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The Impact of Fragility Fractures on Health-Related Quality of Life in Patients With Primary Sclerosing Cholangitis

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Background: Osteoporosis occurs frequently in patients with chronic cholestatic liver diseases, yet data are scarce regarding the prevalence of osteoporosis and fragility fractures and their impact on Health-Related Quality of Life (HRQoL) in Primary Sclerosing Cholangitis (PSC).
Objectives: We aimed to assess Bone Mineral Density (BMD), physical activity and incidence of fragility fractures in patients with PSC. We also sought associations between prior fractures and HRQoL.
Patients and Methods: The study was performed on 33 patients (11 females, 22 males) aged 35.3 ± 13 years. HRQoL was assessed by Short Form (SF)-36, Primary Biliary Cirrhosis (PBC)-40 and PBC-27 questionnaires. BMD was measured by densitometry in the lumbar spine and hip. Physical activity was assessed by questionnaire.
Results: In 32% of patients, BMD measured in the hip or spine was below 1.0 Standard Deviation. A history of fragility fractures (distal forearm and ribs) was reported in six patients (18%). In SF-36 assessment, patients with fractures had lower scores in the role functioning, general health and vitality domains and Physical Component Summary (PCS) than those without fractures. Prior fractures adjusted for gender and PSC duration were associated with lower PCS and Mental Component Summary (MCS) scores. Symptoms and fatigue (assessed by PBC) and prior fractures were inversely associated with MCS ($P = 0.007$).
Conclusions: In middle-aged subjects with PSC, we found a high rate of non-vertebral fractures and a moderately decreased BMD in lumbar spine and hip. Fragility fractures had an impact on physical and mental aspects of HRQoL.

Keywords: Health; Quality of Life; Osteoporosis; Cholangitis, Sclerosis

1. Background

Primary Sclerosing Cholangitis (PSC) is a chronic and progressive disease of the liver. Patients with PSC frequently have asymptomatic and anicteric cholestasis and many of them develop progressive biliary strictures, which lead to recurrent cholangitis, biliary cirrhosis and end-stage liver disease. These complications along with symptoms of the disease, such as chronic fatigue, pruritus, impaired memory and concentration, excessive daytime sleepiness and symptoms of frequently coexisting chronic Inflammatory Bowel Disease (IBD) or liver cirrhosis may substantially influence patients' Health-Related Quality of Life (HRQoL) (1, 2). It is widely accepted that evaluation of HRQoL as a multidimensional construct encompassing physical and cognitive capabilities, functional behavior, emotional status and psychosocial adjustment, plays an important role in the holistic care of patients with chronic liver diseases (3, 4).

Osteoporosis is a frequent comorbidity in chronic liver diseases (1), leading to fragility fractures associated with significant morbidity, mortality and further impairment of HRQoL (5). In contrast to other chronic liver conditions, clinical consequences of osteoporosis in PSC have been less intensively studied. Particularly, to date, there have been no previous reports evaluating the fracture rate and the impact of fractures on HRQoL outcomes in patients with PSC.

2. Objectives

The aim of this study was to assess Bone Mineral Density (BMD) measured by Dual-energy X-ray Absorptiometry (DXA), physical activity and incidence of fragility fractures in patients with PSC. We also sought associations between prior fragility fractures and HRQoL outcomes.

3. Patients and Methods

3.1. Study Population

This study was performed on 33 patients with PSC (11 females, 22 males) aged 35.3 ± 13.38 years (ranged 19.5 to 69.4 years). PSC was diagnosed using the European Association for the Study of the Liver (EASL) criteria as: 1) elevated serum markers of cholestasis; and 2) typical bile duct changes in magnetic resonance imaging or endoscopic cholangiography (6). We included only those patients who had no other acute or chronic medical conditions that required pharmacological treatment or might influence HRQoL outcomes. All women participating in the study were premenopausal. We excluded patients with a history of rapid weight changes within the last 12 months. Among the included patients, six had an established liver cirrhosis and 20 had IBD, including 12 cases with ulcerative colitis, two with Crohn's disease and six with non-classified colitis. The bowel disease was in remission in all patients.

In all subjects, we measured weight and height. Based on available medical reports, we collected the following data on the past fragility fractures, location of the fracture and its severity, time since diagnosis of PSC, X-ray imaging and type of trauma. Fragility fractures were defined as fractures of the distal forearm, neck of the femur, rib and vertebral body occurred as a result of a minimal trauma, such as a fall from a standing height or less or without identifiable trauma. Blood samples were obtained to assess aminotransferases, alkaline phosphatase and bilirubin after an overnight fast from each study participant.

Informed consent was obtained from each patient. The study protocol was approved by the Ethics Committee of the Pomeranian Medical University and conformed to the ethical guidelines of the 1975 Declaration of Helsinki (6^{th} revision, 2008).

3.2. Bone Mineral Density Measurements

Bone Mineral Density (BMD) was measured in the lumbar spine (L1 - L4) and the hip by dual-energy X-ray absorptiometry (DXA) (GE Lunar Prodigy; Madison, WI; USA; software enCORE version 14.1) using automatic scan modes. Osteopenia and osteoporosis were diagnosed according to the World Health Organization (WHO) criteria (7). BMD values were expressed in g/cm^2 as well as z-scores (standard deviation from the mean BMD for normal, age-matched, gender-specific subjects) and t-scores (standard deviation from the mean BMD for normal young individuals). BMD values were compared with expected normal BMD and adjusted for gender and ethnicity using standard values for normal population provided by the manufacturer's reference database.

Additionally, we measured total Body Fat (BF) and lean mass from the total body scan using an automatic scan mode. All measurements and scan analyses were performed by a single operator. The coefficients of variation of lumbar spine, hip and total body measurements were 0.9%, 1.5% and below 1.0%, respectively.

3.3. HRQoL Assessment

Three questionnaires were used for data collection: 1) the Medical Outcome Study Short Form-36 (SF-36); 2) PBC-40; and 3) PBC-27. The Medical Outcomes Study Short Form 36 (SF-36) is a widely used and validated generic questionnaire to measure HRQoL in various populations with a wide variety of medical conditions (8, 9). The disease-specific instruments, PBC-40 and PBC-27 assess the symptoms of chronic cholestasis such as fatigue, excessive daytime sleepiness, pruritus and impaired memory and concentration (3, 4). SF-36 includes 36 items divided into eight domains of physical health (physical functioning, role limitation-physical, bodily pain and general health) and mental health (vitality, social functioning, role limitation-emotional and mental health). Scale scores ranged from 0 (denoting the most impaired HRQoL) and 100 (ideal well-being) and two summary scores; the Physical Component Score (PCS) and Mental Component Score (MCS) were also calculated.

PBC-40 is nowadays commonly used in the assessment of HRQoL in patients with primary biliary cirrhosis (3). Six domains of PBC-40 relate to fatigue, emotional, social and cognitive functions, general symptoms and itching. Answers are marked on a five-point Likert scale (from 1 = never to 5 = always), with higher scores denoting greater impact of symptoms and poorer HRQoL. Possible range of each domain was symptom domain 7 - 35, itching 3 - 15, fatigue 11 - 55, cognitive 6-30 and social and emotional functions 13 - 65 points (10). PBC-40 was also used in HRQoL evaluation in patients with PSC (11).

PBC-27 is an alternative structure of the HRQoL questionnaire for PBC, which appears to be simpler and equivalently sufficient in detecting the impact of PBC on patients' well-being. Twenty seven items are grouped into the following domains: other symptoms (possible range: 3-15 points), dryness (2-10 points), itching (3-15 points), fatigue (8-40 points), cognitive (5-25 points), emotional (3-15 points) and social (3-15 points) functions are evaluated on the same five-point scale as PBC-40 (4).

3.4. Assessment of Physical Activity

The International Physical Activity Questionnaire (IPAQ) was used as a self-report measure of habitual physical activity, with a 7-day recall of physical activity within a month. IPAQ consists of 27 questions regarding four life domains: physical activity associated with the occupation performed, work at home and around the house, moving to various places and mobility during free time devoted to recreation, playing games, sports, tourism

or other muscular work and additional time spending in the sitting position. IPAQ has been validated in many countries worldwide, including Poland (12). Total physical activity as measured by IPAQ is categorized as low (below 600 MET minute/week), moderate (from 600 to 3000 MET minute/week) and vigorous (above 3000 MET minute/week).

3.5. Statistical Analysis

Data are presented as Means ± Standard Deviation (SD) or numbers (proportion) of patients with a condition. Shapiro-Wilk test was used to test for normality, while F-test (Snedecor) and Brown-Forsythe test were used to assess the homogeneity of variances. In the case of a normal distribution and equal variances, means were compared by Student's t-test; otherwise, non-parametric methods were used. The chi-squared test for independence with a Yates' correction was used to analyze qualitative variables. The relationship between pairs of quantitative variables was presented via a Spearman's rank correlation coefficient. Univariate and multiple regression analyses were used to identify independent predictors of HRQoL outcomes. $P < 0.05$ was considered as statistically significant.

4. Results

Baseline characteristics of patients and comparisons between the subjects with and without fractures are summarized in Table 1. In PSC patients, mean BMD of hip was 0.97 + 0.183 g/cm^2 and of spine was 1.11 + 0.161 g/cm^2. In comparison with males, females had lower hip BMD (1.02 ± 0.015 vs. 0.88 ± 0.21 g/cm^2; P = 0.043) and comparable spine BMD (1.12 ± 0.18 vs. 1.07 ± 0.08 g/cm^2). In all subjects, mean BMD values were moderately but significantly lower in PSC than expected in a matched young healthy population of the same gender and ethnicity using the reference values provided by the manufacturer's database (P = 0.011 in the lumbar spine and P = 0.044 in the hip). Based on the WHO densitometric criteria (7), one patient (3%) had osteoporosis and 9 (27.3%) osteopenia either in the lumbar spine or hip. The incidence of a lowered BMD at any site (z-score below –1.0 SD) was not associated with presence of IBD or liver cirrhosis (P > 0.05). Nearly 70% of patients had normal BMD t-scores and z-scores. As many as 75% of patients declared low to moderate physical activity (below 3000 MET/minute/week).

In the SF-36 assessment, patients marked the lowest scoring in the general health domain and the highest in the role emotional domain. In both PBC-40 and PBC-27, patients frequently marked fatigue as well as social and emotional domains as affecting their HRQoL.

A history of fragility fractures was reported by six patients (18%). All fractures were confirmed by medical records and occurred after the diagnosis of PSC. None of the subjects had experienced more than one fracture. All fractures were non-vertebral (distal forearm and ribs). Five of the patients who had experienced fractures also had IBD, while none of them had liver cirrhosis. Three subjects with fractures had the lumbar spine and hip BMD t-scores between 1.0 and 2.5 SD; the remaining had normal BMD.We did not find significant differences in gender distribution, age, duration of PSC, BMD measurement, the incidence of IBD and liver cirrhosis and body composition between individuals with and without fractures. On the other hand, in patients who had experienced fragility fractures, mean scores in role functioning, general health, vitality and PCS domains in SF-36 were lower than subjects without fractures. A similar trend was also observed in respect of the MCS domain. In multiple regression analysis, prior fractures adjusted for gender, age and duration of PSC were significantly associated with lower PCS (β = -0.506; 95% CI: from -0.856 to -0.155; P = 0.006) and MCS scores (β = -0.416; 95% CI: from -0.791 to -0.039; P = 0.031).

MCS and PCS (except for itching) were inversely correlated with all domains tested by PBC-40 and PBC-27 (Table 2). However, in multiple regression analysis, symptoms and fatigue scores and prior fractures were inversely associated with MCS (β = -7.19; 95% CI: from -22.2 to -10.1; P = 0.007), but not PCS scores (P = 0.124). Interestingly, prior fractures were not associated with a lower BMD below –1.0 SD in either sites (R^2 = 0.104; P = 0.144).

In both PBC-40 and PBC-27, patients with fractures reported higher scores in symptoms and fatigue domains than subjects without fractures. Moreover in PBC-27, patients with fractures reported higher scores in dryness and emotional domains.

As shown in Table 3, BMD values did not correlate with age, BMI, duration of PSC, fat mass and total physical activity. There was a positive correlation between lean mass (but not fat mass) and hip BMD. Lean mass was also positively correlated with total physical activity (R = 0.424; P = 0.03).

5. Discussion

In the current study on young and middle-aged subjects with PSC lasting for approximately three years, we found a high rate of fragility fractures and moderately lower BMD values in the lumbar spine and hip. In several studies performed on patients with PSC, similar (13) or even higher rates of low BMD, reaching 50% of patients (14, 15) were observed. Inconsistent to our results, these studies suggested that low bone mass in PSC might be associated with advanced age, low BMI, severity of PSC or long duration of IBD (14). However, patients participating in those studies were older and had a longer duration of PSC than our population. This is consistent with other reports indicating more advanced metabolic bone disease in PSC associated with end-stage liver disease evaluated for transplantation (16) or with advanced liver cirrhosis (17).

Table 1. Characteristics of Study Participants and Comparisons Between Subjects With and Without Fractures [a,b]

Variables	All (n = 33)	Without Fractures (n = 27)	Fractures (n = 6)	P Value
Gender, F/M	11/22	10/17	1/5	0.632
Age, y	35.31 ± 13.38	35.17 ± 14.60	35.80 ± 7.51	0.920
Time from diagnosis, y	3.38 ± 2.85	3.81 ± 2.89	2.99 ± 2.23	0.097
Body mass index, kg/m^2	23.44 ± 3.45	23.33 ± 3.42	23.95 ± 3.90	0.697
Bilirubin, mg/dL	1.14 ± 1.25	1.21 ± 1.34	0.89 ± 0.86	0.654
Alkaline phosphatase, IU/mL	239.21 ± 176.9	240.86 ± 191.0	233.17 ± 124.9	0.926
Alanine aminotransferase, IU/L	74.61 ± 67.46	64.27 ± 54.55	111.80 ± 74.21	0.257
Gamma-glutamyl transferase, IU/mL	245.52 ± 260.2	179.90 ± 175.0	289.61 ± 199.3	0.078
Inflammatory bowel disease [c]	20 (60.6)	15 (55.5)	5 (83.3)	0.632
Liver cirrhosis [c]	7 (21.2)	4 (14.8)	3 (50.0)	0.092
Lean mass, kg	49.36 ± 9.40	49.14 ± 10.06	50.21 ± 6.80	0.807
Total body fat, kg	19.19 ± 8.29	19.60 ± 8.14	17.56 ± 9.47	0.599
Total body fat, %	27.44 ± 10.35	28.15 ± 10.04	24.57 ± 12.03	0.457
Bone mineral density				
Lumbar spine, g/cm^2	1.11 ± 0.16	1.12 ± 0.17	1.05 ± 0.11	0.405
Lumbar spine (z-score)	-0.65 ± 1.39	-0.53 ± 1.48	-1.15 ± 0.78	0.335
Lumbar spine (t-score)	-0.82 ± 1.39	-0.70 ± 1.47	-1.32 ± 0.90	0.339
Hip, g/cm^2	0.97 ± 0.18	0.98 ± 0.19	0.95 ± 0.15	0.726
Hip (z-score)	-0.41 ± 1.00	-0.33 ± 1.00	-0.75 ± 0.99	0.364
Hip (t-score)	-0.62 ± 1.01	-0.54 ± 1.01	-0.97 ± 0.99	0.359
Health-related quality of life SF-36				
Physical functioning	86.25 ± 20.71	91.67 ± 14.55	70.00 ± 28.81	0.128
Role physical	75.67 ± 33.19	82.08 ± 28.17	50.00 ± 41.83	0.031
Bodily pain	72.92 ± 30.68	76.77 ± 31.83	57.50 ± 21.08	0.173
General health	58.47 ± 23.73	63.75 ± 20.81	37.33 ± 24.60	0.012
Vitality	64.37 ± 20.42	69.21 ± 19.03	45.00 ± 13.78	0.006
Social functioning	67.85 ± 25.28	71.79 ± 24.43	52.08 ± 24.26	0.087
Role emotional	89.44 ± 24.24	89.58 ± 24.08	88.89 ± 27.22	0.951
Mental health	72.93 ± 20.63	75.50 ± 20.38	62.67 ± 20.03	0.177
Physical component summary	67.48 ± 21.25	72.86 ± 19.04	45.98 ± 16.06	0.003
Mental component summary	66.57 ± 20.53	70.17 ± 20.95	52.19 ± 10.72	0.053
PBC-40				
Symptoms	12.39 ± 5.16	10.92 ± 3.67	18.50 ± 6.25	0.029
Itching	3.06 ± 2.85	3.32 ± 3.05	2.00 ± 1.55	0.316
Fatigue	22.97 ± 9.06	20.68 ± 8.08	32.50 ± 6.63	0.002
Cognitive	10.13 ± 5.06	9.32 ± 4.57	13.50 ± 6.02	0.068
Social and emotional	25.74 ± 10.20	24.16 ± 10.04	32.33 ± 8.66	0.077
PBC-27				
Symptoms	6.29 ± 3.07	5.68 ± 2.81	8.83 ± 2.99	0.021
Dryness	3.61 ± 1.54	3.20 ± 1.22	5.33 ± 1.63	0.001
Itching	3.06 ± 2.85	3.32 ± 3.05	2.00 ± 1.55	0.316
Fatigue	17.61 ± 6.70	16.00 ± 6.22	24.33 ± 4.03	0.004
Cognitive	8.42 ± 4.11	7.76 ± 3.68	11.17 ± 5.04	0.067
Emotional	6.16 ± 2.78	5.68 ± 2.54	8.17 ± 3.06	0.047
Social	5.77 ± 3.40	5.40 ± 3.54	7.33 ± 2.42	0.217
Physical activity				
MET min/wk	3337 ± 2500	3217 ± 2842	3340 ± 1272	0.998
Below 3000 MET min/wk [c]	25 (75.7)	21 (77.7)	4 (66.7)	0.801

[a] Data are Means ± SD or numbers (proportion).
[b] P value refers to comparisons between subjects with and without fractures.
[c] No (%).

Table 2. Spearman Correlations Coefficients Between Physical and Mental Summary Scores and PBC-40 and PBC-27 Domains

Variables	Physical Component Summary		Mental Component Summary	
	R	P	R	P
PBC-40				
Symptoms	− 0.659	0.0001	− 0.477	0.0089
Itching	− 0.257	0.177	− 0.487	0.010
Fatigue	− 0.689	0.0001	− 0.680	0.0001
Cognitive	− 0.567	0.0001	− 0.567	0.0006
Social and Emotional	− 0.769	0.0001	− 0.769	0.0001
PBC-27				
Symptoms	− 0.608	0.0004	− 0.423	0.022
Dryness	− 0.537	0.0026	− 0.503	0.0054
Itching	− 0.257	0.177	− 0.468	0.010
Fatigue	− 0.668	0.0001	− 0.674	0.0001
Cognitive	− 0.569	0.0013	− 0.593	0.0001
Emotional	− 0.524	0.0035	− 0.528	0.0032
Social	− 0.592	0.0001	− 0.717	0.0001

Table 3. Correlations Between Bone Mineral Density, Age, BMI, Body Composition Parameters and Physical Activity [a]

Variables	Spine BMD, g/cm^2	P Value	Hip BMD, g/cm^2	P Value
Age, y	0.1520	0.4227	- 0.0965	0.6321
Body mass index, kg/m^2	0.2493	0.1689	0.0966	0.6248
Duration of PSC, y	- 0.077	0.6698	- 0.1031	0.5677
Lean mass, kg	0.2814	0.1319	0.4812	0.0071
Total body fat, kg	0.1208	0.5249	0.0678	0.7369
Physical activity, MET min/wk	0.0359	0.8617	0.1799	0.3895

[a] Values in each cell refer to the Spearman rank correlation coefficient.

Additionally, advanced age and low BMI are well-known risk factors for reduced BMD in general population. Our results suggested that even young patients with PSC with a relatively short duration of the disease are at risk of osteoporosis. Previous studies demonstrated that IBD per se is associated with an increased prevalence of bone demineralization and low energy fractures (2). However, IBD associated with PSC usually follows a more quiescent course than patients without PSC (18-20). In patients with PSC, Angulo et al. (14) found a 3.6-fold increased risk for osteoporosis in cases with duration of IBD more than 19 years. Moreover, in their study the rate of bone loss per year was significantly associated with duration of IBD. Hence, we speculate that in patients with a relatively short duration of disease, IBD might be a potential risk factor, but not yet a robust predictor of osteoporosis, although the relative impact of IBD-associated factors and IBD-specific inflammation on bone health is still uncertain (2).

We found a positive correlation between hip BMD and lean mass. Recent meta-analysis (21) and observational studies in men (22) and women (23) demonstrated that lean tissue contributes more to bone mass in the femur than fat tissue during life in healthy population, and now, as suggested by this study possibly also in PSC. This finding underlines the concept that in PSC, in which BMD is frequently lower, physical activity is an important component in the maintenance of bone loss and prevention of osteoporosis. Because lean tissue is composed mainly of skeletal muscles, it influences bone directly via mechanical stimuli and myokines (24). Therefore, a low lean mass seems to be an important risk factor of vertebral and hip fractures, ranking in importance alongside age (21). In line with this concept, we found positive associations between lean mass, hip BMD and the intensity of physical activity.

In the current study, the point prevalence rate of fragility fractures was high, reaching 18% of patients. There have been no previous reports evaluating fracture rate in PSC. In postmenopausal women with primary biliary cirrhosis, Guanabens et al. (25) found a 12% prevalence of non-vertebral fractures. Regardless of the small sample

size, our results suggested that this prevalence may be even higher in PSC.

We found that patients with fractures had significantly lower SF-36 role functioning, general health, vitality and PCS scores than those without fractures; a similar trend was also observed regarding MCS domain. Moreover, in multiple regression analysis, prior fractures adjusted for gender, age and duration of PSC were significantly associated with lower PCS and MCS scores. Poorer MCS outcomes in patients with fractures seem to be, at least partially, associated with higher prevalence of significant subjective symptoms, like systemic symptoms and fatigue, as assessed by the PBC-40 and PBC-27. On the other hand, it has been suggested that fatigue does not seem to be a specific symptom in PSC compared with the general population (26). In a study by Angulo et al (14) comprising 237 participants, aged over 54 years, BMI lower than 24 kg/m^2 and duration of IBD longer than 19 years, correlated with the presence of metabolic bone disease. On the other hand, Campbell et al. (13) showed that low bone density cannot be predicted by severity of liver disease in PSC patients listed for liver transplantation or with hepatic decompensation. Earlier reports pointed more advanced bone disease in PSC patients with end-stage liver disease evaluated for liver transplantation (16) and liver cirrhosis generally was a major risk factor of bone disease in patients evaluated for liver transplantation (17). However, the natural history of PSC is associated with impairment in HRQoL as shown by Benito de Valle et al. (26) and more recently by our group (27). Age was negatively related to all SF-36 physical domain scores and Physical Component Summary (PCS) score and positively to SF-36 mental health, role emotional and Mental Component Summary (MCS) scores. Patients with liver cirrhosis had lower SF-36 scores of physical functioning, role functional, general health, mental health and PCS scores in comparison to non-cirrhotic individuals in Benito de Valle et al. study (26). However, neither fatigue nor psychological distress was more common in PSC patients compared to general population and the disease severity was not a major determinant of HRQoL in unselected patients with PSC (26). Recently, we also found that female gender and older age influenced HRQoL in Polish cohort of PSC patients (27). Mental Component Summary of SF-36 was significantly lower in females than males and men generally showed better quality of life in the study with SF-36, PBC-40 and BC-27 questionnaires (27). The results of the current study to the novel aspect of quality of life in PSC patients, i.e. the impact of fragility bone fractures on HRQoL. We found lower scores of role physical, general health, vitality and PCS scores in respect to SF-36 questionnaire and symptoms in both PBC-40 and PBC-27 tools in PSC patients with fragility osteoporotic bone fractures. These results suggest the impairment of physical aspect of HRQoL in severe osteoporosis associated with PSC.

Fatigue is probably the most intriguing symptom affecting patients with chronic cholestatic disorders (28). However, there is still a controversy about specificity of fatigue in PSC. It did not seem to be a specific complaint of PSC in Benito de Vale et al. study (26), but Al-Harthy et al. found that fatigue was an important, but under reported symptom for patients with PSC, particularly in female patients (11). IBD presence was also associated with more severe fatigue in PSC patients in Al-Rifai et al. study on 138 participants (29). However, the result of our recent study might indicate silent bone complication as a cause of this symptom.

There were certain limitations of our study. The main limitation is its cross-sectional design. Hence, the associations presented between independent factors and outcome variables do not necessarily represent causal relationships. Second, we studied a relatively modest sample of males and females from a single tertiary center, subjected to referral and selection bias. The small sample size limited the power to examine weaker associations. Additionally, males have higher bone mass than females, especially postmenopausal females. To reduce any potential bias associated with gender-specific BMD values, we did not include women after menopause and BMD was expressed in gender-specific z-scores and t-scores. Thirdly, we did not evaluate vertebral fractures by imaging techniques. Vertebral fractures are the most common form of osteoporotic fractures (30) and largely undiagnosed (31). Moreover, vertebral fractures, common among corticosteroid users, are frequently asymptomatic or poorly symptomatic, but they substantially affect quality of life (32). Thus, we cannot exclude that undiagnosed vertebral fractures might influence HRQoL outcomes in our patients.

In conclusion, in young and middle-aged subjects with PSC lasting for approximately three years, we found a high rate of fragility, non-vertebral fractures and moderately lower BMD in the lumbar spine and hip. Fragility fractures have an impact on physical and mental aspects of HRQoL, as assessed by both generic and disease-specific questionnaires.

Authors' Contributions

Study concept and design: Joanna Raszeja-Wyszomirska and Tomasz Miazgowski. Acquisition of data: Robert Kucharski and Marta Zygmunt. Analysis and interpretation of data: Joanna Raszeja-Wyszomirska and Tomasz Miazgowski. Drafting of the manuscript: Joanna Raszeja-Wyszomirska. Critical revision of the manuscript for important intellectual content: Tomasz Miazgowski and Joanna Raszeja-Wyszomirska. Statistical analysis: Krzysztof Safranow. Administrative, technical and material supports: Robert Kucharski and Marta Zygmunt. Study supervision: Tomasz Miazgowski.

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