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Clinical Studies

Undetected low bone mineral density in patients undergoing lumbar fusion surgery—prevalence and risk factors

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ABSTRACT

Background: Sufficient bone quality is a prerequisite for low complication rates and satisfactory outcomes in lumbar fusion surgery (LFS). Low bone mineral density (BMD), including osteoporosis and osteopenia, is linked to adverse postoperative outcomes. Despite reports of a high prevalence of undiagnosed osteoporosis, it is uncertain which risk factors should guide preoperative BMD screening in LFS.

Methods: This secondary cross-sectional analysis of a prospective institutional database at an academic spine center included adult patients undergoing LFS for degenerative conditions between 2014 and 2023. Opportunistic quantitative CT (qCT) at the L1/2 level was performed before surgery, and demographic and medical history data were extracted. Descriptive and comparative statistics, univariable and multivariable logistic regression were performed to determine risk factors for present and undiagnosed osteoporosis.

Results: Of the 675 patients screened, 578 (54% female) were included after excluding those with preoperative lumbar CT scans not suitable for qCT. The median age was 65 years (IQR 58-72), and the median BMI of 28.9 kg/m^2 (IQR 25.2-32.9). Osteoporosis was identified in 182 patients (31%), with 114 previously diagnosed and 68 newly detected via preoperative qCT. Undiagnosed osteoporosis was found in 12% of all patients and 37% of those with osteoporosis. Osteopenia was present in 199 patients (34%), leading to an overall impaired bone quality prevalence of 66%. Multivariable analysis revealed that age and female sex were independent risk factors for osteoporosis, while undiagnosed cases were more common in males, patients with higher BMI, and older individuals.

Conclusions: This study found a high prevalence of abnormal BMD in LFS patients, with a significant proportion of undiagnosed osteoporosis. While osteoporosis was more common in females, male patients with osteoporosis were more frequently undiagnosed. Spine surgeons must remain vigilant about metabolic bone disease in LFS patients to ensure preoperative optimization and prevent complications.

Introduction

Lumbar fusion surgery (LFS) can significantly reduce the disability of patients after conservative treatments have been unsuccessful in addressing disabling degenerative lumbar disorders [1,2]. Musculoskeletal integrity is a prerequisite for successful outcomes. Bone mineral density (BMD) is one component of bone quality which predicts increased fracture risk [3]. Conversely, low BMD is a major risk factor for complications following LFS, such as implant loosening, nonunion and adjunct level fractures, which have a significant impact on patient well-being due to revision surgery, persistent or worsening disability, and increased healthcare costs [4–7].

Early detection of compromised bone quality is crucial for including these patients in perioperative osteological optimization and therapy [6]. The US Preventive Services Task Force (USPSTF) suggests dual energy absorptiometry (DXA) for BMD measurements solely for women aged 65 and older but not men [8], while osteological societies also recommend screening men over 70 years and those at particular risk for osteoporotic fractures [9–11].

Despite these screening recommendations, about 10% of patients undergoing LFS have undiagnosed osteoporosis [12]. DXA has the disadvantage of not being easily acquired preoperatively and may be influenced by spinal degeneration [13,14]. As a result, preoperative osteoporosis evaluation strategies that can identify these cases are prominent topics in current research [14]. Noninvasive diagnostic tools like quantitative bone ultrasound (US) [15], skin US [16,17] or MRI-based proton density fat fraction (PDFF) can improve osteoporosis screening in addition to established indications for DXA, but they need additional clinical resources [14]. Opportunistic screening methods have been developed to assess bone quality in patients scheduled for lumbar surgery that do not require additional radiation or resources [14]. These include using existing preoperative imaging to analyze the MRI derived vertebral bone quality score (VBQ) [18,19], and CT scans to measure vertebral Hounsfield units (HU) [20] or performing asynchronous quantitative CT (qCT). While VBQ offers the advantage of requiring only a preoperative MRI, and HU measurements can be easily obtained from a preoperative lumbar CT scan without the need for additional software, the qCT based volumetric BMD measurements of the L1 and L2 vertebra has the advantage of providing reliable data that correspond with WHO definitions for diagnosing osteopenia (BMD of 120–80 mg/cm^3) and osteoporosis (BMD below 80 mg/cm^3) [21,22]. However, qCT requires, in addition to a preoperative CT scan, asynchronous calibration and specialized software.

Nevertheless, there is limited evidence on how to effectively guide preoperative BMD screening for osteoporosis, osteopenia and undetected osteoporosis in patients undergoing LFS [23]. Also, risk factors associated with undetected osteoporosis specifically in LFS patients, which would warrant a routine bone quality assessment, are not well understood. In our study, we aimed to identify the prevalence of diagnosed and undiagnosed osteopenia and osteoporosis in patients undergoing LFS. We then analyzed the distribution of these conditions among sexes and different age groups to identify risk factors to guide preoperative screening decision making for LFS patients.

Methods

Study design

Patients were queried from an institutional prospective database of lumbar fusion cases at an academic tertiary spine care center between December 2014 and December 2023. The study's documentation complies with the guidelines established by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative [24]. Institutional Review Board (IRB) approval was obtained before the commencement of the study (IRB# 2014-084 and 2015-237). Adult patients (18 ≥ years) scheduled for lumbar fusion surgery were included in the institution's prospective database. All patients underwent a preoperative CT scan as part of their preoperative planning for lumbar fusion surgery. Cases with external CT scans not suitable for qCT BMD measurements were excluded (Fig. 1).

Clinical and anamnestic parameters including osteoporosis diagnosis status

The patient's demographic and surgical data included age, sex, BMI, preoperative severity of back and leg pain (measured using the Numeric Rating Scale, NRS), preoperative Oswestry Disability Index (ODI) [25], pre-existing chronic diseases, and previously diagnosed osteoporosis (based on the medical and surgical documentation available preoperatively and patient-reported history at that time). Additionally, data included alcohol consumption, smoking status, surgery date, and the levels indicated for fusion surgery.

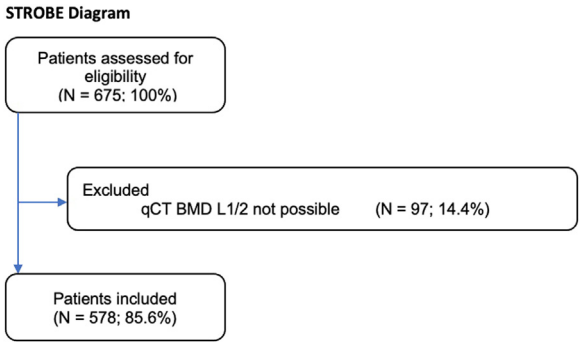

Fig. 1. Strobe diagram for the study.

qCT bone density measurements

As part of the preoperative planning process for lumbar fusion surgery, all patients received a thin-slice CT scan of the lumbar spine (120/140 kV, collimation of ≤0.625 mm, axial slice thickness ≤ 1.25 mm). Scan extent, field of view, and tube current were optimized for each patient in accordance with American College of Radiology (ACR) best practice [25]. qCT BMD measurements were performed in accordance with ACR recommendations [21]. Trabecular BMD of L1 and L2 was measured by placing an elliptical region of interest in the trabecular region of the anterior half of the vertebra avoiding local irregularities in bone density due to spinal degeneration, as previously described [26], and the L1/L2 BMD average was calculated. BMD measurements were performed using Mindways QCT Pro Software with asynchronous ClinQCT BMD measurements extension (Mindways Software, Inc., Austin, TX), which has been previously validated [27,28] and is FDA approved for diagnostic BMD measurements [29].

Osteoporosis prevalence

Osteoporosis was defined as either a previous diagnosis noted in the patient's medical history or a lumbar qCT-derived BMD of <80 mg/cm^3, based on ACR criteria [21,22]. Undetected osteoporosis was defined a BMD of < 80 mg/cm^3 without a prior diagnosis of osteoporosis. Prevalence rates were calculated as follows: overall osteoporosis (all osteoporosis patients/all patients [%]), undetected osteoporosis (undetected osteoporosis/all patients [%]), and undetected osteoporosis among osteoporotic patients (undetected osteoporosis/all osteoporotic patients [%]).

Statistical analysis

The distribution of data for normality was assessed by both visual inspection and the Shapiro-Wilk test. Descriptive statistics included means and standard deviations (SDs) for normally distributed data and medians with interquartile ranges (IQRs) for continuous data that were not normally distributed. Categorical data is presented as percentages and frequencies. The Fisher's exact test or Pearson's chi-squared test, as appropriate, was applied to assess differences between categorical variables. The Wilcoxon rank-sum test was employed for ordinal variables and non-normally distributed continuous variables, respectively. For continuous data that followed a normal distribution, the unpaired 2-tailed Student's t-test was applied. Univariable and multivariable logistic regression models were used for risk factor analysis. Factors included in the multivariable models were selected based on an entry level of $p < .1$ in univariable regression analysis and clinical expertise. Pearson correlation analysis was performed to examine the relationship between BMD and age. Statistical analysis was performed with R Studio (Version 2023.06.2, Posit Software, Boston, Massachusetts, USA). Statistical significance was set at $p < .05$.

Results

Cohort characteristics

Out of 675 patients screened for eligibility, 97 (14%) were excluded because asynchronous BMD measurements could not be made on their CT scans, resulting in a cohort of 578 patients undergoing LFS (Table 1). Of these, 314 (54%) were female with a median age of 65 (inter quartile range (IQR) 58–72) and a median BMI of 28.9 kg/m^2 (IQR 25.5–32.9). The median trabecular BMD at L1/L2 was 111 mg/cm^3. Twenty percent of all patients were previously diagnosed with osteoporosis. Common comorbidities included diabetes mellitus (11%), arterial hypertension (49%), Chronic obstructive pulmonary disease (COPD) (3%) and congestive heart failure (5%). Preoperatively, the median ODI was 44 (IQR), the median NRS back pain 7.2 (IQR 6.0–9.0) and leg pain 7.0 (IQR 4.3–9.0). The median number of levels fused was 2 (IQR 1-3).

Prevalence of impaired bone quality status in LFS

Out of the included patients, 182 patients (31%) were found to be osteoporotic before the LFS either by previous diagnosis or by preoperative qCT screening. One-hundred-fourteen (20%) had a previous diagnosis of osteoporosis and an additional 68 (12%) were diagnosed based on qCT measurements. Previously undiagnosed osteoporosis was found in 37% of all patients with confirmed osteoporosis (Fig. 2). Osteopenia was observed in 199 patients (34%), resulting in a total prevalence of impaired bone quality of 66% (381 patients) and normal bone quality of 34% (197 patients) among all LFS patients in this cohort.

When comparing patients with normal bone quality to those with impaired bone quality (osteopenia or osteoporosis [Supplementary Table 1]), the group with good bone quality was significantly younger (median age: 58 vs. 68 years; $p < .001$), with no significant difference in sex distribution (50% female vs. 57% female; $p = .11$), a higher median BMD (142 vs. 95 mg/cm^3; $p < .001$), and less frequent vitamin D supplementation (7% vs. 24%; $p < .001$) was found.

Comparing patients with preoperative osteoporosis (combining previously diagnosed and undiagnosed cases) to those without osteoporosis

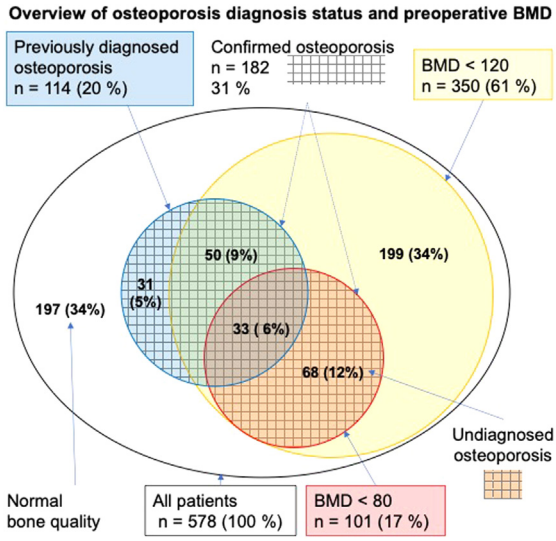

Fig. 2. Euler Diagram of the study cohort showing overlaps, absolute numbers and proportions (relative to the total cohort) of the study cohort (white), patients with a prior diagnosis of osteoporosis (blue), BMD < 120 mg/cm^3 (yellow), and BMD < 80 mg/cm^3 (red). The group combining undiagnosed osteoporosis previously diagnosed osteoporosis is marked with purple squares as confirmed osteoporosis, while patients with a BMD ≥ 120 mg/cm^3 and the absence of previously diagnosed osteoporosis were categorized as having normal bone quality.

Table 1
Demographic overview of the study cohort and stratification by the presence of osteoporosis.

	All patients N = 578*	No osteoporosis N = 396*	Confirmed osteoporosis N = 182*	p-value†
Age	65 (58, 72)	62 (55, 69)	71 (65, 75)	<.001
Sex				<.001
Male	264 (46%)	211 (53%)	53 (29%)	
Female	314 (54%)	185 (47%)	129 (71%)	
BMI	28.9 (25.2, 32.9)	29.3 (26.1, 33.3)	27.6 (24.3, 31.6)	<.001
BMD L1/L2 average	111 (87, 135)	119 (102, 142)	78 (67, 105)	<.001
Previously diagnosed osteoporosis	114 (20%)	0 (0%)	114 (63%)	<.001
Vitamin D supplementation	57 (19%) *(272 missing)*	15 (7.7%) *(201 missing)*	42 (38%) *(71 missing)*	<.001
NRS back pain	7.20 (6.00, 9.00)	7.00 (5.00, 9.00)	8.00 (6.75, 9.00)	.05
NRS leg pain	7.0 (4.3, 9.0)	7.0 (4.0, 9.0)	7.8 (5.0, 9.0)	>.9
ODI	44 (28, 58)	44 (28, 58)	44 (30, 58)	.8
Diabetes mellitus	64 (11%)	43 (11%)	21 (12%)	.8
Arterial hypertension	284 (49%)	189 (48%)	95 (52%)	.3
Congestive heart failure	26 (4.5%)	14 (3.6%)	12 (6.6%)	.1
COPD	18 (3.1%)	11 (2.8%)	7 (3.8%)	.5
Smoking status				.077
Nonsmoker	326 (57%)	233 (59%)	93 (52%)	
Smoker	56 (9.8%)	41 (10%)	15 (8.3%)	
Former smoker	192 (33%)	120 (30%)	72 (40%)	
Alcohol consumption				.8
No alcohol	173 (30%)	121 (30%)	53 (29%)	
Social alcohol	402 (70%)	274 (69%)	128 (70%)	
Self-reported problematic drinking	2 (0.3%)	1 (0.3%)	1 (0.5%)	

* n (%); Median (IQR).
† Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test.

Table 2
Demographic parameters and medical history of osteoporotic patients stratified by osteoporosis diagnosis status.

Confirmed osteoporosis			
Characteristic	Previously diagnosed N = 114*	Undiagnosed N = 68*	p-value†
Age	70 (64, 74)	71 (66, 75)	0.2
Sex			**<.001**
Male	19 (17%)	34 (50%)	
Female	95 (83%)	34 (50%)	
BMI	26.8 (22.8, 31.2)	28.1 (25.2, 33.0)	**.009**
BMD (mg/cm^3)	96 (78, 122)	68 (61, 74)	**<.001**
Vitamin D supplementation	41 (57%)	1 (2.6%)	**<.001**
ODI	44 (28, 58)	44 (34, 56)	>.9
NRS back pain	8.0 (6.0, 9.0)	8.0 (7.0, 9.0)	.6
NRS leg pain	7.0 (3.8, 9.0)	8.0 (6.2, 9.3)	**.049**
DM[a]	11 (9.6%)	10 (15%)	.3
Arterial hypertension	51 (45%)	44 (65%)	**.009**
CHF[b]	6 (5.3%)	6 (8.8%)	.4
COPD	5 (4.4%)	2 (2.9%)	>.9
Smoking status			.2
Nonsmoker	61 (54%)	32 (48%)	
Smoker	6 (5.3%)	9 (13%)	
Former smoker	46 (41%)	26 (39%)	
Alcohol consumption			.4
No alcohol	32 (28%)	21 (31%)	
Social alcohol	82 (72%)	46 (68%)	
Self-reported problematic drinking	0 (0%)	1 (1.5%)	

* Median (IQR); n (%).
† Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test (previously vs undiagnosed osteoporosis).
[a] Diabetes mellitus (DM).
[b] Congestive heart failure (CHF).

(therefore normal or osteopenic one quality, Table 1), patients with osteoporosis were significantly older (median age: 71 vs. 62 years; p < .001), predominantly female (71% vs. 47%; p < .001), had a lower BMI (median: 27.7 vs. 29.3; p < .001) and BMD (78 vs. 119 mg/cm^3; p < .001), but were more frequently supplemented with vitamin D (38% vs. 7.7%; p < .001).

Diagnosed vs. undiagnosed osteoporosis

Patients with undiagnosed osteoporosis were less frequently female (50% vs 83% vs., p < .001), had a higher median BMI (28.1 vs 26.8) and were more often diagnosed with arterial hypertension (65% vs 45%, p = .009), than those with previously diagnosed osteoporosis (Table 2). Undiagnosed osteoporosis patients had a lower median BMD (68 mg/cm3 vs 96 mg/cm3, p < .001), less frequent vitamin D supplementation (3% vs 57%, p < .001), and slightly more severe leg pain (median NRS 8 vs 7, p = .049) in comparison to previously diagnosed osteoporosis. Applying univariable logistic regression analysis, undiagnosed osteoporotic patients were 5 times more likely to be male (OR 5.0, 95% CI 2.52–9.91, p < .001), more likely of higher BMI (OR 1.08, 95% CI 1.03–1.14, p = .003) and older age (OR 1.04 95% CI 1.00–1.08, p = .046), but were fifty times less likely to receive vitamin D supple-

Table 3
Uni- and multivariable logistic regression results for the odds ratios (OR) being undiagnosed in osteoporotic patients.

Undiagnosed Osteoporosis (in patients with osteoporosis)*				
Predictor	univariable analysis†			
	OR*	95% CI		p
Age	1.04	1.00	1.08	**.046**
Sex (male)	5.00	2.52	9.91	**<.001**
BMI	1.08	1.03	1.14	**.003**
Vitamin D supplementation	0.02	0.00	0.15	**<.001**
ODI	1.00	0.98	1.02	.9
NRS back pain	1.00	0.86	1.15	.9
NRS leg pain	1.10	0.98	1.22	.096
DMa	1.61	0.65	4.03	.3
HTAb	2.26	1.22	4.21	**.010**
CHFc	1.73	0.53	5.58	.4
COPD	0.66	0.12	3.50	.6
	multivariable analysis‡			
	OR*	95% CI	p	
Age	1.05	1.01	1.1	**.029**
Sex (male)	4.40	2.14	9.33	**<.001**
BMI	1.07	1.01	1.13	**.035**
HTA	1.26	0.61	2.59	.5

* Osteoporotic patients, $n = 182$, 68 events.
† Univariable logistic regression.
‡ Multivariable logistic regression, including age, sex, BMI and HTA.
[a] Diabetes mellitus (DM).
[b] Arterial hypertension (HTA).
[c] Congestive heart failure (CHF).

mentation (OR 0.02, 95% CI 0.00–0.15, p < .001) than those with a previously established diagnosis. In multivariable logistic regression analysis, being undiagnosed among osteoporotic patients was independently associated with male sex, older age and higher BMI (Table 3).

Risk factors analysis of (undiagnosed) osteoporosis

To optimize screening decisions, risk factors of having osteoporosis or being undiagnosed with osteoporosis in the overall cohort of LFS patients is of relevance. In all LFS patients, univariable linear regression analysis showed that age, female sex, lower BMI, and vitamin D supplementation were significantly associated with higher odds of both confirmed and previously diagnosed osteoporosis cases (Table 4). Age and arterial hypertension, but not sex, were the only significant risk factors associated with higher odds for having undiagnosed osteoporosis among LFS patients without a history of osteoporosis. In the multivariable analysis (Table 5), independent risk factors for the presence for confirmed osteoporosis cases were higher age (OR 1.09, 95% CI 1.06–1.12, p < .001) and female sex (OR 2.67, 95% CI 1.63–4.43, p < .001) but not BMI (OR 1.01, 95% CI 0.96–1.06, p = .7), after adjusting for possible covariates. Age was a consistent independent risk factor for previously diagnosed osteoporosis cases (OR 1.05, 95% CI 1.02–1.09, p < .001) and undiagnosed osteoporosis (OR 1.13 95% CI 1.09–1.17, p < .001). While female sex was a relevant independent risk factor for previously diagnosed osteoporosis (OR 6.11, 95% CI 3.11–13.2, p < .001), sex was not a significant independent risk factor for undiagnosed osteoporosis (OR 1.09, 95% CI 0.62–1.92, p = .8) in patients without a prior history of osteoporosis.

Role of age and sex in bone status and diagnostic awareness in LFS patients

We stratified the patient cohort based on age decade and sex groups, as these were relevant risk factors for the presence of osteoporosis. We then plotted the data based on the absence of impaired bone quality (Fig. 3A) and osteoporosis diagnosis status (Fig. 3B). BMD decreases with age, showing a moderate negative correlation in both women ($R = -0.47$, p < .001) and men ($R = -0.43$, p < .001, Supplementary Fig. 1). The prevalence of normal bone status in all patients ranged from 86% in those aged 20-29 years to 6% in those over 80 years, with no significant sex differences (p = .11). For osteoporosis, the prevalence ranged from 0% in 20 to 29-year-olds to 15% in 40 to 49-year-olds, and up to 56% in octogenarians and older. While the prevalence of confirmed osteoporosis was significantly higher in females across all age groups (41%, $n = 129/314$ female vs 20%, $n = 53/264$ male, p < .001), the proportion of undiagnosed osteoporosis was significantly higher in male patients (64%, $n = 34/53$ male, 26%, $n = 34/129$ female, p < .001). Approximately 70% of osteoporosis cases were undiagnosed in male patients aged 60-69 and 70-79 years, while the rate of undiagnosed osteoporosis was 24% and 29%, respectively, in the corresponding female age decades.

Table 4
Univariable logistic regression results for the odds ratios (OR) for confirmed osteoporosis, previously diagnosed osteoporosis and undiagnosed osteoporosis among all patients/patients stating the absence of osteoporosis.

Predictor	Confirmed osteoporosis† (previously and undiagnosed)				Previously diagnosed Osteoporosis‡				Undiagnosed Osteoporosis§			
	OR*	95% CI		p	OR*	95% CI		p	OR*	95% CI		p
Age	1.10	1.07	1.12	**<.001**	1.06	1.04	1.09	**<.001**	1.13	1.09	1.17	**<.001**
Sex (female)	2.78	1.91	4.04	**<.001**	5.59	3.38	9.71	**<.001**	1.14	0.68	1.91	.6
BMI	0.95	0.92	0.98	**.002**	0.91	0.88	0.95	**<.001**	1.00	0.96	1.05	.9
Vitamin D supplement.	7.30	3.81	14.01	**<.001**	18.02	9.22	36.83	**<.001**	0.32	0.02	1.63	.3
ODI	1.00	0.99	1.01	.8	1.00	0.99	1.01	.9	1.00	0.99	1.02	.7
NRS back pain	1.08	1.00	1.18	.060	1.07	0.98	1.19	.2	1.08	0.96	1.23	.2
NRS leg pain	1.01	0.96	1.07	.7	1.00	0.94	1.07	.9	1.02	0.94	1.10	.7
DMa	1.07	0.61	1.86	8	0.83	0.40	1.58	.6	1.41	0.64	2.86	.4
HTAb	1.19	0.84	1.69	.3	0.80	0.53	1.20	.3	2.00	1.18	3.46	**.011**
CHFc	1.93	0.87	4.26	.1	1.24	0.44	2.99	.7	2.63	0.90	6.82	.057
COPD	1.40	0.53	3.66	.5	1.59	0.50	4.31	.4	1.06	0.16	4.05	.9

* Univariable logistic regression results.
† All patients, $n = 578$, 182 events.
‡ All patients, $n = 578$, 114 events.
§ Patients reporting absence of osteoporosis, $n = 464$, 68 events.
[a] Diabetes mellitus (DM)
[b] Arterial hypertension (HTA).
[c] Congestive heart failure (CHF).

Table 5
Multivariable logistic regression results for the odds ratios (OR) for confirmed osteoporosis, previously diagnosed osteoporosis and undiagnosed osteoporosis including factors reaching p < .1 in univariable logistic regression among all patients/patients stating the absence of osteoporosis.

Predictor	Confirmed osteoporosis† (previously and undiagnosed)				Previously diagnosed Osteoporosis‡				Undiagnosed Osteoporosis§			
	OR*	95% CI		p	OR*	95% CI		p	OR*	95ahve% CI		p
Age	1.09	1.06,	1.12	**<.001**	1.05	1.02,	1.09	**.001**	1.13	1.09	1.17	**<.001**
Sex (female)	2.67	1.63,	4.43	**<.001**	6.11	3.11,	13.2	**<.001**	1.09	0.62	1.92	.8
BMI	0.98	0.94,	1.02	.4	0.95	0.90,	1	.05	1.01	0.96	1.06	.7
NRS Back Pain	1.09	0.99,	1.2	.081	1.07	0.96,	1.2	.2	-	-	-	-
HTAa	0.82	0.50,	1.34	.4	0.64	0.36,	1.13	.12	0.96	0.53	1.77	>.9
CHFb	2.9	0.63,	13.8	.2	4.06	0.70,	20.3	.094	1.78	0.54	5.33	.3

* Multivariable logistic regression results.
† All patients, $n = 408$ with complete dataset for multivariable model, 131 events.
‡ All patients, $n = 408$ with complete dataset for multivariable model, 83 events.
§ Patients reporting absence of osteoporosis, $n = 462$ patients stating the absence of osteoporosis with complete dataset for multivariable model, 68 events.
[a] Arterial hypertension (HTA).
[b] Congestive heart failure (CHF).

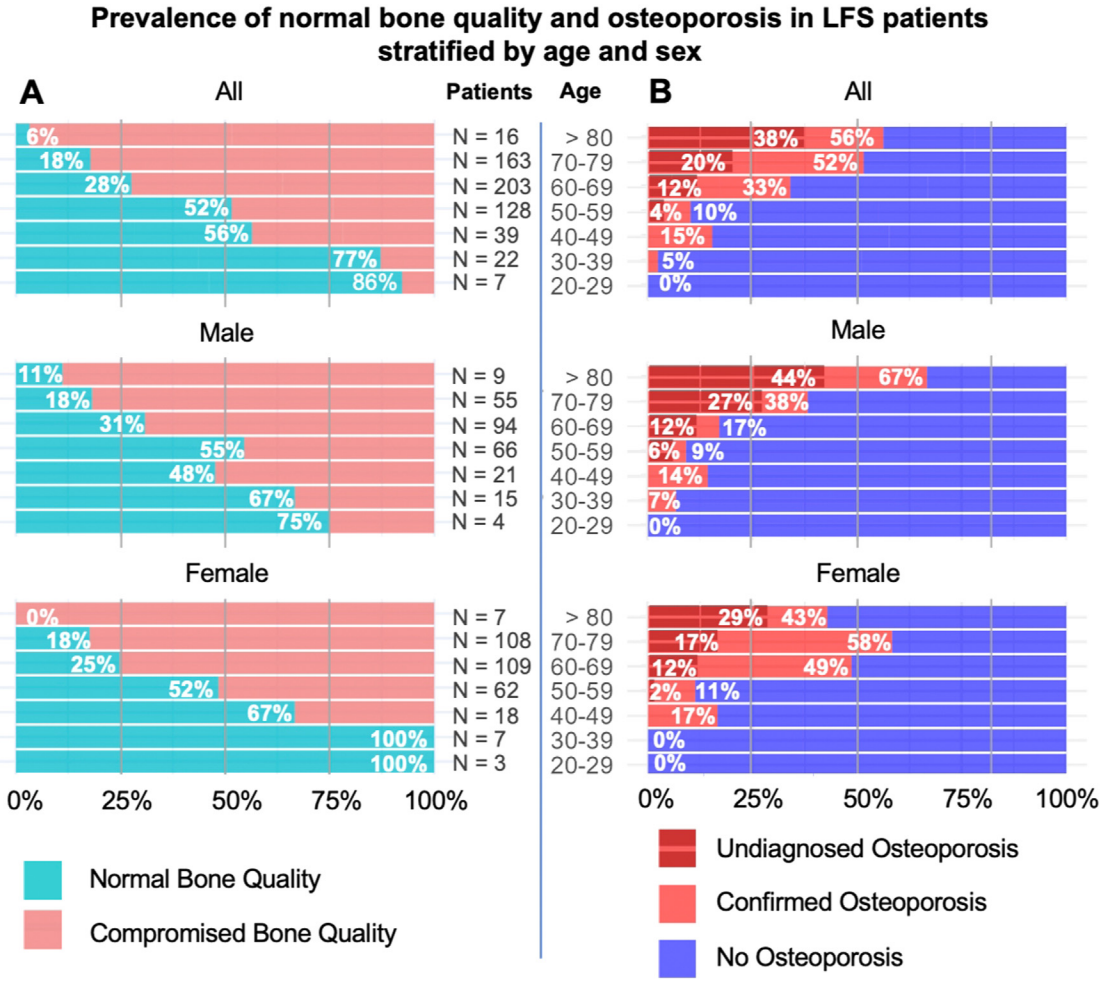

Fig. 3. (A) Overview of the prevalence of normal bone quality defined by BMD ≥ 120 mg/cm^3 and absence of previously diagnosed osteoporosis. (B) Overview of the prevalence of undiagnosed and totally confirmed osteoporosis, defined as BMD < 80 mg/cm^3 or the presence of previously diagnosed osteoporosis.

Discussion

Reliable preoperative identification of cases with impaired bone quality is essential to optimize osteological treatment and surgical management for these LFS patients. We conducted a retrospective, cross-sectional study analyzing qCT-derived vertebral BMD and osteoporosis diagnosis status in patients undergoing LFS to investigate the preoperative prevalence and risk factors for osteopenia, osteoporosis and undiagnosed osteoporosis. Compromised bone quality was present in 66% of patients, increasing from 14% in those aged 20 to 29 years to 94% in patients over 80. Osteoporosis was diagnosed in 31%, with rates ranging from 0% in the youngest group to 56% in the oldest. Among women, 69% had compromised bone quality and 41% had osteoporosis, compared to 63% and 20%, respectively, in men. Undiagnosed osteoporosis was found in 12% of the total cohort, accounting for 37% of osteoporosis cases. Male patients were 4 times more likely to have undiagnosed osteoporosis than females, with 64% of male cases remaining undiagnosed versus 26% in females.

Prevalence of osteoporosis and osteopenia in LFS

In Wright et al.'s U.S. study, among those aged 50 or older, osteoporosis prevalence based on lumbar and femoral DXA, was 10%, and osteopenia was 44%, totaling 54% with compromised bone health. Specifically, in the 60 to 69 age group, the prevalence of osteoporosis was 8% and 44% for osteopenia, while in the 70 to 79 group, osteoporosis was 16% and osteopenia 47%, including both sexes [30].

In our LFS patient cohort, after utilizing preoperative qCT, the prevalence was higher and was 12% for those under 50, and 33% and 52% in the 60 to 69 and 70 to 79 age groups, respectively. Even, when considering only previously diagnosed cases without cases identified by qCT, the prevalence was higher than in the United States general population (21% vs. 8% in 60–69, and 32% vs. 16% in 70–79). Similarly, large differences were observed, when comparing our results to the United States population stratified by gender, e.g. 49% of women and 38% of men aged 60 to 69 undergoing LFS had confirmed osteoporosis, compared to 12% and 3% in the United States general population of the same age group.

The differences between the general population and LFS cohorts lead to 3 distinct interpretations:

1. The prevalence of osteoporosis in LFS patients may be higher than in the general population, therefore lumbar degeneration and disability leading to LFS may be a risk factor for osteoporosis.

In a DXA based study by Chin et al. in Korean patients undergoing major spine surgery [31], 56% and 62% of female patients aged 60-69 and 70-79 had osteoporosis, respectively. In male patients, 9% and 18% aged 60 to 69 and70 to 79 had osteoporosis, respectively. In a recent systematic review of 2,958 patients over the age of 50 undergoing spinal fusion surgery, it was found that approximately 78% had osteopenia or osteoporosis, and 34% with osteoporosis [32]. The authors are not aware of any study reporting a lower than population average prevalence of osteoporosis and osteopenia in LFS patients. Even in young patients in their twenties and thirties undergoing LFS, we observed osteopenia in 14% to 23% of patients.

Mechanistically, disability from spinal degeneration may lead to reduced activity levels, leading to lower loads on the vertebrae, potentially causing disuse osteoporosis. There might be a common biological origin influencing both diminished bone quality and lumbar degeneration leading to LFS. However, the absence of a control group without spine degeneration in our study necessitates further research to validate lumbar degeneration as a possible independent risk factor for osteoporosis. This could potentially justify lower age cut-offs for osteoporosis screening in these patients.

2. Diagnosis of osteoporosis in general practice, based on risk identification and lumbar and femoral DXA, may underestimate the prevalence of osteoporosis, possibly due to lumbar degeneration confounding DXA measurements.

In clinical care, a 10% prevalence of previously undiagnosed osteoporosis in LFS patients aged 50 years or older, has been described [12], which is comparable to our prevalence of 12% undiagnosed osteoporosis, in a cohort including patients younger than 50 years. One major limitation of DXA derived BMD measurements is that they are influenced by the presence of musculoskeletal degenerative findings, such as osteophytes, subchondral sclerosis or vertebral fractures, leading to falsely high BMD estimates despite compromised bone quality [33].

Our analysis showed that female sex was overestimated as a risk factor for osteoporosis, with a discrepancy between previously diagnosed cases (OR 6.1) and confirmed cases (OR 2.67). Additionally, 70% of elderly male patients had undiagnosed osteoporosis, which is significantly higher than the 24% to 29% in comparable female cohorts. These findings are in line with the literature, as male osteoporosis patients receive less timely diagnosis and treatment, have more osteoporosis-related complications and fracture mortality, and are less likely to adhere to therapy [34]. This underscores the need for increased awareness, revised diagnostic protocols for osteoporosis in LFS patients, and new tools to identify otherwise overlooked male osteoporotic patients.

3. qCT-derived trabecular lumbar volumetric BMD may either be more sensitive than DXA or may overestimate the prevalence of osteoporosis in LFS patients.

The classification into normal, osteoporotic and osteopenic bone in this study was performed based on the ACR criteria [21], but there is still a lack of consensus on the optimal thresholding in lumbar qCT derived trabecular volumetric BMD [35]. In spinal surgery, a BMD < 82 mg/cm^3 has been shown to correlate with an enhanced risk for mechanical complications [36], as well as for enhanced risk for osteoporotic vertebral fractures [37], which supports a cut-off around 80 mg/cm^3 from a surgical perspective. Some discordance between DXA and qCT BMD defined osteoporosis diagnosis has been recently described, but with only minor relevance [38]. Furthermore, a recent comparative study in elderly spinal surgery patients and a study in patients over 50 years showed superiority of the lumbar qCT BMD cut-off of 80 mg/cm^3 to the DXA cutoff of a T-Score of −2.5 for the prediction of prevalent osteoporotic vertebral fractures [39,40]. As patients with a diagnosis of osteoporosis usually undergo treatment, we hypothesize that the higher BMDs in previously diagnosed patients are due to treatment. Even if the osteoporosis prevalence in LFS patients might be higher because it is qCT BMD derived, this may be due to better sensitivity for osteoporosis compared to DXA and not a true overestimation of the prevalence [3].

Risk factors for osteoporosis in LFS patients

In our univariable regression analysis, age, female sex, BMI, and vitamin D supplementation were identified as risk factors for osteoporosis, whereas only age and arterial hypertension were linked to undiagnosed osteoporosis. Given that vitamin D is likely administered to osteoporotic patients based on their diagnosis, we excluded it as a predictive factor in the multivariable model. In this model, age and sex were confirmed as independent risk factors for osteoporosis, and age alone predicted undiagnosed osteoporosis, which is in line with general population findings from recent meta-analysis [41].

Male sex was significantly associated with being undiagnosed among osteoporotic patients, but was not predictive of having undiagnosed osteoporosis in the LFS cohort without a history of osteoporosis, most probably due to the lower prevalence of osteoporosis in men compared to women. Nevertheless, as patients with higher BMI and male sex were ad higher odds of being undiagnosed, they might be subjected to a systematically neglected in based on screening decisions guided by female sex and lower BMI as risk factors for osteoporosis.

Recent studies showed that paraspinal muscle degeneration was independently associated with reduced spinal BMD [42,43] and altered bone microstructure [44], indicating that spinal sarcopenia may also contribute to osteoporosis. Despite the broad evidence linking diminished bone quality to postoperative mechanical complications [45], there are only a few, smaller studies that have investigated the presence of undiagnosed osteoporosis prior to LFS [12,46–49], showing comparable prevalence, but did not report independent risk factors. Therefore, this study is the largest analysis of prevalence of undiagnosed and confirmed osteoporosis and the first the describe risk factors for undiagnosed osteoporosis in a cohort of patients undergoing LFS.

Clinical implications

Undiagnosed osteoporosis patients undergoing LFS had significantly lower BMD and were less frequently supplemented with vitamin D then those previously diagnosed, which may lead to an increased risk of complications after LFS. For spinal surgery candidates, the Congress of Neu-

rological Surgeons' guideline mandates preoperative osteoporosis assessment but lacks detailed specifications [23].

Identification of these patients is essential for timely antiosteoporotic treatment to prevent complications. Thus, evidence-based screening algorithms for LFS patients are needed. These should include noninvasive, opportunistic methods such as preoperative MRI or CT-based measurements and targeted DXA or qCT-based BMD measurements, considering the higher prevalence of osteoporosis and osteopenia in LFS patients and the risk of LFS complications in addition to the general risk of osteoporotic fractures in osteoporosis. As male patients and those of higher BMI were more frequently undiagnosed, higher awareness for osteoporosis in this population undergoing LFS seems recommendable. Therefore, future studies are urgently needed to optimize screening decisions for osteoporosis in spinal surgery. Antiosteoporosis therapies, especially osteoanabolic PTH analogs, have been shown to be safely started perioperatively and significantly reduce osseous complications in osteoporotic cases undergoing LFS [6,50,51].

As the prevalence of osteoporosis in this LFS cohort was markedly higher, we advocate for population-based studies, to incorporate lumbar degeneration as a parameter to verify whether it as a risk-factor for osteoporosis.

Male osteoporotic patients and osteoporotic patients of higher BMI were significantly more frequently undiagnosed, which suggests reduced screening awareness in LFS patients not fitting the classic risk factors for osteoporosis. Spine surgeons should remain vigilant for metabolic bone disease in LFS patients and ensure that, at a minimum, general population-based recommendations for DXA screening are followed, while also assessing BMD prior to higher-risk surgical procedures beyond these indications to prevent complications.

When possible, opportunistic screening methods, such as qCT, Hounsfield units, or MRI-derived parameters, could be integrated into the preoperative workup until more robust evidence-based recommendations emerge.

In spine surgical practice, we recommend exhausting these opportunistic screening possibilities for BMD, and advocate for higher awareness for male osteoporosis until more sophisticated screening algorithms are available.

Limitations

The cross-sectional design of the study and the lack of nondegenerative spine cohorts limit the ability to establish a causal relationship or direction of influence between low BMD and spine degeneration. The lack of information on whether and how osteoporosis screening and diagnosis were performed in the LFS cohort prior to presentation at our center prohibits a comparative analysis of the accuracy of DXA and qCT-based osteoporosis diagnoses, or to differentiate between neglected screening and missed diagnosis by other imaging modalities. Given the relative uniform degree of disability in the study sample, likely a consequence of selection bias based on surgical indication, the results' relevance to other populations is limited. The medical history did not include all parameters necessary for FRAX scoring, so a comparison to this established osteoporotic fracture risk tool was not possible. Since osteoporosis treatment status was not analyzed in this study, it is not possible to determine to what extent the nonosteoporotic BMD measurements in osteoporotic patients are due to different treatment regimens. The generalizability of our findings to other bone regions, e.g. femoral neck BMD, is restricted due to the study's focus on the lumbar BMD. Although several confounding variables were accounted for in the logistic regression models, others such as genetic factors, dietary habits, and lifestyle choices and socioeconomic status that could substantially impact the prevalence of osteoporosis and the accessibility of diagnostics, were not considered. Postoperative outcomes were also not analyzed, as the follow-up data collection is ongoing and adherence to treatment and subsequent BMD measurements were not prospectively recorded. Thus, future studies are necessary to explore the long-term impact of undiagnosed osteoporosis on surgical outcomes. It is crucial to acknowledge the study's limitations when interpreting the results and implementing them in wider clinical settings.

Conclusions

This study revealed a high prevalence of low BMD in LFS patients, along with a significant proportion of previously undiagnosed osteoporosis. Despite female patients showing a higher prevalence of osteoporosis prior to LFS, male patients were at increased risk of being undiagnosed. Further research is needed to establish optimal screening strategies in LFS patients, considering both surgical complication risks and osteoporotic fracture prevention, and to evaluate if osteopenic LFS patients might benefit from medical management in addition to adapted surgical planning.

Ethical approval

The study was approved by the HSS' Institutional Review Board (IRB), under the approval number (IRB#2014-084 and 2015-237).

Data availability statement

The underlying data is available on reasonable request to the corresponding author.

Author contributions

Conception and design: Paul C. Köhli Acquisition of data: Erika Chiapparelli, Lukas Schönnagel, Roland Duculan, Ali E. Güven, Paul C. Köhli, Jan Hambrecht Analysis and Interpretation of data: Paul C. Köhli, Jan Hambrecht, Ellen Otto, Arne Kienzle, Alexander P. Hughes Drafting the article: Paul C. Köhli. Critically revising the article: all authors. Preparation of Graphical Content: Paul C. Köhli. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Alexander P. Hughes. Statistical analysis: Paul C. Köhli, Jiaqi Zhu. Administrative/technical/material support: Jennifer Shue, Study supervision: Alexander P. Hughes.

Declaration of competing interests

One or more of the authors declare financial or professional relationships on ICMJE-NASSJ disclosure forms.

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Supplementary materials

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