The incidence of pyogenic spondylodiscitis ranges from 0.2 to 2.4 per 100,000 people per year in Western countries. Its increasing incidence may, in part, be attributable to an aging population with rising comorbidities. Conservative treatment consists of long-term antibiotics optionally combined with bed rest and an orthosis. Surgical treatment of thoracolumbar spondylodiscitis frequently entails pedicle screw fixation. However, pedicle screw loosening remains one of the main reasons for revision surgery after posterior instrumentation. The most frequently reported risk factor for screw loosening is osteoporosis/low bone mineral density (BMD). In patients with osteoporosis, the risk of screw loosening is twice as high as the risk in patients without osteoporosis. However, osteoporosis continues to be substantially underdiagnosed and undertreated, although approximately 200 million individuals suffer from osteoporosis and about 9 million osteoporotic fractures occur each year. Dual x-ray absorptiometry (DXA) remains the diagnostic tool of choice for osteoporosis. Because DXA is underutilized in
clinical practice, alternative tools to increase the detection of osteoporosis may need to be considered in cases in which DXA is not available. Hounsfield unit (HU) values on native CT scans and measurements of BMD obtained with DXA repeatedly showed a strong correlation. A threshold of 110 HUs provided a specificity of more than 90% for distinguishing osteoporosis from osteopenia and normal BMD in a study with more than 1800 patients.

The coexistence of osteoporosis and pyogenic spondylodiscitis has not yet been investigated. Knowledge of osteoporosis in patients with pyogenic spondylodiscitis prior to surgery is very important as it might alter the surgical strategy (such as using multiple points of fixation, varied fixation equipment, and modified screw design/trajectories), and specifically might allow the patient to start a pharmacological treatment (e.g., bisphosphonates or teriparatide), thereby reducing the risk of construct failure. The present analysis was undertaken with the aim to assess the prevalence of subthreshold HU values being compatible with osteoporosis, and the occurrence of implant failure in patients undergoing surgery for thoracolumbar pyogenic spondylodiscitis. We also reviewed the proportion of patients with subthreshold HU values who have received a diagnosis and treatment of osteoporosis within 1 year after spinal instrumentation.

Methods

We retrospectively analyzed a consecutive series of patients with pyogenic spondylodiscitis of the thoracolumbar spine who underwent instrumentation at the Department of Neurosurgery, Georg-August University, in Göttingen, Germany, between 2007 and 2016. CT scans of the thoracolumbar spine were obtained prior to surgery in all patients. We undertook an opportunistic estimation of BMD based on these CT scans. Patients with pyogenic spondylodiscitis of the cervical spine or without a CT scan of the lumbar spine were excluded, as well as patients with pyogenic spondylodiscitis at more than 3 levels of the thoracolumbar spine. Baseline and outcome variables including age, sex, past medical history of osteoporosis, Charlson Comorbidity Index (CCI), smoking, chronic renal failure, diabetes mellitus (DM), liver disease, heart failure, and implant failure were entered into a multivariate logistic regression model for statistical analysis. Osteoporosis interventions (DXA or endocrinological examination and pharmacological treatment of osteoporosis) within 1 year after spinal instrumentation were assessed.

This study was conducted in accordance with the 1964 Helsinki Declaration and its later amendments. Due to its retrospective design, informed consent was not obtained.

Surgical Protocol

All patients underwent posterior instrumentation using standard pedicle screw fixation without interbody lumbar fusion. Surgery was performed using a midline incision and either lateral fluoroscopy-guided or percutaneous robot-assisted insertion of the pedicle screws. Additional decompression was performed in cases of symptomatic spinal epidural abscess.

Imaging Protocol

Based on a validated axial native CT scan (Somatom Emotion, Siemens; tube voltage 120 kV) without contrast, we assessed the average HUs in the vertebral bodies of L1 and L4. If L1 or L4 were affected, we assessed the HUs of the vertebral body below. A region of interest (ROI) was defined at a horizontal plane in the middle of the vertebra, avoiding cortical bone. To obtain the HUs we used a picture archiving and communication system (PACS). Three measurements were performed in 3 different horizontal planes of the middle vertebrae L1 and L4. The average HU value was then calculated for each vertebra, and the final mean HU value was calculated from the average values of L1 and L4. In accordance with the study of Pickhardt et al., a threshold of ≤ 110 HUs was defined as osteoporosis.

Implant Stability

All patients routinely underwent an early postoperative CT scan to confirm correct implant placement. We assessed implant stability on the follow-up CT scans after at least 6 months. Implant stability was graded as screw displacement or halo sign > 2 mm, small halo sign ≤ 2 mm without screw displacement, and no halo sign or screw displacement (Fig. 2). Screw displacement was defined as implant migration or pullout of the pedicle screws.

Statistical Analyses

Descriptive analyses were performed using chi-square tests. Continuous variables were measured as mean or median values and standard deviation. Multivariate logistic regression was performed using a Cox proportional hazards model. The entire analysis was performed using SPSS (version 23.0, IBM Corp.), and p values < 0.05 were considered significant.

Results

Baseline Parameters

Of 216 consecutive patients who underwent posterior instrumentation for pyogenic spondylodiscitis, 200 were included. Sixteen patients were excluded: 6 suffered from cervical pyogenic spondylodiscitis, 5 had pyogenic spondylodiscitis at 3 or more levels, and in 5 patients no preop-
operative lumbar CT scan was available. Sixty-four percent (n = 127) were male (Table 1), and 66% (n = 132) were older than 65 years. A total of 7% (14/200 patients) had a known medical history of osteoporosis.

Imaging Assessment

L1 and L4 measurements revealed mean attenuation HU values of 120.6 ± 47.3 and 118.4 ± 54.6, respectively. With the threshold of 110 HUs, the correlation between the two measured levels was excellent (Pearson correlation coefficient = 0.820, p < 0.001). Applying this threshold of 110 revealed HU values compatible with osteoporosis in 95 patients (48%). In 93% (13/14 patients) the HU measurements confirmed the medical history of osteoporosis (Table 1). Multivariate analysis showed that an age above a threshold of 65 years (Table 2), but not above 50 years (Table 3), was a predictor for subthreshold HU values (OR 5.85, 95% CI 2.7–12.5, p < 0.001 for age older than 65 years; OR 4.52, 95% CI 0.5–39.1, p = 0.17 for age older than 50 years). We did not find a significant association of CCI, smoking, screw malpositioning, wound revision, chronic renal failure, DM, heart failure, or liver disease with subthreshold HU values (Tables 2 and 3). The need for revision surgery due to implant failure showed a trend toward an association with subthreshold HU values (OR 2.11, 95% CI 0.95–4.68, p = 0.067).

Implant Failure

In 60 patients, a CT scan for implant assessment was available after at least 6 months (median follow-up 20.5 months, range 6–97 months). In these patients with an available follow-up CT scan, 30% (18/60 patients) suffered from undiagnosed osteoporosis. The distribution of implant stability is displayed in Fig. 2. The occurrence of implant instability was significantly more frequent in patients with subthreshold HU values, which was compatible with undiagnosed osteoporosis (p < 0.001). The mean time between surgery and the development of implant failure was 12.3 ± 4.9 months.

Diagnostics and Treatment for Osteoporosis

In 81 (41%) of 200 patients, obtained HU values were compatible with unknown osteoporosis. Within 1 year after spinal instrumentation, 4 (5%) of 81 patients underwent DXA with confirmation of osteoporosis and were subsequently treated with bisphosphonates (n = 3) or teriparatide (n = 1). Seventy-one (88%) of 81 patients underwent neither DXA nor endocrine examination nor pharmacological treatment for osteoporosis. In 6 patients (7%), diagnostic and treatment data were inconclusive. Eighteen patients (22%) received vitamin D and 13 patients (16%) received calcium supplementation.

Discussion

Almost half of the patients who underwent surgery for pyogenic spondylodiscitis had low HU values compatible with osteoporosis, confirmed by CT. HU values are eas-

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**Table 1**

| Points | Construct                          |
|--------|-----------------------------------|
| 0      | Screw dislocation or large halo > 2 mm |
| 1      | Small halo ≤ 2 mm without screw dislocation |
| 2      | No halo sign or screw dislocation  |

**FIG. 2.** Distribution of the implant stability in the follow-up cohort. Implant stability was graded by no radiographical sign of screw loosening or halo sign (2 points), halo sign ≤ 2 mm (1 point), and halo sign > 2 mm and screw displacement (0 points). Implant instability occurred significantly more frequently in patients with subthreshold HU values (p < 0.001).
Nal instrumentation is essential. Although screw loosening osteoporotic fracture, usually occurring in the hip, forearm, or vertebra. 24 Osteoporosis remains underdiagnosed and undertreated. 10,11 To determine the BMD prior to spine instrumentation, which documents a substantial underdiagnosed and treated for osteoporosis within 1 year after patients suffering from estimated low BMD were diagnosed and treated for osteoporosis within 1 year after spinal instrumentation, which documents a substantial unawareness of the problem in our and, assumedly, in other institutions.

Prevalence of Osteoporosis
Almost 9 million osteoporotic fractures occur worldwide per year (51% in Europe and the US). 24 One in 3 women and 1 in 5 men older than 50 years are at risk of an osteoporotic fracture, usually occurring in the hip, forearm, or vertebra. 24 Osteoporosis remains underdiagnosed and undertreated. 10,11 To determine the BMD prior to spinal instrumentation is essential. Although screw loosening or implant failure in patients with pyogenic spondylodiscitis has been reported in earlier studies, 20,25,26 there remains a lack of data examining BMD in patients with pyogenic spondylodiscitis. As the use of instrumentation in an infected area of the spine is safe and does not lead to persistence or recurrence of infection, 26–28 it appears possible that cofactors such as low BMD lead to a higher risk for implant failure. In our cohort, 49% of patients with pyogenic spondylodiscitis suffered from estimated low BMD, as reflected by HUs < 110, compatible with osteoporosis. Patients in the subthreshold HU group had a significantly higher risk of implant failure and showed a trend toward subsequent revision surgery. We assume that we found no association between subthreshold HU values and revision surgery, but did find an association with implant failure, because several factors (e.g., poor patient condition, absence of symptoms, or high risk of perioperative morbidity/mortality) might have led to a decision against revision surgery although implant failure occurred. In any case, preoperative knowledge of low BMD/osteoporosis might allow one to use treatment strategies such as using multiple points of fixation, varied fixation equipment, and modified screw design/trajectories 23 to reduce the risk of implant failure and revision surgery.

Diagnosis of Osteoporosis
DXA of the lumbar spine (L1–4) and the proximal femoral bone is usually used in clinical practice for the screening of osteoporosis, revealing a T-score of <−2.5. 9,29 However, as previous studies showed, the accuracy of DXA is affected by several factors, such as lumbar degenerative changes, spinal deformity, previous spinal surgery, or vertebral compressive fractures. 9,30 52.1% of patients with vertebral compressive fractures had false-negative results on DXA imaging. 15,30 Furthermore, DXA is related to additional costs, patient time, technical equipment, and radiation exposure. 15 Quantitative CT (QCT) is an alternative method to assess BMD in clinical practice. It has been shown that a single CT measurement of vertebral attenuation is equivalent to QCT assessment, but was substantially easier to obtain. 15,21 QCT is associated with high costs, requires a phantom, and involves additional time and radiation exposure. 9,15,16,32 For measurements of HU values on CT, excellent interobserver and intraobserver reliability have been proven in earlier studies. 33,34 Although DXA is still routinely used for the diagnosis of osteoporosis, and QCT has been gaining popularity over the last few years, or implant failure in patients with pyogenic spondylodiscitis has been reported in earlier studies, 20,25,26 there remains a lack of data examining BMD in patients with pyogenic spondylodiscitis. As the use of instrumentation in an infected area of the spine is safe and does not lead to persistence or recurrence of infection, 26–28 it appears possible that cofactors such as low BMD lead to a higher risk for implant failure. In our cohort, 49% of patients with pyogenic spondylodiscitis suffered from estimated low BMD, as reflected by HUs < 110, compatible with osteoporosis. Patients in the subthreshold HU group had a significantly higher risk of implant failure and showed a trend toward subsequent revision surgery. We assume that we found no association between subthreshold HU values and revision surgery, but did find an association with implant failure, because several factors (e.g., poor patient condition, absence of symptoms, or high risk of perioperative morbidity/mortality) might have led to a decision against revision surgery although implant failure occurred. In any case, preoperative knowledge of low BMD/osteoporosis might allow one to use treatment strategies such as using multiple points of fixation, varied fixation equipment, and modified screw design/trajectories 23 to reduce the risk of implant failure and revision surgery.

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the results of our study suggest that measurement of HUs on routine CT can be easily obtained and also can be useful to estimate the presence of osteoporosis. However, further prospective validation studies are required before it can be used routinely in clinical practice.

Coincidence of Spondylodiscitis and Osteoporosis

There is a lack of data reporting the coincidence of pyogenic spondylodiscitis and osteoporosis. As noted above, our results suggest a frequent coincidence of osteoporosis and pyogenic spondylodiscitis. This may be explained due to the fact that risk factors for osteoporosis (age, alcoholism, smoking, medication with glucocorticoids, and renal or inflammatory disease) are quite similar to those for pyogenic spondylodiscitis. As shown in earlier studies, we identified age over 65 years as the most reliable predictor for subthreshold HU values, compatible with osteoporosis. Although 50 years of age is a common cutoff used for recommendations for bone health assessment, we identified age over 65 years as the most reliable predictor for subthreshold HU values, compatible with osteoporosis. In our study, we performed a follow-up CT scan after 6 months and later was only acquired, to guide the surgical strategy, start pharmacological treatment of osteoporosis, suggest screening for osteoporosis in patients with pyogenic spondylodiscitis. This may be explained due to the fact that risk factors for osteoporosis (age, alcoholism, smoking, medication with glucocorticoids, and renal or inflammatory disease) are quite similar to those for pyogenic spondylodiscitis. As shown in earlier studies, we identified age over 65 years as the most reliable predictor for subthreshold HU values, compatible with osteoporosis.

Limitations

Our study has several limitations. This was a retrospective analysis undertaking an opportunistic estimation of BMD on CT scans, which have not been verified by DXA, potentially leading to bias. The ROIs for HU measurements were chosen manually, which could lead to a limited repeatability of our results. While a CT scan was routinely performed after surgery within the inpatient stay, a follow-up CT scan after 6 months and later was only performed in 60 of the 200 patients, which also has to be considered a limitation.

Conclusions

Relying on the past medical history of osteoporosis is insufficient in the management of patients with pyogenic spondylodiscitis. Half of the patients presenting with spondylodiscitis also had severely reduced bone mass compatible with a diagnosis of osteoporosis. This is the first study identifying a substantially missed opportunity to detect osteoporosis, to adjust the surgical technique, and to start pharmacological treatment after surgery for prevention of implant failure. We advocate routine opportunistic CT evaluation for a better estimation of bone quality in patients with pyogenic spondylodiscitis to initiate diagnosis and treatment of osteoporosis.

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Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Schatlo, Bettag, Abboud. Acquisition of data: Bettag, Melich. Analysis and interpretation of data: Schatlo, Bettag, von der Brelie. Drafting the article: Bettag. Critically revising the article: Schatlo, Abboud, von der Brelie, Melich, Rohde. Reviewed submitted version of manuscript: all authors. Statistical analysis: Bettag, von der Brelie. Administrative/technical/material support: Abboud, von der Brelie, Melich, Rohde. Study supervision: Schatlo, Rohde.

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