaire. When the variable under study cannot distinguish between the two groups (vertebral fracture cases versus patients with no fractures), the area will be equal to 0.5 (i.e., the ROC curve will coincide with the diagonal). When there is a perfect separation of the values for the two groups, i.e., there is no overlapping of the distributions, the area under the ROC curve will be 1 (the ROC curve will reach the upper left corner of the plot). AUC values > 0.75 are generally considered to represent a good performance (65). From the ROC curves, we computed the optimal cut-off point corresponding to the maximum sum of sensitivity and specificity. The nonparametric Wilcoxon's signed rank test was used to calculate and compare the areas under the ROC curves derived from the patient sample, as suggested by Huley and McNeil (66).

Reliability encompasses the concept that repeated administration of a measurement tool in stable subjects will yield the same results. After a one-week interval, patients were asked by the same data collector to fill out the ECOS-16 questionnaire again with-

out any knowledge of their previous ECOS-16 ratings. Because it is possible for patients to change over a one-week interval, a global 'rating of change' questionnaire was administered concurrently to the subjects. The concept of the "transition" method was originally developed by Jaeschke *et al*. (67) and has since been applied in different rheumatologic settings (68, 69). The so-called "transition questionnaire" investigates current health status compared to that when the first questionnaire was completed (Question: Compared to when you completed the questionnaire regarding your functional disability a week ago, how is your health now?) The possible responses were "much better," "slightly better", "no change," "slightly worse," or "much worse". The questionnaire was designed to be self-administered and the items have been validated in previous studies (68). Subjects who reported no change were considered to be stable and those who reported change were eliminated from this analysis.

The test-retest reliability of the ECOS-16 was analysed using intra-class correlation coefficients (ICCs) in a group of 196 outpatients who declared that their general health status due to osteoporosis had not changed after one week. The ICC reflects both systematic and random differences in test scores. The value for ICC can vary from 1 (perfectly reliable) to 0 (totally unreliable). The ICC was chosen in preference to the Pearson correlation, which may overestimate reliability. One suggestion for acceptable test-retest reliability for the assessment of an individual is an ICC of 0.75 (70, 71). We also assessed reliability in terms of the internal consistency of the ECOS-16 subscales (physical function, pain, fear of illness and psychosocial function) and of the component summary scores (PCS and MCS dimensions). Internal consistency measures the extent to which items within a scale are correlated with each other (71). If the ECOS-16 questionnaire is internally consistent in the osteoporotic population, we would expect items within the individual scales (or dimension) to be highly correlated with one another. The Chronbach alpha statistic (72) is used to estimate the average of the correlations between items within a dimension. According to Steiner and Norman (70) a value of 0.8 is usually regarded as acceptable.

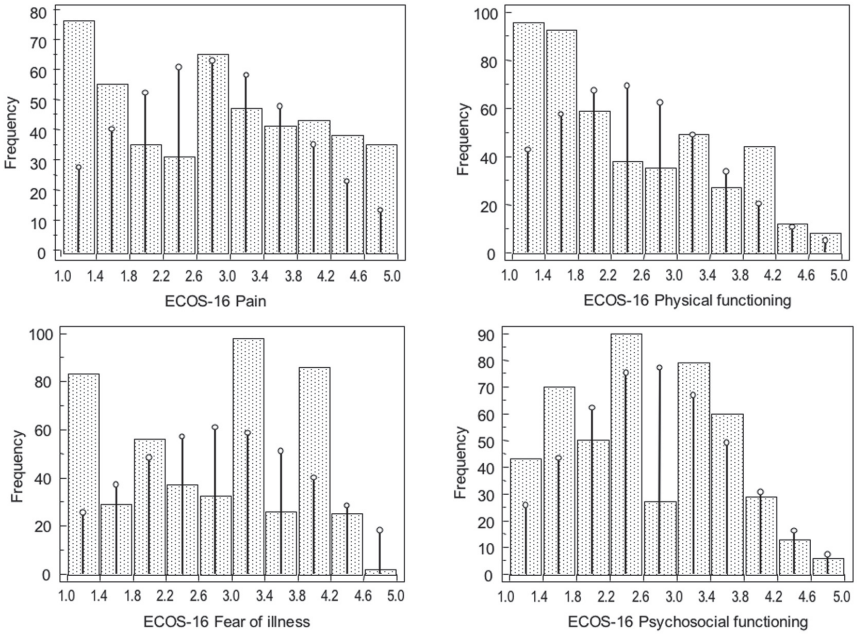


Fig. 1. Distribution of scores in the four subscales covered by the ECOS-16. The horizontal axis shows the scores (range 1-5), with high scores indicating a worse health status. The maximum floor effect was observed in 19.2% of the patients in the physical functioning dimension, in 17.7% of the patients in the pain dimension, and in 17.3% in fear of illness. Concerning the ceiling effects, the maximum possible score was found in 9.3% of the patients in the pain dimension. In the remaining dimensions negligible ceiling effects were found.

Results

Cohort distribution

A total of 478 postmenopausal women were identified for recruitment. The mean age was 68.5 ± 7.8 years (range 48-89) and 59.3% of the patients were married. Their level of education was generally low: 51.3% had received only a primary school education, and only 22.9% had received a high school education. Overall, 201 patients (42.1%) reported one or two comorbid conditions, and 112 patients (23.4%) reported 3 or more (range 3–7). The most frequently reported comorbidities were cardiovascular disorders (27.3%), chronic pulmonary disease (19.1%), metabolic disorders (13.7%), and gastrointestinal diseases (9.2%). Table I shows the main sociodemographic characteristics of the patients by group (those with and those without vertebral fractures): age, years after menopause, educational level, marital status, BMI, number of comorbid conditions, and the SCQ

Table II. Factor analysis: eigenvalues and statistical analysis of ECOS-16 factor structure using the principal component analysis of extraction method.

Component	Initial Eigenvalues			Extraction sums of squared loadings		
	Total	% of variance	Cumulative %	Total	% of variance	Cumulative %
Factor 1 (ECOS-16 PCS)	2.447	61.164	61.164	1.837	45.927	45.927
Factor 2 (ECOS-16 MCS)	1.088	27.207	88.382	1.698	42.455	88.382
Factor 3	0.305	7.634	96.015			
Factor 4	0.159	3.985	100.000			

ECOS-16 PCS: ECOS-16 physical component score; ECOS-16 MCS: ECOS-16 mental component score.

Table III. Factor analysis: rotated component matrix using the principal component analysis extraction method and varimax rotation with Kaiser normalization.

Item	Component	
	Factor 1	Factor 2
ECOS-16 Pain	**0.618**	0.252
ECOS-16 Physical Functioning	**0.512**	0.322
ECOS-16 Fear of Illness	0.235	**0.615**
ECOS-16 Psychosocial Functioning	0.327	**0.598**

The highest loading of each item is in bold type. Items were accepted as the final factors if they had a loading of more than 0.50 on the corresponding factor.

comorbidity score (53). Statistically significant differences ($p < 0.01$) were found for the number of comorbid conditions ($p < 0.0001$), the average SCQ score ($p < 0.001$), and the lumbar T-score obtained by DXA ($p < 0.01$).

Distributions of scores

The distribution of the scores in the ECOS-16 dimensions are presented in Figure 1. The leftmost bar in each graph represents the number of subjects with a score of 1 (floor effect); the rightmost bar represents the number of subjects with the maximum possible score (ceiling effect).

Feasibility

The mean time required to complete the ECOS-16 questionnaire by the patients was 10 ± 3.8 minutes (range 8 –15 minutes). Overall, the ECOS-16 questionnaire was correctly completed by 96.9% of the respondents.

Construct validity

Factor analysis was carried out to examine the factorial structure of the Italian version of the ECOS-16 questionnaire. The analysis revealed a two-factor solution (eigenvalues 2.447 and 1.088) (Table II), with each factor consisting of two items. The first factor, namely the ECOS-16 Physical Component Score (ECOS-16 PCS), accounted for 45.9% of the explained variance. The second factor, the ECOS-16 Mental Component Score (ECOS-16 MCS), accounted for 42.4% of the explained variance.

Table III shows the high loading (more than 0.50) of each question after varimax rotation with Kaiser normalization on the two factors. Each factor loading represents the correlation between that item and the underlying factor. The inter-item correlation between the two factors was r = 0.48.

In testing for convergent validity be-

Table IV. Convergent validity analysis: correlation matrix (Spearman's rho) of the ECOS-16 Questionnaire versus the mini-OQOL, RMDQ, SF-36, and EQ-5D.

	ECOS-16 Questionnaire						
	Pain	Physical functioning	Fear of illness	Psychosocial functioning	PCS	MCS	Total score
ECOS-16 Questionnaire							
Pain	-						
Physical functioning	0.832	-					
Fear of illness	0.481	0.547	-				
Psychosocial functioning	0.668	0.717	0.552	-			
Physical component summary score (PCS)	0.958	0.934	0.537	0.767	-		
Mental component summary score (MCS)	0.629	0.701	0.915	0.834	0.692	-	
Total score	0.861	0.886	0.773	0.843	0.920	0.907	-
Mini-OQOL Questionnaire							
Symptoms	-0.768	-0.698	-0.359	-0.591	-0.778	-0.501	-0.699
Daily living activities	-0.622	-0.636	-0.495	-0.525	-0.655	-0.569	-0.665
Physical functioning	-0.661	-0.686	-0.505	-0.516	-0.695	-0.567	-0.688
Leisure	-0.548	-0.565	-0.414	-0.438	-0.586	-0.481	-0.566
Emotional functioning	-0.472	-0.509	-0.731	-0.441	-0.504	-0.693	-0.635
Total score	-0.731	-0.748	-0.603	-0.592	-0.767	-0.671	-0.779
Roland-Morris Disability Questionnaire	0.698	0.660	0.367	0.534	0.710	0.486	0.659
Medical Outcome Study Short Form-36 (SF-36)							
Bodily pain	-0.497	-0.498	-0.383	-0.438	-0.531	-0.417	-0.523
General health perception	-0.382	-0.446	-0.516	-0.435	-0.438	-0.422	-0.469
Role function – physical aspect	-0.448	-0.501	-0.312	-0.443	-0.492	-0.405	-0.499
Physical functioning	-0.526	-0.582	-0.382	-0.531	-0.571	-0.464	-0.564
Social functioning	-0.479	-0.537	-0.401	-0.418	-0.538	-0.506	-0.571
Role function – emotional aspect	-0.455	-0.454	-0.318	-0.448	-0.463	-0.407	-0.474
Vitality	-0.371	-0.431	-0.307	-0.435	-0.421	-0.402	-0.447
Mental health	-0.343	-0.338	-0.303	-0.459	-0.389	-0.357	-0.404
Physical component summary score (PCS)	-0.512	-0.577	-0.367	-0.435	-0.571	-0.453	-0.561
Mental component summary score (MCS)	-0.355	-0.382	-0.302	-0.429	-0.385	-0.403	-0.431
EUROQoL-5D							
$EQ\text{-}5D_{Utility}$	-0.537	-0.658	-0.447	-0.627	-0.678	-0.583	-0.691
$EQ\text{-}5D_{VAS}$	-0.495	-0.493	-0.397	-0.496	-0.578	-0.486	-0.557

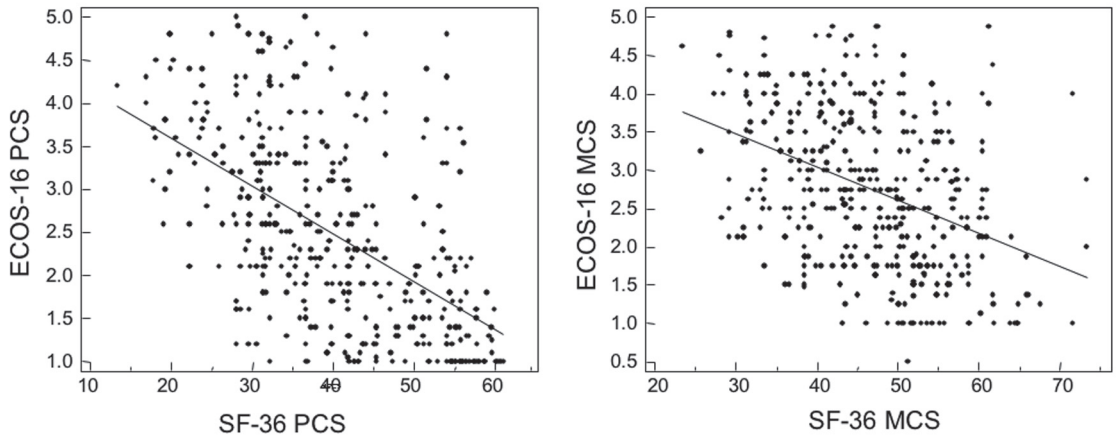


Fig. 2. Scatter plot of the ECOS-16 PCS and MCS (range 1-5) against the SF-36 PCS and MCS (range 0-100) component summary scale scores. Worse function is indicated by high scores for ECOS-16 MCS and low scores for SF-36 MCS. A "best fit" linear regression line has been superimposed.

Table V. Descriptive statistics features of the score distribution and results of the Wilcoxon tests for the four ECOS-16 subscales, dimensions and total scores in patients with or without vertebral fractures due to osteoporosis.

	Osteoporosis with vertebral fractures				Osteoporosis without vertebral fractures				Wilcoxon test	
	Mean score	SD	Median value	Interquartile 25^{th}- 75^{th}	Mean score	SD	Median value	Interquartile 25^{th}- 75^{th}	*z*	*p*
ECOS16 Questionnaire										
Pain	3.299	1.086	3.400	2.600 - 4.200	2.160	1.019	2.000	1.200 - 2.800	-10.467	0.0001
Physical functioning	2.902	1.066	3.000	2.000 - 3.800	1.689	0.716	1.400	1.200 - 2.000	-12.332	0.0001
Fear of illness	3.341	1.114	3.500	2.500 - 4.000	2.370	1.193	2.000	1.000 - 3.000	-8.543	0.0001
Psychosocial functioning	3.053	0.959	3.000	2.500 - 3.750	2.277	0.837	2.250	1.750 - 3.000	-8.428	0.0001
Physical component summary score (PCS)	3.094	1.044	3.200	2.250 - 3.900	1.928	0.799	1.800	1.200 - 2.400	-11.556	0.0001
Mental component summary score (MCS)	3.208	0.916	3.250	2.500 - 4.000	2.323	0.862	2.250	1.750 - 2.875	-9.686	0.0001
Total score	3.131	0.894	3.025	2.488 - 3.862	2.125	0.728	2.031	1.500 - 2.588	-11.440	0.0001

tween instruments (Table IV) we found that the correlation coefficients for the comparable subscales and dimensions of the ECOS-16, mini-OQLQ and SF36 questionnaires ranged from -0.303 to -0.778. Generally, higher significant correlations were seen when comparing the ECOS-16 scales to the mini-OQOL and SF-36 scales, with a high ability to measure pain and physical health. Lower significant correlations were seen when comparing the ECOS-16 scales to the mini-OQOL and SF-36 scales, with a high ability to measure mental health. Of special interest were the correlations between the total ECOS-16 score and the total mini-OQOL score (rho = -0.779; $p < 0.0001$), between the total ECOS-16 score and RMDQ (rho = -0.659; $p < 0.0001$) and between the ECOS-16 and SF-36 PCS and MCS dimensions ($p < 0.0001$) (Fig. 2). The two dimensions of the ECOS-16 (PCS and MCS) correlated significantly with each other (rho = 0.692; $p < 0.0001$).

The results of the Wilcoxon tests for the four subscales, the component summary scale and the total scores for the ECOS-16 are presented in Table V.

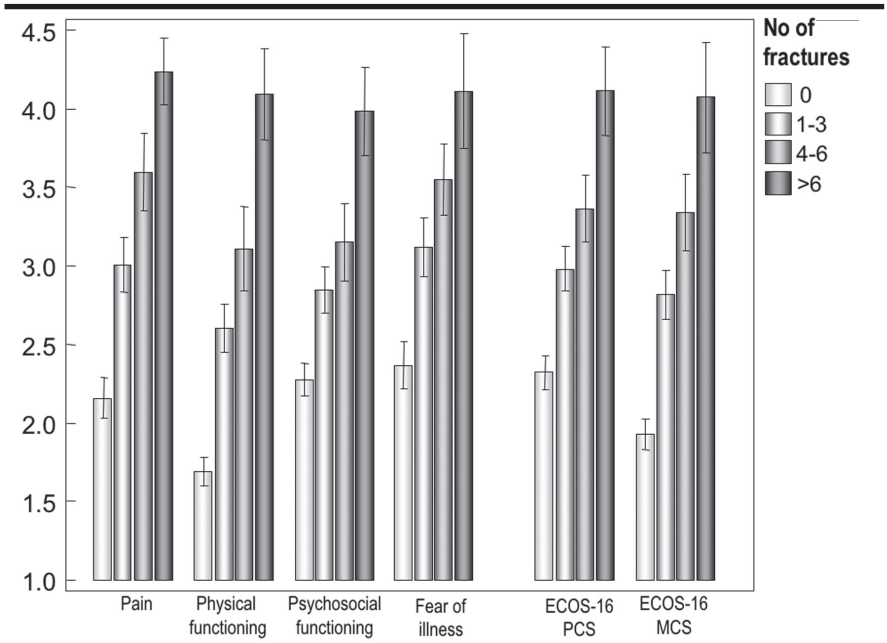


Fig. 3. ECOS-16 subscales, component summary scale scores (PCS and MCS), and the number of prevalent vertebral fractures. For the linear trend for each subscale/dimension, $p < 0.0001$. For subjects with 0 to 1 fracture, $p < 0.01$.

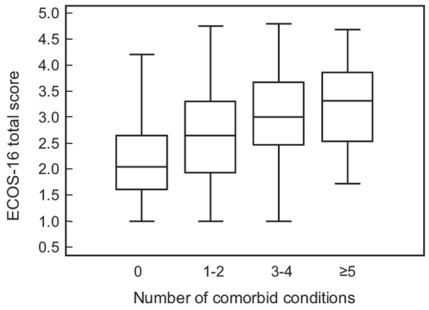


Fig. 4. The median total ECOS-16 score by the number of comorbidities. The box plots provide information on the symmetry of each distribution, the numerical measures of central tendency, and on the variability and spread of the data in the tails of each distribution. The box contains the median values (represented by a horizontal line within the box), 25th and 75th percentiles, and 90th percentiles. The Kruskal-Wallis test was carried out across all four groups (Ht = 52.76, $p < 0.0001$).

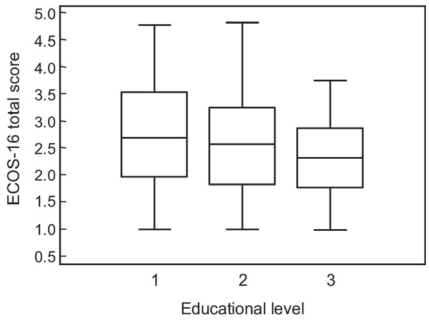


Fig. 5. The median total ECOS-16 score by educational level (1: primary school; 2: secondary school; and 3: high school or university). The Kruskal-Wallis test was carried out across all three groups (Ht = 17.98; $p < 0.001$).

Fig. 6. Receiver operating characteristic (ROC) curves for the performance of the ECOS16 subscales and component summary scale scores (PCS and MCS) in discriminating between vertebral fracture patients and patients without vertebral fractures.

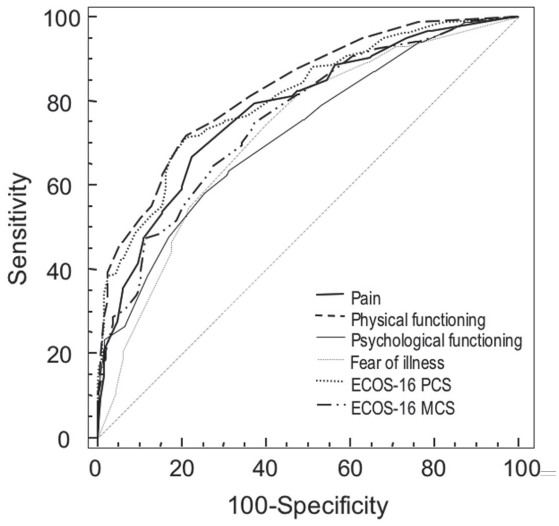
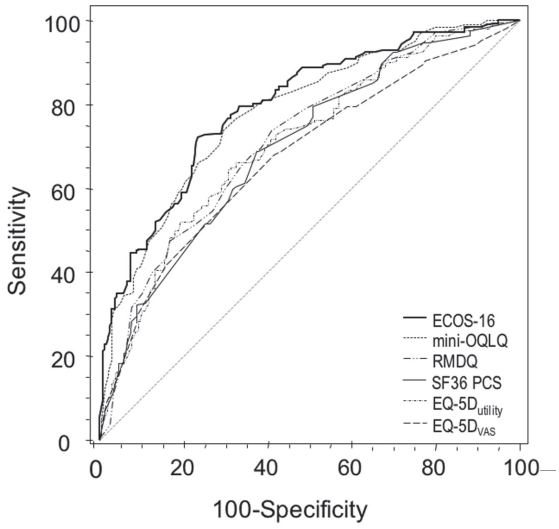


Fig. 7. Receiver operating characteristic (ROC) curves for the performance of the total ECOS16 score, the total mini-OQLQ score, RMDQ, SF-36 PCS and EQ-5D in discriminating between vertebral fracture patients and patients without vertebral fractures.



For all scores of the ECOS-16, we have strong evidence that the mean rank of the scores differ significantly between patients with and patients without vertebral fractures ($p = 0.0001$ in all cases). The total ECOS-16 score progressively increased with the increasing number of prevalent vertebral fractures (Ht = 153.2; $p < 0.0001$) and the effect of the first fracture was already statistically significant ($p < 0.01$) (Fig. 3). Figure 4 shows that there was a larger increase in scores amongst patients with comorbidities (Kruskal Wallis test, Ht = 52.76, $p < 0.0001$). Moreover, a significant correlation was found between the total ECOS-16 score and the SCQ score (rho = 0.358; $p < 0.0001$). Stratification into 3 categories showed that increasing education was associated with a lower total ECOS-16 score (Kruskal Wallis test: Ht = 17.98; $p < 0.001$) (Fig. 5). No significant difference was observed in the comparison between patients subdivided according to age, marital status or BMI.

Figure 6 shows the ROC curve analysis for the individual ECOS-16 subscales and the component summary scores, which was carried out to assess the discriminant capacity between fracture cases and controls. The AUC is used to evaluate the method's performance. ECOS-16 subscales demonstrated significantly better performance for physical functioning (AUC = 0.825) and pain (AUC = 0.778). The ROC curve analysis for the total ECOS-16 score, the total mini-OQOL score, SF-36 PCS, RMDQ, and EQ-5D (EQ-$5D_{Utility}$ and EQ-$5D_{VAS}$) are given in Figure 7. The total ECOS-16 score and mini-OQOL showed a similar performance. The AUC-ROC of the RMDQ and EQ-5D were between 0.684 and 0.723, which implies a significantly lower ($p < 0.001$) discriminant capacity.

Table VI reports the calculated AUC-ROC values (± standard error), 95% confidence intervals and corresponding sensitivity and specificity at the optimal cut-off values for the individual domains, component summary score and total score for the ECOS-16, and for the mini-OQOL total score, the SF-36 PCS, RMDQ, EQ-$5D_{Utility}$ and EQ-$5D_{VAS}$. The optimal cut-off value for the total ECOS-16 score obtained from the ROC analysis was 2.6. Based on this cut-off value, the sensitivity was 74.5% (95% CI for the mean, 69.1–80.9) and the specificity was 77.9% (95% CI for the mean: 71.3–83.8).

Reliability

Of the 478 patients enrolled in the

Table VI. Calculated area under the ROC curve values (± standard error), 95% confidence values, and corresponding sensitivity and specificity at the optimal cut-off value for the ECOS-16 questionnaire (ECOS-16 subscales, dimensions and total score), mini-OQOL (subscales and total score), RMDQ, SF-36 PCS, and EQ-5D (EQ-$5D_{Utility}$ and EQ-$5D_{VAS}$).

	Area under the ROC curve	Standard error	95% CI of the mean	Cut-off value	Sensitivity	Specificity
ECOS16 Questionnaire						
Pain	0.778	0.021	0.736-0.813	2.8	66.7	77.5
Physical functioning	0.825	0.019	0.788-0.858	2.1	71.8	78.8
Fear of illness	0.724	0.023	0.680-0.763	2.5	74.8	55.8
Psychosocial functioning	0.722	0.023	0.681-0.764	2.7	59.1	74.6
Physical component summary score (PCS)	0.805	0.020	0.767-0.840	2.5	71.4	78.7
Mental component summary score (MCS)	0.756	0.022	0.715-0.795	2.5	74.8	62.7
Total score	0.802	0.020	0.764-0.837	2.6	74.5	77.9
Mini-OQOL questionnaire	0.785	0.021	0.746-0.821	4.4	73.5	70.9
Roland-Morris Disability Questionnaire	0.723	0.023	0.665-0.749	6.0	73.9	69.5
Medical Outcome Study Short Form-36 (SF-36) Physical component summary score (PCS)	0.715	0.022	0.672-0.755	38.1	65.1	70.1
EUROQoL-5D						
EQ-$5D_{Utility}$	0.708	0.023	0.665-0.749	0.687	69.2	63.1
EQ-$5D_{VAS}$	0.684	0.024	0.640-0.726	50	68.4	59.4

study, the 196 who did not perceive a change in their general health status due to osteoporosis completed the ECOS-16 questionnaire twice within the stipulated 7 to 10 days (mean 7.9 ± 2.6 days). The test-retest reliability (ICC) was 0.87. The internal consistency of the ECOS-16 subscales was generally good with Cronbach's alpha values ranging from 0.81 to 0.89. Both component summary scale scores of the ECOS-16 showed satisfactory internal consistency according to the standards recommended by Steiner and Norman (70). Cronbach's alpha was 0.87 for the ECOS-16 PCS, and 0.84 for the ECOS-16 MCS. Item-total correlations, which are another measure of internal consistency, compare the scores for the individual items with the overall score of the scale. Items with item-total correlations less than 0.4 should be evaluated for rejection. In our analysis, the item-total correlations for the subscales were very high (Table IV).

Discussion

Vertebral fractures associated with osteoporosis produce pain and other negative effects on a patient's HRQoL, making this an important parameter for assessment (6, 13, 15, 17, 21, 22, 28, 31, 38). For this reason, a number of osteoporosis-specific HRQoL instruments have been developed in recent years (36, 38, 39, 47-49). While clinicians and investigators may utilize a variety of questionnaires to assess their patients' HRQoL, the length of these instruments and the time they take to complete may limit their use. Considerations of greater efficiency, a decreased burden on the respondent, and clinical feasibility have led to the development of shorter questionnaires (47-49). Short questionnaires minimize a patient's time and effort, and thus increase his or her willingness to complete it (33). The ECOS-16 originates from the condensation of two validated and widely used HRQoL questionnaires in osteoporosis patients with vertebral fracture (48, 49).

In the present study, the ECOS-16 was administered to a similar number of patients with and without fractures, in order to examine and validate the psychometric properties of the Italian version of the questionnaire. The findings reported here suggest that the ECOS-16 could offer a valid, reliable and useful instrument wherever a brief, simple method of measuring the HRQoL, as in this type of patient population, is needed. Regarding feasibility, the ECOS-16 was in general very good with no disturbing questions, few confusing items, and a very low percentage of missing data for the items and scales. The patients can complete the questionnaire in a short time (10 minutes) without difficulty. The high CCI coefficients (0.87) obtained from test-retest reliability support this observation.

Factor analysis showed that two primary components of the ECOS-16 questionnaire accounted for 88.4% of the explained variance. The first factor (ECOS-16 PCS, 45.9% of the explained variance) represents the patient's perceived disability in major areas of daily life. The second factor (ECOS-16 MCS, 42.4% of the explained variance) reflects the patient's psychological troubles. Both dimension scales (ECOS-16 PCS and MCS) revealed satisfactory internal consistency. It is worth noting that the two summary scale scores displayed a significant positive inter-correlation of r = 0.48. On the one hand, this inter-correlation is low enough to use both subscales as separate measures, as the results of factor analysis and the eigenvalues suggest, but this correlation is also high enough to allow use of the ECOS-16 questionnaire as an overall measure.

In terms of concurrent validity with the self-administered mini-OQOL, RMDQ, SF-36, and EQ-5D, inspection of the correlations of similar dimensions across the health status instruments revealed the expected convergences. The weak or absent correlations between the total ECOS-16 score and traditional clinical variables (i.e., bone densitometry, BMI, age, years after menopause) are consistent with the findings in earlier studies (33, 34, 44, 46). Based on

ROC curve analysis, in comparison to other established generic instruments such as the SF-36, EQ-5D or disability questionnaires such as the RMDQ, ECOS-16 was shown to be better in discriminating between patients with and without vertebral fractures.

The results of the Kruskal-Wallis analysis confirm that there are differences in the scores between individuals according to the severity of their vertebral fractures in all four dimensions of the ECOS-16 and in both component summary scores. This confirms the widespread impact of chronic pain on all aspects of health, and supports the multidimensional view (23, 38, 43). ECOS-16 scores progressively increased with the number of prevalent vertebral fractures and the effect of the first fracture was already statistically significant ($p < 0.01$). A progressive decline in HRQoL with the increasing number of fractures was reported in the Multiple Outcomes of Raloxifene Evaluation (MORE) multicentre trial using the Osteoporosis Assessment Questionnaire (OPAQ) (38, 73) and the QUALEFFO (23, 42). Most recently, Cickerill *et al*. (74) observed impairment in the HRQoL as measured by the EQ-5D, short form 12, and QUALEFFO in patients with radiographic evidence of recent vertebral fracture in comparison to those with no such signs of fracture, the subjects having being recruited from the European vertebral Osteoporosis Study (EVOS). This impairment was most marked in patients with pre-existing vertebral fracture/deformity (74).

However, one must be cautious in drawing the conclusion that there is a causal relationship. Confounding factors may play a role in the observed association of reduced HRQoL in postmenopausal women with vertebral fractures, including sociodemographic conditions, educational level, psychosocial status, and other traditional risk factors (38, 42, 43, 75, 76). Self-reported chronic pain or reduced physical function, which are common complaints of elderly people, may be secondary symptoms of another condition, such as ischaemic heart disease, pain due to digestive diseases, or chronic peripheral neuropathic pain. Patients with vertebral fractures have been reported to suffer more adverse events than other patients due to comorbidity (1, 77). In addition, comorbidity is known to be an important determinant in fractures. In a retrospective cohort study of 86 United States residents undergoing renal transplantation between 1965 and 1995, high fracture rates were observed, particularly involving the vertebrae and feet (77). Our results show that patients with comorbid conditions have worse total scores for ECOS-16. This observation has already been made in previous studies in patients with other musculoskeletal disorders (78, 79).

In this study a strong association was also noted between ECOS-16 scores and the patient's emotional state (SF-36 MCS). The fact that the ECOS-16 is sensitive to psychosocial factors is not to be attributed to the instrument itself. Self-report instruments are sensitive to these factors and indeed such factors contribute to the actual pain and physical impairment reported by patients. We cannot exclude that this was a coincidental finding, since mental function was found to be the least discriminatory and responsive domain in other studies (43). If, however, a patient's emotional state strongly influences the HRQoL (20, 33, 38, 76, 80), the resultant random measurement error would restrict the validity of the ECOS-16 or other self-report questionnaires to only relatively large studies.

The low level of education in our study cohort must also be taken into account. It is consistent with previous studies (81, 82) and, as in other chronic diseases (78, 79), the level of education may affect an individual's preference values (83). In the present study, we found a significant relationship between the ECOS-16 scores and the level of formal education, suggesting that formal education should be included as a variable in clinical studies of patients with osteoporosis. The mechanism by which education influences HRQoL is unclear, but may be related to an enhanced sense of control and ability to cope, allowing the patient to take advantage of a greater number of pain-reducing modalities. The pattern of association of chronic pain with indicators of socio-demographic status is interesting, and supports previous research on chronic pain (84). It is not clear from this cross-sectional research, however, whether the demonstrated socio-demographic associations represent a cause or an effect.

There are possible limitations to this study, primarily due to the fact that it did not control for certain variables that have been shown to have a clear influence on HRQoL. In particular, the "time passed since the fracture occurred" was not analyzed, even though the subject of the study was women with established osteoporosis. The inclusion of prevalent fractures and the exclusion of incidence fractures led to a smaller variability among the patients in this study and possibly also meant that vertebral fractures had less influence on HRQoL (36, 38). The significance of our results is further limited by the fact that it involved a non-randomly ascertained primary care sample. It can be assumed that a patient's motivation in voluntarily taking part in a study will differ in random population samples, as they tend to aggravate the self-perceived severity of an illness.

In conclusion, the results reported here confirm the psychometric properties of the ECOS-16 questionnaire in patients with osteoporosis. The Italian version of the ECOS-16 questionnaire will increase the comparability of studies conducted in Italy and in English-speaking countries and facilitate international collaboration in this field. The sensitivity of ECOS-16 to longitudinal changes, such as improvement after treatment or deterioration after incident vertebral fracture, needs to be investigated in a prospective multicentre study.

Acknowledgments

We wish to thank all the IMOF study members for their collaboration in this study. The members of the IMOF study are: M. Carotti, M.A. Cimmino, P. Del Medico, L. Di Matteo, A. Farina, M. Frigato, S. Gasparini, R. Girolimetti, W. Grassi, M. Gutierrez, N. Malavolta, E. Manfredini, R. Mule', F. Salaffi, P. Scendoni, A. Stancati, A. Verocchio, and G. Vukatana.

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Appendix

Items of the ECOS-16 questionnaire (Italian version)

Nel corso dell'ultima settimana a causa dei problemi alla schiena dovuti all'osteoporosi:

Quanto spesso ha avuto mal di schiena nel corso dell'ultima settimana?
Quanto è forte il Suo mal di schiena?
Quanto fastidio o difficoltà ha avvertito a causa del fatto che prova dolore nello stare in piedi per lungo tempo?
Quanto fastidio o difficoltà ha avvertito a causa del fatto che prova dolore nel piegarsi?
Il dolore ha disturbato il Suo sonno nel corso dell'ultima settimana?
Quanta difficoltà ha riscontrato nello svolgere le attività domestiche?
E' in grado di salire un piano di scale?
Ha difficoltà nel vestirsi da sola/o?
Quanta difficoltà ha avuto nel chinarsi (ad esempio per raccogliere un oggetto caduto sul pavimento)?
Quanta limitazione ha avvertito nel camminare?
Quanta difficoltà ha avvertito nel recarsi a fare visita a parenti o amici?
Si sente giù di morale?
E' ottimista riguardo al Suo futuro?
Si sente frustrata/o
Ha paura di cadere?
Ha paura di potersi procurare una frattura?

Items of the ECOS-16 questionnaire (English version)

During the last week because of your back problems due to osteoporosis:

How often have you had back pain in the last week?
How severe is your back pain?
How much distress or discomfort have you had because it has been painful to stand for a long time?
How much distress or discomfort have you had due to pain from bending?
Has the back pain disturbed your sleep in the last week?
How difficult has it been for you to carry out household activities?
Can you climb stairs to the next floor of a house?
Do you have problems with dressing?
How difficult has it been for you to bend?
How much has your walking been limited?
How difficult has it been for you to visit friends or relatives?
Do you feel downhearted?
Are you hopeful about your future?
Do you feel frustrated?
Are you afraid of falling?
Are you afraid of getting a fracture?