Association of bone mineral density with reoperation rate following instrumented lumbar spinal fusion: a retrospective cohort and case-control study

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Research article

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Abstract

Background Low bone mineral density (BMD) is believed to influence the outcome of instrumented spinal surgery and can lead to reoperation. Purpose of this retrospective cohort and case-control study was to investigate the association of BMD with the risk of reoperation following instrumented lumbar spinal fusion (LSF).

Methods For the cohort analysis, 81 patients were included who received LSF with and without polymethyl methacrylate (PMMA)-augmentation. For the case-control analysis, 18 patients who had reoperation following LSF were matched to 26 patients who did not have reoperation (matching criteria: sex, age ± 5 years, fused levels, and augmentation). Opportunistic BMD screening was performed in perioperative CT scans using asynchronous calibration. Mean BMD was compared between patients with and without reoperation in augmented and non-augmented surgeries.

Results In the cohort analysis, prevalence of osteoporosis (BMD < 80 mg/cm³) was 29% in non-augmented and 85% in augmented LSF. Seven of 48 patients with non-augmented (15%) and 4 of 33 patients with augmented LSF (12%) had reoperation. In non-augmented LSF, patients with reoperation had significantly lower BMD than patients without reoperation ($p = 0.005$). In the case-control analysis, patients with reoperation presented numerically lower BMD of 78.8 ± 33.1 mg/cm³ than patients without reoperation with BMD of 89.4 ± 39.7 mg/cm³ ($p = 0.357$).

Conclusions Prevalence of osteoporosis in patients undergoing LSF is relatively high. Patients with reoperation following LSF showed slightly lower BMD compared to matched patients without reoperation, but the difference was not statistically significant. Opportunistic BMD screening in preoperative CT is feasible and can provide valuable information about osteoporotic bone status.

Background

Decreased bone mass is the main characteristic of osteoporosis leading to an increased risk of fractures (1). Osteoporosis is the most common metabolic bone disease with 10% prevalence for people aged 50 years and older; the pre-stage (osteopenia) has a prevalence of 40% in the same age group (2). The most common manifestation are osteoporotic vertebral compression fractures (3), which may require surgery with spinal fusion (4–6). The indications for surgical stabilization are similar in osteoporotic and non-osteoporotic patients (7). Osteoporosis is one predisposing factor for degenerative spine disease and micro-instability. On the other hand, limited mobility due to spinal degeneration is a major predisposing factor for osteoporosis. Consequently, the prevalence of osteopenia or osteoporosis in patients undergoing spinal stabilization has been shown to be relatively high (7–9). Vice versa, patients suffering from osteoporosis are more likely to receive surgical treatment by spinal fusion.

Studies over the last three decades continually report failure rates of 13 to 19% for instrumented fusion of the lumbar spine (10–13). There is limited evidence from *in-vivo* studies that associate low bone density with an increased risk of complications and surgical failure rates (14,15), whereas many biomechanical

studies concerning this topic exist (16–20). Surgical failure may be due to impaired screw fixation or purchase (14,21,22), interbody cage subsidence (23), junctional kyphosis adjacent to the instrumented levels (24,25), or reduced osteogenic potential (26). In summary, osteoporosis is believed to be an independent risk factor for instrumentation failure (27), and hence for short- and long-term revision surgery. Therefore, successful instrumented surgery in the osteoporotic spine is especially challenging. Preoperative bone mineral density (BMD) assessment objectifies doubts about bone substance, thus allowing to acknowledge this challenge in the surgical planning process. A survey among spine surgeons showed that prior to instrumented fusion only 44% routinely obtained dual-energy X-ray absorptiometry (DXA) examinations if osteoporosis was suspected (27). Supplementary DXA examinations may become obsolete if volumetric BMD can be opportunistically assessed in preoperative CT imaging. The feasibility and validity of opportunistic BMD screening in existing CT data has been extensively shown (22,28–34).

We carried out a restrospective cohort and a case-control analysis to investigate whether reduced BMD is associated with an increased rate of reoperations following elective lumbar spinal fusion (LSF) and if this association is dependent on the use of polymethyl methacrylate (PMMA)-augmentation.

Methods

Retrospective cohort analysis

We reviewed 1441 consecutive patients who had undergone a neurosurgical operation involving the lumbar spine in our institution in the years 2010 to 2014. We only included patients who had primary elective LSF with either a non-augmented rigid pedicle screw-rod system (Pangea Spine System; Synthes, West Chester, PA, USA) or a rigid system with PMMA-augmented pedicle screw fixation (Expedium, Viper, Matrix and Pangea Spine Systems; Synthes, West Chester, PA, USA; or CD Horizon Longitude Fixation System; Medtronic, Minneapolis, MN, USA). We excluded patients with vertebral neoplasia, without a CT scan in the institution’s imaging database and with non-elective surgeries. Indications for elective LSF were related to degenerative spine disease (spondylolisthesis, spondylolysis, and/or spinal stenosis). Following this algorithm 33 patients with PMMA-augmented LSF and 48 patients with non-augmented LSF were identified (Figure 1). Sociodemographic data and information about index and revision surgeries were extracted from patient files and neurosurgical reports. Seven patients with non-augmented LSF and 4 patients with augmented LSF encountered complications which led to revision surgery (Table 1, Figure 2). Reoperations after immediate surgery related complications, such as misplaced pedicle screws in 2 cases, were not taken into account.

[Figure 1]

Table 1: Complications after lumbar spinal fusion in the retrospective cohort analysis stratified according to the surgical technique.

	PMMA-augmented		Non-augmented	
Complication	n	Reoperation interval, mean (range)	n	Reoperation interval, mean (range)
Instrumentation failure	1	13.1 months	3	21.0 (9.4–43.7) months
Adjacent segment degeneration	2	22.7 (17.7–27.6) months	3	39.9 (18.7–52.8) months
New fracture	1	2.4 months	1	22.4 months
Misplaced pedicle screw			2*	13 (2–24) days

*Reoperations after these complications were not taken into account. PMMA, polymethyl methacrylate

[Figure 2]

Case-control analysis

Eighteen patients with reoperation following LSF were matched by sex, age ± 5 years, fused levels, and use of PMMA-augmentation to 26 patients without reoperation. Again, we only included patients who had primary elective LSF for indication related to degenerative spine disease (spondylolisthesis, spondylolysis, and/or spinal stenosis) with either a non-augmented rigid pedicle screw-rod system or a rigid system with PMMA-augmented pedicle screw fixation. In the hospital's records, patients without reoperation did not present sensory or motor deficits or severe pain at last visit after a median follow-up of 154 days (range 5 days – 5.98 years).

Multidetector computed tomography image acquisition

Preoperative or immediate postoperative CT scans were used for opportunistic BMD screening. CT scans were performed on three multidetector computed tomography (MDCT) scanners in the same hospital (Philips Brilliance 64, Philips Medical Care, Best, The Netherlands; Siemens Somatom Definition AS+ and Definition AS, Siemens Healthineers, Erlangen, Germany), partly with administration of intravenous contrast medium (Imeron 400, Bracco, Konstanz, Germany) depending on the clinical indication for imaging. Image data was acquired in helical mode with a peak tube voltage of 120 kVp for standard and 140 kVp for postmyelography studies.

Opportunistic BMD screening

Volumetric BMD (in mg/cm³) of trabecular bone of at least one lumbar vertebra was opportunistically assessed. Therefore, X-ray attenuation in Hounsfield units (HU) had to be converted to BMD. HU-to-BMD conversion equations for the MDCT scanners used in this study were calculated by asynchronous

calibration as reported in a previous study (34). For postmyelography studies with 140 kVp tube voltage, another previously reported conversion equation was used (22). For contrast-enhanced CT scans, BMD correction offsets for arterial (−8.6 mg/cm³) and portal-venous contrast phase (−15.8 mg/cm³) were added based on previous investigations (35). HU was measured with tools of the institutional picture archiving and communication system software (Sectra IDS7; Sectra AB, Linköping, Sweden). At first, additional sagittal stacks of 15 mm thickness (increment 2 mm) were calculated to average attenuation signals. Herein average HU were extracted from circular regions of interest (ROIs) in the midsagittal plane, placed by an experienced radiologist in the cancellous bone of at least one lumbar vertebral body. Fractured vertebra or those with apparent alterations of the cancellous bone due to degeneration or hemangioma were omitted. ROIs spanning approximately half of the vertebral height in diameter were vertically centered with equal distance to cortical bone and ventrally aligned (22). Following the American College of Radiology practice parameters for bone densitometry, osteoporosis was defined as BMD < 80 mg/cm^3 and osteopenia as 80 mg/cm^3 ≤ BMD ≤ 120 mg/cm^3 (36). For reasons of convenience BMD will refer to volumetric density throughout this text, if not stated otherwise.

Statistical analysis

Descriptive statistics were calculated for patient characteristics and BMD values as derived by opportunistic BMD screening in perioperative CT scans. Means of continuous variables were compared with independent sample t-tests assuming equality of variances depending on Levene's test. Proportions of categorical variables were compared with Pearson's chi-squared test. In a receiver operating characteristic (ROC) analysis, the classification performance of BMD to predict reoperations was tested. BMD thresholds were determined with maximum Youden index. Statistical analyses were conducted with IBM SPSS Statistics 24 (IBM Corp., Armonk, NY, USA). Level of significance for all tests was defined as $p < 0.05$.

Results

In the restrospective cohort analysis, mean BMD was significantly lower in PMMA-augmented surgeries with 60.2 ± 24.1 mg/cm³ than in non-augmented surgeries with 104.8 ± 37.9 mg/cm³ ($p = 0.002$; Table 2). The length of the fixation constructs differed significantly with a median of 2 fused segments in PMMA-augmented versus a median of 1 fused segment in non-augmented surgeries ($p < 0.001$; Table 2). Women had lower mean BMD values with 81.3 ± 42.2 mg/cm³ than men with 94.4 ± 34.5 mg/cm³, but this difference did not reach statistical significance ($p = 0.142$). Patients with non-augmented LSF who underwent reoperation had significantly lower mean BMD of 73.0 ± 18.4 mg/cm³ than those who did not with a mean BMD of 110.2 ± 37.8 mg/cm³ ($p = 0.015$; Table 3). There was no significant difference in BMD between patients with PMMA-augmented LSF who underwent reoperation and those who did not ($p = 0.621$). The best threshold to predict reoperation in non-augmented LSF according to ROC analysis was at a BMD below 83.7 mg/cm³ (area under the ROC curve A = 0.798; 95% confidence interval = 0.649–0.946; $p = 0.013$; Table 3). As the difference of BMD between augmented surgeries with and without

reoperation was not significant, ROC analysis and logistic regression was not performed for this subgroup.

Table 2: Patient characteristics in the retrospective cohort analysis stratified according to the surgical technique.

		PMMA-augmented n = 33	Non-augmented n = 48	PMMA- vs. non-augmented	All n = 82
Women, n (%)		26 (79%)	22 (46%)	p = 0.002	48 (59%)
Age, yrs, mean (range)		76 (51–89)	61 (30–84)	p < 0.001	67 (30–89)
Duration of surgery, min (range)		228 (95–403)	213 (77–385)	p = 0.359	219 (77–403)
Fused segments, n (%)	1	9 (27%)	33 (69%)	p < 0.001	42 (52%)
	2	11 (33%)	11 (23%)		22 (27%)
	3	7 (21%)	3 (6%)		10 (12%)
	4	5 (15%)	1 (2%)		6 (7%)
	5	1 (3%)	0		1 (1%)
Segment L5/S1, n (%)	Included	19 (58%)	33 (69%)	p = 0.309	52 (64%)
	Above	14 (42%)	15 (31%)		29 (36%)
Interbody fusion type, n (%)	TLIF/PLIF	21 (64%)	38 (79%)	p = 0.086	59 (73%)
	XLIF	3 (9%)	2 (4%)		5 (6%)
	ALIF	3 (9%)	7 (15%)		10 (12%)
	No cage*	6 (18%)	1 (2%)		7 (9%)
BMD, mg/cm³, mean (SD)		60.2 (24.1)	104.8 (37.9)	p < 0.001	86.6 (39.5)
Osteoporosis, n (%)		28 (85%)	14 (29%)	p < 0.001	42 (52%)
Osteopenia, n (%)		5 (15%)	19 (40%)	p = 0.012	24 (30%)
Reoperations, n (%)		4 (12%)	7 (15%)	p = 0.754	11 (14%)

*Posterolateral interbody fusion with synthetic bone graft was performed. ALIF, anterior lumbar interbody fusion; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; XLIF,

extreme lateral interbody fusion; BMD, bone mineral density; PMMA, polymethyl methacrylate

Table 3: Mean BMD of patients with/without reoperation in the retrospective cohort analysis stratified according to the surgical technique.

	Group size	BMD, mean, mg/cm³ (SD)	No reoperation vs. reoperation	ROC AUC (CI, Sig.)	BMD threshold, mg/cm³ (Youden index)
Non-augmented without reoperation	41	110.2 (37.8)	p = 0.015	0.798 (0.649–0.946, P = 0.013)	83.7 (J = 0.66)
Non-augmented with reoperation	7	73.0 (18.4)			
PMMA-augmented without reoperation	29	61.0 (24.9)	p = 0.621	*	
PMMA-augmented with reoperation	4	54.5 (19.3)			

*ROC analysis was not performed in absence of significant BMD difference between PMMA-augmented surgeries with/without reoperation. AUC, area under the ROC curve; ROC, receiver operating characteristic; BMD, bone mineral density; CI, confidence interval; PMMA, polymethyl methacrylate

In the case-control analysis, 18 patients with reoperation presented similarly low BMD of 78.8 ± 33.1 mg/cm³ compared to 26 matched patients without reoperation with BMD of 89.4 ± 39.7 mg/cm³ (Table 4). This numerical difference was not statistically significant (p = 0.357).

Table 4: Patient characteristics in the case-control analysis stratified according to the respective group.

		Case n = 18	Control n = 26	Case vs. control
Women, n (%)		12 (67%)	20 (77%)	p = 0.453
Age, yrs, mean (SD)		68.5 (9.5)	69.5 (8)	p = 0.71
BMD, mg/cm³, mean (SD)		78.8 (33.1)	89.4 (39.7)	p = 0.359
PMMA-augmented, n		3	5	p = 0.828
Fused segments, n	1	6	8	p = 0.858
	2	8	12	p = 0.911
	3	3	5	p = 0.828
	4	1	1	p = 0.789
Non-enhanced CT, n		15	20	p = 0.604
Postmyelography CT, n		1	3	p = 0.497

BMD, bone mineral density; PMMA, polymethyl methacrylate

Discussion

In this study, a retrospective cohort and a case-control analysis was conducted to investigate whether opportunistically assessed BMD was associated with the risk of reoperation following instrumented LSF with and without PMMA-augmentation. The retrospective cohort analysis showed that opportunistic BMD assessment on perioperative CT scans allows detection of osteoporotic bone density in patients who are scheduled for LSF. The prevalence of osteoporosis in this elderly group of patients undergoing elective surgery is rather high. We were able to demonstrate that patients with PMMA-augmented LSF exhibited much lower BMD than those with non-augmented LSF, while both groups showed an almost equal rate of reoperations. The case-control analysis showed that lumbar BMD was similar in patients with reoperation compared to matched controls who did not have reoperation. Although not being statistically significant, BMD was numerically lower in cases with reoperations than in controls without reoperation.

Results of this work are in line with previous studies. Low BMD assessed using HU measurements on preoperative CT scans has been associated with adjacent vertebral body fractures after spinal fusion (15). In a case-control study, decreased HU on preoperative CT scans were associated with symptomatic pseudarthrosis on one-year follow-up after posterolateral lumbar fusion (37). Patients with radiographic signs of screw loosening and non-fusion on follow-up after posterior lumbar interbody fusion with pedicle screw fixation had significantly lower areal BMD assessed by DXA compared to patients without these signs (14). Moreover, patients with signs of screw loosening in CT following posterior spinal fixation showed significantly lower BMD assessed by opportunistic screening than patients without signs of

loosening (22). Of note, decreased BMD in the cervical spine was identified as the major predisposing factor for the occurrence of traumatic odontoid fractures in elderly patients (32).

Given that patients in our retrospective cohort analysis with PMMA-augmented LSF had significantly lower BMD than those without augmentation, it is noteworthy that these patients did not show a higher reoperation rate. PMMA-augmented screw fixation is recommended in osteoporotic bone (4,5), because it improves the fixation and fatigue strength *ex vivo* (38), reduces the risk of screw loosening and pullout (39), and increases fusion rates with maintained correction angles *in vivo* (40). In reviews, PMMA-augmented screw fixations and other technical modifications like long-segment constructs is considered to reduce the risk of instrumentation failure in osteoporotic patients (4,41,42). Multiple points of fixation have been recommended in the osteoporotic spine for a long time (43). To avoid ending within a spinal transition zone or a kyphotic section long-segment constructs seems to be beneficial (25,44,45), as these regions are typically prone to adjacent segment degeneration, adjacent vertebral body fractures, or implant failure. In the presented study, patients with augmented LSF had also one more fused segments on average. There might be a positive effect of both these factors – augmentation and longer constructs – leading to a slightly numerically decreased reoperation rate (12% vs. 15%), despite substantially lower BMD. However, a larger scale study is needed to verify if a BMD below 80 mg/cm³ (threshold for osteoporosis) is suitable as a decision point for the use of augmentation, particularly considering other factors such as number of fused levels.

In the retrospective cohort analysis, patients with elective LSF had a mean age of 67 (range 30–89) years and showed a prevalence of 52% for osteoporosis. Women had slightly, but non-significantly lower BMD than men. There was a predominance of women in the group with PMMA-augmented LSF (79%) showing substantially lower BMD compared to non-augmented LSF, which is probably due to postmenopausal changes in bone metabolism. When only looking at the patients who received non-augmented LSF, the prevalence of osteoporotic BMD was still high with 29% vs. 85% in the augmented group. The high prevalence of osteoporosis may be due to the high mean age of our study population. However, indications for LSF in elderly patients persist and favorable clinical outcome after surgery can be achieved in the majority of these patients regardless of an increased overall surgical risk (46). Previously, a prevalence of about 30% of osteoporotic BMD or fragile bone strength has been reported in women between the age of 50 to 70 years undergoing spinal fusion (8). However, equally high rates of osteoporotic BMD were observed in the population of men and women older than 50 years of age prior to spinal fusion surgery (7,9). Thus, biomechanical considerations and the use of the aforementioned surgical techniques are of increasing importance when performing spinal instrumentations in the osteoporotic spine (42,45).

Of note, BMD measurements are not performed on a regular basis prior to surgery in our hospital. We performed opportunistic screening of lumbar BMD in clinical CT scans (31), which has been validated and applied in various studies (22,28–30,32–34,47), showing low short- and long-term reproducibility errors (30). Previous studies demonstrated that lumbar BMD can be assessed in sagittal reformations of contrast-enhanced MDCT and used to differentiate patients with and without osteoporotic fractures (30),

and it could also be used to predict these fractures (29). Linear correction equations can be adjusted for systematic bias of apparent bone density related to different calibration techniques and contrast application (48). We analyzed CT scans obtained on different MDCT devices for indications other than densitometry and applied asynchronous calibration to calculate BMD (22,34). In contrast to direct HU measurements, which are dependent on the specific MDCT device used, calibration enables inter-scanner and/or inter-study comparability of BMD values. Moreover, predefined BMD thresholds for osteoporosis can be used (36). In order to determine whether there is an increased risk of complications and reoperation after LSF, we estimated a BMD threshold of 83.7 mg/cm³ for patients with non-augmented surgeries in our study. In a biomechanical study, BMD of less than 80 mg/cm³ was associated with early screw loosening and unsatisfactory spinal fixation (19). Specifically, a previous study hypothesized that an areal BMD below 0.674 ± 0.104 g/cm² indicates a potentially increased risk of spinal fusion failure (14). Although difficult to compare to volumetric BMD, this value certainly lies within the osteoporotic range. Apparently, the estimated cutoff in our study matches closely with the proposed threshold of lumbar BMD for the diagnosis of osteoporosis (36). This emphasizes the high importance of assessing lumbar BMD prior to spinal instrumentation in the neurosurgical setting.

The presented analyses are based on retrospective data collection and, therefore, are prone to bias. Loss of follow-up is a major confounding factor in the retrospective analysis approach, though expected to be similar across groups. Moreover, there are no objective criteria for reoperation. The decision to have revision surgery is inherently subjective and influenced by the patient's and neurosurgeon's preferences, amongst other factors. Furthermore, the authors are aware that sagittal balance of the spine is another important biomechanical factor, which can have an impact on the outcome subsequent to LSF. Unfortunately, long-standing radiographs that would have allowed the analysis of the sagittal vertebral axis before and after surgery were not available for the presented data since they were not part of routine perioperative workup in our institution regarding the time of data inclusion.

Conclusions

Although presenting with much lower BMD patients with PMMA-augmented LSF showed no higher reoperation rates compared to non-augmented LSF. This could be explained by the improved pedicle screw purchase through augmentation. Patients with reoperation following LSF showed slightly lower BMD compared to matched patients without reoperation, but the difference did not reach statistical significance. Potential loss of follow-up and the lack of objectivity in the decision to undergo reoperation have to be recognized as major limitations of the presented results. However, opportunistic BMD evaluation is feasible and can be advised before LSF, thus informing about osteoporotic bone.

Abbreviations

BMD	Bone mineral density
DXA	Dual-energy X-ray absorptiometry
HU	Hounsfield units
LSF	Lumbar spinal fusion
MDCT	Multidetector computed tomography
PMMA	Polymethyl methacrylate
QCT	Quantitative computed tomography
ROC	Receiver operating characteristic
ROI	Region of interest

Declarations

Ethics approval and consent to participate

The present study was approved by the local institutional review board (ethics committee's reference number: 433/14S). The requirement for informed consent was waived by the institutional review board due to the retrospective character of data collection.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MTL analyzed and interpreted the patient data. MTL, NS, Y-MR, and JSK have drafted the work or substantively revised it. NL, JK, FZ, ES, and AR have made substantial contributions to the acquisition of data. NS, MV, BM, Y-MR, and JSK have made substantial contributions to the conception of the work. All authors read and approved the final manuscript.

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Figures

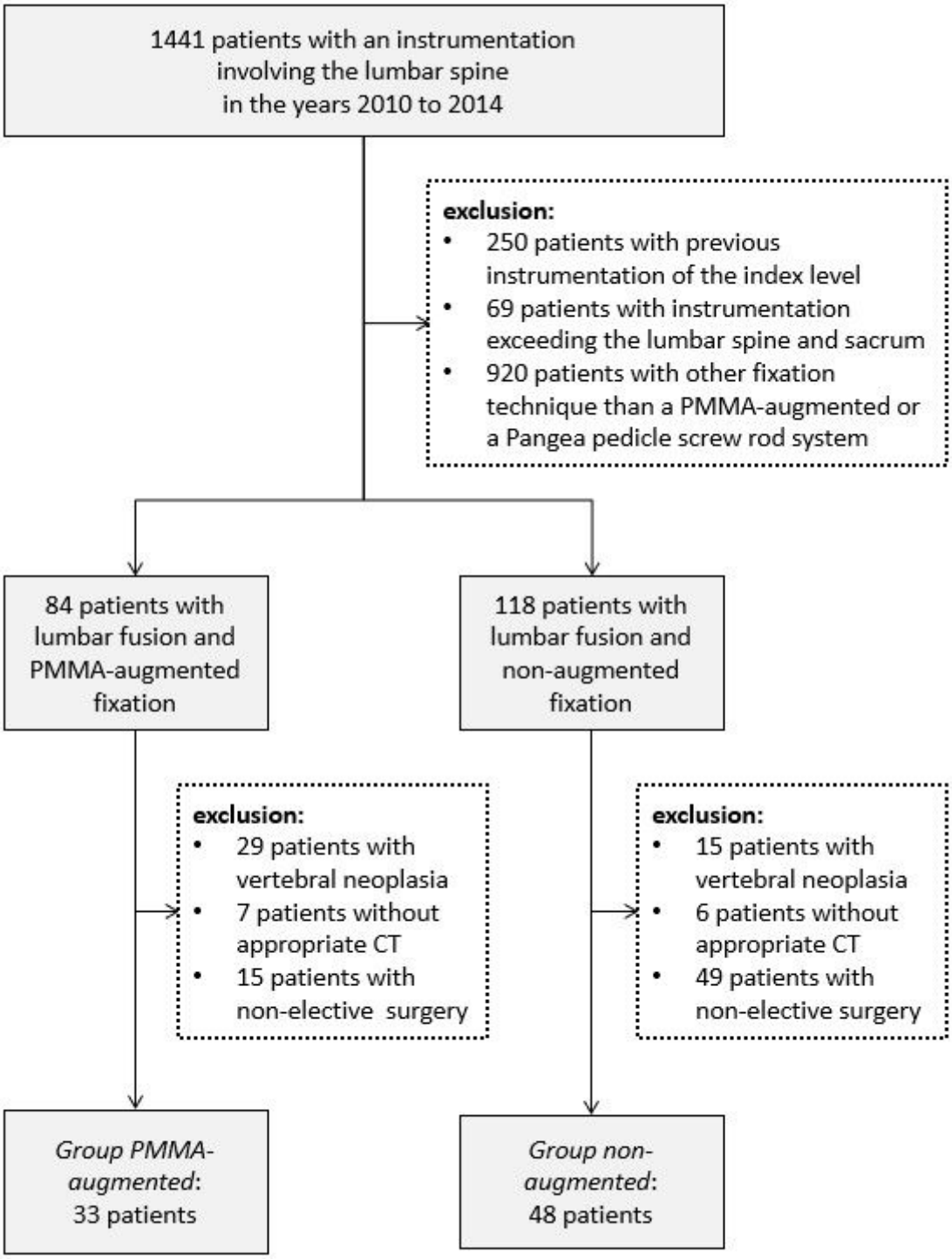

Figure 1

Selection algorithm in the retrospective cohort analysis.

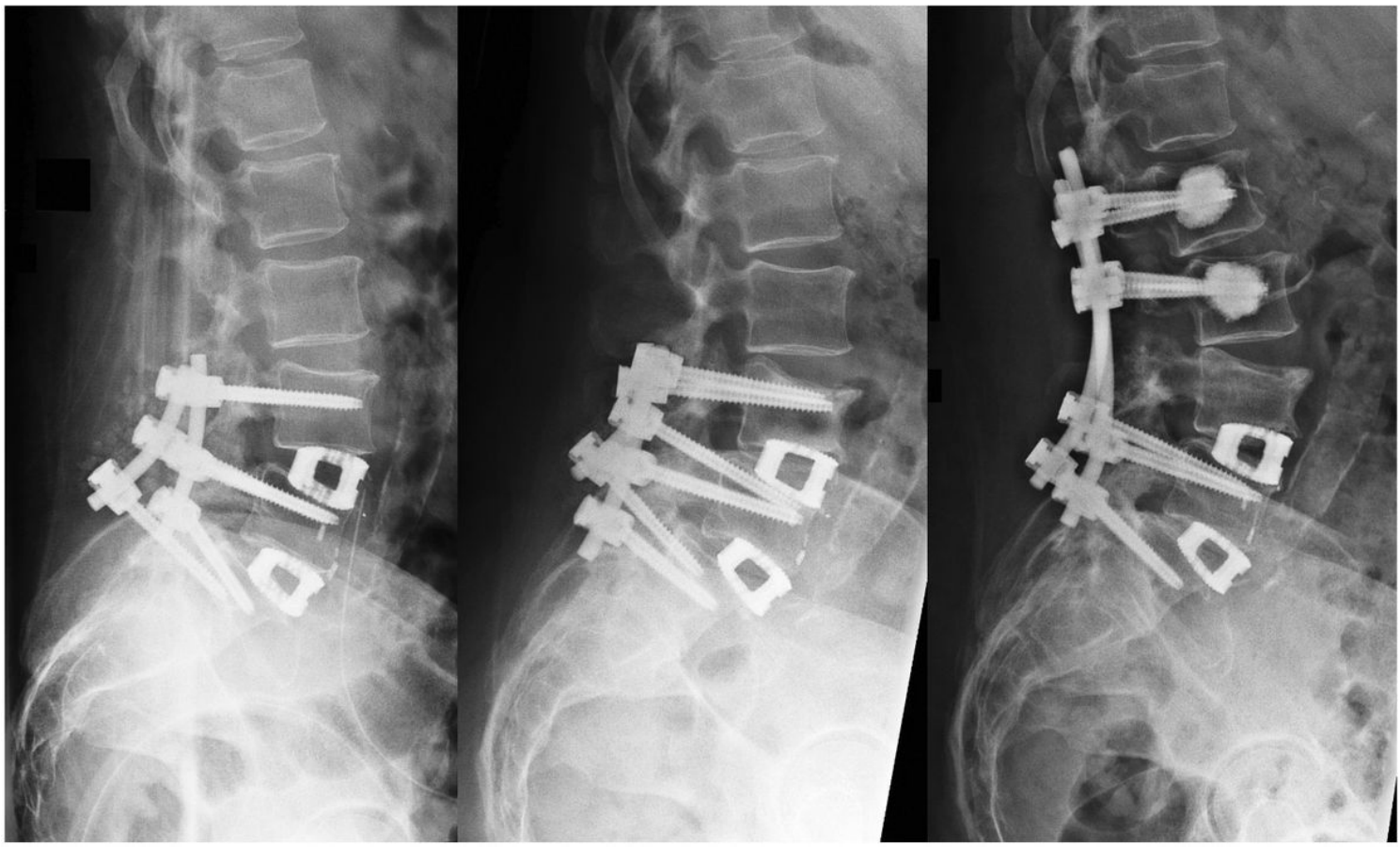

Figure 2

Case of a 76-year old women undergoing instrumented lumbar spinal fusion with ALIF for persistent low back pain because of degenerative instability. BMD was not evaluated preoperatively – our retrospective measurement yielded severely osteoporotic BMD of 57 mg/cm³. Left: Initial non-augmented fusion of vertebral levels L4 to S1. Center: Incidence of a compression fracture of the upper instrumented vertebra 22 months later. Right: Reoperation with extended and PMMA-augmented instrumentation of levels L2 and L3; pedicle screws in the fractured vertebra L4 were removed. ALIF, anterior lumbar interbody fusion; BMD, bone mineral density; PMMA, polymethyl methacrylate