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Systematic Review and Meta-Analysis of the Effect of Osteoporosis on Fusion Rates and Complications Following Surgery for Degenerative Cervical Spine Pathology

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ABSTRACT

Background: As the elderly population grows, the increasing prevalence of osteoporosis presents a unique challenge for surgeons. Decreased bone strength and quality are associated with hardware failure and impaired bone healing, which may increase the rate of revision surgery and the development of complications. The purpose of this review is to determine the impact of osteoporosis on postoperative outcomes for patients with cervical degenerative disease or deformity.

Methods: A systematic review using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and Medical Subject Headings terms involving spine surgery for cervical degenerative disease and osteoporosis were performed. This review focused on radiographic outcomes, as well as surgical and medical complications.

Results: There were 16 studies included in the degenerative group and 9 in the deformity group. Across degenerative studies, lower bone mineral density was associated with increased rates of cage subsidence in osteoporotic patients undergoing operative treatment for cervical degenerative disease. Most studies reported varied results on the relationship between osteoporosis and other outcomes such as revision and readmission rates, costs, and perioperative complications. Our meta-analysis suggests that osteoporotic patients carry a greater risk of reduced fusion rates at 6 months and 1 year postoperatively. With respect to cervical deformity correction, although individual complication rates were unchanged with osteoporosis, the collective risk of incurring any complication may be increased in patients with poor bone stock.

Conclusions: Overall, the literature suggests that outcomes for osteoporotic patients after cervical spine surgery are multifactorial. Osteoporosis seems to be a significant risk factor for developing cage subsidence and pseudarthrosis postoperatively, whereas reports on medical and hospital-related metrics were inconclusive. Our findings highlight the challenges of caring for osteoporotic patients and underline the need for adequately powered studies to understand how osteoporosis changes the risk index of patients undergoing cervical spine surgery.

Clinical Relevance: In patients undergoing cervical spine surgery for degenerative disease, osteoporosis is a significant risk factor for long-term postoperative complications—notably cage subsidence and pseudarthrosis. Given the elective nature of these procedures, interdisciplinary collaboration between providers should be routinely implemented to enable medical optimization of patients prior to cervical spine surgery.

Level of Evidence: 1.

Cervical Spine

Keywords: cervical, degenerative, fusion

INTRODUCTION

Osteoporosis affects nearly 200 million people globally.¹ With an aging population, the increasing prevalence of osteoporosis presents a unique challenge for surgeons.² This age-related process causes decreased bone strength and quality and can contribute to complications such as hardware failure, impaired bone healing, subsequent fractures, and the need for reoperation.¹

Previous studies have also identified a significant correlation between osteoporosis and increased morbidity and mortality.^{3,4} For example, a systematic review by Nazrun et al showed osteoporosis was associated with increased hospital visits, longer hospital stays, and increased health care costs⁴; meanwhile, a 952-patient prospective cohort study by Bliuc et al identified a 10-year increased risk of mortality in osteoporotic patients following low-impact fracture injuries.³

Similarly, cervical spine disease increased in parallel to the aging population. A 2021 retrospective study by Parentreau et al found the prevalence of degenerative disc disease rose from 24.2% in 2005 to 30.1% in 2017.⁵ As the incidence of both osteoporosis and degenerative cervical spine disease continue to increase, there is a need to better understand the interplay between these 2 conditions. The literature currently presents conflicting evidence for many postoperative complications, including rates of cage subsidence, pseudarthrosis, readmission, and reoperation in osteoporotic patients following surgery for cervical spine pathology.⁶⁻¹⁶ Thus, the purpose of this review is to systematically gather and analyze current data to create a more comprehensive understanding of how osteoporosis potentially impacts outcomes following surgery for degenerative cervical conditions.

METHODS

The following systematic review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The guiding research question was as follows: “What effect does a diagnosis of osteoporosis have on the incidence of adverse outcomes following surgical intervention for cervical degenerative pathology?” Furthermore, a search strategy was implemented and eligibility criteria were developed for the screening and inclusion of full texts. Institutional Review Board approval and informed consent were not required because no patient information was collected for this study.

The initial query was carried out on the MEDLINE (PubMed) database, which was searched from 1990 to August 2022. The search contained the following terms: “osteoporosis” AND “cervical” AND (“outcomes” OR “revision” OR “reoperation” OR “complication”).

Inclusion criteria included prospective or retrospective studies in English that examined the relationship between a preoperative diagnosis of osteoporosis and the incidence of adverse radiographic outcomes, surgical outcomes, and clinical outcomes and complications. Patients were determined to have osteoporosis if they were coded as such using International Classification of Diseases codes specific to that study or if they underwent radiographic confirmation of decreased bone mineral density (BMD), either by dual-energy x-ray absorptiometry (DEXA) or computed tomography (CT). Articles were excluded if they were literature or systematic reviews, case reports, technique comparisons, or biomechanical or cadaveric studies. Articles were also excluded if they did not include osteoporotic patients in the study population, if they did

not assess relevant postoperative outcomes, if no surgical intervention was carried out, or if the study used a sample size smaller than 20 patients. Any articles with a vertebral compression fracture, trauma, infection, or neoplasia as indications for surgery were also excluded. Additional exclusion criteria were applied after full-text articles were identified: articles unrelated to degenerative cervical pathology and those in which cement augmentation was utilized as part of the surgical intervention. Finally, all included studies were comparative in that they included cohorts of osteoporotic and nonosteoporotic patients or they assessed outcomes based on a continuous measurement of BMD.

The electronic database search and screening were carried out by 2 independent reviewers. Studies were screened sequentially based on title, abstract, and full text and were included or excluded based on the aforementioned criteria. All eligible articles were saved and pooled, and duplicates were removed. Furthermore, the references of all included full texts were reviewed to find potentially relevant studies that were not identified in the initial query; those studies were subjected to the same screening process and were included in the final pool as appropriate.

A data extraction sheet was developed using the Cochrane Consumers and Communication Review Group’s Data Extraction Template for Included Studies,¹⁷ and 3 authors carried out the review of all eligible articles and extracted the following information from the included studies: author name, publication year, study type, patient populations, indications for surgery, and outcomes assessed. These outcomes were categorized into radiographic outcomes, surgical outcomes, patient-reported outcomes, and complications. The risk of bias was also recorded, which was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method,¹⁸ and articles were assigned a GRADE of either very low, low, moderate, or high.

Data extraction for the meta-analysis was carried out by 3 authors from all eligible articles. Information extracted included, when available, the percentage of osteoporotic and nonosteoporotic patients with a particular outcome, as well as univariate and multivariate analyses linking osteoporosis with outcomes. Outcomes were included in the final analysis if they were present in 2 or more studies and if they were measured similarly between studies. Radiographic outcomes included pseudarthrosis and cage subsidence. The complications category included readmission rate and reoperation rate. Patient-reported outcomes included the Japanese Orthopedic Association (JOA) score¹⁹ and visual analog score (VAS), while surgical outcomes included hospital length of stay.

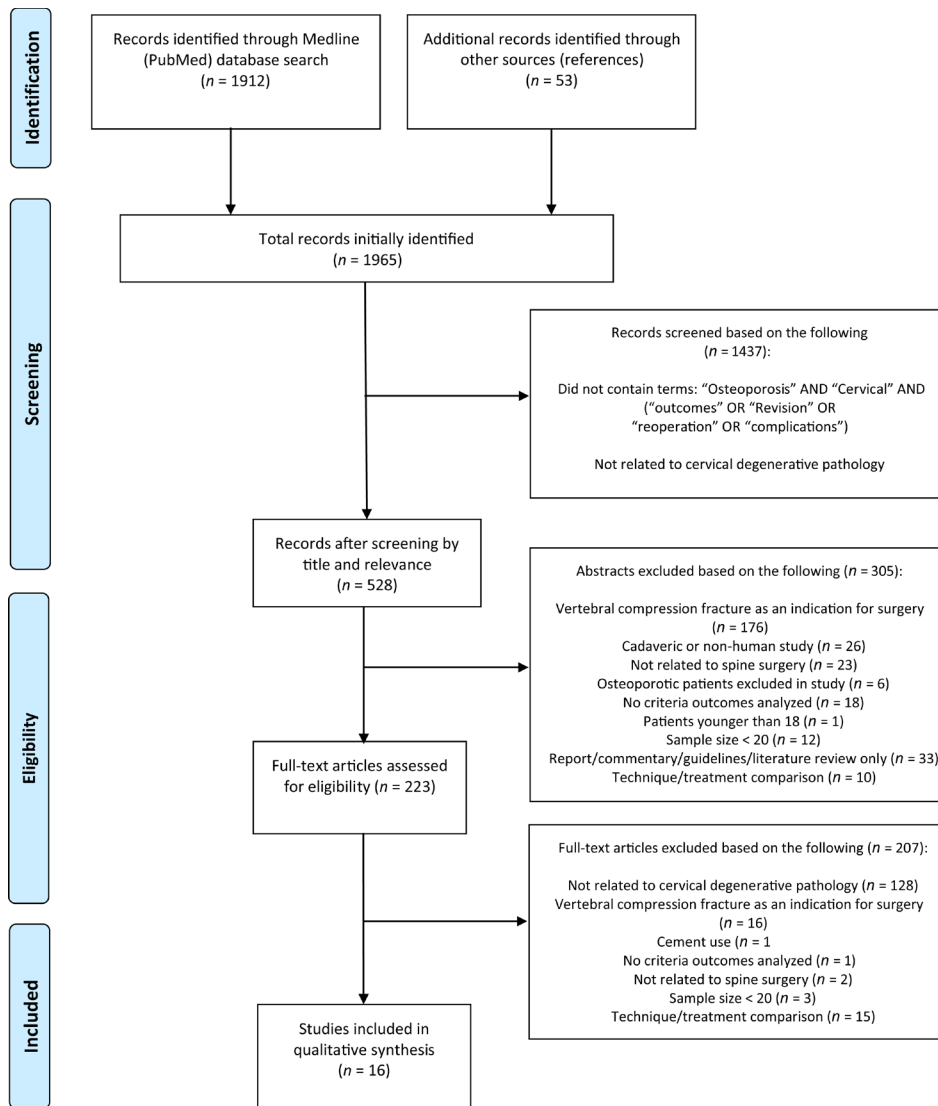


Figure. Study selection flowchart.

Statistical Methods

Comprehensive Meta-Analysis (version 2) was used to perform statistical analysis. The effects of different studies were summed using the random effects model. A *P* value less than 0.05 was considered significant. Variables included in the study were either (1) categorical or (2) means with reportable standard deviations. The standard error of means was calculated from the mean, sample size, and standard deviation.

RESULTS

Study Characteristics

The determination of how studies were included and excluded is outlined in the PRISMA diagram in Figure 1. We initially identified 1912 records, but application of exclusion criteria yielded 1432 articles. An additional 53

records were identified via references and screened for relevance. After screening the titles, 528 records remained, of which 223 full-text articles were assessed for eligibility (*n* = 305 excluded after abstract review). Of these, we included 16 studies related to cervical degenerative pathology, 14 of which were retrospective, and 2 of which were prospective cohort studies. Three studies were included in the final meta-analysis (Table 1).

Risk of Bias and Quality of Evidence

The GRADE guidelines¹⁸ were used to determine the risk of bias, and the level of evidence was determined using the schema from the *Journal of Bone and Joint Surgery* for all 16 included studies.²⁵ One study had a GRADE of moderate, 11 had GRADEs of low, and 4 were very low. In terms of the level of evidence, 14 studies had level III evidence, 1 had level II evidence, and 1 had level I evidence.

Table 1. Characteristics of studies focusing on surgery for cervical degenerative disease.

Study	Type of Study	Patient Population/Indications	Radiographic Outcomes	Surgical Outcomes	Clinical Outcomes	Complications	Level of Evidence	Quality of Evidence (GRADE)
Brenke et al 2015 ⁶	Randomized controlled trial (n = 88)	Patients undergoing ACDF for 1- or 2-level cervical pathology and absence of concomitant spinal disease	Cage subsidence				I	Moderate
Zhang et al 2019 ¹⁶	Retrospective cohort (n = 42)	Osteoporotic patients undergoing ACDF with the Zero-Profile device for symptomatic cervical degenerative disc disease	Cage subsidence; fusion rate; change in cervical lordosis	Operative time; blood loss; hospital LOS; cost of surgery	JOA, NDI, VAS, SF-36 PCS, and SF-36 MCS scores	Cervical soft tissue swelling; dysphagia	III	Very low
Yan et al 2011 ¹⁵	Retrospective cohort (n = 75)	Osteoporotic patients undergoing anterior corpectomy and reconstruction for cervical spondylotic myelopathy	Cage subsidence; change in cervical lordosis		JOA score		III	Very low
Ren et al. 2020 ¹³	Retrospective cohort (n = 295)	Patients undergoing ACDF for cervical spondylotic disease	Cage nonunion		VAS score		III	Low
Bergin et al 2021 ¹⁸	Retrospective cohort (n = 326)	Patients undergoing single-level ACDF utilizing Osteoceil	Pseudarthrosis				III	Low
Lee et al 2020 ¹¹	Retrospective database (n = 85)	Patients undergoing elective primary two-level ACDF for degenerative cervical disease causing radiculopathy or myelopathy	Pseudarthrosis				III	Low
Wang et al 2020 ¹⁴	Retrospective cohort (n = 91)	Patients undergoing single-level ACDF with anterior plate fixation for degenerative cervical disease	Cage subsidence				III	Low
Ji et al 2020 ⁹	Retrospective cohort (n = 73)	Patients undergoing single-level anterior cervical corpectomy and fusion with the use of titanium mesh cage	Cage subsidence				III	Low
Lee et al 2022 ¹⁰	Retrospective cohort (n = 40)	Patients undergoing single-level ACDF using a stand-alone PEEK cage	Cage subsidence				III	Low
Opsenak et al 2019 ⁷	Prospective cohort (n = 61)	Patients undergoing microsurgical 1- or 2-level anterior cervical discectomy for cervical degenerative disc disease	Cage subsidence				II	Very low
Lee et al 2014 ¹²	Retrospective cohort (n = 78)	Patients undergoing single-level ACDF with neck pain and radiculopathy	Cage subsidence				III	Low
Guzman et al 2016 ²⁰	Retrospective administrative database analysis (n = 1,602,129)	Patients with any cervical degenerative disc disease undergoing cervical spine surgery		Hospital length of stay; cost of hospitalization		Revision surgery; wound complications; postoperative hemorrhage	III	Low
Park et al 2016 ²¹	Retrospective national database (n = 7948)	Patients with degenerative cervical spondylotic radiculopathy or myelopathy undergoing discectomy with anterior fusion, corpectomy, laminectomy, with/without posterior fusion, or laminoplasty				Revision surgery	III	Low

Table 1. Continued.

Study	Type of Study	Patient Population/Indications	Radiographic Outcomes	Surgical Outcomes	Clinical Outcomes	Complications	Level of Evidence	Quality of Evidence (GRADE)
Park et al 2016 ²²	Retrospective national database (n = 9071)	Patients with degenerative cervical spondylotic radiculopathy or myelopathy undergoing discectomy with anterior fusion, corpectomy, laminectomy with/without posterior fusion, or laminoplasty				Revision surgery	III	Low
Veeravagu et al 2013 ²³	Retrospective administrative database (n = 28,777)	Patients undergoing single- and multilevel ACDF				Revision surgery Readmission Any perioperative complication Readmission	III	Low
Rumalla et al 2017 ²⁴	Retrospective administrative database (n = 29,990)	Patients undergoing elective posterior cervical spine surgery for degenerative conditions					III	Very low

Abbreviations: ACDF, anterior cervical discectomy and fusion; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; JOA, Japanese Orthopedic Association; LOS, length of stay; MCS, mental component score; NDI, Neck Disability Index; PCS, physical component score; PEEK, polyether-ether-ketone; VAS, visual analog score.

^aIncluded in the meta-analysis portion of this study.

Radiographic Outcomes

A total of 11 studies evaluated the relationship between osteoporosis and various radiographic outcomes, including cage subsidence, pseudarthrosis, and degree of cervical lordosis correction. Nine of these were retrospective cohort or database studies, and 2 were prospective cohort studies.⁶⁻¹⁶ Of the 8 studies that assessed cage migration, 5 found that poor bone stock was associated with the development of this complication.^{7,9,10,14,15} Lee et al calculated Hounsfield units (HUs) based on 6 regions of the cervical spine in a cohort of 40 patients who underwent anterior cervical discectomy and fusion (ACDF) with stand-alone polyether-ether-ketone (PEEK) cages. The authors found that lower regional HU was associated with the development of cage decrement ($P < 0.01$), which is defined as a reduction in the total intervertebral disk height.¹⁰ In contrast, 3 studies did not find that BMD was related to the development of cage subsidence.^{6,12,16} Brenke et al's randomized controlled trial of 88 patients compared 2 cage types but did not find that BMD was related to the rate of cage subsidence in the entire cohort.⁶ In Lee et al's retrospective cohort study of 78 patients who underwent single-level ACDF for neck pain and radiculopathy, osteoporosis was also not found to be a risk factor for subsidence.¹² Lastly, Zhang et al also did not find that low BMD was linked to cage subsidence in their cohort of 42 patients who underwent single-level ACDF with a Zero-Profile device. However, osteoporotic patients in this study underwent medical treatment of their osteoporosis after surgery, an aspect that was undefined in the other studies.¹⁶

Five retrospective studies assessed risk factors for pseudarthrosis following cervical spine surgery with an overall fusion rate in osteoporotic patients ranging from 58.8% to 100% at the final follow-up.^{8,11,13,15,16} Bergin et al reported a 41.2% prevalence of pseudarthrosis at 1 year follow-up in their cohort of 326 patients (OR: 4.97, 95% CI: 1.51–1.64, $P < 0.01$).⁸ Assessment of bony union at earlier time points yielded fusion rates in the range of 60% to 96.2% depending on the time-point.^{11,13,16} Five retrospective studies assessed risk factors for cage pseudarthrosis following cervical spine surgery, wherein 2 studies identified osteoporosis to be significantly predictive.^{8,13} Ren et al's retrospective cohort study of 259 patients with cervical spondylotic disease reported that osteoporosis was an independent predictor of cage pseudarthrosis after ACDF (OR: 1.94, 95% CI: 1.44–2.51, $P = 0.001$).¹³ Similarly, Bergin et al identified osteoporosis as a significant risk factor for pseudarthrosis after ACDF in a retrospective study of 326 patients (OR: 4.97, 95% CI: 1.51–16.4, $P < 0.01$).⁸ In contrast, retrospective cohort studies from Lee et al, Yan et al, and Zhang et al, which included 85, 75, and

42 patients with cervical myelopathy, respectively, were unable to establish osteoporosis as a risk factor for pseudarthrosis.^{11,15,16}

Two studies assessed the degree of cervical lordosis correction before and after surgery. In Yan et al's cohort of 75 osteoporotic patients with cervical spondylotic myelopathy who underwent anterior corpectomy and reconstruction, the C2-C7 lordotic angle was unchanged based on osteoporosis severity.¹⁵ Similarly, Zhang et al found no difference in the C3-C7 Cobb angle between osteoporotic and nonosteoporotic patients in their cohort of 42 patients.¹⁶

Complications

Overall, 6 retrospective studies reported on the relationship between osteoporosis and surgical outcomes, including postoperative complications, reoperation, and readmission rates in patients with degenerative disc disease.

Postoperative Complications

Three studies assessed postoperative complications. Veeravagu et al's retrospective database study of nearly 29,000 individuals who underwent anterior cervical discectomy and fusion (ACDF) procedures showed that patients with osteoporosis had an increased risk of general postoperative complications further defined as postoperative infection, wound dehiscence, chronic pain, pulmonary embolism, deep vein thrombosis, or dysphagia (OR: 1.48, $P = 0.004$).²³ Similarly, a 2016 noninterventional study by Guzman et al found that a diagnosis of osteoporosis was associated with an increased risk of postoperative hemorrhage (OR: 1.70, 95% CI = 1.46–1.98, $P < 0.0001$).²⁰ Lastly, Zhang et al's retrospective study of patients following ACDF found a nonsignificant association between osteoporosis and cervical soft tissue swelling or dysphagia ($P > 0.05$).¹⁶

Need for Readmission

Two studies described the association between osteoporosis and need for readmission. Veeravagu et al found that osteoporosis was significantly linked with any-cause readmission after ACDF in a cohort of nearly 29,000 patients (OR: 1.30, $P = 0.03$)²³; meanwhile, Rumalla et al's database study of 30,000 patients found no association between osteoporosis and readmission following posterior fusion for cervical degenerative disease, reporting rates of 5.5% and 10.0% of 30- and 90-day readmission, respectively, in 1400 osteoporotic individuals.²⁴

Reoperation Rate

There were 4 studies that assessed the relationship between osteoporosis and reoperation rates. Park et al's retrospective study of 8000 patients who underwent ACDF for cervical spondylotic radiculopathy and myelopathy did not identify osteoporosis to be a contributing factor to reoperation rates ($P = 0.857$).²¹ The same authors also compared reoperation rates according to different fusion techniques in a study of more than 9000 patients with degenerative cervical spine disease and found that osteoporosis was not associated with reoperation throughout the entire study period ($P = 0.877$).²² Alternatively, Guzman et al's database study of 1.6 million patients who underwent any type of cervical fusion identified osteoporosis as a significant risk factor for reoperation (OR: 1.54, $P < 0.0001$).²⁰ Similarly, Veeravagu et al also demonstrated that osteoporotic patients were more likely to require reoperation after ACDF (OR: 1.26, $P = 0.0002$).²³

Surgical and Patient-Reported Outcomes

Surgical Outcomes

Two studies assessed both the cost of surgery and length of hospital admission. The first, by Zhang et al, examined outcomes following ACDF surgery in both osteoporotic and nonosteoporotic patients. They found that patients with osteoporosis incurred greater surgical costs ($P < 0.001$) but did not have longer hospital stays.¹⁶ Conversely, Guzman et al found osteoporosis to be linked to significantly greater costs and longer lengths of stay ($P < 0.0001$ for both).²⁰ Zhang et al also assessed surgical parameters such as operative time and intraoperative blood loss during ACDF but did not find a significant difference in either metric between osteoporotic and non-osteoporotic patients.¹⁶

Patient-Reported Outcomes

Two studies investigated patient-reported outcomes. Yan et al focused on the JOA score and VAS pain index in patients with varying degrees of osteoporosis after anterior corpectomy and reconstruction for cervical spondylotic myelopathy.¹⁵ There was no significant association between the degree of osteoporosis and a poor JOA score ($P > 0.05$); similarly, even though scores on the VAS pain index improved significantly for both moderately and severely osteoporotic patients ($P < 0.001$), the difference between the groups was nonsignificant ($P > 0.05$). The study by Zhang et al, which looked at the JOA, VAS, and NDI (Neck Disability Index) scores following ACDF in both osteoporotic and nonosteoporotic patients, also did not find any significant associations ($P > 0.05$).¹⁶

Table 2. Results of the meta-analysis comparing outcomes after surgery for cervical degenerative disease between osteoporotic and nonosteoporotic patients.

Outcome	Osteoporosis	No osteoporosis	P value
Fusion rate at 6 mo	85.0% ± 9.0%	89.4% ± 7.4%	0.708
Fusion rate 1 y	68.5% ± 9.4%	91.3% ± 3.3%	0.023

META-ANALYSIS RESULTS

Three studies met the inclusion criteria and provided appropriate statistical data for use in our meta-analysis. One study reported on rates of pseudarthrosis at both 6 months and 1 year postoperatively in a cohort of 85 patients,¹¹ while the other 2 studies reported on 6-month outcomes in 295 patients¹³ and 1-year outcomes in 326 patients.⁸ While fusion rates at 6-month postoperatively did not differ significantly based on osteoporosis status ($P = 0.708$), results at 1 year indicated otherwise with lower fusion rates observed among osteoporotic patients (68.5% vs 91.3%, $P = 0.023$) (Table 2).

DISCUSSION

In this systematic review and meta-analysis of the literature on operatively treated degenerative cervical spine pathologies, there was a lack of consensus on how osteoporosis affects various outcomes, such as cage subsidence, pseudarthrosis, need for revision surgery, and various patient-reported outcome measures and hospital-related outcomes. Many articles were not included in the final meta-analysis due to a lack of comparative data pertaining to various complications and outcomes. However, we found that fusion rates at 1 year after surgery differed significantly between patients with low and normal BMD (Table 2). Although 3 of 5 investigations into pseudarthrosis rates in the systematic review report a nonsignificant association with osteoporosis, this finding may be explained by an overall low cumulative incidence (0–13.2%). Many studies have identified osteoporosis as a risk factor for poor outcomes following spine surgery due to inferior purchase during screw insertion and impaired bone remodeling that results in increased rates of hardware failure and poor construct healing.^{26,27} For this reason, the use of rigid hardware and augmentation techniques is thought to improve outcomes in patients with osteoporosis.¹⁶

Our systematic review established osteoporosis as a risk factor for cage migration, which has been associated with reduced cervical alignment, reduced foraminal height, adjacent segment disease, and persistent postoperative pain.^{6,7,12,14} Although cage subsidence has been readily identified as a complication of anterior cervical

spine surgery, there is a lack of agreement within the literature as to its ability to predict clinical outcomes.^{28,29} Specifically, several studies have shown that patients both with and without cage subsidence after cervical spine surgery do not have significantly different neck and arm VAS scores, either in the immediate postoperative period or at final follow-up,^{7,9,14} indicating that cage subsidence may represent an incidental radiographic finding rather than clinically relevant criteria used to define successful fusion. The literature, however, highlights a need for further investigation into the clinical impact of cage subsidence.^{12,30}

In addition to the important differences in rates of fusion and cage subsidence, we found that osteoporotic patients incurred much higher costs for both hospitalization and index surgery for cervical degenerative disease. Reasons for the increased costs associated with osteoporosis may include higher rates of postoperative adverse events, longer hospital stays, and greater medication needs.^{20,31} Our review indicates a lack of consensus on whether these outcomes occur more frequently in osteoporotic patients, but 1 large retrospective database review of nearly 30,000 patients by Veeravagu et al identified osteoporosis as a significant predictor of the development of any postoperative complication, such as wound complications, dysphagia, and venous thromboembolic events, in the 180 days following surgery for cervical degenerative pathology.²³ Findings regarding the relationship between osteoporosis and various postoperative complications, however, remain varied across other studies.

A possible explanation for the heterogeneity of our findings may be related to discrepancies in the methodology used to establish a diagnosis for osteoporosis between studies. These included traditional DEXA, CT-based HUs, and Current Procedural Terminology coding for larger database studies. Furthermore, physicians may use various body regions (lumbar spine, cervical spine, and femur) to assess BMD, but emerging studies indicate that in any given individual, BMD can vary between these anatomic locations.^{32,33} In a database study of 3,500 patients, Mounach et al demonstrated that approximately 40% of patients demonstrate discordant T-score values between the hip and spine, with age and obesity as risk factors.³² Although DEXA is the gold standard for BMD measurement, its accuracy in diagnosing osteoporosis can also be limited by cases of severe vertebral degeneration and obesity, as well as the superimposition of other mineralized structures.³⁴ Current management guidelines recommend that physicians obtain patients' BMD, but this is not a

routine practice. Fortunately, spine surgeons routinely obtain preoperative CT scans, especially prior to spinal fusion procedures. For this reason, HU values have emerged as an alternative tool for determining bone quality, and several studies have shown high rates of concordance between HU values and DEXA BMD measurements.³⁴⁻³⁶ In addition to standardizing the acquisition of BMD prior to cervical spine procedures, it may be helpful to establish a validated tool that takes into account the possibility of different values based on technique and location.

Our review has several limitations. The majority of our studies were retrospective in nature, limiting the strength of their conclusions and providing a level of evidence inferior to that of prospective studies. In addition, many studies investigated risk factors for a given primary outcome, rather than comparing the rates of different adverse events between separate cohorts of osteoporotic and nonosteoporotic patients, which often meant that the low number of patients with poor bone quality provided insufficient power to draw conclusions. A similar concern exists with studies where low complication rates were observed. Future studies employing a matched case-control or prospective cohort design would provide stronger evidence, although adequate power is necessary to drive these study designs. Our mixed findings may be related to the high degree of heterogeneity across studies, which includes factors such as inconsistent availability of BMD data, differences in outcome assessments, potential differences in operative techniques, varying follow-up lengths, and different inclusion and exclusion criteria. Specifically, most studies did not specify a history of previous cervical surgery or specify whether patients were medically managed. Future investigations should take care to differentiate between these populations to prevent additional confounding.

CONCLUSIONS

The literature supports the notion that osteoporosis increases risk of cage subsidence and pseudarthrosis after surgical management of cervical degenerative disease. Studies reporting on medical and surgical complications, such as wound complications, distal and proximal junctional kyphosis, readmission rates, and reoperation rates demonstrate varied results, limiting the ability to draw conclusions within the existing literature. Studies that investigate patient-reported outcomes indicate a lack of association between reduced BMD and pain and functionality scores. Overall, our review of the literature indicates that preoperative BMD

assessment can provide valuable information to guide surgical management of patients with disease of the cervical spine. Further research should attempt to prospectively study the relationship between osteoporosis and various postoperative measurements of surgical success and patient satisfaction in order to further inform orthopedic surgeons of avenues to improve outcomes for this vulnerable population.

REFERENCES

- Kushchayeva Y, Pestun I, Kushchayev S, Radzikhovska N, Lewiecki EM. Advancement in the treatment of osteoporosis and the effects on bone healing. *J Clin Med.* 2022;11(24):7477. doi:10.3390/jcm11247477
- Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. *Lancet.* 2011;377(9773):1276–1287. doi:10.1016/S0140-6736(10)62349-5
- Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. *JAMA.* 2009;301(5):513–521. doi:10.1001/jama.2009.50
- Nazrun AS, Tzar MN, Mokhtar SA, Mohamed IN. A systematic review of the outcomes of osteoporotic fracture patients after hospital discharge: morbidity, subsequent fractures, and mortality. *Ther Clin Risk Manag.* 2014;10:937–948. doi:10.2147/TCRM.S72456
- Parenteau CS, Lau EC, Campbell IC, Courtney A. Prevalence of spine degeneration diagnosis by type, age, gender, and obesity using medicare data. *Sci Rep.* 2021;11(1):5389. doi:10.1038/s41598-021-84724-6
- Brenke C, Dostal M, Scharf J, Weiß C, Schmieder K, Barth M. Influence of cervical bone mineral density on cage subsidence in patients following stand-alone anterior cervical discectomy and fusion. *Eur Spine J.* 2015;24(12):2832–2840. doi:10.1007/s00586-014-3725-9
- Opsenak R, Hanko M, Snopko P, Varga K, Kolarovszki B. Subsidence of anchored cage after anterior cervical discectomy. *Bratisl Lek Listy.* 2019;120(5):356–361. doi:10.4149/BLL_2019_058
- Bergin SM, Wang TY, Park C, et al. Pseudarthrosis rate following anterior cervical discectomy with fusion using an allograft cellular bone matrix: a multi-institutional analysis. *Neurosurg Focus.* 2021;50(6):E6. doi:10.3171/2021.3.FOCUS2166
- Ji C, Yu S, Yan N, et al. Risk factors for subsidence of titanium mesh cage following single-level anterior cervical corpectomy and fusion. *BMC Musculoskelet Disord.* 2020;21(1):32. doi:10.1186/s12891-019-3036-8
- Lee JS, Son DW, Lee SH, et al. The effect of hounsfield unit value with conventional computed tomography and intraoperative distraction on postoperative intervertebral height reduction in patients following stand-alone anterior cervical discectomy and fusion. *J Korean Neurosurg Soc.* 2022;65(1):96–106. doi:10.3340/jkns.2021.0131
- Lee NJ, Vulapalli M, Park P, et al. Does screw length for primary two-level ACDF influence pseudarthrosis risk? *Spine J.* 2020;20(11):1752–1760. doi:10.1016/j.spinee.2020.07.002
- Lee Y-S, Kim Y-B, Park S-W. Risk factors for postoperative subsidence of single-level anterior cervical discectomy and fusion: the significance of the preoperative cervical alignment. *Spine.* 2014;39(16):1280–1287. doi:10.1097/BRS.0000000000000400
- Ren B, Gao W, An J, Wu M, Shen Y. Risk factors of cage nonunion after anterior cervical discectomy and fusion. *Medicine.* 2020;99(12):e19550. doi:10.1097/MD.00000000000019550
- Wang M, Mummaneni PV, Xi Z, et al. Lower hounsfield units on CT are associated with cage subsidence after anterior cervical discectomy and fusion. *J Neurosurg Spine.* 2020;33(4):1–8. doi:10.3171/2020.3.SPINE2035
- Yan D, Wang Z, Deng S, Li J, Soo C. Anterior corpectomy and reconstruction with titanium mesh cage and dynamic cervical plate for cervical spondylotic myelopathy in elderly osteoporosis patients. *Arch Orthop Trauma Surg.* 2011;131(10):1369–1374. doi:10.1007/s00402-011-1317-2
- Zhang L, Wang J, Feng X, et al. Outcome evaluation of zero-profile device used for single-level anterior cervical discectomy and fusion with osteoporosis compared without osteoporosis: a minimum three-year follow-up study. *World Neurosurgery.* 2019;124:e1–e9. doi:10.1016/j.wneu.2018.10.024
- Ryan R, Synnot A, Pictor M, Consumers HSC, Group CR. Data Extraction Template for Included Studies. *Group CCAcR.* <https://cccr.org/cochrane.org>.
- Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. introduction—grade evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011;64(4):383–394. doi:10.1016/j.jclinepi.2010.04.026
- Yonenobu K, Abumi K, Nagata K, Taketomi E, Ueyama K. Interobserver and intraobserver reliability of the Japanese Orthopaedic Association scoring system for evaluation of cervical compression myelopathy. *Spine.* 2001;26(17):1890–1894. doi:10.1097/00007632-200109010-00014
- Guzman JZ, Feldman ZM, McAnany S, Hecht AC, Qureshi SA, Cho SK. Osteoporosis in cervical spine surgery. *Spine.* 2016;41(8):662–668. doi:10.1097/BRS.0000000000001347
- Park MS, Ju Y-S, Moon S-H, et al. Reoperation rates after anterior cervical discectomy and fusion for cervical spondylotic radiculopathy and myelopathy: a national population-based study. *Spine.* 2016;41(20):1593–1599. doi:10.1097/BRS.0000000000001590
- Park MS, Ju Y-S, Moon S-H, et al. Reoperation rates after surgery for degenerative cervical spine disease according to different surgical procedures: national population-based cohort study. *Spine.* 2016;41(19):1484–1492. doi:10.1097/BRS.0000000000001581
- Veeravagu A, Cole T, Jiang B, Ratliff JK. Revision rates and complication incidence in single- and multilevel anterior cervical discectomy and fusion procedures: an administrative database study. *Spine J.* 2014;14(7):1125–1131. doi:10.1016/j.spinee.2013.07.474
- Rumalla K, Smith KA, Arnold PM. National rates, causes, risk factors, and outcomes associated with 30-day and 90-day readmissions following degenerative posterior cervical spine surgery utilizing the nationwide readmissions database. *Neurosurgery.* 2017;81(5):740–751. doi:10.1093/neuros/nyx063
- Obremsky WT, Pappas N, Attallah-Wasif E, Tornetta P, Bhandari M. Level of evidence in orthopaedic journals. *The Journal of Bone & Joint Surgery.* 2005;87(12):2632–2638. doi:10.2106/JBJS.E.00370
- Zou D, Muheremu A, Sun Z, Zhong W, Jiang S, Li W. Computed tomography hounsfield unit-based prediction of pedicle screw loosening after surgery for degenerative lumbar spine disease. *J Neurosurg Spine.* 2020;32(5):1–6. doi:10.3171/2019.11.SPINE19868

27. Lehman RA, Kang DG, Wagner SC. Management of osteoporosis in spine surgery. *J Am Acad Orthop Surg.* 2015;23(4):253–263. doi:10.5435/JAAOS-D-14-00042

28. Schmieder K, Wolzik-Grossmann M, Pechlivanis I, Engelhardt M, Scholz M, Harders A. Subsidence of the wing titanium cage after anterior cervical interbody fusion: 2-year follow-up study. *J Neurosurg Spine.* 2006;4(6):447–453. doi:10.3171/spi.2006.4.6.447

29. Wu WJ, Jiang LS, Liang Y, Dai LY. Cage subsidence does not, but cervical lordosis improvement does affect the long-term results of anterior cervical fusion with stand-alone cage for degenerative cervical disc disease: a retrospective study. *Eur Spine J.* 2012;21(7):1374–1382. doi:10.1007/s00586-011-2131-9

30. Lee C-H, Hyun S-J, Kim MJ, et al. Comparative analysis of 3 different construct systems for single-level anterior cervical discectomy and fusion: stand-alone cage, iliac graft plus plate augmentation, and cage plus plating. *J Spinal Disord Tech.* 2013;26(2):112–118. doi:10.1097/BSD.0b013e318274148e

31. Wolfert AJ, Rompala A, Beyer GA, et al. The impact of osteoporosis on adverse outcomes after short fusion for degenerative lumbar disease. *J Am Acad Orthop Surg.* 2022;30(12):573–579. doi:10.5435/JAAOS-D-21-01258

32. Mounach A, Abayi DAM, Ghazi M, et al. Discordance between hip and spine bone mineral density measurement using DXA: prevalence and risk factors. *Semin Arthritis Rheum.* 2009;38(6):467–471. doi:10.1016/j.semarthrit.2008.04.001

33. Younes M, Ben Hammouda S, Jguirim M, et al. Discordance between spine and hip bone mineral density measurement using DXA in osteoporosis diagnosis: prevalence and risk factors. *Tunis Med.* 2014;92(1):1–5.

34. Kim KJ, Kim DH, Lee JI, Choi BK, Han IH, Nam KH. Hounsfield units on lumbar computed tomography for predicting regional bone mineral density. *Open Med.* 2019;14(1):545–551. doi:10.1515/med-2019-0061

35. Marinova M, Edon B, Wolter K, Katsimbari B, Schild HH, Strunk HM. Use of routine thoracic and abdominal computed tomography scans for assessing bone mineral density and detecting osteoporosis. *Curr Med Res Opin.* 2015;31(10):1871–1881. doi:10.1185/03007995.2015.1074892

36. Schreiber JJ, Anderson PA, Rosas HG, Buchholz AL, Au AG. Hounsfield units for assessing bone mineral density and

strength: a tool for osteoporosis management. *J Bone Joint Surg Am.* 2011;93(11):1057–1063. doi:10.2106/JBJS.J.00160

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