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ORIGINAL ARTICLE

Long-term outcome of patients with pregnancy and lactation-associated osteoporosis (PLO) with a particular focus on quality of life

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Abstract

Background Pregnancy and lactation-associated osteoporosis (PLO) is a very rare form of osteoporosis. Vertebral fractures either occur in the last trimester of pregnancy or after childbirth. Pathogenesis is still unclear. Until recently, almost no data existed in regards to the quality of life and long-term clinical outcome of patients with PLO.

Objectives To determine the long-term clinical outcome of patients with pregnancy and lactation-associated osteoporosis (PLO) with respect to the following factors: pain, quality of life, mental condition, vertebral fractures, and capacity to work.

Methods In this single-center retrospective study, patients were reviewed for at least 2 years, more than 50% of them were followed up until menopause. Bone density (DXA) and vertebral fractures were assessed. Standardized questionnaires were used to analyze factors such as quality of life (Qualeffo-41), anxiety and depression (PHQ-4), and pain (the visual analog scale [VAS]). Additionally, a questionnaire was designed in order to evaluate and discuss some of the reasons behind the occurrence of mental distress at the onset of symptoms.

Results Our report shows the clinical course of 20 patients with PLO, 11 of them until menopause (on average 16.3 years after onset of symptoms). When diagnosis was made, 5.4 vertebral fractures were noticed on average. Three of the 20 patients developed subsequent fractures in the following years. The diagnosis of PLO was made on average after 3.3 months after the onset of symptoms. At the beginning of the investigation, physical and mental health of all patients were poor, but improved within the first 2 years and continued doing so until menopause. The average time it took to return to employment was 3.3 years.

Conclusion PLO has a significant impact on pain, mental state, quality of life, and capacity to work. However, the long-term prognosis is promising. The severe mental distress is presumably related to several contributing factors in life such as physical integrity and independence, family life, employment, and financial security.

Key Points
- *PLO has a strong impact on quality of life and can lead to severe mental distress.*
- *At onset of symptoms, patients with PLO are in very poor mental and physical condition; however, the long-term outcome after inpatient rehabilitation seems to be good.*
- *Most patients do not suffer subsequent vertebral fractures until the menopause.*

Keywords Long-term outcome · Mental distress · Osteoporosis · Pregnancy · Rehabilitation · Vertebral fracture

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Introduction

Pregnancy and lactation-associated osteoporosis (PLO) is a rare form of osteoporosis that typically leads to symptoms in the last trimester of pregnancy or post-pregnancy. Approximately 200 cases of PLO have been reported to date. The estimated incidence rate is 4–8 in 1 million pregnancies. The exact pathogenesis of PLO is still unclear. Hadji et al.

identified excessive dental problems as well as lack of exercise in childhood as risk factors associated with both PLO and pregnancy-associated transient osteoporosis of the hip (TOH) [1, 2]. During pregnancy and lactation, maternal calcium is transferred to the infant resulting in a loss of maternal bone mass. This process is controlled by a complex hormonal interaction between the mother and child. During lactation, elevated prolactin levels and secondary amenorrhea lead to a further loss of calcium [3, 4]. A recent prospective study was able to show pathogenic variants of bone-specific genes in three of seven patients (genes LRP5, COL1A1, and COL1A2). Butscheidt et al. described the existence of a previously unrecognized monogenetic bone disorder in patients with PLO. During their study, they considered the loss of calcium during pregnancy as a possible risk factor, which might lead to osteoporosis in individuals who carry these underlying mutations [5].

The key symptoms of PLO include severe lower back pain and, less commonly, pelvic or femoral pain. The diagnosis of PLO is made, when typical clinical features of osteoporosis, such as spontaneous vertebral fractures and reduced bone density (DXA-measurement), occur during pregnancy or lactation and other causes of secondary osteoporosis have been previously excluded. Hematological, endocrine, rheumatologic, gastrointestinal, nephrological disorders and drugs that might cause osteoporosis have to be ruled out as well [6]. Most authors note that several vertebral fractures occur at the onset of symptoms. O'Sullivan studied a group of 11 women with PLO and reported that they had low-trauma vertebral fractures (median: 3, range: 2–5). Phillips et al. studied a group of 13 patients; 8 of them with vertebral fractures and 5 with involvement of the hip. Both studies reported a reduced bone density in the patients that increased significantly in the following years [7, 8].

Back pain that occurs in young patients during or after pregnancy might be misinterpreted as non-specific lumbar pain. This can cause a delay in diagnosing vertebral fractures. This article discusses severe mental distress observed in daily clinical practice. Postpartum depression in patients with PLO has previously been discussed [9]. However, little is known about mental distress as a direct result of PLO.

Given the comparatively small number of patients affected, a valid therapeutic recommendation cannot be made. Almost all authors recommend discontinuing breast feeding [6, 7]. However, the value of drug therapy for PLO is still vague. A study with nine patients treated with bisphosphonates over the course of 2 years found an increase of bone mineral density. Additional cases have been reported where treatment of patients with bisphosphonates led to an increase of bone mineral density and prevention of further fractures [10–14].

A study with three patients reported successful treatment with teriparatide [15].

Different case reports also reported an increase of bone density while treated with teriparatide [16, 17]. However, it remains uncertain, whether treatment with bisphosphonates or teriparatide has additional benefits towards the outcome. There are no prospective studies comparing clinical course of untreated disease to clinical course with drug treatment [18]. Nakamura et al. have reported that vitamins D and K are of paramount importance when it comes to increasing BMD and preventing fragile fractures [19].

Laroche et al. published a retrospective multicenter study with 52 patients that were hospitalized in the last 10 years. A total of 19.2% (10 of these 52 patients) suffered from repeated fractures between 4 and 36 months after the diagnosis was made. The majority of these patients with subsequent fractures (7 out of 10) had no specific therapy. BMD was monitored in 18 of the 52 patients (mean follow-up for 2.5 years). Patients treated with bisphosphonates ($n = 7$) showed an annual mean gain in BMD measured at the spine of 10.2% and patients treated with teriparatide ($n = 4$) showed a gain of 14.9%. Patients that received no specific therapy ($n = 5$) showed only an increase of 6.6% [20]. Phillips et al. followed 13 patients up to 8 years after pregnancy [8]. Few articles describe the specific effects of rehabilitation [13, 21]. Currently, there are no studies reporting about neither the long-term outcome nor the quality of life until menopause.

Main aim of this study

To determine the long-term clinical outcome of patients with pregnancy and lactation-associated osteoporosis (PLO).

Secondary aim of this study

To specify the following factors: pain, quality of life, mental condition, vertebral fractures, and capacity to work.

Materials and methods

Patients and setting

In this single-center retrospective study, 20 patients with PLO were included.

Diagnostic criteria

The diagnosis of PLO was made when typical clinical features of osteoporosis such as spontaneous vertebral fractures and reduced bone density (DXA-measurement) occur during pregnancy or lactation. Other causes of secondary osteoporosis had to be excluded [1, 6]. The vertebral

fractures were postpartum diagnosed by X-ray. In some cases, also magnetic resonance imaging (MRI) was used to detect vertebral fractures. Patients with hip pain received a pelvic MRI to detect hip edema.

Inclusion criteria

Patients who first received a 3-week inpatient rehabilitation in our specialized osteological clinic between 1991 and 2016. The diagnosis of PLO had to be made during the rehabilitation period and patients had to be followed up on a regular basis as outpatients in the clinic until presently.

Exclusion criteria

Patients presenting with additional possible reasons such as hematological, endocrine, rheumatological, gastrointestinal, and nephrological disorders as a cause for osteoporosis or fractures were excluded from this study. Patients taking glucocorticoids, patients with osteomalacia, patients with osteogenesis imperfecta, and patients who are extremely underweight (body mass index/BMI < 15 kg/m^2) were also excluded.

Selection of patients

Between 2016 and 2019, patients were selected for the study during another inpatient rehabilitation or during the follow-up in the outpatient department of the clinic. All these patients had already initially completed the inpatient rehabilitation between 1991 and 2016.

Patients were eligible for the study if they fulfilled the inclusion and exclusion criteria and gave consent to participate in the study.

Setting

The 3-week inpatient rehabilitation included pharmacological pain management (analgesia in compliance with WHO guidelines) as well as daily physiotherapy to improve muscular coordination and increase strength of the proximal skeletal muscles [22]. Patients dependent on walking aids (crutches, wheelchairs, or walking frames) received additional walk training. All patients were fitted with a spinal orthosis. Spinal orthoses have been proven to increase trunk muscle strength and quality of life, while reducing pain in patients suffering from osteoporotic vertebral fractures [23].

Additionally, during rehabilitation, the patients received two psychological interventions per week. Telephone contact was initiated and maintained with the patients previously treated on inpatient basis at the hospital (this included one or two calls; 30 to 60 min in duration).

Data collected

Data was collected between 2016 and 2019 and based on the documentation, collected during the initial inpatient rehabilitation and during the follow-up rehabilitation, either as inpatients or outpatients. This documentation included clinical information as well as the questionnaires that had been completed regularly by the patients. Previous diagnoses and accompanying illnesses (excluding osteoporosis), age, body mass index (BMI), number of pregnancies, and pre-medication (relevant for osteoporosis) were documented. Number of vertebral fractures, incidences of hip edema, and time of onset of symptoms until diagnosis were also noted.

Patients completed standardized questionnaires including the Qualeffo-41, PHQ-4, and a visual analog scale (VAS) for pain at the time of diagnosis (baseline) and after one, as well as 2 years. Eleven patients continued completing questionnaires after menopause. An additional questionnaire was designed to investigate the reason behind mental distress at the onset of symptoms. This questionnaire was filled out once retrospectively by the patients at the time of patient selection for the study (from 2016 to 2019).

At the time of diagnosis (baseline), patients were asked about their ability to care for the baby and about their dependency on walking aids (crutches, wheelchair, walking frame).

Bone density (lumbar spine and hip total) of all patients was measured at baseline and after 18 months. Eleven patients were additionally measured after onset of menopause.

During the clinical follow-up, patients were asked about symptoms of further vertebral fractures. An increase of pain or a loss of body height was used as criteria to perform additional x-rays of the thoracic and lumbar spine in order to look for new vertebral fractures.

The period of time it took to return to work (defined as three or more hours per day) was recorded. Patients that did not return to work within the time of observation were contacted after 3 and 4 years via telephone to gather these information.

Qualeffo-41

Qualeffo-41 is a questionnaire for measuring the quality of life of patients with vertebral fractures. It includes the domains pain, general health, perception, physical function, mental function, and social function. The score ranges from 0 to 100. A result of 100 complies with lowest quality of life, while 0 is equated to the highest quality of life [23].

Qualeffo-41 was measured at baseline, after 1 and after 2 years after onset of symptoms. Eleven patients were additionally followed up until after menopause.

PHQ-4

PHQ-4 is a questionnaire to detect anxiety and depression. The score ranges from 0 to 12. A result of 12 complies

with maximal psychological strain (anxiety and depression); a result of 0 is equal to no psychological strain [24].

PHQ-4 was measured at baseline, after 1 and 2 years. Eleven patients were additionally accessed after menopause.

Visual analog scale (VAS) for pain

Pain was measured by VAS. The scale ranges from 0 to 10. Ten corresponds to maximum pain intensity, 0 corresponds to no pain.

VAS was measured at baseline, after 1 and 2 years. In the case of 11 patients, it was additionally performed after menopause.

Questionnaire "Reason for mental distress at onset of symptoms"

A list of potential reasons for mental distress in patients with PLO was compiled by the authors. Patients were asked to rate retrospectively the impact of each reason on mental discomfort. Each answer was allocated to 0 to 3 points (0 = no impact, 1 = slight impact, 2 = moderate impact, 3 = strong impact). Arithmetic mean, standard deviation, median, and range were calculated.

DXA

Delphi W (Hologic) was used for measurement of bone density at lumbar spine and total hip.

Statistical analysis

Mean value, median, and standard deviation of all questionnaires were calculated at any three points in time (baseline, after 1 year, and after 2 years) for all questionnaires ("Qualeffo-41","PHQ-4", and "VAS pain"). For 11 patients, this was additionally performed after menopause. Significance was calculated by using the *t* test (paired sample *t* test) comparing the points of time "one year", "two years", and "menopause" with baseline. The graphs were made by using Excel 2013 (MS office).

Results

Period of observation

All 20 patients took part in a follow-up over a period of at least 2 years.

Eleven of these patients were followed up on until menopause: 16.3 years after onset of symptoms (median 16, range 4–27), aged 49.5 years (median 50, range 46 to 51).

Demographic data

A total of 20 patients were included in this study (Table 1). All patients except one were primiparas. Time from onset of symptoms until diagnosis of PLO amounted to 3.3 ± 2.0 months (range: 1–7).

Risk factors

Patients with major risk factors for osteoporosis had been excluded (exclusion criteria); however, 70% (13 of 20 patients) had at least one minor risk factor: 35% of the patients (7 of 20) had a positive family history of osteoporosis, 25% patients (5 of 20) were slightly underweight (BMI 15–20 kg/m^2), 10% of the patients (2 of 20) had a history of oral anticoagulation (Phenprocoumon) for more than 5 years and heparin therapy during pregnancy. Thirty-five percent of the patients (7 of 20) had no risk factors at all.

Fracture data, subsequent fractures, and hip edema

Patients had a mean of 5.4 ± 2.8 vertebral fractures (median 6, range 0–10) when diagnosis was made (baseline). Eighty-five percent (17 of 20 patients) developed no subsequent fractures, whereas three patients developed further fractures. All subsequent fractures happened within the first 2 years after baseline.

One patient suffered from one vertebral fracture due to an adequate trauma, one patient suffered from three vertebral fractures due to an inadequate trauma (this patient had a history of oral anticoagulation and heparin therapy), and one patient suffered from six vertebral fractures with no trauma. None of these patients developed any further vertebral or non-vertebral fractures until menopause. Four patients showed edema of the femur (visualized by magnetic resonance imaging/MRI) in addition to the vertebral fractures. One of these patents was additionally diagnosed with an osteonecrosis of the femur.

Longitudinal BMD

Bone density (DXA) was low at baseline: lumbar spine − 3.3 ± 0.9 SD/T-score (median − 3.2, range − 1.3 to − 5.2) and total femur − 2.3 ± 1.0 SD/T-score (median − 2.1, range − 0.9 to − 3.8). DXA improved significantly after 18 months: lumbar spine − 2.4 ± 0.9 SD/T-score (median − 2.3, range − 0.7 to − 4.3) and total femur − 1.8 ± 1.0 SD-T-score (median − 2.1, range − 0.5 to − 3.7). After that up until menopause, no further improvement of bone density was measured: lumbar spine − 2.6 ± 0.8 SD/T-score (median − 2.4, range − 1.4 to − 3.9) and total femur − 2.0 ± 0.8 SD/T-score (median − 2.0, range − 0.4 to − 3.2) (Graph 1).

Table 1 Baseline table, anthropometric data, and clinical features at baseline

	Mean value ± standard deviation	Median (range)
Age (years)	33.9 ± 4.6	34 (27–42)
Body mass index/BMI (kg/m^2)	23.5 ± 5.4	21.7 (16.9–39)
Time from onset of symptoms until diagnosis (months)	3.3 ± 2.0	3 (1–7)
Number of vertebral body fractures at diagnosis	5.4 ± 2.8	6 (0^x - 10) *(^{X}sacrum fracture)*
	Percentage of patients (number of patients)	Details
Edema of the hip	20% (4 of 20)	
Not able to care for the baby	80% (16 of 20)	
Dependent on walking aids (crutches, wheelchair, walking frame) at onset of symptoms	30% (6 of 20)	
	Characterization of patients	Details
Drug therapy Started at baseline	Teriparatide 9 Bisphosphonates 8 Denosumab 1 None 2	Teriparatid had been given 2 years, Bisphosphonates 5 years Two patients received after teriparatide, 5 years bisphosphonates
Risk factors for osteoporosis	• 35% (7 of 20 patients) had a positive family-history of osteoporosis • 25% (5 of 20 patients) had slight underweight (BMI 15–20 kg/m^2 • 35% (7 of 20 patients) had no risk factors at all	*All Patients with major risk-factors have been excluded*
Premedication (relevant for osteoporosis)	• 2 patients had a history of oral anticoagulation (phenprocoumon) and a 7-month history of heparin.	*All Patients with cortisone therapy have been excluded*
Number of pregnancies	all patients but one were primiparas	

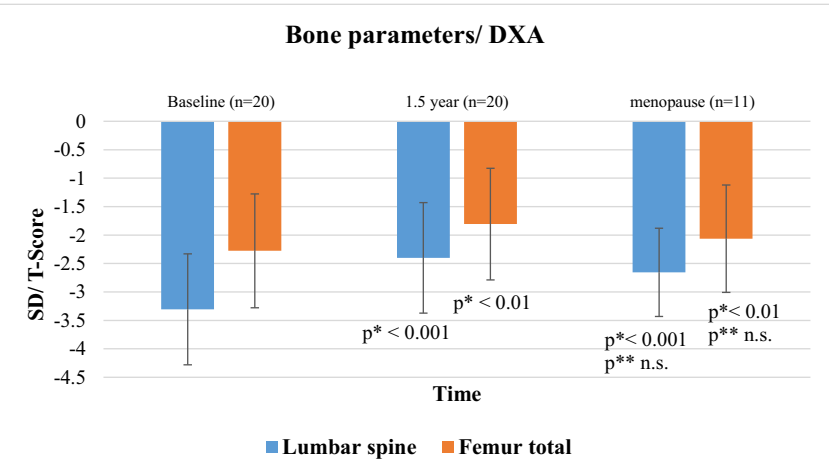
Treatment

All patients received 1000 IE vitamin D daily. At baseline, nine patients were additionally treated with teriparatide, eight patients with bisphosphonates, one with denosumab, and two patients received no further medications. Teriparatid was given 2 years, bisphosphonates 5 years. Two patients continued with 5 years of bisphosphonates, after initially receiving teriparatide.

At baseline, all patients underwent a 3-week inpatient rehabilitation.

Quality of life and psychological data

At baseline, 80% (16 of 20) patients were not able to take care of their babies (changing diapers, pushing baby carriage, lifting the baby etc.), 30% (6 of 20) were



Graph 1 Bone parameters. Follow-up BMD measurement at the lumbar spine and the femur (T-score). For all patients ($n = 20$), T-score was measured at baseline and after one and a half year. Of these patients, 11 patients were additionally followed up until menopause. Significance was calculated by *t* test. Menopause: 16.3 years after onset of symptoms (median 16, range 4–27), aged 49.5 years (median 50, range 46 to 51). Abbreviations: SD: standard deviation. n.s.: not significant. *P*: level of significance. *In comparison to baseline. **In comparison to 1.5 years

dependent on walking aids (crutches, wheelchair, walking frame).

At the onset of symptoms (baseline), all patients were in very poor physical and mental condition. Qualeffo-41, PHQ-4, and VAS-for pain scored highly at baseline: Qualeffo-41 = 75.3 ± 15.8 (median 77, range 38 to 95), VAS pain = 9.8 ± 0.5 (median 10, range 8 to 10), PHQ 4 = 9.8 ± 3.9 (median 12, range 0 to 12). However, already after 1 year and even more after the second year, a highly significant decrease in pain levels and mental stress, as well as a highly significant increase in quality of life, was observed. After 2 years: Qualeffo-41 = 34.4 ± 17.3 (median 35, range 5 to 65), VAS pain = 3.4 ± 2.0 (median 3, range 0 to 8), PHQ 4 = 2.8 ± 2.0 (median 3, range 0 to 7). This positive trend continued until menopause: Qualeffo-41 = 24.6 ± 8.5 (median 24, range 16 to 46), VAS pain = 2.6 ± 2.4 (median 3, range 0 to 7), PHQ 4 = 1.5 ± 1.5 (median 1, range 0 to 4) (Graph 2). Patients rated all items included in the questionnaire "Reasons for mental distress at onset of symptoms" to be relevant for the poor psychological condition. The items "Incapacity to take care for the baby" and "Intensity of pain" had the greatest impact. Furthermore, the items "Limitation of daily activity", "Time span until diagnosis", "Underestimation of symptoms by physicians", "Fear of the future", "Limitations in performing house work", "Problems with dressing, washing and practicing personal hygiene", "Worries about career options", Medical advise against further pregnancies", and "sleep disorders" were rated to have a moderate to strong impact on mental health (Graph 3).

Ability to work

Time to return to work was a median period of 3 years (arithmetic mean 3.3 ± 2.9, range 0.5–10). This was calculated using 17 patients. Three patients did not return to work during the follow-up period of 2 years nor at the time of the telephone interview 3 years after baseline.

Discussion and conclusions

Vertebral fractures and bone density

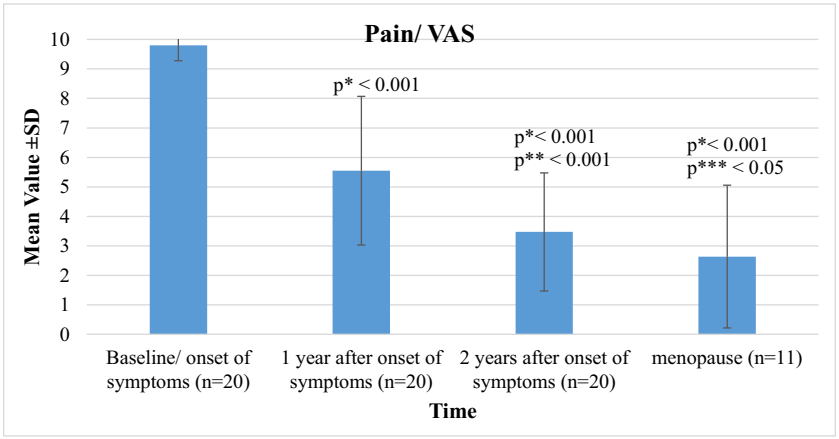
The number of vertebral fractures at baseline (5.4 ± 2.8) in this study is higher than in most previous studies [1, 7, 8]. Fifteen percent (3 of 20) of the patients in this study developed further vertebral fractures in the following years. These findings correlate well with the study of Laroche et al. which reported that 19.2% (10 of 52) showed consecutive vertebral fractures [21]. However, the number of patients with subsequent fractures in our study is clearly lower than described by the study of Kyvernitakis et al. that showed 24.3% (26 of 107) patients with subsequent fractures. Also, the number of vertebral fractures counted in Kyvernitakis et al. baseline was lower (4.2 ± 2.4) than the number counted in our study [26]. Our data was collected from patients performing at baseline an inpatient rehabilitations that were followed up in the outpatient clinic and in further inpatient rehabilitations, whereas data used in Kyvernitakis et al. study was collected only in an ambulatory setting. This might explain the higher number of vertebral fractures at baseline in our study (inpatient versus outpatient) and the lower level of subsequent fractures (tight follow-up in our study on inpatient and outpatient basis). Bone density improved significantly within the first 1.5 years, but showed no further improvement until menopause.

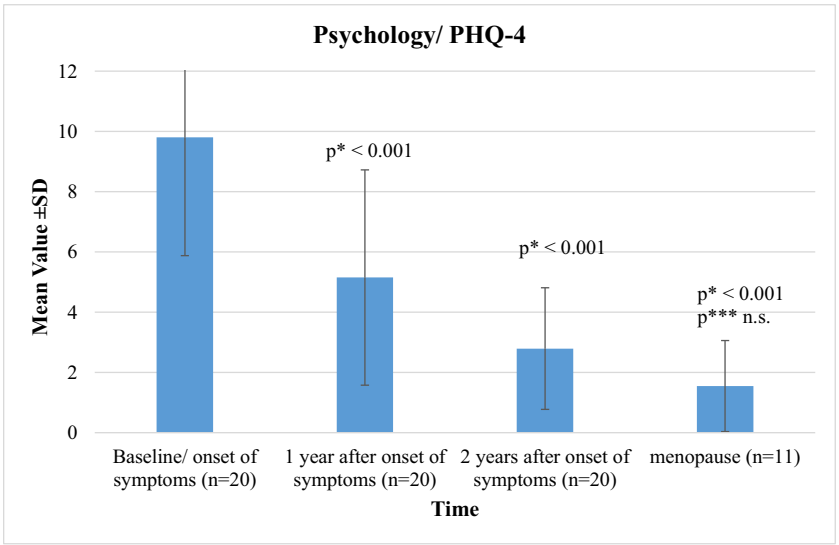
Risk factors

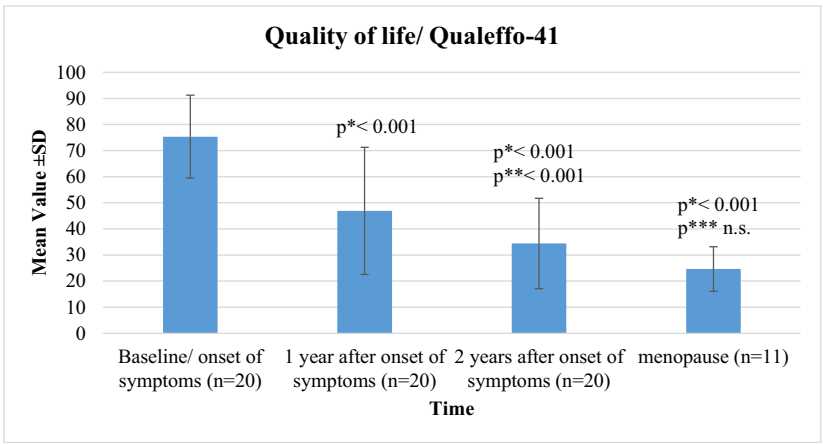
Major risk factors of osteoporosis led to an exclusion of patients in this study. However, 35% of the patients had a positive family history of osteoporosis. This might fit the hypothesis of an unrecognized genetic bone disorder in a subset of patients with PLO, in which the onset of symptoms is promoted by pregnancy and lactation [5].

Quality of life

Our findings show that PLO has a strong impact on quality of life and can lead to severe mental distress. Eighty percent of the patients were not able to care for their baby by, for example, completing tasks such as changing diapers, pushing the carriage, and lifting the baby. At the onset of symptoms, one third of the patients were dependent on a wheelchair, walking frame, or crutches for mobility. The time span until diagnosis was made was 3.3 ± 2.0 months. As the questionnaire "Reasons for mental distress at onset of symptoms" has never been validated, systematic bias cannot be totally excluded. However, our data indicate that the patients perceived the underestimating of symptoms by physicians and family and the limitations of activities of daily living (such as difficulty with dressing, washing, practicing personal hygiene, cooking, and doing housework) to be very stressful. Sleep disorders and severe pain were traumatizing and caused a strong fear of the future. Presumably, the amount of anxiety and depression occurring is related to the onset of symptoms occurring in a vulnerable period of the patient's life. This study indicates that the following several dimensions of life were simultaneously affected:



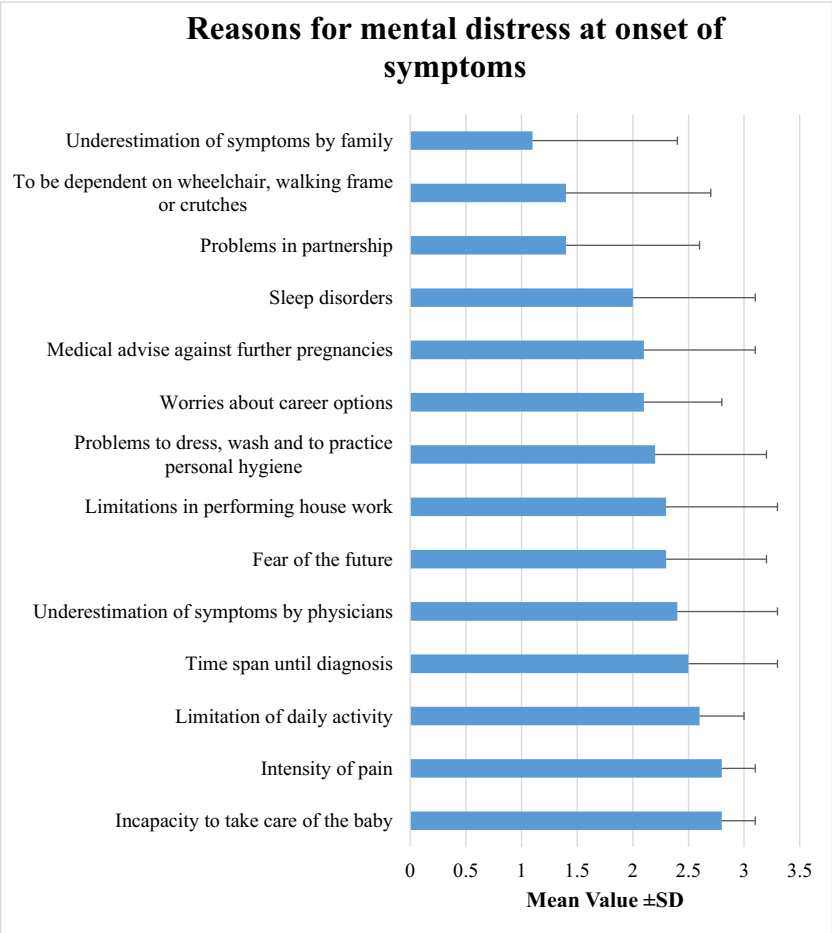




Graph 2 Questionnaires (pain, mental parameters, functional parameters). The results of questionnaires (mean value and standard deviation) VAS-pain, PHQ-4, and Qualeffo-41 were documented. All patients were followed up for at least 2 years (points of time: baseline, 1 year, and 2 years). Of these patients, 11 patients were additionally followed up until menopause. Significance was calculated by *t* test. Menopause: 16.3 years after onset of symptoms (median 16, range 4–27), aged 49.5 years (median 50, range 46 to 51). • Visual analog scale (VAS) for pain: the scale ranges from 0 to 10. Ten corresponds to maximal pain, 0 to no pain. • PHQ-4: the score ranges from 0 to 12. A result of 12 complies with maximal psychological strain (anxiety and depression), a result of 0 means no psychological strain [25]. • Qualeffo-41: the score ranges from 0 to 100. A result of 100 complies with maximal reduction of quality of life, while 0 equals to no reduction of quality of life [24]. Abbreviation: SD: standard deviation, *p* = level of significance calculated by *t* test. *In comparison to baseline. **In comparison to 1 year. ***In comparison to 2 years. n.s.: not significant

physical integrity and independence, family life, employment, and financial security. This led to a decline in confidence and self-efficacy. The reason of the decline in self-confidence and the analysis of the factors contributing to the decline can lead to an important therapeutic approach during rehabilitation and consecutive psychotherapy [27].

Keeping in mind the severity of symptoms on first presentation, all patients had residual disorders and limitations after two or more years. However, the symptoms were significantly diminished in comparison to time of the onset of the disease. This positive trend continued until menopause. Even patients with multiple vertebral



Graph 3 Questionnaire "Reasons for mental distress at onset of symptoms". All patients ($n = 20$) were asked for the reasons for mental distress. The questionnaire was designed by the authors. Patients were asked retrospectively to assess each item with 0 point (no impact) until a maximum of 3 points (strong impact). 0 = no impact. 1 = slight impact. 2 = moderate impact. 3 = strong impact

fractures were able to return to work (defined as light physical work more than 3 h a day) after a median period of time of 3 years. The knowledge of an overall positive prognosis for quality of life might be a very relevant factor in patient disease management. This can be communicated to patients both on a rational level (e.g., by referring to this study) and on an emotional level (e.g., by establishing contact to other patients who are at a later stage of the disease).

Strength and limitations of the study

The strength of this study lies in the long period of observation. This study is the first one to follow up 11 patients until menopause. Despite the comparatively small number of patients, the cohort of this study is one of the largest ones published on PLO. Furthermore, this study is the first one to describe the intensity of mental distress over the clinical course until menopause, as well as the first to give insight into possible reasons for the high intensity of mental distress at the beginning of the disease. In contrast to other studies on PLO, all patients with additional reasons for osteoporosis have been strictly excluded in this study [21].

One of the limitations of the study includes the retrospective design and the small number of patients, limiting the explanatory power. Further prospective studies are necessary to get more information about the quality of life and mental distress. As this study is lacking a control group, it is not possible to evaluate the effects of medication or rehabilitation on the clinical course of the disease.

Conclusion

In conclusion, PLO has a strong impact on quality of life. In addition to physical problems, mental distress is a major component and should be included when planning a treatment strategy. The knowledge behind the reasons for mental distress might lead to a specific psychological intervention, which can be included in the treatment plan alongside physical therapy.

Keeping in mind the relatively good long-term outcome and the excellent prognosis to return to work after some years might help patients to cope with mental distress caused by the disease.

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Authors' contributions MG wrote the manuscript. All authors contributed substantially to the elaboration of this study. All authors approved the final version of this article.

Compliance with ethical standards

Conflict of interest/disclosure Martin Gehlen, Ana Doina Lazarescu, Christian Hinz, Michael Schwarz-Eywill, Michael Pfeifer, Subathira Balasingam and Anna Maier declare that they have no conflict of interest. The authors declare no competing financial interests.

Patient consent Informed consent was obtained from all participants included in the study.

Ethical standards Retrospective study. For this type of study, formal consent is not required.

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