The effect of sarcopenia on outcomes following orthopedic surgery

The effect of sarcopenia on outcomes following orthopedic surgery: a systematic review

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ABSTRACT

Background

Sarcopenia is characterised by a generalised progressive loss of skeletal muscle mass, strength, and physical performance. This systematic review evaluated the effects of sarcopenia on postoperative functional recovery and mortality in patients undergoing orthopaedic surgery and secondarily assessed the methods used to diagnose and define sarcopenia in the orthopaedic literature.

Methods

A systematic search was conducted in MEDLINE, EMBASE and Google Scholar databases according to the PRISMA guidelines. Studies involving sarcopenic patients that underwent defined orthopedic surgery and recorded postoperative outcomes were included. The quality of the criteria by which a sarcopenia diagnosis was made was evaluated. Publication quality was assessed using Newcastle-Ottawa Scale.

Results:

A total of 365 studies were identified and screened, 26 full text records were reviewed, and 19 publications included in the review. In total 3009 patients were included, of which 2146 (71%) were female and 863 (29%) were male. Mean age of the participants was 75.1yrs (SD 7.1). Five studies included patients who underwent spinal surgery, 13 included hip or knee surgery and a single article evaluated distal radius fixation. Mean follow up was 1.9 years (SD: 1.9 years). There was wide heterogeneity in measurement tools and evaluated parameters across the included papers. Sarcopenia was associated with at least one deleterious effect on surgical outcomes in all 19 studies. Post-operative mortality rate was reported in 11 papers and sarcopenia was associated with poorer survival

in 73% (8/11) of these. The most commonly utilised outcome was the Barthel index (4/19), and sarcopenic patients recorded lower scores in 75% (3/4) of these. Sarcopenia was defined using the gold standard three parameters (muscle strength, muscle quantity or quality and muscle function) in 21% of studies, using two parameters in 21% studies and one in the remaining 58%. The methodological quality of included papers was moderate -high.

Conclusions

The orthopaedic literature suffers from heterogeneity in outcomes and classification of sarcopenia diagnostic parameters. However, what data exists suggests that sarcopenia impairs recovery and increases postoperative mortality, especially in the trauma setting. Further research is required to create processes for the accurate diagnosis of sarcopenia in orthopaedics, which may facilitate targeted pre-operative interventions that aim to improve outcomes.

KEY WORDS

Sarcopenia, orthopaedics, outcomes, muscle, aging

INTRODUCTION

The ageing population brings with it the challenge of an increased prevalence in age-related health issues such as sarcopenia (1). This degenerative process affecting muscle fibre size and number has been shown to be associated with a number of impairments including functional deterioration, physical disability, increased morbidity and mortality, as well as increased healthcare costs (2).

Sarcopenia is known to be associated with poor surgical outcomes. Systematic reviews have outlined that patients with sarcopenia undergoing abdominal surgery have higher rates of postoperative complications, longer length of hospital stay, higher mortality, and lower disease-free survival (3,4). The same issues have been reported in older patients following blunt trauma (5). In urological, oncological and colorectal surgery, sarcopenia has been found to be associated with adverse outcomes (6–8), while sarcopenic patients undergoing vascular surgery have been shown to have increased healthcare costs (9). Sarcopenia has also been associated with an increased risk of perioperative infection in patients undergoing reconstructive flap based procedures (10). However, the literature is limited regarding the influence of sarcopenia on the outcomes of orthopaedic interventions, despite some 44% of elderly patients undergoing orthopaedic interventions being sarcopenic (11). Despite the recognized general association between frailty, sarcopenia and poorer surgical outcomes, there is no consensus as to the effect of sarcopenia on outcomes following orthopaedic intervention. A further issue is that there is no agreed definition of sarcopenia within orthopedic research communities.

The criteria that determine the clinical assessment of sarcopenia is heterogeneous. To address this the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) issued guidelines in 2018 that proposed a sarcopenia diagnosis should be confirmed by the presence of reduced muscle strength and either low muscle quantity or quality; with cut-off values to meet criteria set 2.0 standard deviations below the mean of a young adult healthy reference population (12). Probable sarcopenia is identified by the presence of low muscle strength alone and the diagnosis is confirmed by presence of low muscle mass or quality. However, muscle strength does not depend solely on muscle mass, and the relationship between strength and mass is not linear (13). Additional demonstration of low

physical performance is defined as severe sarcopenia (12). Further distinction defines primary sarcopenia as age related muscle decline, where no other cause or co-morbidities are contributing to muscle loss. Secondary sarcopenia, in contrast, is described when other systemic diseases and co-morbidities are contributing to the aging process and muscle decline (14). Complicating this are reports, which suggest that clinical sarcopenia criteria may vary between different countries due to inherent human phenotypic differences associated with different ethnicities (1).

Various tools can estimate muscle mass and quality. Muscle mass is measured using bioelectrical analysis (BIA) or dual-energy X-ray absorptiometry (DXA), which estimates the appendicular skeletal muscle mass (ASM). To obtain more accurate estimates of muscle mass, ASM can be adjusted for variables, which exist between patients. ASM normalized to patient's height is defined as the skeletal muscle index (SMI). ASM can also be normalized to weight and BMI. Suggested cut-off values for low SMI are 7.0 kg/m^2 in men, 5.4kg/m^2 in woman or SMI >2 standard deviations below average for healthy men and women (15). Computer tomography (CT) or magnetic resonance imaging (MRI) measurements of psoas major and other abdominal muscles can also estimate central muscle quantity and quality. Crude cross sectional area of psoas is defined as Total Psoas Area (TPA), which also may be normalized to patient's vertebra size and is defined as the psoas:lumbar vertebral index (PLVI) or to patient's height, defined as psoas major index (PMI) (16). Muscle quality can additionally be assessed using the measured psoas attenuation on CT imaging, a measure of muscle density, which shows the degree of muscle infiltration with adipose tissue (17). Muscle strength is the key feature of sarcopenia diagnosis and mainly measured by handgrip strength (HGS). Low strength is generally indicated as the inability to record 26–30 kg for men and 16–20 kg for women on a hand held dynamometer (1). Finally, physical performance can be measured by gait speed and timed up and go test (TUG). Walking a distance of <400 m in 6 minutes is indicative of sarcopenia (15). For simplicity, a single cut-off speed ≤0.8 m/s is advised by EWGSOP2 as an indicator of severe sarcopenia (12). Detailed methods of assessing parameters of sarcopenia are supplied in Supplementary Table 1.

The purpose of this review is to evaluate the influence of sarcopenia on the outcomes of orthopaedic surgery and secondarily to investigate and qualify the definition of sarcopenia applied in these reports.

METHODS

A systematic review was conducted according to the updated Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines (18). We searched Ovid MEDLINE and EMBASE for English language peer-reviewed published papers from earliest records until 3rd January 2021. The search was conducted by a single author (FB) and two authors (FB and DH) independently screened titles and abstracts. In cases of disagreements papers were included for full review.

Search terms and inclusion criteria

The search terms were "Sarcopenia" AND "Orthopaedic procedures" [MeSH terms] OR "fracture" [MeSH terms], OR "arthroplasty" [MeSH terms]. Independent searches using the same MeSH terms were carried out in each database and the results were combined.

Studies assessing the influence on sarcopenia on clinical outcomes following orthopaedic intervention were included. Randomized controlled trials and cohort studies were considered. Nonclinical studies, reviews, case reports, unpublished data and conference reports were excluded. Studies were also excluded where sarcopenia or the orthopaedic intervention was not clearly defined or reported. Bibliographies of all relevant papers and review articles were manually searched in Google Scholar.

Data extraction

One author (FB) performed the data extraction. Relevant data (authors, study date, study type, numbers of participants, patient demographics, sarcopenia definition, orthopaedic intervention and associated surgical outcomes) was exported to a bespoke database for analysis. Definitions of sarcopenia and criteria for assessment were considered as per EWGSOP guidance. Microsoft Excel

was used to calculate the mean and standard deviation of the age and BMI of patients, male to female ratio and mean follow up periods.

Risk of bias assessment

All papers were individually assessed for methodological quality by 2 authors (FB and DH) using the Newcastle-Ottawa Scale (NOS) (19). This quality assessment tool consists of 9 items addressing the selection of the study groups; the comparability of the groups; and the ascertainment of the outcome of interest. Based on the NOS, each study was evaluated using a scoring system, quantified by the number of stars awarded. When a study included relevant information that was associated with methodological quality of the NOS tool, one star was awarded. Studies assigned 7-9, 4-6, and 0-3 stars were identified as high quality, moderate quality and low quality respectively. Studies were also assessed independently for quality of sarcopenia detection. Studies, which did not employ two parameters to detect sarcopenia, were deemed to have inadequate ascertainment of exposure (sarcopenia status).

RESULTS

The initial search yielded 362 publications. Three studies were subsequently added through searching the Google Scholar search engine. After screening of article titles and abstracts, 26 studies were included for review (Figure 1). Following full text evaluation, a further 7 were excluded, leaving 19 studies that met the inclusion criteria. The included papers comprised 6 prospective and 13 retrospective cohort studies (Table 1). In total there were 3009 patients, of which 2146 (71%) were female and 863 (29%) were male. Mean age of the participants was 75.1yrs (SD: 7.1). The average age of patients in sarcopenic and non-sarcopenic cohorts was reported in 18 studies. The mean age of sarcopenic patients was 78.2 (SD: 5.7) and the mean age of the non-sarcopenic patients was 74.5 (SD: 6.5). BMI differences were reported in 13 studies, with the mean reported BMI being 23.2 (SD:1.9) and 26.2 (SD: 2.9) in the sarcopenic and non-sarcopenic groups respectively.

The papers reflected a variety of orthopedic interventions, primarily aimed at treatment of elderly trauma and osteoarthritis conditions. Fourteen studies were performed on trauma patient cohorts, two studies on elective patients and two studies on mixed cohorts of trauma and elective patients. Five studies included patients who underwent spinal surgery (vertebroplasty and kyphoplasty), 13 included hip or knee surgery (total hip arthroplasty, hemiarthroplasty or internal fixation, and a single cohort of total knee arthroplasty). Additionally, a single article evaluated distal radius fixation. Nine studies reported data from Asia, 6 from North America and 4 from Europe. Mean period of follow up for clinical outcomes was 1.9 years (SD: 1.9, range 5 days to 5.6 years).

Effect of sarcopenia on outcomes

Sarcopenia was associated with at least one deleterious effect on surgical outcomes in all 19 studies. Post-operative mortality rates were reported in 58% (11/19) of included studies. Significantly increased post-operative mortality rates for patients defined as sarcopenic were reported in 73% (8/11), while 27% (3/11) showed no statistical difference in mortality outcomes. Moreover, mortality rates were measured in 64% (9/14) of studies assessing strictly trauma patient cohorts and in 50% (1/2) studies strictly assessing elective patients. Sarcopenia was associated with increased mortality in 78% (7/9) of the studies where surgical intervention was indicated for traumatic fractures, whereas Charest-Morin et al., 2018 showed that sarcopenia did not affect mortality rates in the elective orthopaedic patient cohort (20).

In the setting of hip fracture surgery, Deren et al., 2017 showed that the 1 year mortality rate was 28.6% in the sarcopenic group compared with 12.3% in the control *(P* = 0.0419), whereas Bae and Moon et al., 2020 showed no difference in 1 year mortality (*P* = 0.512) (21,22). Kim et al., 2018 showed no difference in 1-year mortality rates between the sarcopenic cohort and the control (*P* = 0.793), but a significant difference in the 5-year mortality rate was detected (*P* = 0.028) (23). Independently, psoas:lumbar vertebral index (PLVI) as a marker of central sarcopenia was predictive of increased risk of mortality in spinal surgery. The follow up period to assess mortality in studies

ranged from 6 months to 5 years. The range of follow up periods and the heterogeneity in the performed orthopaedic procedures may explain the differences in recorded mortality outcomes.

In the elective setting, Babu et al., 2019 showed that a higher psoas:lumbar vertebral index (PLVI) measurement was protective against infection (odds ratio 0.28, 95% confidence interval 0.109-0.715, $P = 0.008$) in patients undergoing THA and TKA, noting that this may be as a result of secondary sarcopenia and underlying diseases such as diabetes and other conditions leading to immunosuppression. Charest-Morin et al. showed that sarcopenia had no effect on postoperative infection rates in patients undergoing primary elective thoracolumbar surgery (20,24). Similarly, Deren et al. showed no difference in post-operative infection rate for patients undergoing THA for traumatic acetabular fractures (21).

There were 21% (4/19) of studies that used the Barthel Index to record postoperative activities of daily living after hip fracture surgery. Significantly lower Barthel Index was recorded in 75% (3/4) of those that reported this outcome. Barthel Index scores range from 0 (total functional dependency) to 100 (total functional independency) and Landi et al. highlighted that the scores at the time of discharge from a rehabilitation unit after hip surgery were 58.9 in the sarcopenic group and 69.2 in the non-sarcopenic group ($P < 0.001$) (25). However, Malafarina et al. found no significant difference in Barthel Index at time of discharge (26).

Other measured outcomes found that sarcopenic cohorts were associated with greater care costs, transfusion rates and increased likelihood of advanced imaging postoperatively (27). Bokshan et al. showed that patients defined as sarcopenic had a hospital length of stay 1.7-fold longer compared with the control (8.1 vs. 4.7 days; P = 0.02) (11). Roh et al. (Table 1) also showed the association of sarcopenia with poorer Michigan Hand Questionnaire score after distal radius fracture surgery (28).

Sarcopenia definition

The gold standard three sarcopenia parameters (muscle strength, muscle quantity or quality and muscle function) were measured in 21% (4/19) of studies and sarcopenia was diagnosed when at least two of the three parameters met the threshold criteria. Two parameters were measured in a further 21% (4/19) studies, where both parameters had to be present to diagnose sarcopenia. Only one sarcopenia parameter was recorded in the remaining 58% (11/19) of the studies (Table 2). No study made the distinction of diagnosing patients with likely primary or secondary sarcopenia. Likewise, no study categorized patients as "pre-sarcopenic", "sarcopenic" or "severely sarcopenic" based on EWGSOP2 guidelines (12).

All 19 studies estimated patient's muscle mass, for which 53% (10/19) of the studies used CT imaging, 21% (4/19) used DXA imaging, 21% (4/19) used BIA and 5% (1/19) used anthropometry skin fold measurements. Muscle mass was determined through CT imaging; five times at the L4 vertebra and five times and at the L3 vertebra level. CT scan derived muscle mass size was normalized to lumbar vertebra size (PLVI) in 3 studies and to patient's height in 4 studies (NTPA, SMI and PMI).

Six papers determined sarcopenia or low muscle mass based on the total cohort's muscle mass distribution measurements. Sarcopenia or low muscle mass was determined if the measurement was below the mean value in one study, the median value in two studies, the tertile value in two studies and the quartile value in two studies. Two studies adjusted muscle mass measurement threshold values to the studied population (23,29). Handgrip strength was measured in 42% (8/19) of the studies and the gait speed was measured in 16% (3/19) of the studies. Low gait speed was consistently defined as walking speed ≤0.8 m/s. Low handgrip strength was defined as < 26 kg in men and < 18 kg in women in 6 studies and as HGS < 30 kg in men and < 20 kg in women in 2 studies.

Quality assessment (NOS)

Based on the Newcastle-Ottawa Scale, 74% (14/19) studies scored 7 or more and were therefore of high quality. The remaining 5 studies were of moderate quality. In particular, the assessment of the

presence of sarcopenia was unsatisfactory. Assessment of clinical outcome was poorly reported and only 4 studies included independent blinded assessment of measured outcomes, where separate assessors were determining presence of sarcopenia and the outcomes of interest. Length of follow-up was deemed adequate in 74% (14/19) studies, when outcomes were measured at a minimum of 1-year to assess mortality or functional outcomes.

DISCUSSION

This systematic review is limited by the heterogeneity in outcomes reported and the definition of sarcopenia diagnostic parameters used, however, the data suggests that the presence of sarcopenia generally increases postoperative mortality and impairs recovery in patients undergoing orthopaedic surgery. Though formal meta-analysis was not feasible, clear trends were apparent. All studies included in this review broadly suggested a deleterious effect of sarcopenia on postoperative outcomes. Importantly, of the studies, which reported mortality, 73% showed an association with sarcopenia. Moreover, where only trauma patients were included, increased mortality rates were reported in 78% of the studies. Notably, Deren et al. showed that 1-year mortality could be as high as 28.6% in sarcopenic patients compared to 12.3% mortality rate in a control cohort. No specific surgical intervention was highlighted to yield particularly poor survival outcomes for sarcopenic patients. However, due to variations in elective and emergency procedures, the type of surgery performed and the duration of the period for mortality follow up, it was not possible to quantify accurately the effect of sarcopenia on survival from the available data.

Sarcopenic patients were also shown to have poorer recovery outcomes following surgery. While there was some variation in this data (Table 1), all reports indicated either worse or equivalent outcomes across assessed parameters for patients with sarcopenia. Significantly lower Barthel Index scores were reported in sarcopenic patients in 3 of the 4 studies assessing activities of daily living after hip fracture surgery. Roh et al. also showed that sarcopenic patients were likely to have lower activities of daily living scores using the Michigan Hand Questionnaire 6 and 12-months after distal

radius fracture surgery (p<0.001) (28). Lower function after surgery in sarcopenic cohort was also determined by an increased likelihood of discharge to a nursing home (OR 3.2) (30) and by increased hospital length of stay (1.7-fold longer compared with the control, 8.1 vs. 4.7 days) (11). Poorer recovery outcomes may also translate into greater care costs, with the in hospital cost of sarcopenic patients suggested to be 1.75-fold greater than of the non-sarcopenic groups (27).

The variation in outcomes data may be influenced by the different methodologies used to define sarcopenia. All the studies included in this review were published after 2010 and therefore should follow the EWGSOP reporting guidelines that were introduced in 2010, which include at least two sarcopenia parameters. However, of the 19 studies in this review, only 8 used two or more parameters (31). Over half of the studies utilized CT imaging for muscle mass detection, which may be explained by frequent preoperative use of CT imaging for patients who are admitted with acute trauma and may reflect a convenient data resource. Unfortunately, recent publications suggest that there is no standardized protocol for image acquisition of body fat and muscle mass using this technique (32). Currently, in sarcopenia research, an accurate and most frequently used landmark among sectional body composition studies is the L3 level of the lumbar vertebra, used for the measurement of total abdominal muscle area (33). Schweitzer et al. studied L1 to L5 cross sections to determine the best estimates of skeletal muscle and visceral fat using single slice image of MRI and confirmed that L3 level showed highest correlation with whole-body skeletal muscle and visceral fat volume (34,35). In our systematic review, L3 and L4 landmarks were used equally. This review also highlights the disparity in CT scan cross-sectional methods of determining cut off points; Byram et al. used a psoas:lumbar vertebral index (PLVI) threshold of 0.603, whereas Babu et al., 2019 used as PLVI 0.842 threshold (24,36). Nevertheless, once a standardized method is available, a tool like PLVI, which may be derived quickly from preoperative imaging may help with preoperative planning and aid in the decision making (37).

Another potential issue was defining sarcopenia based on a low muscle mass threshold value derived from the studied cohort's mean, median, tertile or quartile; methods which may be subject to sampling

bias. Likewise, studies originating from different continents were likely composed of different ethnicities known to require differing thresholds and this was seldom controlled for. Single publications offer unique parameters or cut-off values for specific populations, although what actually constitutes a different sarcopenic population is a question fraught with difficulty (38). For example, Bahat et al. has recommended a HGS threshold values of <32 kg for men and <22 kg for women in the Turkish population, distinct from the EWGSOP2 guidelines (12,39). Better-defined threshold values for specific populations would eliminate confounding and would improve accuracy in sarcopenia diagnosis. This is difficult though where multiple ethnic groups live together and epigenetics as well as social factors may influence the development of sarcopenia. Our review highlights that the available data for outcomes following orthopaedic surgery comes from multiple populations across the globe, with the majority of reports originating from Asia. Until population specific evidence is available, future orthopaedic studies should adhere to the EWGSOP2 guidelines, where cut off points for low HGS are <27kg for men and <16kg for women. Likewise, CT calculated ASM values based on CT imaging: <20kg for men and <15kg for women and ASM/height2 values: <7.0kg/m2 for men and <5.5kg/m2 for women. Moreover, the general lack of a measure of muscle strength and functional parameters in 11 of the included studies can be considered the more pressing issue in our literature base and may have contributed to inaccurate sarcopenia detection.

This study has several limitations. The included papers were heterogeneous in design and contained a variety of measured outcomes at assessment time points. These factors precluded a meaningful meta-analysis of the mortality results or of the functional outcomes. As there is no standardised approach to preoperative sarcopenia detection, all methods measuring parameters of sarcopenia were accepted, which may also have affected the observed results. The included studies did not specify if the patients were likely to have “primary” or “secondary” sarcopenia and whether the patients were “pre-sarcopenic”, “sarcopenic” or “severely sarcopenic”. The later distinctions were most likely impossible to make in the majority of the studies, as there was an inadequate number of sarcopenia parameters measured. Furthermore, study selection was limited to publications that explicitly defined the sarcopenic cohort and the orthopaedic intervention. As such, it is possible that there was an omission

of publications where sarcopenic patients underwent orthopaedic intervention but were poorly described.

No system exists which stratifies patients into risk groups based on the extent of sarcopenia and the associated burden on patient's physiological reserve. Such preoperative stratification could be used to better inform the shared decision-making process between surgeons and patients, as well as targeting early interventions to these patients. Future research should define acceptable methods for sarcopenia diagnosis in context of elective and acute trauma orthopaedic surgery, where fractures may impair muscle strength or function measurements. Such a tool would assist in preoperative decision-making, particularly for patients who are at high risk of postoperative complications or mortality. Moreover, recognition of sarcopenia could highlight the patients that may benefit from enhanced postoperative recovery protocols. Logistical difficulties of obtaining sarcopenia parameters in day to day clinical orthopaedic practice will likely be a limiting factor in assessing patients for sarcopenia, particularly in the trauma setting. We propose that further research assesses the role of sarcopenia screening questionnaires such as the SARC-F, as proposed by the EWGSOP2 guidelines (40,41) as these tools may prove more feasible. Further research is also needed in the elective setting for pre-operative risk stratification. However we propose that in preoperative arthroplasty clinics, assessing muscle hand grip strength and additionally muscle function performance tests such as the timed-get-up-and-go, would likely be feasible. Most research studies utilise CT imaging for muscle mass detection, although this is neither practical nor resource efficient. Trials have been conducted in ultrasound imaging in the clinic setting for rectus femoris muscle mass detection. This may be more feasible and has been shown to have good intra- and inter-observer reliability, even in older patients (39,42).

It may also be that the effects of sarcopenia when recognized can be ameliorated. In the context of elective surgeries, evidenced-based guidelines for the prevention and improvement of sarcopenia by the American Medical Directors Association are available. These suggest that sufficient protein intake (>1.2 g/kg/d) slows loss of muscle mass and leucine-enriched amino acids can enhance muscle strength (43). Further, resistance exercise has been established as a reliable treatment option for

sarcopenia (44). In the context of trauma setting, Ekinci et al., 2016 highlights possible dietary augmentation with calcium β-Hydroxy-β-methylbutyrate (CaHMB), vitamin D, and protein supplementation in sarcopenic patients after a hip fracture, showing improvement in muscle strength and function outcomes (45). There is further hope in selective androgen receptor modulators, selective to skeletal muscle for patients with severe muscle wasting, however studies on this are still in the early stages (46).

In conclusion, the orthoapedic literature suffers from heterogeneity in outcomes and classification of sarcopenia diagnosis parameters. However, what data exists broadly suggests that sarcopenia impairs recovery and increases postoperative mortality, especially in the trauma setting. Further research is required to create systems that allow for accurate diagnosis of sarcopenia in both elective and trauma settings, and if sarcopenic patients could be accurately identified, they stand to benefit from targeted pre-operative interventions that aim to improve outcomes.

FIGURES

Figure 1. PRISMA flow diagram showing the systematic selection process of records.

TABLES

Table 1. Descriptive and summary outcomes data of included studies

Author Year Country	Study Design	Study Size Mean age (Y) Sex (M/F)	Follow-up Period	Orthopedic Intervention	Mortality and Morbidity Outcomes	Recovery Outcomes
Bae and Moon 2020 (22) South Korea	Retrospective	*n* = 126 83.0 103/23	1 year	THA, BH, IF	No significant difference between the mortality rate of osteosarcopenic and control group (*P* = 0.512).	H index and HHS significantly lower scores in the osteosarcopenia and control group at 6 weeks, 3 months, and 1 year after surgery (*P* < .001)
Bayram et al., 2020 (36) Turkey	Retrospective	*n* = 103 72.3 64/39	1 year	Vertebroplasty and Kyphoplasty	PLVI independently associated with a poor overall survival in multivariate analysis (*P* = 0.02).	
Chen et al., 2020 (47) Taiwan	Prospective	*n* = 139 80.7 103/36	6 months	Hip Fracture Surgery (Not specified)	No significant difference in 6-month mortality rate. (*P* = 0.118).	Sarcopenic patients with hip fracture have a lower Barthel Index score (*P* = 0.001) 6 months after surgery.
Shin et al., 2020 (48) South Korea	Retrospective	*n* = 135 74.1 100/35	< 1 year	THA, BH, IF	Non-union identified 0% in sarcopenic group and 10% in control (*P* = 0.288). Mean union time in sarcopenia group was 4.0 months and control 4.4 months (P = 0.210).	HHS and Parker's mobility score; 81.7 and 6.9 in the sarcopenic group, 77.6 and 6.3 in control (*P* = 0.149 and 0.122).
Babu et al., 2019 (24) USA	Retrospective	*n* = 99 70.7 45/54	1 year	THA, TKA	Higher PLVI protective against infection (OR 0.28, 95%CI 0.109-0.715, *P* = 0 .008).	
Lim et al., 2019 (49) South Korea	Prospective	*n* = 80 81.0 62/18	6 months	THA, BH, IF		Sarcopenic group did not differ in ambulation or other functions at follow up compared to control (P < 0.001 or *P* = 0.001).
Malafarina et al., 2019 (26) Spain	Prospective	*n* = 187 85.2 137/50	3.9 years	THA, BH, IF	Sarcopenia associated with increased mortality during study duration (HR 1.67, 95%CI 1.11–2.51).	No significant difference in Barthel Index between groups at discharge (*P* = 0.069).
Wang et al., 2019 (50) China	Retrospective	*n* = 237 70.6 201/36	1 year	Percutaneous Kyphoplasty	In multivariable analysis, sarcopenia an independent predictor of osteoporotic vertebral compression refractures (OR 2.271; 95% CI 1.069–4.824, P = 0.033).	
Charest-Morin et al., 2018 (20)	Retrospective	*n* = 102 60.1	5 days	Thoracolumbar Surgery	NTPA was not predictive of death (OR 1.12, 95% CI 0.83–1.53, *P* = 0.47).	NTPA was not predictive of discharge home (OR: 0.95, 95% CI 0.76–1.20, *P* = 0.7)

Canada		51/51				
Kim et al., 2018 (23) South Korea	Retrospective	*n* = 91 75.3 64/27	5 years	THA, BH, IF	Sarcopenia does not affect 1-year mortality rate (*P*=0.793) but had a significant effect on the 5-year mortality rate (*P* = 0.028).	
Mitchell et al., 2018 (51) USA	Retrospective	*n* = 146 70.1 107/39	1 year	Acetabular Fracture Surgery (Not specified)	Operatively treated and non-operatively treated combined sarcopenic rate of mortality 32.4%, compared with control 11.0% (OR: 4.04; 95% CI: 1.62–10.1).	No significant difference between number of patients operatively treated between sarcopenic 48.7% and non-sarcopenic group 64.2% (*P* = 0.09)
Steihaug et al., 2018 (30) Norway	Prospective	*n* = 282 79.4 214/68	1 year	Hip Fracture Surgery (Not specified)	Sarcopenia was associated with the combined end point of becoming a nursing home resident or death (OR 3.6, 95% CI 1.2 to 12.2, *P* = 0.02).	Sarcopenia did not predict change in mobility (*P* = 0.6). Sarcopenia associated with becoming a nursing home resident (OR 3.2, 95% CI 0.9 to 12.4, P = 0.048).
Bokshan et al., 2017 (27) USA	Retrospective	*n* = 50 72.6 24/26	4.6 year	Thoracolumbar Surgery	Mean hospital costs were 1.75-fold greater for sarcopenic patients compared with control (*P* = 0.04). Sarcopenic patients were 2.1 times as likely to require a blood transfusion (*P* = 0.04). Sarcopenic patients had a 2.6-fold greater usage of advanced imaging (*P* = 0.002).	
Deren et al., 2017 (21) USA	Retrospective	*n* = 99 74.3 38/61	16 to 120 months	THA	Sarcopenia significantly associated with increased 1-year mortality compared with control (28.6 vs 12.3% P = 0.0419). Sarcopenic group reported 2.4% surgical site infction rate and control group 3.5% (*P* = 1.0)	
Landi et al., 2017 (25) Italy	Prospective	*n* = 127 81.3 82/45	3 months	THA		Sarcopenia patients showed lower Barthel index scores at the time of discharge (69.2 versus 58.9, respectively; *P* < 0.001) and 3 months after discharge (90.9 versus 80.5, respectively; *P* = 0.02)
Roh et al., 2017 (28) South Korea	Prospective	*n* = 157 61.3 99/58	1 year	Volar Plate Fixation of Distal Radius	No significant difference in range of motion 6 and 12 months after surgery between sarcopenic and control group.	Michigan Hand Questionnaire score lesser in sarcopenic group compared with control at the 6 and 12-month follow-up (*P* < 0.001).
Yoo et al., 2018 (52) South Korea	Retrospective	*n* = 324 77.8 246/78	1 year	Hip Arthroplasty, IF	A 1-year mortality of osteosarcopenia (15.1%) was higher than that of other groups; control: (7.8%), osteoporosis only (5.1%), sarcopenia only (10.3%) (*P* = 0.050).	

Bokshan et al., 2016 (53) USA	Retrospective	*n* = 46 72.2 24/22	5.2 years	Thoracolumbar Surgery	Sarcopenic patients had a 3-fold increase in postoperative in-hospital complications (1.2 vs 0.4; *P* = 0.02). Patients with sarcopenia had a significantly lower cumulative survival (log rank=0.007).	Patients with sarcopenia had a hospital length of stay 1.7-fold longer than those without sarcopenia (8.1 vs 4.7 days; *P* = 0.02).
González-Montalvo et al., 2016 (29) Spain	Prospective	n = 479 85.3 382/97	5 days	Hip arthroplasty, IF		Sarcopenia was associated with residence in nursing homes (30.5% vs 19.6%, P = 0.030).

THA: Total Hip Arthroplasty, TKA: Total Knee Arthroplasty, IF: Internal Fixation, BH: Bipolar hemiarthroplasty, OR: Odds Ratio, 95% CI: 95% Confidence Interval,

Table 2. Summary of parameters and reference values for sarcopenia definition

Author	Measured Sarcopenia Parameters	Sarcopenia Diagnostic Reference Values
Bae and Moon 2020 (22)	Psoas muscle index (PMI): summed psoas muscles CSA at L3 vertebra level measured by CT scan and normalised to patient's height.	Sarcopenic group defined as PMI below the cohort's mean value (4.01 cm^2/m^2).
Bayram et al., 2020 (36)	Psoas:Lumbar Vertebral Index (PLVI): CSA at L4 vertebra measured on a CT scan and normalized to area of L4 vertebral body.	Sarcopenic group represented as PLVI below the cohort's median value (0.603).
Chen et al., 2020 (47)	Relative Appendicular Skeletal Mass (RASM): lean muscle mass measured by DXA and normalized to patient's height. Hand Grip Strength (HGS): measured using dynamometer.	Low muscle mass defined as RASM <7.0 kg/m^2 in men and <5.4 kg/m^2 in women. Low muscle strength defined as HGS < 26 kg in men and < 18 kg in women. * Sarcopenia diagnosed when both low HGS and low RASM present.
Shin et al., 2020 (48)	Skeletal Muscle Index (SMI): lean muscle mass measured using DXA and normalized to patient's height.	Sarcopenia defined as SMI below 7.0 kg/m^2 in men and below 5.4 kg/m^2 in women. * Sarcobesity defined as the co-existence of sarcopenia and BMI > 25.0 kg/m^2.
Babu et al., 2019 (24)	Psoas:Lumbar Vertebral Index (PLVI): CSA at L4 vertebra measured on a CT scan and normalized to area of L4 vertebral body.	Sarcopenic group defined as PLVI below the studied cohort's median value (0.842).
Lim et al., 2019 (49)	Appendicular Skeletal Mass (ASM): body composition measured using bioelectrical impedance analysis (BIA) and generated ASM normalized to patient's height. Hand Grip Strength (HGS): measured using dynamometer.	Low muscle mass defined as SMI < 7.0 kg/m^2 in men and < 5.7 kg/m^2 in women. Low muscle strength defined as HGS < 26 kg in men and < 18 kg in women. * Sarcopenia diagnosed when both low HGS and low SMI present.
Malafarina et al., 2019 (26)	Skeletal Muscle Index (SMI): lean muscle mass measured using bioelectrical impedance analysis and normalized to patient's height. Hand Grip Strength (HGS): measured using dynamometer. Gait speed: 4 meter walking pace.	Low muscle mass defined as SMI <7.0 kg/m^2 in men and <6.0 kg/m^2 in women. Low muscle strength defined as < 26 kg in men and < 18 kg in women. Low gait speed defined as ≤0.8 m/s. * Sarcopenia diagnosed when both low HGS and low SMI present.
Wang et al., 2019 (50)	Skeletal Muscle Index (SMI): entire skeletal muscle CSA at L3 vertebra measured on a CT scan and normalized to patient's height Hand Grip Strength (HGS): measured using dynamometer. Gait speed: 6 meter walking pace.	Low muscle mass defined as SMI ≤ 36.0 cm^2/m^2 in men and ≤ 29.0 cm^2/m^2 in women Low muscle strength defined as HGS < 26 kg in men and < 18 kg in women. Low gait speed defined as ≤0.8 m/s. * Sarcopenia diagnosed when two out of three of the above criteria present
Charest-Morin et al., 2018 (20)	Normalised total psoas area (NTPA): cross sectional area at L3 vertebra level measured on a CT scan and normalised to patient's height.	Sarcopenic group defined as sex adjusted NTPA below the studied cohort's bottom quartile (500 mm^2/m^2 women, 749 mm^2/m^2 men).
Kim et al., 2018	Skeletal Muscle Index (SMI): entire skeletal muscle CSA at L3 vertebra	Sarcopenic group defined as SMI <42.2 cm^2/m^2 in men and <33.9 cm^2/m^2 in women (SMI

(23)	measured on a CT scan and normalized to patient's height.	threshold adjusted to Korean population).
Mitchell et al., 2018 (51)	Psoas:Lumbar Vertebral Index (PLVI): CSA at L4 vertebra measured on a CT scan and normalized to area of L4 vertebral body.	Sarcopenic group defined as PLVI below the studied cohort's lowest quartile value (0.64).
Steihaug et al., 2018 (30)	Appendicular Lean Mass: (ALM): body composition measured using arm circumference with triceps skinfold and normalized to patients BMI: ALM (BMI). Hand Grip Strength (HGS): measured using dynamometer. Mobility and function: Danish New Mobility Score (NMS) interview	Low muscle mass defined as ALM ≤7.25 kg/m^2 in men and ≤5.67 kg/m^2 in women Low muscle strength defined as HGS < 30 kg in men and < 20 kg in women. Low mobility defined as NMS < 5 * Sarcopenia diagnosed when low lean mass and either low HGS or low NMS
Bokshan et al., 2017 (27)	Total psoas area (TPA): cross sectional area at L4 vertebra measured on CT scan.	Sarcopenic group defined as sex adjusted TPA in lowest tertile of the study's cohort (numerical cut off threshold not in record).
Deren et al., 2017 (21)	Skeletal Muscle Index (SMI): entire skeletal muscle CSA at L3 vertebra measured on a CT scan and normalized to patient's height.	Sarcopenic group defined as SMI <55.4 cm^2/m^2 in men and <38.5 cm^2/m^2 in women.
Landi et al., 2017 (25)	Appendicular Lean Mass: (ALM): body composition measured using bioelectrical impedance analysis (BIA) and normalized to patients BMI: ALM (BMI).	Sarcopenic group defined as ALM (BMI) <0.789kg in men and <0.512kg in women or crude ALM <19.75kg in men and <15.02kg in women.
Roh et al., 2017 (28)	Appendicular Skeletal Mass (ASM): lean muscle mass measured using dual energy X-ray absorptiometry (DXA) and normalized to patient's height. Hand Grip Strength (HGS): measured using dynamometer. Gait speed: 6-meter walking pace.	Low muscle mass defined as SMI <7.0 kg/m^2 in men and <5.4 kg/m^2 in women. Low muscle strength defined as HGS < 26 kg in men and < 18 kg in women. Low gait speed defined as ≤0.8 m/s. * Sarcopenia diagnosed when low lean mass and either low muscle strength or low gait speed present.
Yoo et al., 2018 (52)	Skeletal Muscle Index (SMI): lean muscle mass measured using dual energy X-ray absorptiometry (DXA) and normalized to patient's height. Hand Grip Strength (HGS): measured using dynamometer.	Low muscle mass defined as SMI <7.0 kg/m^2 in men and <5.4 kg/m^2 in women. Low muscle strength defined as HGS < 26 kg in men and < 18 kg in women. * Sarcopenia diagnosed when both low HGS and low SMI present.
Bokshan et al., 2016 (53)	Total psoas area (TPA): cross sectional area at L4 vertebra measured on CT scan.	Sarcopenic group defined as TPA in lowest tertile of the study's cohort (numerical cut off threshold not in record).
González-Montalvo et al., 2016 (29)	Skeletal Muscle Index (SMI): lean muscle mass measured using bioelectrical impedance analysis (BIA) and normalized to patient's height. Hand Grip Strength (HGS): measured using dynamometer.	Low muscle mass defined as SMI <8.31 kg/m^2 in men and <6.68 kg/m^2 in women (SMI threshold adjusted to Spanish population). Low muscle strength defined as HGS < 30 kg in men and < 20 kg in women. *Sarcopenia diagnosed when both low HGS and low SMI present.

Table 3. Newcastle-Ottawa Scale quality assessment of included papers

Study	Selection				Comparability	Outcome			Total Score
	Representativeness of exposed cohort (Maximum:★)	Selection of non-exposed cohort (Maximum:★)	Ascertainment of exposure (Maximum:★)	Demonstration that outcome of interest was not present at start of study (Maximum:★)	Comparability of cohorts on the basis of the design or analysis* (Maximum:★★)	Assessment of outcome (Maximum:★)	Was follow up long enough? (Maximum:★)	Adequacy of follow up of cohorts (Maximum:★)	(out of 9)
Bae and Moon (22)	★	★	-	★	★★	-	★	★	7
Bayram (36)	★	★	-	★	★★	-	★	★	7
Chen (47)	★	★	★	★	★★	★	-	★	8
Shin (48)	★	★	-	★	★★	-	★	★	7
Babu (24)	★	★	-	★	★★	★	★	★	8
Lim (49)	★	★	★	-	★★	-	-	★	6
Malafarina (26)	★	★	★	★	★★	-	★	★	8
Wang (50)	★	★	★	★	★★	-	★	★	8
Charest-Morin (20)	★	★	-	★	★★	-	★	★	7
Kim (23)	★	★	-	★	★★	-	★	★	7
Mitchell (51)	-	★	-	-	★★	-	★	★	5
Steihaug (30)	★	★	★	-	★★	-	★	★	7
Bokshan (27)	- (small study)	★	-	★	★★	-	★	★	6

Deren (21)	★	★	-	★	★★	-	★	★	7
Landi (25)	★	★	-	★	★★	-	-	★	6
Roh (28)	★	★	★	-	★★	★	★	★	8
Yoo (52)	★	★	★	★	★★	★	★	★	9
Bokshan, (53)	- (small study)	★	-	★	★★	-	★	★	6
González-Montalvo (29)	★	★	★	★	★★	-	-	★	7

** Comparability assessed as the following: one star rewarded if study adjusted outcomes for sex, another star rewarded if study adjusted for any other factor.

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APPENDICES

Supplementary (online only material)

S.Table 1. Summary of methods and measurements used to assess sarcopenia

Muscle Mass	Muscle Quality	Muscle Strength	Physical Performance
Dual energy X-ray absorptiometry • Appendicular skeletal muscle mass (ASM) • Skeletal Muscle Index, ASM normalized to height (ASM/ht^2),	Computer tomography (CT) derived muscle attenuation • Expressed in Hounsfield Units	Hand Grip Strength (HGS)	Gait speed
Bioelectrical impedance (BIA) • Skeletal muscle mass (SMM) • Appendicular skeletal muscle mass (ASMM)	Magnetic resonance imaging (MRI)	Knee Extension Strength	400m walk test
Computer tomography • Total Psoas Area (TPA) • Psoas:Lumbar Vertebral Index (PLVI • Psoas major index (PMI), which is TPA normalized to height	Muscle Biopsy		Short physical performance battery (SPPB)
Magnetic resonance imaging (MRI)			Timed up and go test (TUG)

S.Table 2. Search strategy for Medline search engine.

[The same search strategy was applied and adjusted for Embase]

Search Strategy for Medline	
1	Sarcopenia
2	Orthopedic procedures
3	Fracture Fixation, Internal/ or Spinal Fractures/ or Fractures, Bone/ or Hip Fractures
4	Arthroplasty/ Replacement
5	2 or 3 or 4
6	1 and 5
7	Limit to English language and Human studies