



The Relation of Osteoporotic Vertebral Fractures and Sarcopenic Characteristics on the Occurrence of Complications: A Systematic Review

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Study Design: Systematic review.

Purpose: As the number of elderly increases, age-related changes of body composition like osteoporosis and sarcopenic muscle changes contribute to higher morbidity, less quality of life and higher health care costs. Data on the effect of muscle atrophy on osteoporotic vertebral fractures is limited. We systematically reviewed the current literature for the influence of preexisting degenerative muscle changes in patients with OVF on the occurrence of complication during and after treatment.

Methods: A systematic literature review adherent to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines was performed using the Web of Science and Medline databases. We considered English and German articles from January 1990 to December 2022. Inclusion criteria covered patients with OVF and muscle degeneration with complications during and after treatment. Included trials were cohort studies and case series.

Results: Eight Studies were included in this systematic review. One studied the role of degenerated paravertebral muscle during conservative treatment. One article analysed the influence of sarcopenia after dorsal instrumentation in patients with OVF, another the effects of muscle degeneration after dorsal instrumentation or kyphoplasty. The other studies evaluated complications after percutaneous vertebroplasty or kyphoplasty. Seven studies described an increased risk for subsequent fracture following OVF treatment in case of muscle degeneration, despite differing methods and cut-offs for muscle degeneration.

Conclusion: Subsequent fractures were the most frequently analysed complication, others were scarcely analysed. Most studies found a correlation of paravertebral muscle degeneration and the occurrence of secondary OVFs. However, very different methods and cut-offs for sarcopenia assessment were used and it remains unclear what defines muscle changes that lead to an increased risk for complications.

Keywords: osteoporotic vertebral fracture, sarcopenia, muscle degeneration, osteoporosis, refracture

Introduction

Vertebral fractures are the most common form of osteoporotic fractures and affect the quality of life due to their high mortality and morbidity risk.^{1,2} Different conservative and surgical treatment strategies offer effective ways for pain relief and improve quality of life. Sequential and adjacent vertebral fractures are complications. Several risk factors like bone quality, age, gender, steroid use, and medical comorbidities were analyzed by previous studies.³

Recently sarcopenia, meaning low muscle strength in combination with low muscle quality and quantity according to European Working Group on Sarcopenia in older people (EWGSOP), is gaining researchers interest as well as a risk factor for osteoporotic fractures.^{4,5} The relationship between osteoporosis, sarcopenia, and vertebral fractures is complex but increasingly recognized in the literature. Both osteoporosis and sarcopenia involve the progressive decline of skeletal

health, but they affect different aspects of the musculoskeletal system. Though different in their primary targets (bones vs muscles), these conditions are closely linked because muscle mass plays a critical role in maintaining bone strength. Osteoporosis can increase the risk of falls and fractures, which can also lead to reduced physical activity, thus exacerbating the loss of muscle mass. Sarcopenia can lead to postural abnormalities increases spinal loading, imbalance, and increased fall risk, which, in turn, elevates the chances of experiencing a fracture. This vicious circle that can emerge from the combined effects of osteoporosis and sarcopenia can severely affect quality of life causing chronic pain, loss of independence and mobility.

Vertebral fractures are among the most common types of fractures associated with osteoporosis, and both osteoporosis and sarcopenia contribute to their occurrence:

Muscle degeneration increases the risk of falls and fractures and impairs mobility and quality of life. Osteoporosis and sarcopenia can occur simultaneously and lead to increased risk of fragility fractures in elderly.⁶ A role of muscle degeneration in occurrence and reoccurrence of osteoporotic vertebral fractures (OVF) seems obvious, but little data exists to prove this hypothesis.

The purpose of this study was to systematically review the current literature for the influence of degenerative muscle changes in patients with OVF for the occurrence of complications.

Methods

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we performed a systematic electronic search of the Web of Science and Medline databases from January 1990 to December 2022. A broad search strategy was favored with the keywords in order to capture as many potentially relevant articles as possible. Databases were queried with the following search terms: (spine AND fracture AND (sarcopenia OR atrophy OR fatty degeneration OR muscle). Only studies in the English or German language evaluating humans were included.⁷

The Population, Intervention, Comparison, and Outcome (PICO) question for this systematic review was: “In a population of patients with osteoporotic vertebral fractures, considered patients with a vertebral fracture after no or an inadequate trauma (P), do muscular changes like sarcopenia, muscle atrophy or fatty degeneration (I) have an influence on the occurrence of complications (O)?”⁸

The systematic review was performed and registered on the International Prospective of systematic reviews (PROSPERO, registration number: CRD42021252980).

Inclusion criteria were defined as

1. Patients with thoracic or lumbar OVF in
2. randomized or nonrandomized controlled trials, any cohort study or case series ($n \geq 10$) evaluating
3. the role of muscular changes like sarcopenia, muscle atrophy or fatty degeneration in the
4. occurrence of complications like refracture, deformity, implant failure, surgical site infection and general complication.

Exclusion criteria were: a) case reports or case series with less than 10 patients, b) review articles or meta-analysis, c) cadaver studies, d) biomechanical studies or models relying on imaging data.

If 2 studies were encountered with shared data, the study with the largest dataset was to be preferred.

Results from both databases were combined and duplicates removed. Two reviewers (ER and DW) independently screened the titles and abstracts of all returned search results. Following this, full-text articles of the retrieved studies were assessed for suitability of inclusion. Discrepancies were discussed until consensus attained. The references of all included studies were reviewed for further eligible articles.

The flowchart of selection process is shown in [Figure 1](#).

We extracted data concerning study characteristics including authors' names, title, year of publication, journal of publication, number of patients, time of follow-up and type of study. For the description of the study population, number

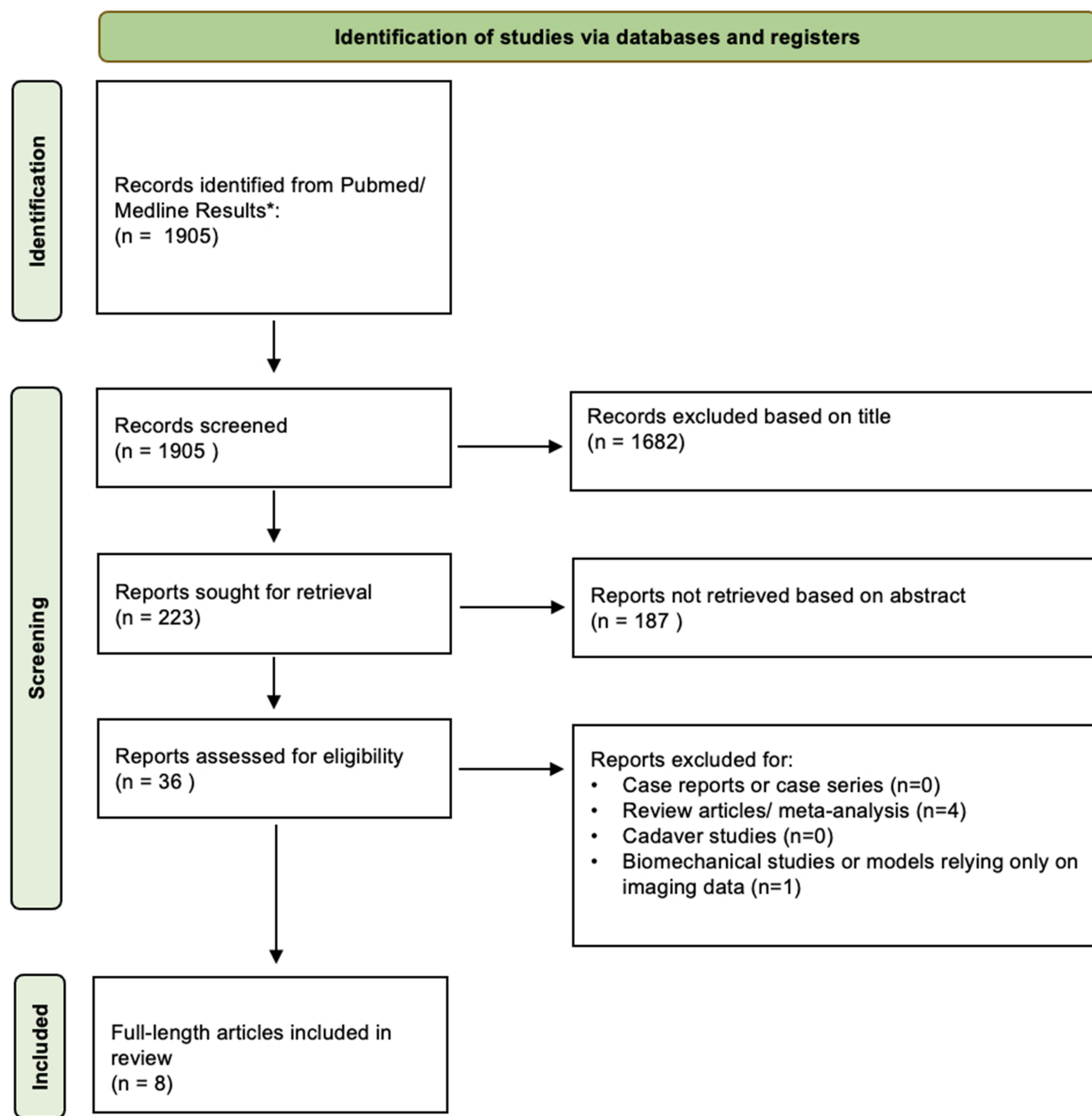


Figure 1 Study selection process according to PRISMA Guidelines 2020. Adapted from Page M J, McKenzie J E, Bossuyt P M, Boutron I, Hoffmann T C, Mulrow C D et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021; 372 :n71. Creative Commons.

of patients and age were collected. Outcome parameters were analyzed according to the inclusion criteria and were assigned to five predicted outcomes: 1) sequential fracture (vertebral/others), 2) implant failure.

Due to heterogeneity of the evaluated studies a meta-analysis was not possible. Quality assessment was performed using Newcastle-Ottawa Scale (Table 1).

Results

Study Selection

Eight articles met the inclusion criteria (Tables 2 and 3). Publication dates ranged from 2019 to 2022. Absence or missing information on osteoporosis or on sarcopenia, absence of vertebral fractures or information missing on complications as

Table 1 Quality Assessment of Bias Using New-Castle Ottawa Scale

Studies		Selection				Comparability	Exposure			Total Quality Score
Authors	Year	Is the Case Definition Adequate?	Representativeness of the Cases	Selection of Controls	Definition of Controls	Comparability of Cases and Controls	Ascertainment of Exposure	Same Method of Ascertainment for Cases and Controls	Non-Response Rate	
Habibi et al ⁹	2021	1	1	0	1	1	1	1	1	7
Wang et al ¹⁰	2019	1	1	0	1	1	1	1	0	6
Si et al ¹¹	2022	1	1	0	1	1	1	1	1	7
Chen Q. et al ¹²	2022	1	1	0	1	1	1	1	1	7
Zhao et al ¹³	2021	1	1	0	1	1	1	1	1	7
Chen Z. et al ¹⁴	2022	1	1	0	1	1	1	1	1	7
Krenzlin et al ¹⁵	2022	1	1	0	1	1	1	1	1	7
Osterhoff et al ¹⁶	2021	1	1	0	1	1	1	1	0	6

Table 2 The Characteristics of Included Studies

Author	Year	Study Type	Population Characteristics	Age/Gender	No.	Follow-Up	Sarcopenia Definition	Methods for Muscle Evaluation
Habibi et al ⁹	2021	Multicenter prospective cohort study	≥65 years old with a fresh fragile symptomatic vertebral fracture	79.1 ± 7.2 years; 80.3 female	117	6 months	N.A.	CSA (ES +MF) at Level of L1 and L5; FI %
Wang et al ¹⁰	2019	Case control study	Patients with single-level osteoporotic vertebral compression fractures who underwent PKP	70.6 ± 8.9 y; 84.8% female; 20.3% sarcopenic	237	1 year	EGWSOP, AGSW	SMI at L3 in CT Grip strength
Si et al ¹¹	2022	Case control study	Patients with osteoporotic vertebral compression fractures who underwent single-level PKP	70.35y; 73.7% female#	202	26.2 months (range 12.7–55.4 month)	N.A.	CSA (ES, MF and PM) at L4-5 and FSF in T2 weighted MRI
Chen Q et al ¹²	2022	Case control study	Patients with OVF undergoing single level PKP	77.98 ± 3.92y; 67% female; 32.2% sarcopenic	214	N.A.	AWGS	Handgrip strength AMI by DEXA CSA (ES+MF) at level L3 in MRI Physical performance (6m gait speed)
Zhao et al ¹³	(2021).	Retrospective single-center case control study	Patients with single-level OVF undergoing PKP	75.3 ± 8.5y; 67.4% female	92	247 ± 90.5 days (range 96–461 days)	N.A.	CSA of PVM (ES + MF) at level of OVF and Signal intensity of PVM. In axial MRI
Chen Z et al ¹⁴	2022	Case control study	Patients with lumbar OVF undergoing PVP or PKP	Non-refracture group (age: 77.16 ± 7.682y; 68.8% female); refracture group (age: 76.25 ± 7.344y; 81.3% female)	144	n.d. (at least 3 month)	N.A.	Preoperative CSA L4 and FI (PS+ES+MF)
Krenzlín et al ¹⁵	2022	Retrospective single-center cohort study	Patients with OVF undergoing dorsal instrumentation	73.7 ± 7.9, 60.3% female, 47.1% sarcopenic,	68	14.1 ± 15.5 months	EGWSOP	$zSMA_{HT}$ at L3 by axial CT images (SMA z-score adjusted for optimal height and BMI); $SMA_{(ES+PM)}$
Osterhoff et al ¹⁶	2021	Monocentric retrospective cohort study	Patients with isolated thoraco-lumbar OVF (T5 to L5) without neurologic deficits treated operatively	77± 8, 60.7 female	191	12 months	N.A.	CSA_{MF} at two levels above and below T12; Goutallier classification for fatty degeneration

Table 3 Treatment and Outcomes

Author	Treatment General	Vertebral Refracture	Other Complications	Conclusion
Habibi et al ⁹	Non-operative, soft vs hard brace, antiosteoporotic treatment	11 (9.4%)	N.A.	Fl% of the PVM in the thoracolumbar region is highly correlated with the occurrence of new OVF, and the Fl% of the PVM in the lumbar region is related to remaining LBP.
Wang et al ¹⁰	Operative PKP + osteoporotic medication (Vitamin D)	64 (27%); non-sarcopenic 43 (22.8%); sarcopenic 21 (43.8%)	N.A.	Sarcopenia is among others an independent risk predictor of osteoporotic compression refractures (OR 2.271; 95% CI 1.069–4.824, $p = 0.033$)
Si et al ¹¹	Operative PKP single level and 6 months anti-osteoporotic medication (calcitonin, calcium carbonate, calcitriol)	54 (26.7%)	N.A.	Subsequent OVFs occurred in 54 of 202 patients (26.7%). FSF _{ES} (OR = 1.064; $P = 0.001$), FSF _{PM} (OR = 1.326; $P < 0.001$), and the difference index of the muscle CSA _{MF/PM} (OR = 1.048; $P < 0.001$) were independent risk factors for the occurrence.
Chen Q. et al ¹²	PKP, antiosteoporotic medication (bisphosphonates, calcium supplementation, vitamin D)	74 (34.6%); 84% in sarcopenic patients	N.A.	Sarcopenia (OR= 5.47; $p = 0.005$) and fatty infiltration of PVM (OR=1.13; $p=0.015$) are independent risk factor for sequential vertebral fracture
Zhao et al ¹³	Single level PKP, postoperatively rigid brace for 3 month	33 (35.9%)	N.A.	Patients with sequential OVF had an significantly decreased CSA during follow-up ($p<0.05$) along with an increase of SI (representing fat content of the muscle)
Chen Z. et al ¹⁴	PVP or PKP single-level	16 (11.1%)	N.A.	In the refracture group CSA _{PM} was significantly smaller ($p<0.003$) and higher FI _{ES+MF} ($p< 0.008$) und FI _{PM} ($p<0.05$) were found
Krenzlin et al ¹⁵	Dorsal spinal instrumentation	N.A.	19 implantfailures, 14 cases in sarcopenic patients. Cementleakage (n=4 out of 28 with cement augmentation), hematoma n=1, surgical site infection n=2; 7 complication in 6 patients, complications only occurred in sarcopenic patients ($p=0.01$)	zSMAHT ($p = 0.0057$) and BMD ($p = 0.0041$) were significantly related to implant failure occurrence.
Osterhoff et al ¹⁶	PKP 27.7%, percutaneous posterior fixation 49.7%,and open fixation 22.5%	23 patients (12%)	N.A.	Multifidus area and multifidus fatty infiltration had no significant effect on the occurrence of adjacent vertebral fractures within one year after the index fracture.

well as non-original were common reasons for exclusions. The articles were divided into two main groups: conservative treatment (one study) and operative treatment (8 studies).

Conservative Treatment

Habibi et al conducted the only eligible study using conservative treatment for thoracolumbar and lumbar OVs consisting of use of soft or hard brace for 2–3 month. In this multicenter prospective study with a follow up of 6 months, 11 out of 117 patients (9.4%) had a sequential OV. The fat infiltration percentage (FI%) of paravertebral muscles (Multifidus and Erector spinae) was associated with the occurrence of new OVs in thoracolumbar region. FI% of the lumbar region was related to remaining back pain. Regarding the cross-sectional area of the back muscles, no significant difference was noted. Based on their findings, Habibi et al recommended paying close attention to fatty degeneration of the paravertebral muscles (PVM) in patients with OVs as this cases may require a more potent treatment.⁹

Operative Treatment

This group consisted of seven studies dealing with OVs treated by percutaneous vertebroplasty (PVP) or percutaneous kyphoplasty (PKP), one study using dorsal instrumentation and another PKP or dorsal instrumentation.

All studies concerning PKP or PVP were case control studies.

Three studies evaluated the relationship between sarcopenia and refracture after both percutaneous kyphoplasty and anti-osteoporotic treatment.^{10–12} In each of these studies more than 200 patients were included and baseline characteristics were similar for age and gender among the groups with and without muscle atrophy. Different methods for muscle evaluation and different muscles were assessed. Anti-osteoporotic treatment differed in each study and included the sole application of vitamin D,¹⁰ or combination therapy with bisphosphonates¹¹/ calcitonin¹² and calcium. Complications other than subsequent fractures were not studied.

Following EWGSOP and AWGS standards Wang et al¹⁰ assessed muscle mass and strength using skeletal muscle index at level of L3 in axial CT scans and grip strength by hand dynamometer. 237 patients were included with a follow-up of one year, 64 secondary vertebral fractures occurred in 64 patients (27%). Sarcopenia was present in 48 patients of whom 21 had secondary fractures and had a higher risk for secondary fractures compared to non-sarcopenic patients. Sarcopenia, lower BMD, advanced age (≥ 75) and female sex were independent risk factors for refracture.¹⁰

Si et al measured the cross-sectional area (CSA) and fat signal fraction (FSF) of Erector spinae (ES), Multifidus (MF) and Psoas Major (PM) in T2 weighted axial MRI at L4-5 to quantify the muscle degeneration. Among the 202 enrolled patients, 54 (26.7%) patients developed new OVs during a mean follow-up of 26.2 month. The FSF of erector spinae (OR = 1.064) and psoas major (OR = 1.326) and the difference index of the muscle CSA between multifidus and psoas major (OR = 1.048) were independent risk factors for the reoccurrence of OVs.¹¹

According to AWGS, Chen Qi et al evaluated muscle degeneration by appendicular muscle mass index, by DEXA, CSA of paravertebral muscles, grip strength and 6m gait speed for physical performance in 214 patients. Subsequent OVs were found in 74 patients, 58 of them in sarcopenic patients. Fatty infiltration of PVM and sarcopenia were independent risk factors for recurrent OV.¹²

In one study dealing with PKP and additional brace for 2–3 month the authors could show a significant decrease of CSA of paravertebral muscles (–10.1%) at the level of the fractured vertebra from preoperative to follow-up MRI in the refracture group (n = 33 out of 92). PVM in this study consisted of Erector spinae, Multifidus and fat tissue inside the lumbosacral fascia posteriorly. As a second parameter for muscle evaluation the authors chose the signal intensity of PVM represented by the grayscale of the region of interest quantified by the software. This parameter showed a significant increase in the refracture group, indicating fatty degeneration, taking into account no difference in between the two group preoperatively.¹³

Chen et al included 144 patients with OV undergoing vertebral augmentation in their study, not differing between PKP and PVP. In preoperative MRI scans, CSA and fatty infiltration at L4 of Erector spinae, Multifidus and Psoas major were measured. Subsequent fractures occurred in 16 patients who showed significantly smaller relative CSA and higher

fatty infiltration of ES and MF. The authors could not validate this parameter as independent risk factors in univariate analysis, however.¹⁴

Krenzlin et al conducted a single-center cohort study to evaluate the effect of sarcopenia and bone mineral density on implant failure after dorsal instrumentation (244 segments) in 68 patients with OVF. Using height and body mass adjusted skeletal muscle area z-scores (Level L3 on axial CT-Scans) as surrogate parameter for muscle mass and fatty degeneration, they revealed that sarcopenia was significantly related to implant failure. General complications (n = 7) like cement leakage, hematoma and surgical site infection occurred in six patients, all were sarcopenic.¹⁵

In contrast, Osterhoff et al measured multifidus muscle atrophy and fatty degeneration in 191 patients before surgery for an OVF. Symptomatic adjacent OVCFs were observed in 23 patients (12%) at mean 12 weeks postoperatively. Multifidus area and multifidus fatty infiltration had no significant effect on the occurrence of adjacent vertebral fractures within one year after the index fracture. The only detected risk factor in this study was pre-existing medication with corticosteroids.¹⁶

Discussion

The systematic review of literature from 1990 to 2022 about a potential effect of sarcopenia on complications after treatment of OVF revealed only eight studies to be included. The prevalence of sarcopenia ranges from 5 to 17% in elderly depending on the utilized definition.^{17,18} Some studies found a combined effect between osteoporosis and sarcopenia, increasing the risk of falls, reduced mobility and fragility fractures.¹⁹ Each vertebral fracture brings a heavy economic burden. In 2010 the direct cost of all osteoporotic fractures in the five largest European countries to be €29 billion.²⁰ As this number will rise due to demographic changes, it is important to understand bone-muscle-interaction in ageing patients and its conclusion for therapeutic strategies.

The studies included in this analysis mainly used the definitions of sarcopenia by the EWGSOP and the AWGS which differ in their cut-offs.²¹ Both state cut-offs for bioelectrical impedance or dual-energy x-ray absorptiometry, but miss thresholds for lumbar 3rd vertebra imaging by computed tomography. This technique is significantly correlated with whole-body muscle mass,²² but in the revised European consensus on sarcopenia (EWGSOP2) it is listed as a future/alternative technique. Most studies (Tables 2 and 3) used MRI scans for CSA measurements with variations in the chosen vertebra level. Muscles accounting for paravertebral muscle measurement varied and sometimes included erector spinae and multifidus or the psoas muscle.

Fat signal intensity as a surrogate parameter for fatty muscle degeneration is widely used to describe poor muscle quality, but it actually differs from sarcopenia, which focusses more on external muscle function.^{23,24} Fatty infiltration of paravertebral muscle is associated with lower back pain and disability.²⁵ Several studies reported the impact of PVM of OVFs, especially about the reduction of PVM after OVF and its relation to delayed union.²⁶ Nevertheless, data on the role of fatty degenerated paraspinal muscle as a potential risk factor for complications or secondary fractures after OVFs is scarce.

Five studies showed that the decrease in CSA was related to occurrence of a secondary fracture. Habibi et al revealed only the FI of the paraspinal muscle, but not the CSA, was significantly correlated with the refractures.⁹ On the other hand, Zhao et al could not show any difference of the CSA preoperatively in refracture and no fracture group, but the authors found a significantly decreased CSA in patients with subsequent fracture in follow-up.¹³ Krenzlin et al showed a significant lower height and BMI adjusted skeletal muscle area in cases of implant failure after spinal instrumentation in OVFs.¹⁵

Seven studies showed that paraspinal muscle degeneration plays an important role of subsequent vertebral fractures after OVFs, but other complications were rarely examined.

In contrast, Osterhoff et al found no association between secondary symptomatic vertebral fractures and fatty infiltration or CSA in their sample of 191 patients.¹⁶

This systematic review was limited by the number of eligible articles, their heterogeneity and level of evidence. Despite differing methods and study quality, all authors agreed on the impact of sarcopenia on the occurrence and reoccurrence of OVFs. Except for the study by Habibi et al on conservative treatment, all studies were retrospective cohort studies. None of the studies combined the measurements for sarcopenia with an assessment for general fragility.

Further prospective studies are necessary to evaluate sarcopenia in paravertebral muscles and its effect on the treatment of OVF. Assessing the muscle condition before treatment may be beneficial to recognize high risk patients and to prevent complications via early detection and treatment of sarcopenia.

Conclusions

Subsequent fractures were the most frequently analysed complication, others were scarcely analysed. Most studies found a correlation of paravertebral muscle degeneration and the occurrence of secondary OVFs. However, very different methods and cut-offs for sarcopenia assessment were used and it remains unclear what defines muscle changes that lead to an increased risk for complications.

Abbreviations

AMI, Appendicular muscle mass index; AWGS, Asian working group of sarcopenia; CSA, Cross-sectional area; EGWSOP, European Working Group on Sarcopenia in older people; ES, Erector spinae; FI%, Fat infiltration %; FSF, Fat signal fraction; IF, Implant failure; LBP, Lumbar back pain; MF, Multifidus; OVF, Osteoporotic vertebral fracture; PKP, Percutaneous kyphoplasty; PM, Psoas major; PVM, Paravertebral muscles; PVP, Percutaneous vertebroplasty; SI, Signal intensity; SMA, Skeletal muscle area; SMI, Skeletal muscle index.

Data Sharing Statement

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

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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