Systematic Literature Review and Meta-Analysis on the Clinical Outcomes of Spine Surgeries in Patients with Concurrent Osteoporosis

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Abstract:

Background: Osteoporosis is common among elderly patients and can result in vertebral fractures requiring surgical treatment. This study assessed clinical outcomes associated with spinal surgery in patients with osteoporosis/osteopenia with an additional focus on Asian patients.

Methods: A PRISMA-compliant systematic review and meta-analysis were conducted using the PubMed and ProQuest databases to identify articles published up to May 27, 2021, that included outcomes for patients with osteoporosis or osteopenia undergoing spinal surgery. Statistical analysis was conducted comparing rates of proximal junctional kyphosis (PJK)/proximal junctional failure (PJF), implant loosening, and revision surgery. A qualitative summary of Asian studies was also conducted.

Results: A total of 16 studies comprising 133,086 patients were included; among the 15 studies reporting rates of osteoporosis/osteopenia, 12.1% (16,127/132,302) of patients overall and 38.0% (106/279) of Asian patients (n=4 studies) had osteoporosis/osteopenia. The risks of PJK/PJF (relative risk [RR]=1.89; 95% confidence interval [CI]=1.22-2.92, p=0.004), screw loosening (RR=2.59; 95% CI=1.67-4.01, p<0.0001), and revision surgery (RR=1.65; 95% CI=1.13-2.42, p=0.010) were higher in patients with poor bone quality compared with those with healthy bone. In the qualitative review of Asian studies, all studies found that osteoporosis increased the risk of complications and/or revision for spinal surgery patients.

Conclusions: This systematic literature review and meta-analysis indicate that spinal surgery patients with compromised bone quality have more complications and higher healthcare utilization than those with normal bone quality. To our knowledge, this is the first study to focus on the pathophysiology and disease burden among Asian patients. Given the high rate of poor bone quality in this aging population, additional high-quality Asian studies, with uniform definitions and data reporting, are needed.

Keywords:
Spinal Fusion, Osteoporosis, Spine Surgery, Degenerative Spine Disease, Asia-Pacific

Introduction

Osteoporosis predominantly affects older people and is a major risk factor for bone fractures[1]. Estimates of osteoporosis prevalence vary greatly, but a recent meta-analysis reported a global prevalence of 23.1% (95% confidence interval [CI] 19.8-26.9) in women and 11.7% (95% CI 9.6-14.1) in men, with the highest rates among Asian and African women (24.3% and 42.4%, respectively)[2]. The overall osteoporosis rate in Asia was estimated at 16.7%[2], though a country-specific meta-analysis undertaken in China found an overall osteoporosis rate of 20%[3], and a study of several industrialized countries found that the prevalence of osteoporosis in the spine or hip was highest in Japan (26.3%)[4]. Among osteoporotic fractures, vertebral fractures are extremely common[5], with a lifetime risk of at least 15.6% in

white women and 5.0% in white men[6], and a true incidence that is likely higher given that many vertebral fractures are asymptomatic and never diagnosed[7].

As populations age, the prevalence of osteoporosis and associated vertebral fractures is expected to increase[8,9]. In particular, between 2019 and 2050, the proportion of older people in Asia is projected to at least double[10]; as a result, vertebral fractures are likely to rise substantially in this region[11]. Currently, the rates of osteoporotic vertebral fractures in Asia are not well documented. A study in India using two population-based databases reported 42.7% and 27.7% of subjects had osteoporosis of the spine, respectively[12], and a study conducted in Japan reported a prevalence of osteoporotic vertebral fractures of 17.8%[13]. Given the wide variation in reported rates and scarcity of data, additional studies of Asian osteoporotic patients are needed.

Although most symptomatic osteoporotic vertebral fractures require conservative management, a subset with spinal canal compromise and neurological deficit require surgery[14]. Osteoporosis increases the risk of complications during surgery[15-17] and is associated with vertebral fractures after instrumentation, pseudoarthrosis, implant failure[15], and a significant risk for revision surgery[15,18-20].

Given the aging of the world population, particularly in the Asia-Pacific region, the accumulated evidence on the prevalence and clinical outcomes of surgical management of vertebral fractures in patients with osteoporosis can inform current challenges and future best practices. This systematic review and meta-analysis assessed clinical outcomes associated with surgical management of vertebral fractures in patients with concurrent osteoporosis or osteopenia compared with those with normal bone quality. Studies conducted in Asian countries were also qualitatively assessed to evaluate what is known about spinal surgery patients with osteoporosis compared with those without osteoporosis in this population.

Methods

The study protocol was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement[21].

Literature search

The literature search was performed with the PubMed (on May 27, 2021) and ProQuest (on March 29, 2021) databases. Detailed search terms are shown in Table S1. Duplicate articles were excluded. Two independent reviewers screened titles and abstracts, and, when necessary, full texts; disagreements were adjudicated by a third independent reviewer. Study selection followed the PRISMA flow diagram presented in Fig. 1.

Study selection criteria

Studies of adult (>18 years) patients with compromised bone quality (osteoporosis or osteopenia) undergoing spine surgery published between January 1, 2015, and May 27, 2021, in English, Chinese, Japanese, or Korean that reported one of the primary outcomes of interest by osteoporosis status were eligible for inclusion. Patients could be from any geographical region. Surgical management procedures included open reduction and internal fixation, conducted either at the thoracic, lumbar, thoracolumbar, lumbosacral, or sacral spine. Surgical management using instruments, implants or screws, vertebral body augmentation, kyphoplasty, stenting, and vertebroplasty were eligible for inclusion. All comparative studies were eligible for inclusion.

Studies were excluded for the following reasons: 1) patients did not have concurrent osteoporosis or osteopenia; 2) the study described conventional nonsurgical management or pharmacological or experimental treatments; 3) the study was not an appropriate article type (technical article, including animal, biomechanical or cadaver studies; case report; narrative review; editorial; opinion piece or letter; ongoing clinical trial; or conference abstract that did not report results on outcomes of interest); or 4) the study did not include comparative data between patients with and without osteoporosis.

Outcomes

The primary outcomes were the rate of proximal junctional kyphosis (PJK)/proximal junctional failure (PJF), implant-related complications/implant loosening, and revision surgery.

Data collection

Pre-determined items were extracted by one reviewer and independently checked for accuracy by a second reviewer. Reviewers were not blinded to the authors' names, institutions, journal of publication, or study results. Conflict resolution was done through discussion or by a third reviewer. The extracted data included: study reference, objective, study design, patient counts, demographics and comorbidities, indication for surgery, follow-up time, study groups and treatments, and complications (PJK, PJF, implant-related complications/implant loosening, revision surgeries).

Quality assessment

All included studies were rated by two independent researchers as low, good, or high-quality using the Evidence Level and Quality Guide from Johns Hopkins Nursing Evidence-Based Practice (Table S2)[22]. Quality was primarily determined by the principles of hierarchy of evidence and evidence-based practice guidelines. The quality of the study results within each level of evidence was also assessed. Publication bias was assessed for all outcomes with at least 10 data points using funnel plots.

Statistical analysis

A meta-analysis was performed to compare patients with and without osteoporosis on primary outcomes of interest. For binary outcomes, aggregate risks with 95% CIs were
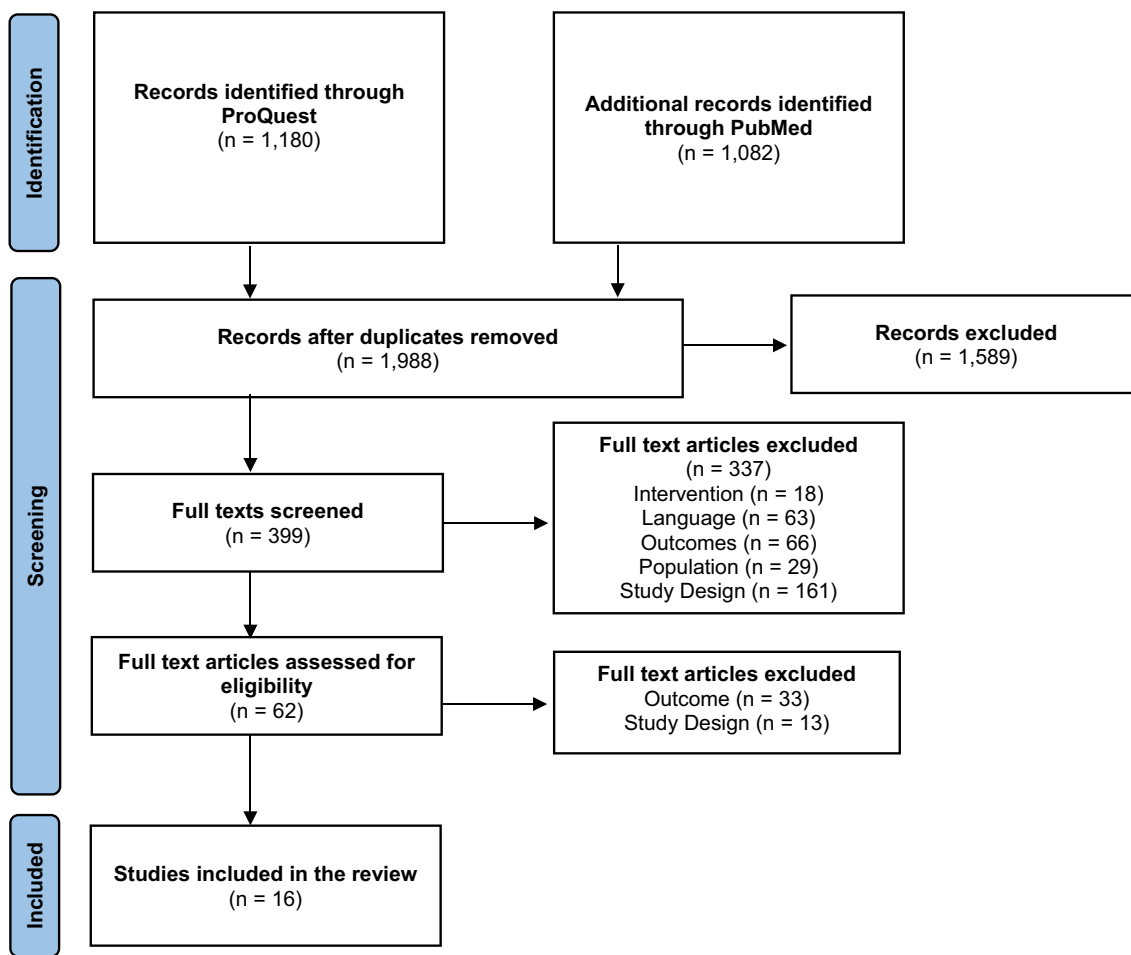
Figure 1. PRISMA study flow diagram.

calculated and pooled risk ratios between cohorts with and without osteoporosis were estimated. The DerSimonian and Laird random-effects model was used when there was high heterogeneity (I^2>50%); otherwise, fixed-effect models were applied. Statistical heterogeneity was assessed using I^2 statistics. A p-value of <0.05 was considered statistically significant. Review Manager (RevMan) [Computer program]. Version 5.5, The Cochrane Collaboration, 2020 was used for statistical analysis.

Results

The literature searches yielded 2,262 citations (1,180 through ProQuest; 1,082 through PubMed). A total of 274 duplicate citations were removed, and 1,589 studies did not meet the inclusion and exclusion criteria. Full texts of the remaining studies were screened and 381 were excluded (Fig. 1). A total of 16 articles were deemed eligible and included in the analysis, including 11 cohort studies, two case series, one case-control study, one registry, and one economic study. One study reported lumbar levels rather than number of patients and reported that 72 of 881 lumbar levels had osteoporosis and 809 had either osteopenia or no osteoarthritis/osteopenia. Excluding this study, the 15 remaining studies comprised 132,302 patients, among whom

16,127 had a compromised bone quality condition (14,244 had osteoporosis and/or osteopenia, and 1,883 had osteopenia).

The study characteristics are presented in detail in Table 1. Most (n=9) studies were conducted in the US, followed by Korea (n=3), Japan (n=2), and Germany (n=2). The size of the patient population in the included studies ranged from 18[23] to 116,749[24]. Fifteen studies reported data on sex (78,368 females and 54,718 males). The mean age at the time of surgery ranged from 33[23] to 71.5 years[25]. Fifteen studies were graded as level III evidence while the remaining study had level IV[23].

Primary outcomes

PJK and PJF

Four studies reported rates of PJK and PJF (Table 2). Of these studies, two had sufficient data to compare the risk for PJK/PJF between those with and without compromised bone quality[17,26]. A forest plot of the random-effects model is shown in Fig. 2. The studies exhibited low heterogeneity (I^2=0%). Those with compromised bone quality were at higher risk for PJK and PFK (relative risk [RR]=1.89; 95% CI=1.22-2.92, p=0.004) compared with those with normal bone quality.

Table 1. Characteristics of the Included Studies.

Study	Study Design	Country	Level of Evidence	Patients (n)				Treatment	Female (n)	Mean Age at Surgery (Years)	Follow-up (Months, Unless Indicated)
				Total	With Osteoporosis	With Osteopenia	Without Osteoporosis/Osteopenia*				
Loffler et al. (2021) [28]	Case-Control	Germany#	III C	46	13	20	13	Primary surgery w/ semi-rigid instrumentation of the lumbar spine	28	69.9	Mean, 12.2
Roberts et al. (2021) [16]	Cohort	USA#	III C	4,743ᵘ	3,162ᵘ	NR	1,581ᵘ	Posterior lumbar fusion w/ or w/out bisphosphonate	NR	NR	≥12
Sumiya et al. (2021) [29]	Cohort	Japan#	III C	76	33	NR	43	Long posterior spinal instrumented fixation at ≥3 levels	29	69.2	2 days
Khalid et al. (2020) [36]	Cohort	USA#	III B	5,169	1,723	1,723	1,723	Single-level lumbar fusion	4,413	NR	24
Park et al. (2020) [26]	Cohort	Korea#	III B	63	18	NR	45	Long instrumented fusion stopping at thoracolumbar junction in adult spinal deformity	57	67.2	Mean, 51.7
Rentenberger et al. (2020) [33]	Cohort	USA#	III C	133	33	58	42	Lateral lumbar interbody fusion	82	67.5	≥12
Rodriguez-Fontan et al. (2020) [17]	Cohort	Germany#	III C	80	28	NR	52	Posterior instrumented fusion with or without Mersilene tape	51	62.3	24
Sharma et al. (2020) [24]	Economic	USA#	III B	116,749	7,145	NR	109,604	Lumbar fusion	69,421	57	≥24
Shimizu et al. (2020) [23]	Case Series	USA	IV C	18	1	NR	17	Pre-operative halo-gravity traction; definitive fusion by 1 or 2-staged posterior-alone approach w/ osteotomies depending on severity	7	33	3
St Jeor et al. (2020) [31]	Cohort	USA#	III B	140	14	82	44	Primary posterior thoracolumbar or lumbar fusion	88	68.8	Mean, 2.1 years (minimum 1 year)
Varshneya et al. (2020) [25]	Cohort	USA#	III B	2,564	971	NR	1,593	Thoracolumbar adult spinal deformity surgery	1,755	71.5	24
Park et al. (2019) [30]	Cohort	Korea	III B	881 lumbar levels (784 patients)	72 lumbar levels (T-score≤ −2.5)‡	Combined with No Osteoporosis patients‡	809 lumbar levels (T-score> −2.5)Φ	Transforaminal lumbar interbody fusion with a bilateral pedicle screw	483	63.3	18
Cho et al. (2018) [15]	Cohort	Korea	III B	86	31 (T-score≤ −2.5)	NR	55 (T-score≥ −1.0)	Posterior lumbar interbody fusion w/ pedicle screw fixation followed by interbody poly-etheretherketone cage	60	66	>24
Uei et al. (2018) [34]	Cohort	Japan#	III C	54	24 (Osteoporosis or Osteopenia)	Combined with Osteoporosis patients	30	Spinal deformity patients ≥65 years treated with correction and fusion surgery of ≥4 levels	50	NR	Mean, 38

Table 1. continued.

Study	Study Design	Country	Level of Evidence	Patients (n)				Treatment	Female (n)	Mean Age at Surgery (Years)	Follow-up (Months, Unless Indicated)
				Total	With Osteoporosis	With Osteopenia	Without Osteoporosis/ Osteopenia*				
Formby et al. (2016)[27]	Case Series	USA	III B	88	18	NR	70	Instrumented transforaminal lumbar interbody fusion w/ pedicle screw instrumentation with polyetheretherketone cage	34	NR	Mean, 35.8
Puvanesarajah et al. (2016)[32]	Registry	USA	III C	2,293	1,030	NR	1,263	Posterolateral fusion of ≥8 levels	1,810	<75, n=1,676; ≥75, n=617	5 years

*In studies that do not include osteopenia patients (all except for Park et al., 2019), this group consists of patients without osteoporosis only.
#Country inferred through author's affiliation.
†T-score, a measure of bone density measured in standard deviations from the average bone density of healthy same-sex 30-year-olds.
ΦT-score between 1 and 2.5 standard deviations below the young adult mean (−1 to −2.5) is considered low bone density, or osteopenia.
¤Numbers following matching of three groups: osteoporosis patients w/ and without bisphosphonate use, and non-osteoporosis patients without bisphosphonate use.
NR, not reported; USA, United States of America

Implant-related complications/screw loosening

Seven studies reported rates of implant-related complications (Table 3)[15,16,27-31]. Four of these studies had sufficient data to compare rates of screw loosening by bone quality[15,27-29]. A forest plot of the random-effects model for the screw loosening analysis is presented in Fig. 3. The studies have low heterogeneity ($I^2=0\%$). Those with compromised bone quality were over two times more likely (RR=2.59; 95% CI=1.67-4.01, p<0.0001) to have screw loosening compared with those with normal bone quality.

Revision surgery

Ten studies reported rates of revision surgeries by osteoporosis status (Table 4)[16,23-25,27,32-36]. Four studies compared the risk for revision surgery by bone quality[24,32,33,36]. A forest plot of the random-effects model for the revision analysis is presented in Fig. 4. The studies exhibited high heterogeneity ($I^2=88\%$). The risk for revision surgery was higher among those with compromised bone quality than for those with normal bone quality (RR=1.65; 95% CI=1.13-2.42, p= 0.010).

Outcomes among asian patients

Five of the included studies were conducted in Asian countries. As noted above, one study conducted in Korea reported an osteoporosis rate of 8.2% (72/881) among lumbar levels[30]. Among the four studies that reported rates among patients, 38.0% of Asian spinal surgery patients had osteoporosis (none of the studies reported rates of osteopenia). All five studies found that osteoporosis increased the risk of complications and/or revision for spinal surgery patients[15,26,29,34]. Three of the studies focused on screw loosening or implant failure (Table 3). The study by Sumiya et al. on Japanese patients retrospectively analyzed the risk of pedicle screw pull-out in 76 patients (746 screws) who underwent at least triple-level posterior fixation for thoracic or lumbar spinal injury, spinal metastasis, or pyogenic spondylitis. By comparing intraoperative cone-beam computed tomography scans with two-day postoperative computed tomography scans, the authors found that patients with screw pull-out were more likely to have osteoporosis than those without (17 vs. 15 patients, p=0.0038)[29]. Similarly, Park et al. found that among 784 Korean patients undergoing transforaminal lumbar interbody fusion, osteoporosis was a significant risk factor for cage migration with subsidence (OR 5.77, p<0.001), cage migration without subsidence (OR 8.73, p<0.001), and cage retropulsion (OR 7.86, p<0.001)[30]. Cho et al. also evaluated the impact of osteoporosis on the clinical and radiological outcomes among Korean patients. Results from 86 Korean patients at least 2 years after undergoing one-level posterior lumbar interbody fusion indicated that even though osteoporosis patients had higher cage subsidence (65.4% vs. 17.6%, p<0.001) and pedicle screw loosening rates (32.3% vs. 12.7%, p<0.029), these did not significantly affect the fusion rate (p=0.727)[15].

Table 2. Studies Reporting Proximal Junctional Kyphosis and Failure.

Study	Study Groups	Proximal Junctional Kyphosis n/N (%)	Additional Analysis	Proximal Junctional Failure n/N (%)	Additional Analysis
Park et al. (2020) [26]	Osteoporosis	NR	NR	10/18 (55.6)	NR
	No Osteoporosis	13/45 (28.9)		NR	
Rodriguez-Fontan et al. (2020) [17]	Osteoporosis	13/28 (46.4) (Both PJK and PJF)	Osteoporosis vs. No Osteoporosis, OR 2.6 (95% CI 0.9–6.8, p=0.08)	Values combined with PJK	Values combined with PJK
	No Osteoporosis	13/52 (25.0) (Both PJK and PJF)			
Shimizu et al. (2020) [23]	Osteoporosis	0/1 (0.0)	NR	NR	NR
	No Osteoporosis	3/17 (17.6)			
St Jeor et al. (2020) [31]	Osteoporosis	5/14 (35.7) (Pooled rate of ORCs*)	Osteoporosis vs. No Osteoporosis/Osteopenia, p=0.138	NR	NR
	Osteopenia	33/82 (40.2) (Pooled rate of ORCs*)	Osteopenia vs. No Osteoporosis/Osteopenia, p=0.005		
	No Osteoporosis/ Osteopenia	7/44 (15.9) (Pooled rate of ORCs*)			

*Osteoporosis-related complications (ORCs) are defined as one of the following: revision surgery, compression fracture, proximal junctional kyphosis, pseudarthrosis, accelerated adjacent segment disease, or instrumentation failure (including screw loosening).
NR, not reported; OR, odds ratio; ORC, osteoporosis-related complication; PJF, proximal junctional failure; PJK, proximal junctional kyphosis

Figure 2. Risk ratio for proximal junction kyphosis and failure in patients with versus without osteoporosis/osteopenia.

Two studies in Asia focused on patients with adult spinal deformity (ASD)[26,34]. Uei et al. examined 54 elderly Japanese with ASD treated with correction and fusion at four or more levels and found that elderly patients who required revision surgery within 2 years had significantly lower mean bone densities of vertebral bodies at T8 (158 vs. 213 Hounsfield units, p=0.03) and T9 (158 vs. 203 Hounsfield units, p =0.02) (Table 4)[34]. Park et al. investigated the risk factors for PJF following long instrumented fusion stopping at the thoracolumbar junction (TLJ) in Korean ASD patients to determine which cases are suitable for TLJ stop without increasing the risk for PJF (Table 2). Osteoporosis was identified as a significant risk factor for PJF in patients with TLJ as the uppermost instrumented vertebra (OR 4.459, p= 0.033), making this level unsuitable for osteoporotic patients[26].

Discussion

According to this systematic review and meta-analysis, poor bone quality is associated with worse outcomes after spinal surgery. Compared with patients without osteoporosis/ osteopenia, those with osteoporosis/osteopenia undergoing spinal surgery are at higher risk of PJK/PJF, screw loosening, and revision surgery. Additionally, our review of Asian studies underscores the burden of poor bone quality in this population and highlights the need for further study and focus on these patients. Similar to previous studies[37,38], we found that many patients undergoing spinal surgery have compromised bone quality. Bjerke et al. reported that among 140 patients undergoing primary posterior thoracolumbar or lumbar fusion, 22.7% had normal bone density, 32.9% had osteopenia, and 50.0% had osteoporosis[37]. Given the high proportion of patients with poor bone quality undergoing spinal surgery, it is critical to understand how outcomes differ among these patients. Our results indicate that in addition to a high risk for primary surgery, osteoporotic patients are also more likely to need revision surgery. Indeed, the increased rate of revision surgery is quite notable; Khalid et al. found that patients with compromised bone quality were almost three times more likely (odd ratio 2.73, 95% CI 1.89-3.94) to need revision surgery than those with normal bone quality[36]. Additionally, the increased risk for screw loosening and PJK//PJF among these patients further under-

Table 3. Studies Reporting Implant-related Complications, Including Screw Loosening by Osteoporosis/osteopenia Status.

Study	Study Groups	Implant-related Complications n/N (%)	Additional Analysis
Loffler et al. (2021) [28]	Osteoporosis Osteopenia No Osteoporosis/Osteopenia	11/13 (84.6) (screw loosening) 9/20 (45.0) (screw loosening) 3/13 (23.1) (screw loosening)	NR
Roberts et al. (2021) [16]	Osteoporosis No Osteoporosis	192/3,162 (6.1) (instrumentation failure) 76/1,581 (4.8) (instrumentation failure)	Osteoporosis w/ bisphosphonate vs. No Osteoporosis, OR 1.20 (95% CI 0.88–1.65); Osteoporosis w/out bisphosphonate vs. No Osteoporosis, OR 1.35 (1.00–1.84)
Sumiya et al. (2021) [29]	Osteoporosis No Osteoporosis	17/33 (51.5) (screw pull-out) 9/43 (20.9) (screw pull-out)	NR
St Jeor et al. (2020) [31]	Osteoporosis Osteopenia No Osteoporosis/Osteopenia	5/14 (35.7) (pooled rate of ORCs*) 33/82 (40.2) (pooled rate of ORCs*) 7/44 (15.9) (pooled rate of ORCs*)	Osteoporosis vs. No Osteoporosis/ Osteopenia, p=0.138 Osteopenia vs. No Osteoporosis/ Osteopenia, p=0.005
Park et al. (2019) [30]	Osteoporosis (T-score≤−2.5) # No Osteoporosis/Osteopenia (T-score≤−2.5) ‖	7/72 lumbar levels (9.7%) (CM w/o subsidence) 13/72 lumbar levels (18.1%) (CM w/ subsidence), 9/72 lumbar levels (12.5%) (CR) 13/809 lumbar levels (1.6%) (CM w/o subsidence), 23/809 lumbar levels (0.1%) (CM w/ subsidence), 8/809 lumbar levels (1.0%) (CR)	Osteoporosis was a risk factor for: CM w/out subsidence, OR 8.73, p<0.001; CM w/ subsidence, OR 5.77, p<0.001; CR, OR 7.86, p<0.001
Cho et al. (2018) [15]	Osteoporosis (T-score≤−2.5) # No Osteoporosis (T-score≥−1.0) #	10/31 (32.3) (screw loosening) 17/24 (70.8) (cage subsidence) 7/55 (12.7) (screw loosening) 9/39 (23.1) (cage subsidence)	Osteoporosis vs. No Osteoporosis, screw loosening, p=0.029; cage subsidence, p<0.001
Formby et al. (2016) [27]	Osteoporosis No Osteoporosis	4/18 (22.2) (pedicle screw loosening) 6/70 (8.6) (pedicle screw loosening)	Osteoporosis vs. No Osteoporosis p=0.14

*Osteoporosis-related complications (ORCs) were defined as one of the following categories: revision surgery, compression fracture, proximal junctional kyphosis, pseudarthrosis, accelerated adjacent segment disease, or instrumentation failure (including screw loosening).

#T-score, a measure of bone density measured in standard deviations from the average bone density of healthy same-sex young adults.

‖T-score between 1 and 2.5 standard deviations below the young adult mean is considered low bone density, or osteopenia.

CI, confidence interval; CM, cage migration; CR, cage retropulsion; OR, odds ratio; ORC, osteoporosis-related complications; NR, not reported
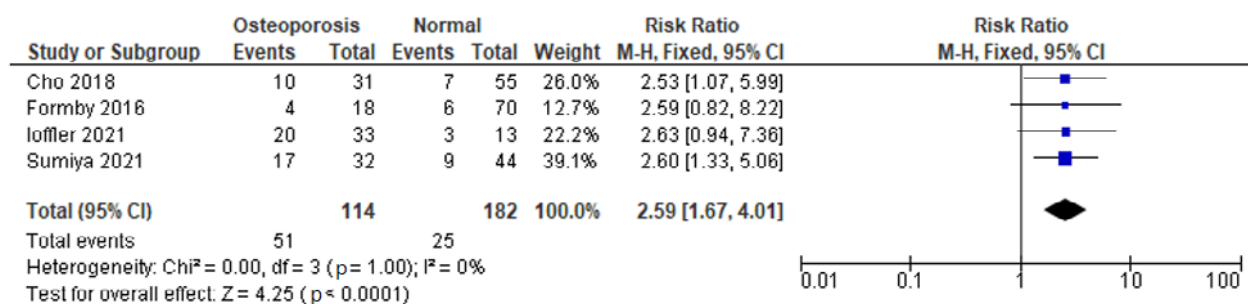

Figure 3. Forest plot for screw loosening in patients with versus without osteoporosis/osteopenia.

scores the increased risk for additional surgery as both are associated with pain and neurological issues that can require reoperation[39-45]. Costs associated with both primary and revision surgery can result in a heavy and increasing economic burden[46]. According to a report published by the Health Insurance Review and Assessment Service in South Korea, osteoporosis-related medical costs increased by 35% from 2007 to 2011[47]. These costs will likely grow substantially as the population ages.

To our knowledge, this is the first review to focus on the pathophysiology of poor bone quality among the Asian population overall. We found that the rate of osteoporosis was higher overall in studies conducted in Asian countries compared with that in all the included studies. This is consistent with other studies that have suggested that regional and country-specific osteoporosis prevalence varies greatly[4,5,48]. A comprehensive review of prevalence rates in several industrialized countries in people above 50 years old documented the wide variation in disease burden with rates of 26.3% in Japan, 21% in the US, 14.3% in Germany, 9.9% in France, 9.7% in Italy, 7.8% in the United Kingdom, 6.3% in Spain, 2.6% in Canada, and 2% in Australia[4]. The

Table 4. Studies Reporting Revision Surgery.

Study	Study Groups	Revision Surgery Definition	Follow-up (Months)	Revision Surgery n/N (%)	Additional Analysis
Roberts et al. (2021) [16]	Osteoporosis No osteoporosis	NR	6 12 6 12	143/3,162 (4.5) 197/3,162 (6.2) 54/1,581 (3.4) 73/1,581 (4.6)	Osteoporosis w/ bisphosphonate vs. No Osteoporosis, OR 1.37 (95% CI 0.96–1.96, p=0.085) (at 6 months); Osteoporosis w/out bisphosphonate vs. No Osteoporosis, OR 1.31 (95% CI 0.91–1.88, p=0.143) (at 6 months) Osteoporosis w/ bisphosphonate vs. No Osteoporosis, OR 1.38 (95% CI 1.01–1.88, p=0.042) (at 1 year); Osteoporosis w/out bisphosphonate vs. No Osteoporosis, OR 1.37 (95% CI 1.00–1.86, p=0.049) (at 1 year)
Khalid et al. (2020) [36]	Osteoporosis Osteopenia No Osteoporosis/Osteopenia	NR	24	127/1,723 (7.4) 108/1,723 (6.3) 41/1,723 (2.4)	Osteoporosis vs. No Osteoporosis/Osteopenia, OR 3.25, 95% CI 2.27–4.65, p=0.02 Osteopenia vs. No Osteoporosis/Osteopenia, OR 2.73, 95% CI 1.89–3.9, p=0.02
Rentenberger et al. (2020) [33]	Osteoporosis Osteopenia No Osteoporosis/Osteopenia	Any secondary surgery/ recommendation of surgery including the index lateral lumbar interbody fusion levels and/or adjacent levels	12	9/33 (27.0) 9/58 (15.5) 7/42 (16.7)	Revision patients vs. nonrevision patients by bone status (Osteoporosis, Osteopenia, No Osteoporosis/Osteopenia), p=0.37
Sharma et al. (2020) [24]	Osteoporosis No Osteoporosis	Refusion	6 12 24 6 12 24	54/7,145 (0.8) 106/7,145 (1.5) 182/7,145 (2.5) 482/109,604 (0.4) 1136/109,604 (1.0) 2,318/109,604 (2.1)	Osteoporosis vs. No Osteoporosis, OR 1.947 (1.456, 2.604), p≤0.001 (6 months); OR 1.559 (1.269, 1.916), p<0.001 (12 months); OR 1.272 (1.087, 1.487), p=0.002 (24 months)
Shimizu et al. (2020) [23]	Osteoporosis No osteoporosis	NR	3	0/1 (0.0%) 3/17 (17.6%)	NR
St Jeor et al. (2020) [31]	Osteoporosis Osteopenia No Osteoporosis/Osteopenia	NR	≥12	5/14 (35.7) (pooled rate of ORCs*) 33/82 (40.2) (pooled rate of ORCs*) 7/44 (15.9) (pooled rate of ORCs*)	Osteoporosis vs. No Osteoporosis/Osteopenia, p=0.138 Osteopenia vs. No Osteoporosis/Osteopenia, p=0.005
Varshneya et al. (2020) [25]	Osteoporosis No Osteoporosis	NR	24	NR NR	Osteoporosis was a risk factor for revision surgery within 2 years, OR 1.58, 95% CI 1.29–1.92, p<0.0001
Uei et al. (2018) [34]	Osteoporosis No Osteoporosis	Revision surgery associated with PJK or additional vertebral fracture	24	6/24 (25.0) 8/30 (26.7)	NR
Formby et al. (2016) [27]	Osteoporosis No Osteoporosis	NR	6	3/18 (16.7) 10/70 (14.3)	Osteoporosis vs. No Osteoporosis, p=0.78

Table 4. continued.

Study	Study Groups	Revision Surgery Definition	Follow-up (Months)	Revision Surgery n/N (%)	Additional Analysis
Puvanesarajah et al. (2016)[32]	Osteoporosis	ICD-9 Codes: P78.69, P81.30, P81.34, P81.35, P81.36, P81.37, P81.38, P81.39, P86.22, CPT Codes: CPT-22010, CPT-22015, CPT-22830, CPT-22850, CPT-22852	12 24 36 48 60	131/1,030 (12.7) 203/1,030 (19.7) 227/1,030 (22.0) 242/1,030 (23.5) 246/1,030 (23.9)	Multivariate analysis at 5 years of follow-up: Osteoporosis associated with an increased revision risk, OR 1.98, 95% CI 1.60–2.46, p<0.0001
	No Osteoporosis		12 24 36 48 60	110/1,263 (8.7) 151/1,263 (12.0) 167/1,263 (13.2) 175/1,263 (13.8) 178/1,263 (14.1)	

CI, confidence interval; CPT, current procedural terminology; ICD-9, International Classification of Diseases, 9th Revision; NR, not reported; OR, odds ratio

prevalence of osteoporosis in many parts of Asia is not well-documented, but according to a meta-analysis, that in China from 2003 to October 2015 was 15.3% in men and 25.4% in women[3]. Given the size and aging of the Asian population worldwide, studies have projected that by the year 2050, Asian patients will account for more than 50% of global osteoporotic hip fractures[49,50]. Moreover, the International Osteoporosis Foundation reported that osteoporosis has been greatly underdiagnosed in Asia, particularly in rural areas[12]. Additionally, almost all Asian countries fall far below the World Health Organization recommendations for appropriate calcium intake (between 1,000 and 1,300 mg/day); for example, the calcium intake for Malaysia, the Philippines, and India remains <500 mg/day[12]. The findings from the studies conducted in Asian countries included in our review underscore the fact that elderly patients in the Asia-Pacific region are a high-risk population for osteoporosis-related ailments. Sufficient studies were not available to perform a meta-analysis on the Asian population overall, highlighting the need for additional research on this population to guide policy development on prevention and treatment in this region.

Limitations

This study had multiple limitations, including incomplete or nonstandardized outcome reporting in the included publications, which limited the number of studies included in the meta-analyses. A second limitation was the relatively low quality of published studies reporting the outcomes of interest; the included studies were cohort studies, which may suffer from selection bias. Third, a lack of large-scale population-based studies and the lack of osteoporosis-oriented studies limited the scope of generalizations and comparisons. Fourth, additional potential complications (distal junctional kyphosis, distal junctional failure, adjacent level fracture, etc.) that may be associated with compromised bone quality were not included in this study, as the relationship between these outcomes and compromised bone quality may be difficult to determine due to limited data. Finally, in many large-scale retrospective studies, osteoporosis was part of multivariate analysis, but further subgroup analysis was not presented. The results of such studies should be interpreted with caution.

Conclusions

According to this systematic review and meta-analysis, patients with poor bone quality undergoing spinal surgery are at higher risk for complications and healthcare utilization than those with normal bone quality. A focus specifically on patients in Asian countries underscored that this patient population is at high risk for osteoporosis-related complications. High-quality studies with uniform definitions and data reporting are needed, particularly among Asian patients, to confirm the study findings and inform strategies for prevention of postoperative complications.
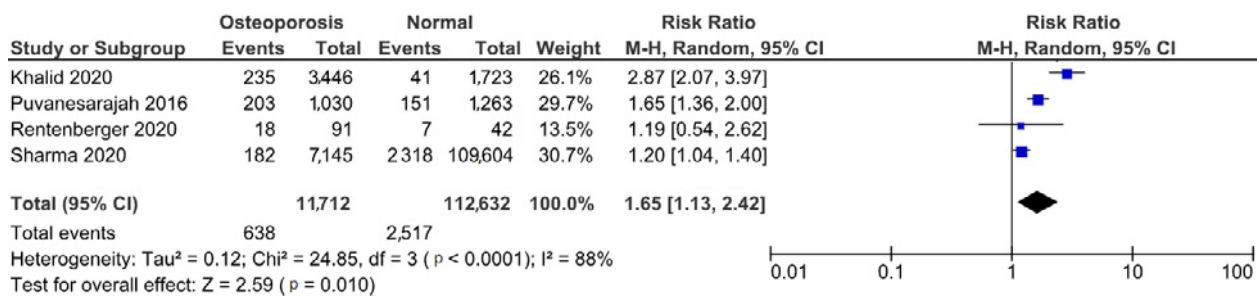
Study or Subgroup	Osteoporosis Events	Total	Normal Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Khalid 2020	235	3,446	41	1,723	26.1%	2.87 [2.07, 3.97]
Puvanesarajah 2016	203	1,030	151	1,263	29.7%	1.65 [1.36, 2.00]
Rentenberger 2020	18	91	7	42	13.5%	1.19 [0.54, 2.62]
Sharma 2020	182	7,145	2 318	109,604	30.7%	1.20 [1.04, 1.40]
Total (95% CI)		11,712		112,632	100.0%	1.65 [1.13, 2.42]
Total events	638		2,517			

Heterogeneity: Tau² = 0.12; Chi² = 24.85, df = 3 (p < 0.0001); I² = 88%
Test for overall effect: Z = 2.59 (p = 0.010)

Figure 4. Forest plot for revision surgery in patients with and without osteoporosis/osteopenia.

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Ethical Approval and Patient Consent: Institutional Review Board approval and patient consent are not required for this study type.

Data Availability: All data relevant to the study are included in the article or uploaded as supplementary information.

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