Relationship of Health Related Quality of Life to Prevalent and New or Worsening Back Pain in Postmenopausal Women with Osteoporosis

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ABSTRACT. ***Objective.*** To examine the association between back pain and health related quality of life (HRQOL) in postmenopausal women with osteoporosis.

Methods. The Fracture Prevention Trial was a prospective double blinded, placebo controlled study designed to compare the proportion of women receiving teriparatide who experienced a new fracture to the proportion of women receiving placebo who experienced a new fracture. Subjects were ambulatory postmenopausal women with osteoporosis and prior vertebral fracture. As part of this trial, English-speaking women from Canada, New Zealand, Australia, and the United States participated in a HRQOL substudy using the Osteoporosis Assessment Questionnaire (OPAQ). OPAQ was administered at baseline, 12 months, and at study termination (median treatment duration 19 mo). Back pain data were collected as part of the adverse event monitoring during the trial. Subjects considered to have experienced back pain reported this event spontaneously and were not queried specifically. We examined the influence of prevalent back pain on HRQOL after controlling for spine deformity index score, and the influence of new or worsening back pain on HRQOL after controlling for incident vertebral fracture.

Results. Of 471 women who completed OPAQ at baseline, 172 reported back pain that was associated with a mean decrease in all OPAQ dimension scores ($p < 0.05$). Of 429 women who completed OPAQ at all timepoints, 88 experienced new or worsening back pain that was associated with a mean decrease in physical function, emotional status, and symptoms scores ($p < 0.01$ for each). In a subset of 65 women who experienced moderate to severe back pain, all OPAQ dimensions were significantly reduced ($p < 0.05$).

Conclusion. Both prevalent back pain and new or worsening back pain affected HRQOL negatively. Osteoporosis therapies that prevent the development of back pain in postmenopausal women may also prevent decreases in HRQOL. (J Rheumatol 2005;32:2405–9)

Key Indexing Terms:
OSTEOPOROSIS ASSESSMENT QUESTIONNAIRE
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Osteoporosis is a chronic disease of low bone mass, diminished bone strength, and skeletal fragility. Approximately 10 million people are affected in the United States[1]. The most common clinical manifestation of osteoporosis is vertebral fracture[2]. Vertebral fractures increase the risk of future vertebral fractures, precipitating height loss and kyphosis[3-5]. Impaired physical functioning, immobility, loss of self-esteem, and depression may result[6-8]. Assessments of fracture and bone mineral density can provide useful information about the physical influence of osteoporosis. However, these quantitative results do not provide qualitative information regarding the association with daily living activities.

Health related quality of life (HRQOL) is a multidimensional concept characterizing the health of individuals according to specific dimensions, namely physical, social, emotional, and functional well being[9]. It is commonly assessed by subject questionnaires that can be classified as general or disease-specific. General questionnaires may contain unessential information, but allow for comparison of different diseases[10]. Examples include the Nottingham Health Profile, the Sickness Impact Profile, the Short Form-36 of the Medical Outcomes Study, and the EuroQol. There are 6 osteoporosis-specific questionnaires, including the quality of life questionnaire of the European Foundation for Osteoporosis (QUALEFFO) and the Osteoporosis Assessment Questionnaire (OPAQ).

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While both general and disease-specific instruments have demonstrated that vertebral and hip fractures are associated with a decrease in HRQOL[10], only a few large clinical trials have examined HRQOL in postmenopausal women with osteoporosis. In the Multiple Outcomes of Raloxifene Evaluation (MORE) trial, which examined the effect of raloxifene on vertebral and nonvertebral fracture risk in postmenopausal women[11], HRQOL was measured in a subset of European women using QUALEFFO. During the conduct of the MORE trial, HRQOL was also measured in a subset of English-speaking women from Australia, Canada, New Zealand, and the United States using OPAQ. Both instruments confirmed that postmenopausal women who experienced a vertebral fracture had decreased HRQOL compared to those who had not[12,13].

In the Fracture Prevention Trial, a study designed to examine the effect of teriparatide on vertebral and nonvertebral fracture risk in postmenopausal women with osteoporosis, OPAQ was again administered to a subset of English-speaking women. The data showed that postmenopausal women who experienced an incident vertebral or nonvertebral fracture had a significant reduction in HRQOL[14]. Analyses were not performed to determine the influence of back pain on HRQOL. We hypothesized that OPAQ composite dimension scores (i.e., HRQOL) for trial participants who spontaneously reported back pain were lower than OPAQ dimension scores for trial participants who did not. To test this hypothesis, we examined the effect of prevalent and incident back pain on HRQOL in the Fracture Prevention Trial.

MATERIALS AND METHODS

A detailed description of the Fracture Prevention Trial has been published[15]. Briefly, 1637 ambulatory postmenopausal women with osteoporosis, ranging in age from 42 to 86 years, were recruited from 99 centers in 17 countries. Women were randomized to daily self-administered subcutaneous injections of placebo, teriparatide 20 µg or teriparatide 40 µg with daily calcium (1000 mg) and vitamin D (400–1200 IU) supplement.

Measurements

OPAQ. As OPAQ was available only in English at the time of the study, it was administered only to women from English-speaking countries. These included 521 women from Australia, Canada, New Zealand, and the United States. OPAQ was administered at baseline, Month 12, and at study endpoint (median duration 19 mo). OPAQ has demonstrated reliability and validity as a disease-targeted instrument in postmenopausal women with osteoporosis[16]. It is a validated, self-administered instrument of 49 questions representing 4 composite dimensions of health status. The physical function dimension consists of 6 domains (walking/bending, standing/sitting, dressing/reaching, household/self-care, transfers, and usual work). The emotional status dimension consists of 4 domains: fear of falling, level of tension, body image, and independence. The symptoms dimension includes the domains of back pain and fatigue, while the social interaction dimension includes social activity and support of family and friends. There are also 6 individual questions, including one pertaining to overall HRQOL, and 12 domain-weighting questions. Scoring can be performed by domain or composite health dimension. Because of the relatively small number of subjects, this report will focus on the 4 composite dimensions.

Back pain. Back pain data were collected as adverse events at baseline and at each study visit. Subjects considered to have experienced back pain reported this event spontaneously and were not queried specifically. Women were characterized as having new or worsening back pain if they reported a case of back pain with greater severity than that experienced prior to randomization. The timing of the new or worsening back pain was the date of the visit when it was first reported. A physician assessed back pain severity as follows: If the subject reported no change in physical activity and required only occasional medication use for pain, the back pain was considered mild; if the subject reported mild disruptions in daily physical activities and required regular medication use, the back pain was considered moderate; and if the subject reported major disruption in normal daily activities, additional medication use, and/or hospitalization, the back pain was considered severe. Subjects with mild back pain at baseline could be categorized as having only moderate or severe worsening back pain at subsequent visits, and subjects with moderate back pain at baseline were only at risk for severe worsening back pain during the study.

Vertebral fracture diagnosis and Spine Deformity Index (SDI) score. The diagnosis of vertebral fracture has been described in detail[15]. Briefly, fracture severity was assessed by a semiquantitative vertebral deformity (SQ) score. The SQ score represents an accurate and reproducible method of assessing fracture severity that has been tested and applied in many clinical studies[17]. SQ scores were assigned to each individual vertebra from T4 to L4[18]. An SQ score of 0 was assigned to normal, nonfractured vertebra; 1 for a mild deformity; 2 for a moderate deformity; and 3 for a severe deformity. A mild fracture was defined as a 20%–25% reduction in anterior, middle, or posterior vertebral height. Moderate and severe vertebral fractures were defined as 25%–40% reduction and > 40% reduction in vertebral height, respectively. The SDI score for a subject was defined as the sum of the individual vertebral deformity scores. By combining the number and severity of vertebral fractures, the SDI score provides a valuable descriptor of fracture burden[19].

Statistical analysis. An analysis of variance model was used to compare OPAQ scores between women with or without back pain at baseline. The term SDI score was also included in the model to ensure that the effect of back pain was not confounded with this variable. The difference in mean OPAQ scores between women who did and did not experience new or worsening back pain during the trial was compared using an analysis of covariance model that included the terms of baseline OPAQ score, incident vertebral fracture (yes/no), and back pain (yes/no). The term incident vertebral fracture was included in the model to ensure that the effect of back pain was not confounded with this variable. To compare the percentages of women in each group who experienced significant reductions in HRQOL, a logistic regression model was used. A significant loss in HRQOL was defined as a decrease in OPAQ score of more than 1 standard deviation (SD) from baseline to study endpoint.

RESULTS

Study population demographics. Completed baseline OPAQ were received from 471 women. The demographic data of those who presented with back pain were similar to those who did not, except for the SDI score, which was higher in women who presented with back pain (Table 1). Four hundred twenty-nine women completed OPAQ at all timepoints. Of these, 88 experienced new or worsening back pain and a subset of 65 women experienced moderate to severe back pain. There were no significant differences in demographic data between those who did and those who did not experience new or worsening back pain (Table 2). The mean SDI score in women who did not experience new or worsening back pain (3.09 ± 2.48) was similar to that in women who

Table 1. Baseline characteristics (mean ± SD) of women who did and did not spontaneously report back pain at baseline*.

	No Back Pain, n = 299	Back Pain, n = 172
Age, yrs	70.5 ± 6.7	71.4 ± 7.2
BMI, kg/m^2	26.7 ± 4.6	26.3 ± 4.4
Years postmenopausal	23.3 ± 9.3	25.2 ± 8.6**
Current smokers, %	14.7	16.9
Alcohol, %	45.5	43.6
Caucasian, %	95.7	98.3
Lumbar spine BMD, g/cm^2	0.86 ± 0.19	0.83 ± 0.17
SDI score	2.90 ± 2.49	3.66 ± 2.72**

* Of the 478 English-speaking women, 471 completed OPAQ at baseline. BMI: body mass index, BMD: bone mineral density, SDI: Spine Deformity Index, OPAQ: Osteoporosis Assessment Questionnaire. ** $p < 0.05$ between groups.

Table 2. Baseline characteristics (mean ± SD) of women who did and did not spontaneously report new or worsening back pain during the trial*.

	No New or Worsening Back Pain, n = 341	New or Worsening Back Pain, n = 88
Age, yrs	70.6 ± 6.9	70.5 ± 6.1
BMI, kg/m^2	26.6 ± 4.7	26.7 ± 4.4
Years postmenopausal	23.5 ± 9.1	25.1 ± 8.9
Current smokers, %	14.1	14.8
Alcohol, %	43.1	50
Caucasian, %	97.1	95.5
Lumbar spine BMD, g/cm^2	0.86 ± 0.19	0.84 ± 0.19
SDI score	3.09 ± 2.48	3.05 ± 2.68

* Of the 478 English-speaking women, 429 completed OPAQ at baseline, 12 months, and at study termination. BMI: body mass index, BMD: bone mineral density, SDI: Spine Deformity Index, OPAQ: Osteoporosis Assessment Questionnaire.

developed back pain (3.05 ± 2.68) or moderate to severe back pain (3.03 ± 2.75). Among the women who developed back pain during the trial, 79 had radiographs at study endpoint. An incident vertebral fracture was experienced by 17.7% (n = 14) of these women. In the no back pain group, 287 women had radiographs at study endpoint. Of these, 5.2% (n = 15) experienced an incident vertebral fracture. Baseline characteristics were similar between the overall study population and the English-speaking subset (data not shown).

Association between back pain and HRQOL. Prevalent back pain was associated with a mean decrease in OPAQ dimension scores for physical function, emotional status, symptoms, and social interaction (Table 3; $p < 0.05$ for all). Prevalent back pain also was associated with a significantly reduced overall HRQOL score ($p < 0.01$). For women experiencing new or worsening back pain during the trial, there was a mean decrease in OPAQ dimension scores for physical function, emotional status, and symptoms (Table 4; $p < 0.01$ for each). New or worsening back pain was also associated with a significantly reduced general overall HRQOL score ($p < 0.01$). Women who experienced moderate to severe back pain had significantly reduced scores for all OPAQ dimensions (Table 4; $p < 0.05$ for all). Moderate to severe back pain was also associated with a significantly reduced overall HRQOL score ($p < 0.01$). Women who reported prevalent or new or worsening back pain scored significantly lower in the back pain domain of the symptoms dimension ($p < 0.001$).

Table 3. Mean (± SD) OPAQ dimension scores in subjects who did and did not spontaneously report back pain at baseline.

OPAQ Dimension	No Back Pain at Baseline, n = 299	Back Pain at Baseline, n = 172
Physical function	87.8 ± 14.4	76.0 ± 19.2*
Emotional status	72.0 ± 14.6	62.5 ± 18.4*
Symptoms	67.9 ± 17.5	53.3 ± 19.9*
Social interaction	65.9 ± 15.2	62.0 ± 15.7*

* $p < 0.05$ between groups, OPAQ: Osteoporosis Assessment Questionnaire.

Proportion of women with back pain and a significant loss in HRQOL. Higher percentages of women with new or worsening back pain experienced significant reductions (> 1 SD from baseline) in OPAQ dimension scores for physical function and symptoms (Table 5; $p < 0.01$). Higher percentages of women with moderate to severe back pain also experienced significant reductions in OPAQ dimension scores for physical function, emotional status, and symptoms (Table 5; $p < 0.05$).

DISCUSSION

Osteoporosis has significant psychological and social consequences, including anxiety and depression as well as social withdrawal and isolation. These factors can have a significant negative impact on quality of life[20]. While BMD and fracture status provide information about the physical effects of osteoporosis, they do not account for these social and psychological aspects. HRQOL encompasses the psychological, social, and physical aspects of osteoporosis and thus provides a comprehensive assessment of burden of this disease.

The decrease in HRQOL seen in people with osteoporosis is conferred by fracture[21,22]. In particular, multiple vertebral fractures and hip fractures appear to have the greatest influence[10], and more severe vertebral fractures are associated with greater decreases in HRQOL[23]. While longer periods of time after fracture are associated with improvements, HRQOL is not completely restored[10], although in a study of 600 women with osteoporotic fractures, HRQOL scores, assessed by the Short Form-36 of the Medical Outcomes Study, were found to be normal 2 years after a forearm fracture[24].

Table 4. Mean (± SD) changes in OPAQ dimension scores in subjects who did not spontaneously report new or worsening back pain compared to OPAQ dimension scores in women who spontaneously reported new or worsening back pain or moderate/severe new or worsening back pain.

OPAQ Dimension	No New or Worsening Back Pain, n = 341	New or Worsening Back Pain n = 88	New or Worsening Moderate/Severe Back Pain, n = 65†
Physical function	–0.27 ± 10.9	–5.51 ± 17.1**	–7.69 ± 18.9**
Emotional status	0.49 ± 10.4	–3.49 ± 10.1**	–4.46 ± 10.6**
Symptoms	2.51 ± 12.9	–3.97 ± 18.9**	–4.85 ± 18.9**
Social interaction	1.86 ± 14.0	–1.31 ± 15.1	–1.27 ± 14.4*

† Back pain severity was assessed by the physician. These data represent a subgroup of the new or worsening back pain group. * $p < 0.05$, ** $p < 0.01$ versus corresponding mean change in score for women not experiencing new or worsening back pain after adjusting for incident vertebral fracture. HRQOL: health related quality of life, OPAQ: Osteoporosis Assessment Questionnaire.

Table 5. Percentage of women who experienced a significant loss (> 1 SD) in HRQOL as measured by OPAQ dimensions.

OPAQ Dimension	No New or Worsening Back Pain (n = 321), %	New or Worsening Back Pain (n = 88), %	New or Worsening Moderate/Severe Back Pain† (n = 65), %
Physical function	6.1	16.9**	22.6**
Emotional status	5.8	9.5	12.9*
Symptoms	4.2	17.4**	21.9**
Social interaction	9.6	9.3	9.4

† Back pain severity was assessed by the physician. These data represent a subgroup of the new or worsening back pain group. * $p < 0.05$, ** $p < 0.01$ versus corresponding percentage of women not experiencing new or worsening back pain after adjusting for incident vertebral fracture. HRQOL: health related quality of life, OPAQ: Osteoporosis Assessment Questionnaire.

In our analysis we controlled for SDI score and incident vertebral fracture when assessing the effects of prevalent and new or worsening back pain on HRQOL. While the mean SDI score in women who presented with back pain at baseline was significantly greater than the mean SDI score for women who did not, back pain was still associated with a decrease in HRQOL after controlling for this factor.

In regard to new or worsening back pain, the mean baseline SDI scores were similar between those who did and those who did not develop back pain. However, the percentage of women in the new or worsening back pain group who experienced an incident vertebral fracture was higher than in the group not experiencing new or worsening back pain. Since previous results showed that a composite endpoint of incident vertebral and nonvertebral fracture was associated with decreased HRQOL[14], we controlled for incident vertebral fracture. New or worsening back pain was associated with a decrease in HRQOL after controlling for incident vertebral fracture.

Higher percentages of women who experienced new or worsening back pain had significant reductions in physical function, emotional status, and symptom scores. These effects were even more profound in the subset of women who developed moderate to severe back pain. Only moderate to severe new or worsening back pain significantly reduced the social interaction score from baseline, and there was no significant difference between the percentages of women with or without new or worsening back pain who experienced a significant reduction in the social interaction score. This general lack of effect on social interaction score may be a function of the sensitivity of the OPAQ or the design of this dimension, which measures domains — in particular, support from friends and family — that may not be negatively affected by back pain. A previous analysis reported a similar lack of effect of prevalent vertebral fracture[12]. It should be acknowledged that back pain is one of the 2 domains of the symptoms dimension; therefore, patients who spontaneously reported back pain would be expected to have lower scores for this dimension.

Only a small percentage of women in this analysis devel-

oped an incident vertebral fracture during the trial. This raises the issue of why new back pain developed or worsened in the absence of radiographically diagnosed new vertebral fracture. Possible explanations include propagation of microfractures, changes in biomechanical loading, muscular pain, and psychosocial issues. Of all women enrolled in the Fracture Prevention Trial, 90% had one or more prevalent vertebral fracture at baseline.

Even though teriparatide reduced the risk of back pain in the full trial population, there were no differences between treatment groups and placebo in any HRQOL domain in this subset. This may be attributed to the fact that only a small percentage of women developed back pain (21%), and of these only a small percentage (< 17.5%) experienced a significant loss in physical function, emotional status, and symptom scores. Further, significant losses in these domains were seen in a very small number of women not experiencing new or worsening back pain (4.2%–6.1%).

Our results suggest that both prevalent and new or worsening back pain have a negative impact on HRQOL in postmenopausal women with osteoporosis — an effect that occurs after controlling for SDI score and incident vertebral fracture. Therefore, postmenopausal women with osteoporosis who spontaneously reported back pain had a greater decrease in HRQOL than matching postmenopausal women with osteoporosis who did not spontaneously report back pain. Osteoporosis therapies that prevent the development of new or worsening back pain in postmenopausal women may also prevent decreases in HRQOL.

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