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Clinical Study

BMI and gender increase risk of sacral fractures after multilevel instrumented spinal fusion compared with bone mineral density and pelvic parameters

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Abstract

BACKGROUND CONTEXT: Sacral fractures are a rare but potentially devastating complication. Long-fusion constructs, including the sacrum, that do not extend to the pelvis may result in sacral fractures. Besides established risk factors including gender, age, and number of levels fused, body mass index (BMI), pelvic parameters, and bone mineral density (BMD) have also been proposed as potential risk factors for postoperative sacral fractures. The literature supporting this, however, is limited.
PURPOSE: The aim of the present study was to assess whether preoperative pelvic parameters, BMI, or BMD of patients with sacral fracture are different compared with age, gender, and fusion level-matched non-fracture controls.
STUDY DESIGN/SETTING: This is a case-control study.
PATIENT SAMPLE: Patients undergoing posterior instrumented fusion at a single academic institution between 2002 and 2016 were included in the study.
OUTCOME MEASURES: The outcome measure was occurrence of a postoperative sacral fracture.

FDA device/drug status: Not applicable.

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METHODS: Patients with sacral fractures after posterior instrumented spinal fusion, including the sacrum, were retrospectively identified and matched 2:1 with non-fracture controls based on gender, age, and number of levels fused. Patients with concurrent spinopelvic fixation or missing preoperative computed tomography (CT) imaging were excluded. Preoperative sagittal balance was assessed using lateral radiographs. Quantitative computed tomography (QCT) assessment included standard measurements at L1/L2 and additional experimental measurements of the S1 body and sacral ala.
RESULTS: Twenty-one patients with sacral fracture were matched to non-fracture controls. The majority of the patients with sacral fracture was female (76.2%) and of advanced age (mean 66.4 years). Fracture and control groups were well matched with respect to gender, age, and number of levels fused. Standard measurements at L1/L2 showed no significant difference in BMD between the fracture and the control groups (109.9 mg/cm^3 vs. 116.4 mg/cm^3, p=.414). Similarly, there was no significant BMD differences between the groups using the experimental measurements of the S1 body (183.6 mg/cm^3 vs. 176.2 mg/cm^3, p=.567) and the sacral ala (8.9 mg/cm^3 vs. 4.8 mg/cm^3, p=.616). Mean preoperative pelvic incidence-lumbar lordosis mismatch and pelvic tilt were not significantly different between the groups. Univariate conditional logistic regression analysis revealed that the odds of experiencing a sacral fracture was approximately six times higher for obese patients compared with normal or underweight patients. After controlling for BMI in multivariate conditional logistic regression models, BMD was still not significantly associated with the odds of experiencing sacral fractures.
CONCLUSIONS: To our knowledge, this is the first study to assess the association of preoperative BMD measured by QCT, pelvic parameters, and BMI with postoperative sacral fractures in a large patient cohort. Interestingly, our data do not show any difference in preoperative pelvic parameters and BMD between the groups. This is in line with previous reports that indicate only a few patients with sacral fracture after fusion surgery have clear evidence of osteoporosis. Bone mineral density as a measure of bone quantity, rather than bone quality, may not be as important in these fractures as previously thought. Obesity, however, was associated with higher odds of experiencing postoperative sacral fractures. The present study thereby challenges the widespread concept that obesity is a protective factor against fractures in the elderly. In summary, our results suggest that BMI and gender, more than pelvic parameters and BMD, are risk factors for postoperative sacral fractures.

Keywords: Bone mineral density; Instrumented spinal fusion; Obesity; Quantitative computed tomography; Risk factor; Sacral fracture

Introduction

Sacral fractures after instrumented spinal fusion are a rare but potentially devastating complication. Long-fusion constructs, including the sacrum, that do not extend to the pelvis can cause a redistribution of forces through the sacrum, which may result in sacral fractures [1–3]. Besides established risk factors including gender, age, and number of levels fused, bone mineral density (BMD), pelvic parameters, and body mass index (BMI) have also been proposed as potential risk factors for postoperative sacral fractures [1–4].

Osteoporosis is associated with insufficiency fractures at different anatomical locations [5]. It has also been proposed as an important risk factor for sacral fractures after spinal fusion; however, data supporting this are primarily anecdotal [6–8]. More importantly, previous larger reports indicate that only a few patients sustaining sacral fractures after fusion surgery had clear evidence of osteoporosis [2,3].

Besides BMD, abnormal spinopelvic alignment might also play a role in the development of postoperative sacral fractures. Pelvic incidence-lumbar lordosis (PI-LL) mismatch, one of the main indicators of appropriate spinal alignment, has been proposed as a possible risk factor [4].

Obesity is generally considered a protective factor against osteoporotic fractures [9]. However, previous case reports and series indicate that many of the patients with sacral fracture had an increased BMI [1,2,10]. There is a paucity of evidence in the spine literature assessing the influence of preoperative patient factors including BMI, pelvic parameters, and BMD on the development of postoperative sacral fractures.

The aim of the present study was thereby to assess whether preoperative pelvic parameters, BMI, or BMD of patients with sacral fracture are different compared with age, gender, and fusion level-matched non-fracture controls. For the purpose of the present study, a novel quantitative computed tomography (QCT) measurement method of the sacrum was used and is described in detail.

Materials and methods

This study was approved by the institutional review board at our hospital.

Subjects

We retrospectively identified patients with sacral fractures after posterior instrumented spinal fusion including the sacrum. All patients were treated at our institution by a fellowship-trained spinal surgeon between 2002 and 2016. The identified fracture cases were then matched (with

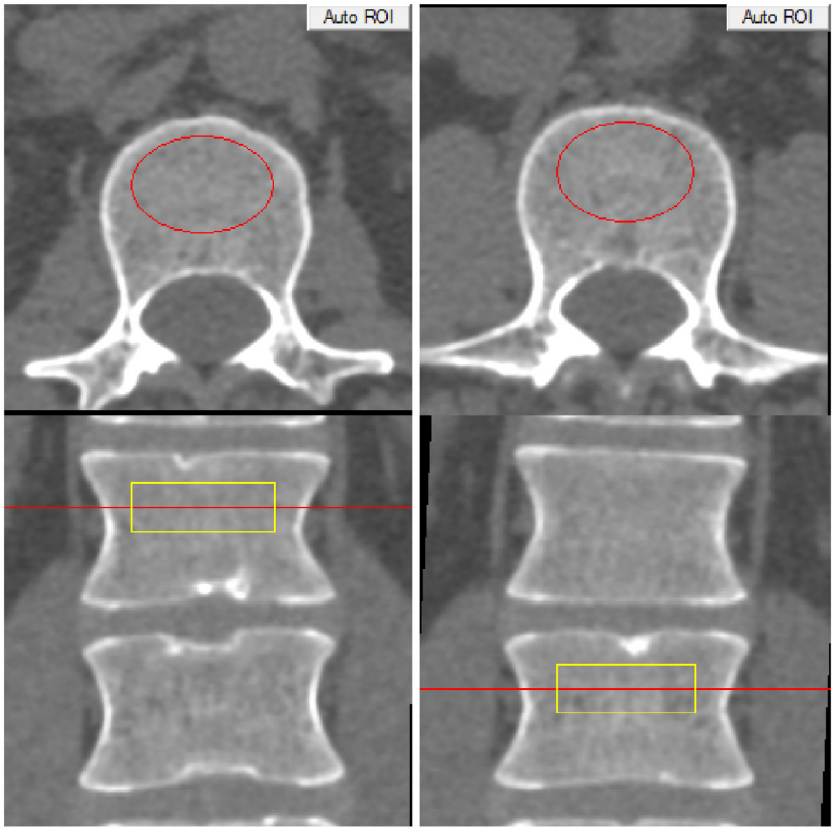

Fig. 1. Axial and coronal view of the L1 and L2 region of interest (ROI).

replacement) 2:1 to non-fracture controls based on gender, age, and number of levels fused. Minimum required postoperative follow-up was 6 months. Body mass index, preoperative pelvic parameters, and BMD were not matched to evaluate their effect on the risk of sacral fractures. Patients with concurrent spinopelvic fixation or missing preoperative computed tomography (CT) imaging were excluded. Inpatient and outpatient medical records were reviewed. Demographic and clinical data included age, gender, BMI, and operative details. The following BMI ranges were used: underweight (<18.5 kg/m^2), normal weight (18.5–25 kg/m^2), overweight (25–30 kg/m^2), and obese (>30 kg/m^2).

Assessment of sagittal balance

Radiological assessment of sagittal balance was performed using preoperative lateral radiographs. Measurements of pelvic incidence, lumbar lordosis, and pelvic tilt (PT) were done using the picture archiving and communication system. The PI-LL mismatch was calculated [11].

Measurement of BMD

Bone mineral density measurements were performed by analyzing preoperative CT scans with Mindways QCT Pro (Mindways Software, Inc, Austin, TX, USA). All preoperative CT scans were performed without a bone density-appropriate phantom at the time of the examination. To obtain BMD information contained on the preoperative CT scans, a newly developed method called asynchronous QCT was applied. This method does not require a phantom to be present during the patient examination. Asynchronous QCT uses quality assurance phantom data obtained independently from the patient scan to convert the observed Hounsfield units (HU) to BMD values. The HUs were divided by the appropriate calibration factor to derive a BMD value in mg/cm^3 [12]. The calibration data for the various CT scanner models used over the study period were provided by Mindways (Mindways Software, Inc).

The Mindways QCT Pro software (Mindways Software, Inc) was used to calculate an HU value by placing an elliptical region of interest limited to the medullary space of each vertebral level that excluded the adjacent cortical bone. According to the recommended methodology, for each area the largest possible region of interest was selected. Standard QCT measurements were performed at the L1 and L2 vertebra (Fig. 1), which is a conventional method to assess BMD in the clinical setting in addition to dual-energy x-ray absorptiometry (DEXA). The American College of Radiology defines the QCT spine BMD thresholds at L1/L2 as follows: osteoporosis (BMD<80 mg/cm^3), osteopenia (80 mg/cm^3≤BMD≤120 mg/cm^3), and normal (BMD>120 mg/cm^3) [13].

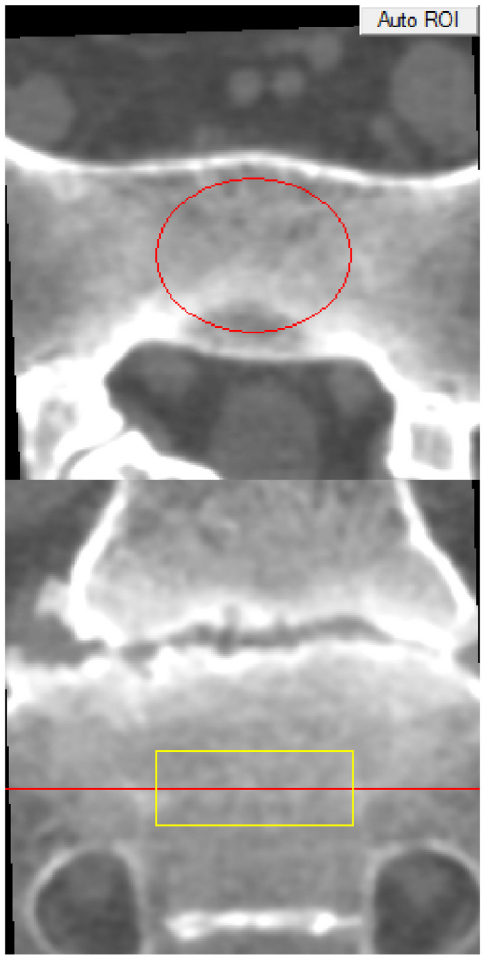

Fig. 2. Axial and coronal view of the S1 body region of interest (ROI).

After customizing the QCT software configurations to allow measurements of the S1 body (Fig. 2) and the left and right sacral ala (Fig. 3), experimental BMD measurements of the sacrum were performed. All measurements were performed by one investigator trained on the technique and reviewed by an attending radiologist. As there were no significant BMD differences between the L1 and L2 levels, measurements from those two levels were averaged. The same method was applied to the left and right sacral ala BMD values.

Statistical analysis

Descriptive statistics were summarized by case status using Fisher exact test for categorical variables, paired Student *t* test for normally distributed continuous variables, and the Wilcoxon rank-sum test for non-normally distributed continuous variables. Conditional logistic regression was performed to examine the association between BMD and risk of sacral fractures to account for the matched study design. The statistical significance level was set at $p<.05$. All the analyses were carried out in Stata 14.0 SE (StataCorp, College Station, TX, USA).

Results

Twenty-one patients with sacral fracture were matched to non-fracture controls. Patients underwent the index procedure for a wide variety of indications including degenerative kyphoscoliosis, spondylosis, degenerative disc disease, spinal stenosis with spondylolisthesis, and symptomatic pseudarthrosis. The mean time from index surgery to fracture was 87 days, with 76% of the fractures occurring within the first 3 months postoperatively. Patients with sacral fracture typically presented with postoperative axial low back or buttock pain. Notably, the majority of the patients with sacral fracture was female (76.2%), of advanced age (mean, 66.4 years), and underwent multisegmental fixation with a mean of 5.6 levels fused. Because gender, age, and number of levels fused are well-established risk factors for postoperative sacral fractures, we matched our study groups by these three variables. Demographic data of the fracture and control groups are detailed in Table 1. Fracture and control groups were well matched with respect to gender, age, and number of levels fused.

A statistically significant difference was found between fracture versus non-fracture groups in BMI distribution (underweight/normal 28.6% vs. 33.3%, overweight 19.0% vs. 54.8%, obese 52.4% vs. 11.9%, p=.002) (Table 1).

Mean preoperative PI-LL mismatch was not different between the groups (fracture group 14.1° vs. control group 15.8°, p=.693). There was also no difference in PT between the fracture and the control groups (26.3° vs. 26.2°, p=.981) (Table 1).

Standard QCT measurements of the L1/L2 average showed no significant BMD difference between the fracture and the control groups (109.9 mg/cm^3 vs. 116.4 mg/cm^3, p=.414). Similarly, there was no significant difference between the fracture and control groups using the experimental BMD measurements of the S1 body (183.6 mg/cm^3 vs. 176.2 mg/cm^3, p=.567) and the average of the left and right sacral ala (8.9 mg/cm^3 vs. 4.8 mg/cm^3, p=.616) (Table 1, Fig. 4).

Univariate conditional logistic regression analysis revealed BMD of the L1-L2 body, the left and right sacral ala, and the S1 body were not associated with the odds of experiencing sacral fractures. However, the odds of experiencing a sacral fracture was approximately six times higher for obese patients compared with normal or underweight patients (Table 2).

After controlling for BMI in multivariate conditional logistic regression models, BMD of the L1-L2 body, the left and right sacral ala, and the S1 body were not significantly associated with the odds of experiencing sacral fractures (Table 3).

Discussion

To our knowledge, this is the first study to assess the association of preoperative pelvic parameters, BMI, and BMD measured by QCT with postoperative sacral fractures in a large

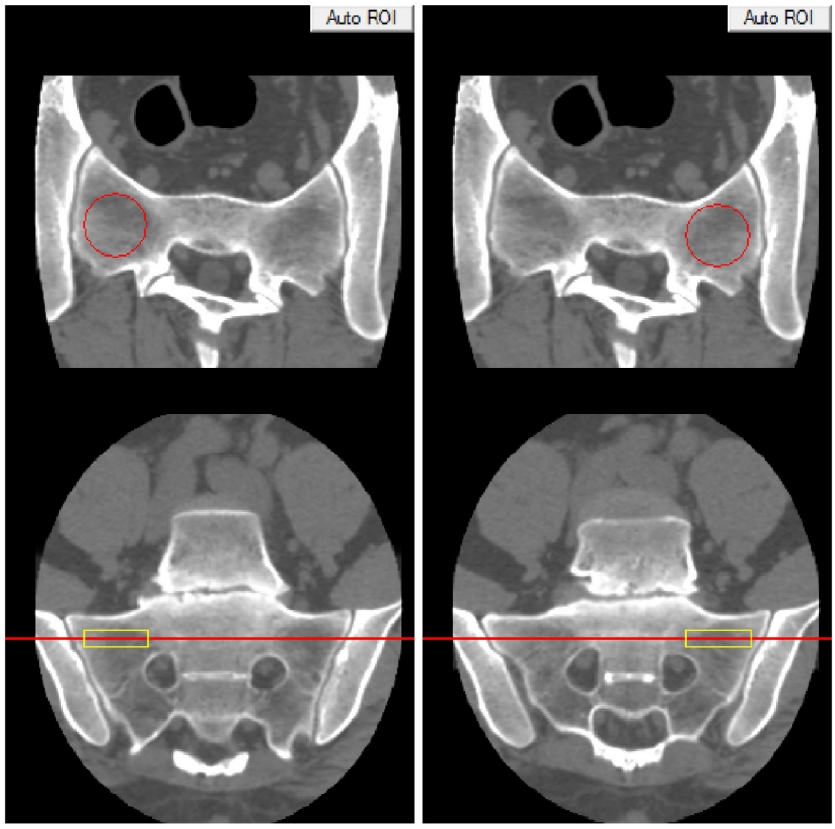

Fig. 3. Axial and coronal view of the right and left sacral ala region of interest (ROI).

Table 1
Description of the study population

Characteristics	Fracture group N=21	Non-fracture group N=42	p-Value
Gender, N (%)			
Female	16 (76.2)	32 (76.2)	
Male	5 (23.8)	10 (23.8)	—*
Age, y, mean (SD)	66.4 (8.5)	65.3 (7.9)	.601*
No. of levels fused, mean (SD)	5.6 (3.0)	5.1 (2.4)	.517*
BMI, mean (SD)	30.0 (7.4)	26.4 (5.0)	.027
BMI, %			
Underweight/Normal	6 (28.6)	14 (33.3)	
Overweight	4 (19.0)	23 (54.8)	
Obese	11 (52.4)	5 (11.9)	.002
PI-LL, mean (SD)	14.1 (14.4)	15.8 (15.4)	.693
PT, mean (SD)	26.3 (9.3)	26.2 (9.9)	.981
L1, mean (SD)	109.9 (32.5)	116.9 (27.5)	.370
L2, mean (SD)	109.9 (41.6)	115.9 (27.6)	.491
Average L1-L2, mean (SD)	109.9 (35.7)	116.4 (26.6)	.414
Ala right, mean (SD)	8.8 (37.6)	7.6 (28.8)	.887
Ala left, mean (SD)	8.9 (33.4)	1.9 (28.5)	.391
Average ala, mean (SD)	8.9 (35.0)	4.8 (27.8)	.616
S1, mean (SD)	183.6 (44.0)	176.2 (50.8)	.567

y, years; SD, standard deviation; BMI, body mass index; PI-LL, pelvic incidence-lumbar lordosis mismatch; PT, pelvic tilt.

* Matched variables.

patient cohort. Our data do not show any significant difference in preoperative pelvic parameters or BMD using both standard and experimental measures between the study groups. Obesity, however, was associated with approximately six times higher odds of experiencing postoperative sacral fractures. In addition, more than three quarters of our patients with fracture were women, confirming female gender is a major risk factor.

There is a paucity of literature on sacral fractures after posterior instrumented spinal fusion. To date, primarily case reports [8,14–18] and case series [1–3,6,7,10,19–21] have been published on this topic. In general, sacral fractures are considered an uncommon complication after fusion surgery. Meredith et al. [3] reported an overall incidence of 6.1% in patients undergoing instrumented posterior spinal fusion including the

Table 2
Univariate conditional logistic regression

Parameters	Odds ratio (95% CI)	p-Value
L1-L2 average	0.99 (0.97, 1.01)	.401
Ala left and right average	1.01 (0.99, 1.03)	.579
S1	1.00 (0.99, 1.02)	.589
BMI		
Underweight/Normal	Ref	
Overweight	0.42 (0.10, 1.76)	.232
Obese	5.99 (1.19, 30.18)	.030

CI, confidence interval; BMI, body mass index; Ref, reference group.

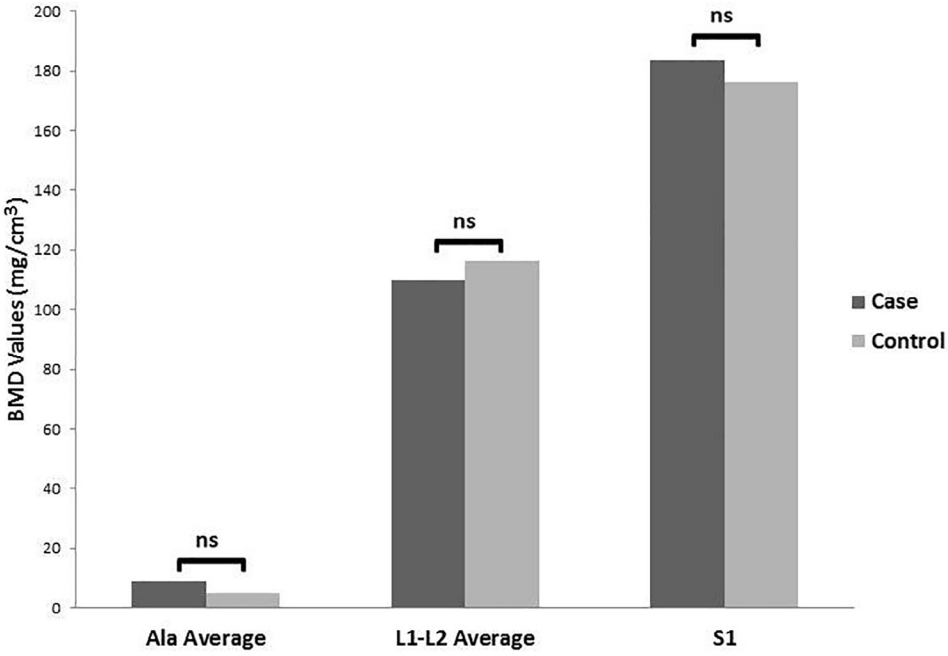

Fig. 4. Mean values are shown for BMD measurements of the L1-L2 body, the sacral ala, and the S1 body for the fracture and control groups. BMD, bone mineral density, ns, not significant.

sacrum. However, Wang et al. [18] suggested that this entity might be underreported in the literature as most of these fractures are not visible on plain radiographs, and fracture healing without intervention can occur.

Various risk factors for sacral fractures after spinal fusion have been proposed. Female gender and advanced age are commonly reported. Consistent with previous reports [1–4,6,7,10], our sacral fracture cohort was mainly female (76.2%) and of advanced age (mean 66.4 years). Additionally, the majority of patients underwent multisegmental fixation, with a mean of 5.6 levels fused. The long moment arm of these multilevel fusion constructs may result in increased forces through the sacrum leading to fracture [4]. To take the aforementioned points into account, the identified fracture cases were matched to non-fracture controls based on gender, age, and number of levels fused in the present study.

Table 3
Multivariate conditional logistic regression

	Odds ratio (95% CI)	p-Value
L1-L2 average	0.99 (0.97, 1.01)	.335
BMI		
Underweight/Normal	Ref	
Overweight	0.42 (0.10, 1.79)	.240
Obese	6.45 (1.19, 35.00)	.031
S1	1.01 (0.99, 1.02)	.509
BMI		
Underweight/Normal	Ref	
Overweight	0.35 (0.07, 1.65)	.184
Obese	5.65 (1.11, 28.88)	.037
Ala average	1.00 (0.98, 1.03)	.880
BMI		
Underweight/Normal	Ref	
Overweight	0.40 (0.09, 1.78)	.230
Obese	5.79 (1.08, 30.87)	.040

CI, confidence interval; BMI, body mass index; Ref, reference group.

Osteoporosis is one of the most commonly quoted risk factors for sacral fractures after spinal fusion. However, this is often only a presumption made by various authors because of the female gender and postmenopausal age of most patients with fracture [2,10]. In many cases, diagnostic measurements by DEXA are unavailable and information on the severity of the metabolic bone disease is incomplete. More importantly, several case series indicate that only a few patients sustaining sacral fractures after fusion surgery have clear evidence of osteoporosis. In the series by Vavken and Krepler [6], two of the four reported cases had sacral fractures despite normal bone density measurements. Similarly, in the largest series of 24 patients with sacral fracture by Meredith et al. [3], several patients without osteoporosis had postoperative fractures of the sacrum. In another series by Wilde et al. [2], only 4 of 23 patients who sustained sacral fractures had clear evidence of osteoporosis. In line with these previous reports, our data do not show any significant association of preoperative BMD and the occurrence of sacral fractures.

Given the conflicting results in the current literature, we put a special emphasis on BMD assessment in the present study. The clinically used QCT measurements of the L1 and L2 vertebra were performed to globally assess the bone density status of our patients. To assess possible regional differences, experimental measurements of the sacrum were performed as well. Our results of the BMD measurements at L1/2, the S1 body, and the sacral ala are largely in agreement with the results by Hoel et al. [22]. In this recent study, they reported mean CT attenuations of 224 HU of the S1 body,

165 HU of the L1 vertebra, and 24 HU of the central sacral ala. A direct comparison of their results, however, is difficult because Hoel et al. reported on HU rather than BMD in mg/cm^3. In addition, the mean patient age in their study was 47 years and thereby almost 20 years younger than that of our patient population [22]. A continuous decrease in BMD with age after reaching the peak bone mass around the age of 25 has been described [23].

The present study showed significant regional differences in BMD within the lumbosacral spine. The BMD of the S1 body (fracture group: 183.6 mg/cm^3, control group: 176.2 mg/cm^3) was significantly higher than that of the sacral ala (fracture group: 8.9 mg/cm^3, control group: 4.8 mg/cm^3) and the L1/L2 average (fracture group: 109.9 mg/cm^3, control group: 116.4 mg/cm^3). This regional variation is consistent with previous studies assessing the BMD throughout various regions of the sacrum [22–24]. As described by de Peretti et al., the low BMD of the sacral ala is related to the high marrow fat and the few spongy trabeculae in this anatomical region [24,25]. It has been shown that the high fat content of this "fatty sphere" or "ala void" region might also result in an underestimation of trabecular BMD with QCT, which might explain the very low sacral ala BMD observed in the present study [24,26].

Lumbar spine BMD strongly correlates with BMD of the sacrum [22,24]. In line with this finding, both of our measurements (lumbar and sacral) showed no association between preoperative BMD and sacral fractures after instrumented fusion. Bone mineral density is often used as a surrogate marker for overall bone health. Nonetheless, BMD is a quantitative rather than a qualitative marker. To assess bony microarchitecture and tissue quality, a bone biopsy is required [27].

Besides the evaluation of BMD, we also assessed the role of abnormal spinopelvic alignment in the development of postoperative sacral fractures. Odate et al. retrospectively reviewed all patients undergoing lumbosacral fusion at their institution. Out of a total of 116 patients, they identified 5 sacral fracture cases, all of whom were female patients. In their patient cohort, the fracture group had larger mean preoperative pelvic incidence-lumbar lordosis mismatch compared with the non-fracture group. They did not find any difference in preoperative PT between the groups [4]. In contrast to the present study, our results show no difference in both preoperative pelvic incidence and pelvic incidence-lumbar lordosis mismatch. Possible explanations for the difference between the study by Odate et al. and the results presented here include the use of a different patient sample and a larger fracture group in our study (21 cases vs. 5 cases).

Obesity has traditionally been considered a protective factor against osteoporotic fractures. However, recently there is growing evidence that challenges this widespread concept. Some studies even suggest that obesity might be a risk factor for fractures at various anatomical sites. Possible mechanisms include the production of inflammatory cytokines (interleukin 6 and tumor necrosis factor alpha) in excessive abdominal fat and changes in 25-hydroxyvitamin D levels (fat-soluble vitamin), which might lead to a reduction in bone strength [9].

In the present study, the odds of experiencing a sacral fracture was approximately six times higher for obese patients compared with normal or underweight patients. This study finding is similar to previous case series that indicate many patients with sacral fracture had an increased BMI [1,2,10]. Besides the biochemical mechanisms leading to reduced bone strength, obesity in connection with long fusion constructs might biomechanically result in increased forces through the sacrum that can ultimately lead to sacral fractures [1,2].

Several previous biomechanical studies assessed the pull-out strength and insertion torque of S1 screws. Biomechanical advantages of bicortical over unicortical S1 screws have been reported [28–30]. There were no differences in sacral fixation between our study cohorts, and bicortical fixation was obtained for both groups.

The present study has a number of unique strengths. First, the study design allowed us to match the groups on established risk factors (gender, age, and number of levels fused) and to assess for additional previously proposed risk factors. In contrast to previous studies, BMD information was available for the entire patient population because of the use of QCT rather than DEXA. Most importantly, with 21 sacral fracture cases, this is the most comprehensive case-control study on this topic in the current literature.

The present study has several limitations. Bone mineral density measurements with DEXA were not available in enough patients to directly compare the two measurement methods. However, previous studies show correlations between these two modalities, with some authors even suggesting CT-based evaluation as the preferred method of evaluation over DEXA because of inherent shortcomings of DEXA in the lumbar spine [22,31]. An additional limitation of the present study is the unavailability of information about factors affecting bone quality such as laboratory markers of the patients, including vitamin D, parathyroid hormone, bone turnover markers, and metabolic bone disease therapeutics. Furthermore, follow-up time was not matched between the cohorts. However, given that the vast majority of the fractures occurred within the first 3 months postoperatively, we established a minimum postoperative follow-up of 6 months. Lastly, both of our cohorts included patients with various number and type of interbody devices (PLIF, TLIF, LLIF, ALIF) and graft materials (ICBG, bone marrow aspirate, allograft, local bone, BMP) used. Although we matched the cohorts on gender, age, and number of posterior levels fused, due to sample size, we were unable to control for interbody and graft material usage.

In conclusion, our data do not show any difference in preoperative pelvic parameters or BMD between the groups. This is in line with previous reports that indicate only a few patients with sacral fracture after fusion surgery have clear evidence of osteoporosis. Bone mineral density as a measure of bone quantity, rather than bone quality, may not be as important in these fractures as previously thought. Besides BMD contributing to bone strength and fracture risk, qualitative

markers including micro- and macro-architecture, material properties, and bone turnover might play a role in this specific fracture type [32,33]. Interestingly, obesity was associated with approximately six times higher odds of experiencing postoperative sacral fractures. The present study thereby challenges the widespread concept that obesity is a protective factor against fractures in the elderly. In addition, more than three quarters of our fracture patients were women, which confirms that female gender is a major risk factor. In summary, our results suggest that BMI and gender, rather than pelvic parameters and BMD, are risk factors for postoperative sacral fractures.

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