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Comparing 15D and SF-6D performance in fragility wrist and hip fracture patients in a two-year follow-up case control study.

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Abstract

Aims: To examine and compare the two utility and health related quality of life (HRQOL) measures 15D and SF-6D in fragility wrist and hip fracture patients and controls, study the responsiveness of 15D and SF-6D and examine the impact of these fractures on changes in 15D and SF-6D scores over two years.

Study population: A total of 152 wrist fracture patients and 164 controls and 61 hip fracture patients and 61 controls with 15D and SF-6D scores were studied.

Results: The mean 15D score decreased significantly in wrist fracture patients between baseline and two year follow-up (p=0.003). A wrist fracture was a significant predictor of a decrease in the 15D scores two years after fracture (B=-0.016, p=0.049), along with low body mass index (B=-0.002, p=0.009). In hip fracture patients both 15D and SF-6D scores decreased significantly (p<0.001). A hip fracture was a significant predictor of a decrease in 15D (B=-0.060, p=0.001) and SF-6D scores (B=-0.096, p=0.001)

Conclusion: Our data suggest that a fragility wrist fracture has a long term negative effect on HRQOL, but not as strong as for fragility hip fractures. 15D seems to be more responsive than SF-6D when assessing HRQOL in patients with fragility fractures.

Keywords: Utility measures, health related quality of life, fragility fractures, prospective study

Running title: 15D and SF-6D in patients with fragility fracture

Abbreviations

ART - antiresorptive treatment, BMD - bone mineral density, BMI - body mass index, DXA - dual-energy X-ray absorptiometry, ES – effect size, GLM - General Linear Model, HRQOL - health related quality of life, MCS - mental component summary, PCS - physical component summary, SF-36 - Short Form-36, SF-6D Short Form – 6D, SPSS - Statistical Package for Social Sciences, WHO -World Health Organization

Introduction

Fragility fractures may be devastating for the individual, challenging for the health care system due to increased demand of health care and a burden to society because of increased costs (1). The most frequent sites for non-

vertebral fragility fractures are wrist and hip. Previous studies have consistently reported that patients with a fragility fracture at hip experience a long term negative impact on health related quality of life (HRQOL) and the patients do not regain pre-fracture HRQOL levels (2-6). For fragility wrist fracture, however, several studies indicate no long term negative effects on HRQOL (7-9).

HRQOL can be used for economic evaluation (cost-utility analysis) and several generic utility instruments (e.g. 15D, SF-6D and EQ5D) have been developed. The underlying idea is that the utility (value) of a health state can be measured on a scale from death (0.0) to perfect health (1.0). Such utility measures also can be used to calculate quality- adjusted life years (QALYs) (10;11). The ability of the instruments to detect clinically important differences and changes is vital to their usefulness and applicability in clinical practice. This ability may be assessed by exploring the responsiveness of the instruments, which may be considered as one form of validity (12;13).

There is a general lack of knowledge regarding changes in HRQOL in patients with fragility fractures compared with individuals from the general population, in particular as assessed by utility instruments (2;11). Apart from two studies, no previous studies of patients with fragility fractures have compared results from utility-measures to those of other generic HRQOL measures such as SF-36 (2;14).

From a prospective case control study we have recently published long term SF-36 (HRQOL) data in patients with fragility wrist and hip fracture, reporting long term reduction in SF-36 HRQOL in hip fracture patients after two years (15), but no long term reduction in patients with wrist fracture after one year (9).

From this same study population of wrist and hip fracture patients and controls we now aim to examine and compare the two utility measures 15D and SF-6D. Further, our aim is to study the responsiveness of 15D and SF-6D and examine the impact of a fragility wrist or hip fracture on changes in 15D and SF-6D scores after one and two years.

Methods

Study population and data collection

Patients with fragility wrist or hip fractures aged 50 years and older attending a regional hospital in the southern part of Norway in a two year period were invited to the Osteoporosis Centre for assessment of bone mineral

density (BMD) and health status, and participation in a two year prospective case control study. The controls were recruited consecutively from the same geographic area. Patients with confusion or dementia, serious infection, tourists, patients not capable of giving informed consent, and patients unable to speak Norwegian were excluded. Study design and data collection, demographic, clinical, bone density and SF-36 (HRQOL) data from this study have previously been described in details (9;16;17). For the wrist fracture patients only 1 year follow up data have been published previously (9). In our study wrist fracture, also called distal radius fracture in the literature, was defined as a fracture located within 3 cm of the radiocarpal joint.

In the two year inclusion period, 324 patients with fragility wrist fractures were treated at the hospital, and 249 of the patients were clinically examined at the Osteoporosis Centre (30 patients were excluded and 45 declined BMD assessment). Of the 249 patients with wrist fractures examined at the Osteoporosis Centre, 181 met the inclusion criteria and were willing to enroll in this study (21 patients were excluded and 47 were unwilling to participate), which give a response rate of 66%. At one year follow up, data were available in 160 patients (21 dropped out) and 169 controls (9) and at two year follow up in 152 patients (17 dropped out) and 164 controls.

Four-hundred and fifty-six patients with fragility hip fracture were treated at the hospital. Among them 307 patients were clinically examined at the Osteoporosis Centre (137 patients were excluded and 12 declined BMD assessment). Of the 307 patients with hip fractures at the Osteoporosis Centre, 97 met the inclusion criteria and were willing to enroll in this prospective study (134 patients were excluded and 76 were unwilling to participate), yielding a response rate of 52%. Among the hip fracture patients 72 had one year data (5 died and 20 dropped out) and 61 patients had two year data (five died and six dropped out) (15). The 61 patients with a hip fracture who were still in the study at two years follow-up were age and sex matched with 61 of the controls (± 5 years) that had valid measures at baseline and at one- and two-year follow-ups (15).

At baseline the patients were asked to report their status prior to fracture and the controls at the time prior to inclusion. With regard to the 15D questionnaire the patients were asked to report their HRQOL at the time before fracture and the controls at the time before inclusion, and in SF-36 the four weeks before fracture for patients and the controls the four weeks before inclusion. The same data collection performed at baseline was repeated after one and two years.

The collected data included demographical and clinical data, exercise (more than 30 minutes three times a week), smoking habits, medication, previous fragility fractures after the age of 50 years, number of falls the

year before the fracture, and co-morbidity (heart diseases, pulmonary diseases, neurological disorders, urogenital disorders, gastrointestinal disorders, endocrine disorders, inflammatory joint disorders and connective tissue disorders, cancer, mental disorders) as listed in table 1. For co-morbidity, we also computed a sum score of the number of diseases for each patient.

BMD was measured at femoral neck, total hip, and lumbar spine (L2-4) using the same dual energy X-ray absorptiometry (DXA) equipment (General Electric, Lunar Prodigy), previously described in detail (9). Osteoporosis was defined as T-score ≤ -2.5 SD, osteopenia as T-score > -2.5 and < -1.0 and normal BMD as T-score > -1.0, according to the WHO definition for osteoporosis (18).

The utility measures 15D and SF-6D

The 15D questionnaire is a generic, multidimensional, standardized evaluation tool of HRQOL that can be used primarily as a single index measure, but also as a profile utility measure. It describes the health status, assessing the 15 dimensions; mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity (19). Each dimension comprises one question with five response categories. A single utility index score is obtained by incorporating population based preference weights to the dimensions. The algorithm has been developed on the basis of multi-attribute utility theory and the 15D weights are based on a Finnish study from 2001 (19). The algorithm has also been used in Norwegian studies (20;21). The utility scores fall between 0.0 (being dead) and 1.00 (no problems on any dimension). Regression analyses were performed to impute missing values. The questionnaire has been thoroughly tested for psychometric properties in other studies, within several countries (19-21).

The SF-6D is a utility instrument in which SF-36 or SF-12 scores can be translated into this utility score by means of an algorithm based on a standard gamble (SG) technique (10). The SF-6D is based on 11 questions from the SF-36 and includes six dimensions, each with 4-6 levels. The SF-6D utility scores range from 0.29 to 1.00, with 1.00 indicating "full health". The Norwegian standard SF-36 v. 1.00 was used to derive the SF-6D. The different health states are assigned values derived from valuations of SF-6D health status using SG in a representative sample of the UK population. Regression analyses were performed to impute missing values. The questionnaire has been tested for psychometric properties in other studies, in several countries (10).

Statistical analysis

Statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) for Windows (version 18.0). Chi-square tests and t-tests were used to compare differences between subgroups. Paired samples *t* tests were used to compare changes in 15D and SF-6D scores between baseline and one-year follow-up, and between baseline and two-year follow-up, within each patient group and within controls. General linear model (GLM) (repeated MANOVA) was also applied to examine differences in the repeated HRQOL measures within the groups (12;22). Mean 15D and SF-6D –change-scores (SD) over the two year period were calculated within the groups. Independent sample *t* tests were used to compare differences in 15D and SF-6D scores between patients and controls at baseline, one- and two-year follow-up. Pearson correlation coefficients between 15D and SF-6D two year change scores were calculated.

To examine the internal responsiveness of the instruments, the observed change and effect size (ES) related to the change in the 15D and SF-6D scores were calculated within patients and within controls. ES were calculated by subtracting the mean 15D and SF-6D scores at inclusion from the mean scores of the one- and two-year follow-ups, and then dividing by each group's *SD* at inclusion (23). We applied Cohen standards for effect sizes as: small effect 0.2, medium effect 0.5 and large effect 0.8 (22).

Multiple linear regression analysis (procedure GLM in the SPSS) was used to examine the impact of a fragility wrist or hip fracture on 2 years changes in the 15D and SF-6D scores. Independent variables in the multiple regression analyses were the demographic variables of age, gender, and marital status (cohabiting/living alone), and the clinical variables of BMD (normal BMD/ osteopenia/osteoporosis), and patients/controls. These variables showed correlations with the patients/controls dichotomy at baseline and have been shown to be covariates of HRQOL in earlier studies (12). The regression analyses were adjusted for 15D or SF-6D scores at baseline. To test if the effects of independent variables in the regression models (potential predictors of change) on our dependent variables were significantly different for patients and controls, interaction terms involving the patient/control dichotomy and each of the independent variables were entered in the equations, one pair at a time, while retaining the other independent variables (i.e. main effects) in the model. The level of significance was set at 0.05.

Ethics

The study was approved by the Regional Committee for Medical Research Ethics and by the National Data Inspectorate.

Results

Demographical and clinical characteristics

Socio-demographical and clinical characteristics at baseline of those participants who completed all baseline, one and two year follow-up assessments are shown in table 1. Patients with fragility wrist fracture were more often living alone ($p=0.012$), had fewer years of education ($p=0.008$), had lower BMI ($p=0.049$), and were more frequently classified with osteoporosis ($p<0.001$) compared to the controls. Patients with hip fracture were more likely to live alone ($p=0.045$), exercise less ($p=0.033$), smoke more ($p=0.019$) and more frequently have osteoporosis ($p<0.001$) compared to the controls.

Table 1 about here

Changes in the 15D and SF6D scores

In the fragility wrist fracture group significant changes for 15D scores were found from baseline to one and two year follow-up (table 2). For SF-6D scores no significant changes between baseline and follow-up values were found. In the controls no significant changes in 15D or SF-6D scores were seen.

For both 15D and SF-6D scores in the fragility hip fracture group, significant changes between baseline and follow-up values were found for one year and two year follow-ups (table 3). In the hip fracture controls no significant changes in 15D and SF-6D scores were seen. For both fracture groups and controls no significant changes in 15D and SF-6D scores were seen between one and two year follow-up. Due to multiple comparisons, we also applied repeated MANOVA on the changes in 15D and SF-6D scores within patients and within controls, and the same pattern persisted.

Table 2 and table 3 about here

Differences in the utility-scores between patients with wrist fractures and controls and patients with hip fractures and controls

At baseline the patients with wrist fractures reported significantly higher 15D scores compared to controls ($p=0.042$). However, at one and two years follow-up no significant differences between the groups were seen ($p=0.504$ and $p=0.968$, respectively). Comparing SF-6D scores for patients and controls at baseline, one and two years follow-up, revealed no significant differences ($p=0.675$, $p=0.661$ and $p=0.254$ respectively).

The patients with hip fractures reported significantly lower 15D scores compared to controls at baseline ($p=0.039$) and at one and two year follow-up ($p<0.001$). For SF-6D scores significant differences between hip fracture patients and controls were also found at baseline ($p=0.011$) and at one and two years follow-up ($p<0.001$).

Correlations between the 15D and SF-6D change scores over a two year period were 0.356 in the patients with wrist fracture ($p<0.001$), 0.259 in the controls ($p=0.002$), 0.624 in patients with hip fracture ($p<0.001$), and 0.353 in controls ($p=0.010$)

Responsiveness

Effect sizes (ES) expressing internal responsiveness for 15D and SF-6D scores are displayed in table 2 and table 3 for patients with fracture and controls. A small change in the 15D scores in patients with wrist fracture was seen between baseline and one year (ES = -0.3) and two year follow-up (ES = -0.3). In patients with hip fractures medium changes in 15D scores between baseline and one year (ES= - 0.6) and two year follow-up (ES= - 0.6) were seen. For wrist fracture patients the ES for SF-6D scores between baseline and follow-up was 0.1 and 0. 0, respectively. In hip fracture patients the ES for SF-6D scores between baseline and one and two year follow-up was -0.5 and -0.4.

The impact of a fragility wrist or hip fracture on changes in 15D and SF-6D scores two years after fracture

When comparing patients with wrist fracture and controls, worsened 15D score was predicted by being a patient with distal fracture (B = –0.016, p=0.049) and having low BMI (B = –0.002, p=0.009). Interaction terms between pairs of each independent variable and patients/controls (tested one pair at a time) revealed that having low BMD (osteoporosis) at baseline had a significantly stronger (negative) effect on changes in HRQOL among patients with wrist fracture than among controls. Worsened SF-6D scores were only predicted by low BMI (B=-0.004, p<0.001), but not by having a wrist fracture (table 4).

When comparing patients with hip fracture and controls, worsened 15D scores were predicted by being a patient with hip fracture (B=-0.060, p=0.001) and low BMI (B= -0.005, p=0.018), while worsened SF-6D scores were predicted by being a patient with hip fracture (B= -0.095, p=0.001) and old age (B= -0.003, p=0.013) (Table 5).

Table 4 and table 5 about here

Discussion

To our knowledge, this is the first study which uses the utility measures 15D and SF-6D to study changes in HRQOL in patients with a fragility fracture at wrist or at the hip. In our study, the two utility instruments revealed different findings in wrist fracture patients. A significant decrease in HRQOL in our wrist fracture patients after one and two years follow-up was only found when assessed by 15D but not by SF-6D. A reduction in 15D scores took place in the first year, which remained during the second year of follow up. The changes in HRQOL measured by 15D seem to be attributable to the wrist fracture. This appears to be slightly at odds with findings from previous studies, which indicate no reduction in long term HRQOL following a wrist fracture (7;8). In a previous report from this same wrist fracture cohort we found no significant changes in SF-36 (9). This may indicate that responsiveness for the 15D may be better than for the SF-6D. In our patients with hip fractures a decrease was seen for both 15D and SF-6D scores. For hip fracture the literature has been consistent in reporting a reduction in HRQOL after hip fracture (3;5-8;24). From this same hip fracture cohort we have previously also reported a persistent long term reduction in SF-36 (15).

A strength of our study is the study design comparing patients with age and gender matched controls recruited from the background population of the fracture patients. In the control groups, both for the wrist and the hip fracture patients, no significant changes in 15D or for SF-6 D scores were found over the two- year-period.

The differences in changes after the fracture using different generic HRQOL utility instruments might be attributed to the nature of the health items included and the way the questions are asked. On the other hand most generic instruments intended for HRQOL assessment include at least some items that focus upon physical, emotional and social functioning, which is also the case in the HRQOL instruments 15D and SF-6D used in the present study (13). The decrease in the mean 15D score two years after fracture might also be partly attributed to higher 15D scores prior to wrist fracture compared to baseline scores in the controls. The higher 15D scores in wrist patients might in part be explained by a tendency of a higher total co-morbidity score in the controls compared to wrist patients, however not statistical significant. A mean decrease of 0.02 in 15D scores between baseline and one and two-year follow-up might be considered as not being a clinically important difference. However according to Sintonen it has been documented that a 15D score change of 0.02-0.03 is detectable and recognizable for the individual (19). Another explanation of the decrease in 15D score over the two year period might be that our findings for wrist fracture patients only is a result of random fluctuations. However, we believe

it is rather unlikely that 15D scores in the wrist fracture patients remained significantly reduced not only after one year but also at two years follow-up.

The stronger effect size revealed in 15D compared with SF-6D within the wrist fracture patients over the two year period might be seen as a sign of higher internal responsiveness for 15D compared to SF-6D. However, the effect size for 15D of -0.3 was small, and the results have to be interpreted with caution. According to Cohen, effect sizes in the range 0.2 to 0.5 should be defined as small (12;22). In our patients with hip fracture, the effect size for 15D was also slightly higher than for SF-6D, which further might indicate a higher responsiveness in 15D. For hip fracture patients the effect size for 15D at two year follow-up was -0.6 which is defined as medium effect whereas for SF-6D the effects size was -0.4 which is defined as small effect according to Cohen. In previous studies including 15D and SF-6D, Stavem et al (21) reported no evidence of a better responsiveness of the 15D compared to EQ-5D and SF-6D in patients with HIV/AIDS . While Kontodimopoulos et al (25) showed that 15D might be more sensitive in diabetic intervention compared to EQ-5D and SF-6D, which they explain by 15D comprising a richer descriptive system. Kvam et al (26) reported an acceptable responsiveness of 15D in patients with multiple myeloma, yet not as good as for EQ-5D and EQTRC (European Organization for Research and Treatment of Cancer) QLQ-30. And with regard to SF-6D, Buitinga et al (27) reported that the SF-6D was more responsive than EQ-5D in patients with rheumatoid arthritis. In the literature there is no unequivocal evidence of better or worse responsiveness of 15D compared to SF-6D across studies within different patient groups. The better responsiveness of 15D compared to SF-6D in our study also was rather weak and one may argue that these differences are not of clinical relevance. Demographic and clinical characteristics (except osteoporosis) in patients with wrist fracture all in all are comparable with the controls, which supports previous findings indicating that wrist fractures mostly occur in otherwise relatively healthy middle-aged and elderly individuals, with an active lifestyle, good physical and mental health, but with reduced BMD (28-30). And in some cases, the fracture happened just because of bad luck. In patients with hip fracture our findings indicate a different pattern. Hip fracture occurs in elderly individuals characterized by a large complexity in their underlying conditions, co-morbidities, and clinical histories compared to control, which also have been seen in previous findings (31-35).

Using retrospective reports for the collection of HRQOL data prior to fracture is a limitation of our study, because ideally such data should have been collected before the fracture occurred. However, for practical reasons it is of course almost impossible to collect HRQOL data prospectively for a population with a specific injury, and alternative methods relying on pre-injury recall, have been used in several previous trauma studies

(14;36-38). Retrospective evaluations can be biased by recall problems and response shifts caused by the trauma under investigation (13;39;40). To minimize this problem, it is recommended that HRQOL assessments should be performed within the shortest possible time period after the fracture event, which was indeed the aim in our study (12;13). To further minimize the limitations of our study design, the questionnaires were administered with an instruction that the patient should report their status before the fracture. The response options given in the 15D and SF-36 are different in their nature (19;41-43), and might be influenced differently by potential recall problems and response shift. The 15D asks about the response option that best describe the health status before the fracture, while the SF-36 asks about limitations or problems during the past four weeks before fracture. However, as previously mentioned, most generic instruments intended for HRQOL assessment include at least some items that focus upon physical, emotional and social functioning, which is also the case in the HRQOL 15D and SF-6D instruments in this study (13). A further potential limitation of our study is the patients who were lost to follow-up. They were characterized by lower 15D and SF-6D scores at baseline, and a higher number of diseases. Reduced health in patients who are lost to follow-up has been reported in other studies as well (8), and may influence the results. Reduced HRQOL prior to fracture might also be seen as a potential risk factor of decreased health and death in the study population and thereby a predictor of future objective health and HRQOL, especially in the patients with fragility hip fracture. The aim in our study, however, was to compare the self-reported health measures and examine the impact of fragility fractures on 15D and SF-6D scores over a two year period and rather than exploring their role as predictors of objective health outcomes such as hospitalizations, death etc..

The patients included in the present study were probably among the healthiest patients. The patients who were unwilling to participate and thus excluded from the study we know were older and probably less healthy than the patients included in the study (44). Furthermore, the patients who dropped out during the two year follow-up period seemed to be less healthy than the patients who attended the two-year follow-up (9;15). Our findings therefore should be interpreted with caution. On the other hand, it seems unlikely that HRQOL in less healthy fragility fracture patients would be influenced to a lesser extent by the fracture.

Conclusion

Our findings nuance previous findings reporting no long term reduction in HRQOL following a fragility wrist fracture. The data in the present study indicate that a fragility wrist fracture may indeed negatively impact on HRQOL. Our study confirms that hip fracture has a sustained, long term negative effect on HRQOL as assessed

both by 15D and SF-6D. Our data indicate that 15D seems to be more responsive than SF-6D when assessing utility and HRQOL in both types of fractures, although the results should be interpreted with caution. This may be of importance for health economic analyses (cost-utility analyses), for calculation of QALYs in fracture patients, and for the proper interpretation of studies of health utility and HRQOL.

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Table 1. Baseline demographical and clinical characteristics in patients with distal radius fracture and controls and in patients with hip fractures and controls who visited the osteoporosis centre both at baseline and at two years follow-up. Mean (SD) for continuous variables and numbers (%) for categorical variables.

	Distal radius fracture	Controls	p*	Hip fracture	Controls	p**
	n=152	n=164		n=61	n=61	
Demographics						
Age (years; mean (SD))	67 (9)	66 (9)	0.588	74 (10)	73 (8)	0.502
Females	136 (90)	147 (90)	0.963	46 (75)	46 (75)	1.00
BMI (kg/m^2)	25.7 (4.4)	26.7 (4.4)	0.049	23.6 (3.7)	26.8 (3.7)	<0.001
Menarche (years; mean (SD))	13.9 (1.5)	13.6 (1.4)	0.089	14.3 (1.9)	13.7 (1.1)	0.064
Menopause (years; mean (SD))	49.0 (4.5)	49.6 (4.1)	0.277	48.3 (5.6)	50.0 (3.4)	0.090
Education			0.008			0.525
< 10 years	50 (36)	68 (42)		26 (46)	22 (37)	
11–13 years	60 (43)	43 (26)		18 (32)	21 (35)	
> 13 years	30 (21)	52 (32)		12 (21)	17 (28)	
Co-habiting	82 (54)	111 (68)	0.012	26 (44)	38 (62)	0.045
Regular exercise***	113 (74)	123 (75)	0.893	36 (59)	47 (77)	0.033
Current smoker	22 (15)	20 (12)	0.551	16 (36)	6 (10)	0.019
Clinical characteristics						
Current calcium and/or vitamin D treatment	36 (24)	40 (24)	0.909	12 (20)	18 (30)	0.207
Current ART	26 (17)	26 (15)	0.653	9 (15)	10 (16)	0.803
Previous fractures	79 (52)	75 (47)	0.337	28 (46)	29 (48)	0.362
≥ 1 fall in the previous year	62 (46)	47 (36)	0.118	27 (47)	19 (37)	0.289
Osteoporosis spine/hip****	48 (32)	28 (18)	<0.001	35 (58)	12 (20)	0.001
Femoral neck *****			0.001			0.023
Normal BMD	20 (14)	49 (31)		6 (20)	13 (23)	
Osteopenia	80 (56)	82 (52)		7 (23)	28 (49)	
Osteoporosis	42 (30)	28 (17)		17 (57)	16 (28)	
Total hip *****			<0.001			<0.001
Normal BMD	32 (21)	73 (45)		5 (9)	21 (36)	
Osteopenia	92 (62)	71 (44)		24 (43)	30 (51)	

Osteoporosis	25 (17)	18 (11)		27 (48)	8 (14)	
Lumbar spine L2-4 *****			<0.001			0.018
Normal BMD	25 (16)	62 (38)		19 (31)	31 (52)	
Osteopenia	79 (52)	72 (44)		19 (31)	19 (31)	
Osteoporosis	48 (32)	29 (18)		23 (28)	10 (17)	
Heart diseases	45 (30)	57 (35)	0.328	28 (48)	30 (49)	0.856
Pulmonary diseases	18 (12)	12 (7)	0.170	10 (16)	5(8)	0.168
Neurological diseases	10 (7)	13 (8)	0.645	8 (13)	3 (5)	0.114
Endocrine disorders	14 (9)	20 (12)	0.392	5 (8)	4 (7)	0.729
Gastrointestinal disorders	6 (4)	21 (13)	0.005	6 (10)	11 (18)	0.191
Urogenital disorders	4 (3)	1 (1)	0.150	5 (8)	2(3)	0.243
Inflammatory joint disorders and connective tissue disorders	31 (20)	44 (27)	0.179	16 (26)	13 (21)	0.523
Cancer	14 (9)	17 (10)	0.730	8 (13)	6 (10)	0.570
Mental disorders	4 (3)	7 (4)	0.428	3 (5)	2 (3)	0.648
Co-morbidities	1.0 (1.0)	1.2 (1.1)	0.073	1.2 (1.1)	1.5 (0.9)	0.218
(range 0-6)						

*P-values indicate differences between the patients with distal radius fracture and controls

**P-values indicate differences between the patients with hip fracture and controls

*** Exercise more than 30 minutes three times a week.

**** Osteoporosis was defined as T-score ≤ -2.5 SD

***** The numbers differs between the measures site due to some invalid measures (eg. due to hip-replacement)

SD: standard deviation; BMI: body mass index; ART; antiresorptive treatment, a specific osteoporosis treatment comprising bisphosphonates, or selective oestrogen-receptor modulators.

Table 2. The 15D and SF-6D scores at baseline, one and two year follow-up in patients with distal radius fracture (n=152) and in controls (n=164). Data are given as means with standard deviation

	Baseline	One year	Two years	p-values	Mean change	Effect size
	Distal radius fracture patients					
15D	0.92 (0.08)	0.90 (0.10)	0.90 (0.09)	<0.001[a] , 0.003[b] , 0.239[c]	-0.023 (0.067)[a], -0.018 (0.071)[b], 0.005 (0.054)[c]	-0.3[a], -0.3[b], 0[c]
SF-6D	0.77 (0.14)	0.78 (0.13)	0.77 (0.13)	0.564[a], 0.296[b], 0.198[c]	0.006 (0.106)[a], -0.013 (0.128)[b], -0.012 (0.094)[c]	0.1[a], 0[b], -0.1[c]
	Controls					
15D	0.90 (0.09)	0.90 (0.09)	0.90 (0.10)	0.448[a], 0.851[b], 0.604[c]	0.003 (0.057)[a], -0.001 (0.067)[b], -0.002 (0.059)[c]	0[a], 0[b], 0c
SF-6D	0.78 (0.12)	0.78 (0.13)	0.79 (0.13)	0.660[a], 0.784[b], 0.935[c]	0.004 (0.097)[a], -0.002 (0.090)[b], 0.001 (0.101)[c]	0[a], 0[b], 0.1[c]

Paired sample t-tests were applied to detect significant differences between baseline and follow-up. Mean changes and effect size were also applied.

a = between baseline and one year follow-up, b = between baseline and two year follow-up, c= between one and two year follow-up.

15D and SF-6D, where 1.00 means perfect health.

Table 3. The 15D and SF-6D scores at baseline, at one and two year follow-up in patients with hip fracture (n=61) and in controls (n=61). Data are given as means with standard deviation

	Baseline	One year	Two years	p-values	Mean change (SD)	Effect size
	Hip fracture patients					
15D	0.87 (0.10)	0.82 (0.12)	0.82 (0.11)	<0.001[a], <0.001[b], 0.899 [c]	-0.055 (0.080) [a], -0.054 (0.099)[b], 0.001 (0.074)[c]	-0.6[a], -0.6[b], 0.02[c]
SF-6D	0.71 (0.14)	0.64 (0.13)	0.65 (0.15)	0.001[a], 0.004[b], 0.983 [c]	-0.070 (0.127)[a], -0.063 (0.141)[b], 0.000 (0.120) [c]	-0.5[a], -0.4[b],-0.1[c]
	Controls					
15D	0.91(0.08)	0.90 (0.08)	0.90 (0.09)	0.652[a], 0.573[b], 0.758 [c]	-0.004 (0.059)[a], -0.005 (0.061)[b], -0.002 (0.053)[c]	-0.1[a], -0.1[b], 0.0[c]
SF-6D	0.78 (0.12)	0.79 (0.11)	0.78 (0.11)	0.178 [a], 0.931[b], 0.237 [c]	0.019 (0.094)[a,] -0.001 (0.101) [b,] -0.017 (0.095)[c]	0.1[a], 0.1[b], -0.1[c]

Paired sample t-tests were applied to detect significant differences between baseline and follow-up. Mean changes and effect size were also applied .

a = between baseline and one year follow-up, b = between baseline and two year follow-up. c = between one and two year follow-up.

15D and SF-6D, where 1.00 means perfect health.

Table 4. Predictors of two years change in health related quality of life (delta 15D and delta SF-6D) in patients with distal radius fracture (n=152) and controls (n=164). Regression analyses of demographics, clinical characteristics, and 15D/SF-6D scores at baseline of changes in 15D or SF-6D scores. Adjusted unstandardized regression coefficients, 95% CI, p values.

	Adj B 15D (95% CI)	p-values	Adj B SF-6D (95% CI)	p-values
Demographic				
Age*	0.000 (0.000,0.000)	0.240	-0.001 (-0.001,0.001)	0.279
Male	-0.021 (-0.045,0.004)	0.105	0.000 (-0.041, 0.040)	0.985
Living alone	0.000 (-0.017,0.016)	0.975	0.013 (-0-014,0.041)	0.341
BMI	-0.002 (-0.004,-0.000)	0.009	-0.004 (-0.008, -0.002)	0.001
Clinical				
Radius patients	-0.016 (-0.032,-0.000)	0.049	-0.010 (-0.036, 0.017)	0.478
Osteopenia**	-0.001 (-0.020,0.017)	0.899	-0.019 (-0.049, 0.011)	0.212
Osteoporosis**	-0.014 (-0.037,0.010)	0.255	-0.037 (-0.078, 0.004)	0.074
Baseline HRQOL				
15D \SF-6D	-0.181 (-0.278,-0.091)	<0.001	-0.369 (-0.470, -0.002)	<0.001
R^2 adj	6.4%		18.4%	

* Age in decades.

** Osteopenia/osteoporosis at total hip and/or spine L2–L4.

BMD= bone mineral density, BMI=body mass index,

15D and SF-6D, where 1.00 means perfect health.

Table 5. Predictors of two years change in health related quality of life (delta 15D and delta SF-6D) in patients with hip fracture (n=61) and controls (n=61). Regression analyses of demographics, clinical characteristics, and 15D/SF-6D scores at baseline of changes in 15D or SF-6D scores. Adjusted unstandardized regression coefficients, 95% CI, p values.

	Adj B 15D (95% CI)	p-values	Adj B SF-6D (95% CI)	p-values
Demographic				
Age*	-0.002 (-0.003, 0.000)	0.074	-0.003 (-0.006, -0.001)	0.013
Male	0.000 (-0.036, 0.035)	0.988	-0.009 (-0.063, 0.045)	0.734
Living alone	0.011 (-0.022, 0.043)	0.520	0.004 (-0.045, 0.052)	0.880
BMI	-0.005 (-0.009, -0.001)	0.018	-0.003 (-0.009, 0.052)	0.361
Clinical				
Hip patients	-0.060 (-0.094, -0.026)	0.001	-0.095 (-0.147, -0.042)	0.001
Osteopenia**	-0.006 (-0.046, 0.033)	0.752	-0.013 (-0.071, 0.044)	0.648
Osteoporosis**	-0.041 (-0.088, 0.007)	0.093	-0.005 (-0.075, 0.066)	0.898
Baseline HRQOL				
15D\SF-6D	-0.211 (-0.387, -0.036)	0.018	-0.481 (-0.657, -0.305)	<0.001
R^2 adj	16.6%		28.7 %	

* Age in decades.

** Osteopenia/osteoporosis at total hip and/or spine L2–L4.

BMD= bone mineral density, BMI=body mass index,

15D and SF-6D, where 1.00 means perfect health.