The impact of frailty and sarcopenia on postoperative outcomes in adult spine surgery. A systematic review of the literature

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Abstract

STUDY DESIGN: Systematic review.
OBJECTIVES: To identify currently used measures of frailty and sarcopenia in the adult spine surgery literature. To assess their ability to predict postoperative outcomes including mortality, morbidity, in-hospital length of stay (LOS), and discharge disposition. To determine which is the best clinical measure of frailty and sarcopenia in predicting outcome after spine surgery.
SUMMARY OF BACKGROUND DATA: Frailty and sarcopenia have been identified as predictors of mortality and adverse-events (AEs) in numerous nonsurgical and nonspine populations. This topic is an emerging area of interest and study in patients undergoing spinal surgery.
METHODS: A systematic literature review using the PRISMA methodology of MEDLINE, PubMed, Ovid, EMBASE, and Cochrane databases was performed from January 1950 to August 2017. Included studies consisted of those that examined measures of frailty or sarcopenia in adult patients undergoing any spinal surgery. The literature was synthesized and recommendations are proposed based on the GRADE system.
RESULTS: The initial search yielded 210 results, 11 of which met our complete inclusion criteria. Seven reported on measures of frailty and four reported on measures of sarcopenia. Frailty, assessed using a variety of measurement tools, was a consistent predictor of mortality, major and minor morbidity, prolonged in-hospital LOS, and discharge to a center of higher care for adult patients undergoing spinal surgery. The relationship between sarcopenia and postoperative outcomes was inconsistent due to the lack of consensus regarding the definition, measurement tools, and wide variability in sarcopenia measured in the spinal population.
CONCLUSIONS: Frailty is predictive of AEs, mortality, in-hospital LOS, and discharge disposition in a number of distinct spinal surgery populations. The impact of sarcopenia on postoperative outcomes is equivocal given the current state of the literature. The relationship between spinal pathology, frailty, sarcopenia, and how they interact to yield outcome remains to be clarified. Frailty and sarcopenia are potentially useful tools for risk stratification of patients undergoing spinal surgery.

This systematic review was registered with PROSPERO, registration number 85096.

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Keywords: Adverse Events; Complication; Discharge Disposition; Frailty; Length of Stay; Mortality; Morbidity; Sarcopenia; Total Psoas Area.

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**Introduction**

In the modern era of spine surgery, a growing number of interventions are performed in the setting of advancing patient age and the presence of multiple comorbidities. Spine surgeons face the challenge of determining what, if any, is the appropriate surgical intervention in the aging population. Surgical intervention aims to improve the quality of life with no or acceptable additional morbidity. Patient factors such as frailty and sarcopenia may guide surgical decision-making in terms of candidacy, type, and magnitude of procedure and the specifics of informed consent.

Frailty is a cumulative age-related decline in multiple physiological reserves causing an inability to respond to provoked stress [1,2]. Frailty can be measured through a variety of parameters using clinical, biochemical and radiological markers [3]. Clinical markers such as the accumulation of comorbid burden, reduced activities of daily living and quality of life, increased functional dependence and decreased cognition have been integrated into tools which measure and stratify frailty severity [3,4]. Likewise, biochemical markers such as reduced serum albumin and elevated inflammatory markers (erythrocyte sedimentation rate (ESR), interleukin-6 (IL-6) and ferritin levels) have been integrated into similar tools [5,6]. Recently radiological markers have been introduced that quantify reductions in muscle area or density, indicative of sarcopenia, which act as a further method of measuring and stratifying frailty severity [7]. The fact that multiple measuring systems exist reflects the reality that frailty has no universally accepted definition or gold standard method of assessment [3].

Frailty may explain some of the observed heterogeneity in postoperative outcomes amongst elderly patients, particularly those who do not tolerate even a minor stressor. In multiple nonspine surgical populations, frailty is a significant independent risk factor in predicting postoperative adverse events (AEs) and mortality [8–10].

Frailty and sarcopenia, while linked, are distinctly different health and disease concepts. The hallmark of frailty is a loss of functional capacity that can occur in association with sarcopenia, which is defined as a decline in skeletal muscle mass, strength, and endurance [7]. Sarcopenia described by Cruz-Jentoft et al. is evaluated via a radiological technique known as morphometrics [2,7]. Morphometrics is the radiological measurement of patients muscle areas on either computed-tomography (CT) or magnetic resonance imaging (MRI) modalities [7,11]. The most common muscles groups assessed for sarcopenia are the psoas and paraspinous muscle areas and to a lesser extent the quadriceps [7,11]. Recent literature has suggested that sarcopenia may be an independent and important risk factor in predicting mortality and adverse-events across multiple surgical and medical fields [8–10,12,13]. However, there is currently no consensus as to the most appropriate methodology of measuring sarcopenia or in determining sarcopenia cutoffs that may be clinically relevant [7].

Since frailty and sarcopenia appear to be useful in the surgical decision process in nonsurgical and nonspinal populations, a systematic review of the literature was performed using the PRISMA (Preferred Reporting Items of Systematic reviews and Meta-Analyses) guidelines to clarify its use in the context of adult spine surgery.

Our systematic review was designed to answer the following research questions:

1. In adult patients undergoing spinal surgery, what clinical measure of frailty and sarcopenic measurement technique is the most appropriate that allows for the prediction of postoperative outcomes including mortality, morbidity, in-hospital length of stay (LOS) and discharge disposition?
2. In which adult population(s) undergoing spinal surgery does frailty and/or sarcopenia have the most clinically significant role in predicting postoperative outcomes?

**Methodology**

Systematic reviews are important in health care. Clinicians read them to keep up-to-date with the most current clinical knowledge within their field of medical or surgical practice and they are used as starting points for developing clinical guidelines. As with all research, the value of a systematic review depends on what was done, what was found, and the clarity of reporting. As with other publications, the reporting quality of systematic reviews varies, limiting readers’ ability to assess the strengths and weaknesses of those reviews. In 2009, the original Quality of Reporting of Meta-analysis (QUOROM) guidelines for meta-analyses was updated to address several conceptual and practical advances in the science of systematic reviews and was renamed PRISMA [14]. The PRISMA is an evidence-based minimum set of 27 items for reporting in systematic reviews and meta-analyses [14]. The checklist has been provided as supplemental material for this systematic review.

This systematic review was registered with PROSPERO, registration number 85096. The PROSPERO is an international database of prospectively registered systematic reviews with a focus on health-related outcomes. The PROSPERO provides a comprehensive listing of systematic reviews registered at the time of inception to help avoid duplication and reduce the opportunity for reporting bias by enabling comparison of the completed review with what was planned in the protocol. The PROSPERO is produced by University of York’s Center for Reviews and Dissemination and funded by the National Institute for Health Research.

**Eligibility criteria**

All articles included in our review were published in the English language between January 1st, 1950 and August
21st, 2017 and if they met the following eligibility criteria:

1. Population studied: adult (age ≥18 years) undergoing any surgical spine procedure.
2. Intervention: measurement of frailty and/or sarcopenia with explicitly described measurement tools and/or parameters.
3. Comparative: patients measured as frail compared with nonfrail and patients measured as sarcopenic compared with nonsarcopenic.
4. Outcome: postoperative mortality, all postoperative major and minor AEs, reoperation, in-hospital LOS and discharge disposition.
5. Length of follow up: postoperative acute care hospitalization.
6. Study design: prospective, retrospective and ambispective cohort studies.

Studies were excluded if:

1. No objective quantifiable measure of frailty or sarcopenia was provided.
2. They included nonsurgical methods of intervention.
3. They were published in a language other than English.

Search strategy

The following databases were searched for relevant literature on August 21st, 2017 which included:MEDLINE, PubMed, Ovid, EMBASE, and Cochrane. The search terms used were frailty, sarcopenia, elderly, old-age, muscle weakness, spine surgery, thoracolumbar, cervical, sacral, fusion, outcome, adverse-event, disposition, length-of-stay, complication, and mortality. Citations of eligible studies relevant to the review were identified and included in the search process. Preliminary restrictions such as: English language, period of publication (January 1st, 1950-August 21st, 2017), full text, and study design (retrospective, prospective, ambispective, small and large cohort) were subsequently applied. Eligible studies included in this review were evaluated by two independent reviewers (E.M; E.B-M.). The two reviewers independently performed the literature review. The initial articles selected by each reviewer for inclusion were further reviewed by two additional senior authors (R.C-M. and J.S.) and the final studies to be included in the analysis were confirmed. The reviewers then independently examined each of the studies, using the PRISMA guidelines, analyzing the results, points of future discussion, and quality of evidence for each study. Bias identification and risk assessment were performed, as per PRISMA, to identify potential biases and to assess the effect of these biases on an outcome level and on the cumulative evidence within individual studies and across all studies respectively. Finally, an evidentiary table was created by the reviewers, using the PRISMA guidelines, which was used for the writing of the manuscript. This table has been provided as supplementary material.

All of our study’s authors participated in a panel discussion using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system to rate the quality of the scientific evidence and develop recommendations or guidelines based on the best available evidence [15]. The panel included spine surgeons and spine anesthesiologists with established expertise and a track record of previous publications on the topics of frailty, sarcopenia, and spinal surgery outcomes.

Results

The initial literature search yielded a total of 210 articles (Figure). After the full inclusion and exclusion criteria were applied, 11 articles [16–26] were included in the systematic review. Figure shows the overall process of article extraction and screening with the electronic search strategy used to identify relevant literature from the databases. There was 100% agreement between the two reviewers with respect to the final determination of eligible studies for inclusion and to the PRISMA based findings from the included studies. All studies utilized multivariable logistic regression to assess the predictive impact of frailty and sarcopenia on postoperative outcomes independently against other variables. These variables included: Body Mass Index (BMI), smoking status, patient age, sex and race, surgical procedure and approach, and American Society of Anesthesiology (ASA) score. Only one study compared frailty against control populations and not against previously described variables [22].

Measures identified

Frailty measures

Frailty was quantified with the modified Frailty Index (mFI), Frailty Basic Score (FBS) or Metastatic Spine Tumor Frailty Index (MSTFI) (Table 1).

Sarcopenia measures

Morphometrics is assessed on axial imaging on CT or MRI imaging modalities to determine psoas muscle area (mm²) at either the level of L3 or L4 [23–26]. Right and left psoas areas are combined to create the total psoas area (TPA). TPA’s can be stratified in tertiles to categorize sarcopenia severity [23,24]. Further normalization of TPA’s against Ver tebral Body Area (VBA) (mm²) is an alternative measure when compared by quartiles for identifying sarcopenia [26]. Charest-Morin et al. 2017 standardized psoas areas against patient height (m²) to create the normalized total psoas area (NTPA) (mm²/m²) [25]. Three studies utilizing morphometrics carried out inter-rater observations to ensure accurate collection of musculoskeletal measurements [24–26].

Outcome databases

Seven articles obtained postoperative outcome data from the American College of Surgery National Surgical Quality Improvement Program (ACS-NSQIP) database. The ACS-NSQIP database prospectively collects data from multiple hospitals on the occurrence of surgical complications throughout all adult surgical fields [16].

The Henry Ford Health System (HFHS,) utilized by Zakaria et al. is a unicentre database which prospectively collects patient data [23]. Patient data included

The Spine Adverse Events Severity (SAVES) system was used in one study [25]. Previously described by Street et al. it is a system which prospectively collects postoperative complications on patients undergoing adult spine surgery [25,27,28]. The database records 14 intraoperative and 22 postoperative AEs and their associated severity.

Finally, the Nationwide Inpatient Sample (NIS) database, utilized by De la Garza et al. is a multicenter administrative database containing diagnostic, procedural and complication codes from a 20% sample of nonfederal community hospitals in the United States [22].

High-quality data collection was reported throughout all databases by rigorous training of the clinical reviewers. Inter-rater reliability audits were conducted to ensure data accuracy and consistency [22,23,28]. The predictive effect (s) and size(s) of frailty on postoperative outcomes were reported as either odds ratio (OR), crude rate (%) or size effect (No.). A 95% Confidence Interval (CI) was set when comparing cohorts. A p-value of less than .05 was considered the threshold for statistical significance in all studies.

Reported outcomes

The results of the included studies are summarized in Table 2 (frailty measures) and Table 3 (sarcopenia measures).

Frailty studies

We identified seven studies, all retrospective, using clinical measures of frailty to stratify frailty severity and...
### Table 1
Measures of frailty identified in adult spine surgery literature

<table>
<thead>
<tr>
<th>Frailty measure</th>
<th>Description</th>
<th>Variables (n)</th>
<th>Cut-Off Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>mFI*</td>
<td>Measures burden of disease by summing together 11 variables (n) present in the CSHA-FI. The score is calculated by the number of deficits present divided by 11 (n/11).</td>
<td>Dependent functional status, diabetes mellitus, respiratory problems, congestive cardiac failure, myocardial infarction, cardiac problems, hypertension, impaired sensorium, prior transient ischemic attack, cerebral vascular accident, peripheral vascular disease.</td>
<td>Flexman et al.: Non Frail (mFI = 1), PreFrail (mFI &gt; 0 and &lt; 0.21), Frail (mFI &gt; 0.21) [16]. Phan et al.: NonSpecific cutoff values: mFI = 0; mFI = 0.09; mFI = 0.18; mFI = 0.27 [19]. Ali et al.: Severely Frail: mFI &gt; 0.27 [18]. Leven et al.: NonSpecific cutoff values of: mFI = 0.09; mFI &gt; 0.18; mFI &gt; 0.36 [17]. Shin et al.: NonSpecific cutoff values of: mFI = 0; mFI = 0.09, mFI = 0.18, mFI &gt; 0.27 [20].</td>
</tr>
<tr>
<td>FBS[1]</td>
<td>Measures burden of disease by summing together 20 variables (n), 12 of which included in the CSHA-FI. The score is calculated by the addition of each variable value creating a total score out of 22.</td>
<td>Serum albumin &lt; 3.4g/dL, weight loss &gt; 10% of body weight in 6 months, diabetes mellitus, chronic obstructive pulmonary disease, pneumonia, congestive heart failure, myocardial infarction, angina, peripheral arterial disease, steroids, coagulopathy, paraplegia, impaired sensorium, disseminated cancer, dialysis, dyspnea, ascites, BMI &lt; 18.5 (All scored 1); dependent functional status and sepsis (each scored 2).</td>
<td>Abnormal Score ≥ 1 [21].</td>
</tr>
<tr>
<td>MSTFI</td>
<td>Measures burden of disease and surgical factors by summing together 9 variables (n) associated with 30-day postoperative AEs. The score is calculated by the addition of each variable value creating a total score out of 10.</td>
<td>Anemia, chronic lung disease, coagulopathy, electrolyte abnormalities, renal failure, malnutrition, emergent/urgent surgical case, anterior or combined surgical approach (all scored 1); and pulmonary circulatory disorders (scored 2).</td>
<td>NonFrail (MSTFI = 0), Mildly Frail (MSTFI = 1), Moderately Frail (MSTFI = 2), Severely Frail (MSTFI ≥ 3) [22].</td>
</tr>
</tbody>
</table>

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* mFI - no known cut off values for determining nonfrail versus frail populations; study dependent cutoff values.

| FBS - no known cut off values for determining nonfrail versus frail populations. |

**Abbreviations:** Canadian Study of Health and Aging Frailty Index (CSHA-FI), Modified Frailty Index (mFI), Frailty Basic Score (FBS), Metastatic Spinal Tumor Frailty Index (MSTFI), Adverse Events (AEs), Body Mass Index (BMI)
Table 2
Summary of included studies on frailty and adult spine surgery

<table>
<thead>
<tr>
<th>Articles</th>
<th>N</th>
<th>Outcome Database</th>
<th>Population /Procedure</th>
<th>Frailty measure</th>
<th>Primary outcomes of study</th>
<th>Adjusted outcomes</th>
<th>Potential bias(es)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexman et al. [16]</td>
<td>52,671</td>
<td>ACS-NSQIP</td>
<td>Degenerative spine population /All procedures</td>
<td>mFI</td>
<td>30-Day mortality</td>
<td>30-day mortality OR: 1.44 (95% CI: 1.15–1.81 p &lt; .005)* 30-day morbidity OR: 1.15 (95% CI: 1.09–1.21 p &lt; .0005) * Discharge disposition increased In-Hospital LOS OR: 1.27 (95% CI: 1.19–1.35 p &lt; .0005) * Discharge to center of higher care OR: 1.32 (95% CI: 1.24–1.40 p &lt; .0005) *</td>
<td>Selection bias Sample bias</td>
</tr>
<tr>
<td>Leven et al. [17]</td>
<td>1,001</td>
<td>ACS-NSQIP</td>
<td>Adult spinal deformity/Posterior fusion ≥ 3 levels or anterior fusion ≥ 4 levels or combined anterior-posterior approach</td>
<td>mFI</td>
<td>30-day mortality</td>
<td>Selection bias Sample bias</td>
<td></td>
</tr>
<tr>
<td>Ali et al. (18)</td>
<td>18,294</td>
<td>ACS-NSQIP</td>
<td>Not specified/All procedures</td>
<td>mFI</td>
<td>30-day mortality</td>
<td>Selection bias Sample bias</td>
<td></td>
</tr>
<tr>
<td>Phan et al. (19)</td>
<td>3,920</td>
<td>ACS-NSQIP</td>
<td>Degenerative lumbar spine population/ALIF</td>
<td>mFI</td>
<td>30-day composite AEs</td>
<td>Selection bias Sample bias Post-Hoc bias</td>
<td></td>
</tr>
<tr>
<td>Shin et al. (20)</td>
<td>6,965</td>
<td>ACS-NSQIP</td>
<td>Degenerative cervical spine population/Cervical fusion</td>
<td>mFI</td>
<td>30-day composite AEs</td>
<td>Selection bias Sample bias</td>
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<tr>
<th>Articles</th>
<th>N</th>
<th>Database</th>
<th>Population/Procedure</th>
<th>Frailty measure</th>
<th>Primary outcomes of study</th>
<th>Adjusted outcomes</th>
<th>Potential bias(es)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medvedev et al. (21)</td>
<td>5,627</td>
<td>ACS-NSQIP</td>
<td>Degenerative and metastatic cervical pathology/PCF or combined ACDF and PCF</td>
<td>FBS</td>
<td>30-day composite AEs</td>
<td>30-day composite AEs OR: 1.78 (95% CI: 1.61–1.96, p&lt;.0001)</td>
<td>Selection bias Sample bias</td>
</tr>
</tbody>
</table>
| De La Garza Ramos et al. (22)  | 4,583  | NIS          | Metastatic spine population/All procedures | MSTFI           | 30-day mortality         | 30-day mortality rate (%):  
  * MSTFI Score of 0 → 5: 1.0% to 9.6% (P<.001)  
  * MSTFI Score of 2 versus 0: OR 5.15 (95% CI:2.44–10.86, p<.001)  
  * MSTFI Score of ≥ 3 versus 0: OR 5.74 (95% CI:2.69–12.24, p<.001)  
  * MSTFI Score of 0 → 7: 6.7% to 100% (P<.001)  
  * MSTFI Score of 1 versus 0: OR 1.88 (95% CI:1.33–2.66, p<.001)  
  * MSTFI Score of 2 versus 0: OR 3.83 (95% CI:2.71–5.41, p<.001)  
  * MSTFI Score of ≥ 3 versus 0: OR 6.97 (95% CI:4.98–9.74, p<.001)  
  In-hospital LOS (Days):  
  * MSTFI Score of 1 versus 0: LOS 3.3±0.4 Days (P<.001)  
  * MSTFI score of 2 versus 0: LOS 5.6±0.4 Days (P<.001)  
  * MSTFI score of ≥ 3 versus 0: LOS 6.4±0.4 Days (P<.001) | Sample bias Misclassification bias Ascertainment Bias |

* Per 0.10 increase in mFI score.  
† Per one unit increase in FBS score.  

Abbreviations: American College of Surgeon - National Surgical Quality Improvement Program (ACS-NSQIP), Anterior Lumbar Interbody Fusion (ALIF), Anterior Cervical Discectomy and Fusion (ACDF), Posterior Cervical Fusion (PCF), Posterior Lumbar Interbody Fusion (PLIF), Modifiable Frailty Index (mFI), Frailty Basic Score (FBS), Metastatic Tumor Frailty Index (MSTFI), Length of Stay (LOS), Adverse Events (AEs), Odds Ratio (OR), Confidence Interval (CI); Nationwide Inpatient Sample (NIS) Database.
<table>
<thead>
<tr>
<th>Articles</th>
<th>N</th>
<th>Outcome Database/Design</th>
<th>Population/Procedure</th>
<th>Sarcopenia measure</th>
<th>Primary outcomes of study</th>
<th>Adjusted outcomes</th>
<th>Quality of evidence</th>
</tr>
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<tbody>
<tr>
<td>Gakhar et al. [26]</td>
<td>86</td>
<td>Single center/Ambispective</td>
<td>Thoracolumbar procedures for metastatic spine disease</td>
<td>NTPA and TPA/ VB Ratio at L3 on CT scan</td>
<td>1-year mortality</td>
<td>1-year mortality rate(^{3})</td>
<td>Selection bias</td>
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<tr>
<td></td>
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<td>TPA at L4 and Paraspinous at T12 on MRI</td>
<td>90-day composite AEs</td>
<td>90-day composite AEs OR: 1.70 (95% CI: 1.04–2.79 p=.035)*</td>
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<td>In-hospital LOS (Days)*</td>
<td>In-hospital LOS (Days)* OR: 1.06 (95% CI: 0.91–1.23 p=.45)</td>
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<td>30-day composite AEs (No.)*</td>
<td>30-day composite AEs (No.)* OR: 0.3±0.2 (P=.04)</td>
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<td>30-day major morbidity (No.)*</td>
<td>30-day major morbidity (No.)* OR: 0.03±0.1 (P=0.04)</td>
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<td></td>
<td>Discharge disposition</td>
<td>Discharge to center of higher care (Rate)*</td>
<td></td>
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<tr>
<td>Zakaria et al. [23]</td>
<td>395</td>
<td>Single Center HFHS/Retrospective</td>
<td>Thoracolumbar procedures: laminectomy-lumbar arthrosis and lumbar interbody arthrosis</td>
<td>TPA at L4 on CT scan</td>
<td>30-day AEs</td>
<td>30-day AEs OR: 2.42 (95% CI: 1.17–5.01 p=.016)*</td>
<td>Sample bias</td>
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<td>30-day major and minor morbidity</td>
<td>30-day major morbidity OR: 2.68 (95% CI: 1.25–5.35 p=.007)</td>
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<td>In-hospital LOS (Days)*</td>
<td>In-hospital LOS (Days)* OR: 0.95 (95% CI: 0.76–1.20 P=.70)</td>
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<td>Discharge disposition</td>
<td>Discharge to center of higher care (Rate)*</td>
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<tr>
<td>Bokshan et al. [24]</td>
<td>46</td>
<td>Single center/Retrospective</td>
<td>Thoracolumbar procedures including scoliosis surgery, fracture, degenerative and infection</td>
<td>TPA at L4 on CT scan</td>
<td>30-day AEs</td>
<td>30-day composite AEs OR: 1.70 (95% CI: 1.04–2.79 p=.035)*</td>
<td>Sample bias</td>
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<td>Discharge disposition</td>
<td>Discharge to center of higher care (Rate)*</td>
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<tr>
<td>Charest-Morin et al. [25]</td>
<td>102</td>
<td>Single Center SAVES/Ambispective</td>
<td>Elective noncomplex degenerative lumbar spine procedures</td>
<td>NTPA at L3 on CT scan</td>
<td>30-day composite AEs</td>
<td>30-day composite AEs OR: 1.06 (95% CI: 0.91–1.23 p=.45)</td>
<td>Selection bias</td>
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<td>30-day mortality</td>
<td>30-day mortality OR: 1.12 (95% CI: 0.83–1.53 P=.47)</td>
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<td>Discharge disposition</td>
<td>Discharge to center of higher care OR: 0.95 (95% CI: 0.76–1.20 P=.70)</td>
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</table>

* Total Psoas Areas (TPA): Lowest tertile vs. middle and highest TPA tertiles.
† Per 100 mm²/m² in NTPA.
‡ Total Psoas Area (TPA)/Vertebral Body Area (VB) Ratio: Lowest quartile vs. high quartile.

Abbreviations: Length of Stay (LOS), Adverse Events (AEs), Odds Ratio (OR), Confidence Interval (CI), Spine AdVerse Events Severity (SAVES) system; Henry Ford Health System (HFHS), Magnetic Resonance Imaging (MRI), Computed Tomography (CT), Total Psoas Area (TPA), Normalized Total Psoas Area (NTPA), Vertebral Body (VB), Total Psoas Area - Vertebral Body Ratio (TPA/VB)
quantify its predictive effect on postoperative AEs [16–22]. Five articles used mFI while the last two articles used FBS and MSTFI respectively to quantify frailty severity. All studies reported a positive relationship between frailty and its impact on postoperative AEs. Our expert panel determined all seven articles included in this review, which utilized clinical measures of frailty, were a GRADE score of very low for their quality of evidence.

### 30-day postoperative mortality

Six studies using clinical markers of frailty reported on the impact of frailty on 30-day postoperative mortality [16–20,22]. Five studies measured frailty with mFI while the last study utilized MSTFI. Only one study by Phan et al. reported a negative outcome between frailty and its impact on 30-day postoperative mortality [19].

Ali et al. studied 18,294 patients undergoing all spinal procedures and found incremental increases in mFI score from 0 to ≥0.27 were associated with higher 30-day postoperative mortality rates of 0.1% to 2.3% (p < .001) after multivariable analysis [18].

Leven et al. studied 1,001 patients undergoing long spinal fusion for spinal deformity and after multivariable analysis, they reported increased mFI scores from 0 to ≥0.27 were associated with higher 30-day postoperative mortality rates of 0.3% to 10% (P = .001) [17].

Shin et al. studied 6,965 patients undergoing either an anterior cervical discectomy and fusion (ACDF) or posterior cervical fusion (PCF) for cervical spondylosis. In the ACDF population they reported increased mFI scores from 0 to ≥0.27 were associated with increased 30-day postoperative mortality rates of 0.1% to 3.0% (P < .001) [20]. In the PCF cohort, they described incremental gains in mFI scores from 0 to ≥0.36 were associated with higher 30-postoperative mortality rates of 0% to 10.0% with (P < .001) [20]. All outcomes were reported on after multivariable analysis.

Flexman et al. studied 52,671 patients undergoing all spinal procedures for degenerative spinal conditions and found for every incremental increase in mFI score by 0.10, the likelihood of 30-day postoperative mortality increased by OR 1.44 (95% CI: 1.15–1.81 p < .005) after multivariable analysis [16].

Phan et al. studied 3,920 patients undergoing anterior lumbar interbody fusion (ALIF) for degenerative spinal conditions. After multivariable analysis they found no association between mFI and 30-day postoperative mortality in the mild OR 3.9 (95% CI: 0.4–38.2 p = .996), moderate OR 3.1 (95% CI: 0.2–52.4 p = .774) or severely frail OR 19.5 (95% CI: 1.0–387.8 p = .077) populations when compared against the nonfrail cohort [19].

De la Garza et al. studied 4,583 patients undergoing all spinal procedures for metastatic disease to the spine. They found after multivariable analysis that moderately and severely frail patients had higher odds of 30-day postoperative mortality of OR 5.15 (95% CI: 2.44–10.86) and OR 5.74 (95% CI: 2.69–12.24) respectively when compared against the nonfrail cohort (P < .001) [22]. They also described higher MSTFI index scores of 0 to 5 were associated with higher crude mortality rates of 1.0% to 9.6% (P < .001) [22].

### 30-day postoperative morbidity and composite AEs

All seven studies using clinical measures of frailty reported on the predictive impact of frailty on either 30-day postoperative morbidity and/or 30-day postoperative composite AEs [16–22]. Four studies only reported on 30-day postoperative morbidity [16–18,22], while another two reported on only 30-day postoperative composite AEs [19,21]. The remaining one study reported on both 30-day postoperative morbidity and composite AEs [20]. Five studies used mFI while the last two studies used FBS and MSTFI respectively to quantify frailty severity. Only one study by Phan et al. reported a negative outcome between frailty and its impact on 30-day postoperative mortality [19].

Ali et al. found in patients undergoing any surgical procedure of the spine that increased mFI scores from 0 to ≥0.27 were associated with higher 30-day postoperative morbidity rates of 0.8% to 7.1% (P < .001) after multivariable analysis [18].

Leven et al. found patients undergoing long spinal fusion procedures that increased mFI scores from 0 to ≥0.27 were associated with higher 30-day postoperative morbidity rates of 35% to 60% (P = .002) [17]. After multivariate logistic regression analysis, they found mFI scores of 0.09 and ≥ 0.18 are independent risk factors for composite AEs with the following odds of OR 1.7 (95% CI: 1.3–2.2 P < .0001) and OR 1.6 (95% CI: 1.1–2.4 P = .010) [17].

Shin et al. found in the ACDF population that increased mFI scores of 0 to ≥0.27 were associated with higher postoperative 30-day morbidity rates of 0.8% to 5.6% and composite adverse-event rates of 2.0% to 9.0% (P < .001) after multivariable analysis [20]. Likewise in the PCF population after multivariable analysis, they reported increased mFI scores from 0 to ≥0.36 were associated with higher 30-day morbidity rates of 0.7% to 5.8% and composite adverse-event rates of 4.1% to 35.0% (P < .001) [20].

Flexman et al. found in patients undergoing all spinal procedures for degenerative spinal conditions, that for every incremental increase in mFI score by 0.10, the likelihood of 30-day postoperative mortality increased by OR 1.44 (95% CI: 1.15–1.81 p < .005) after multivariable analysis [16].

Medvedev et al. studied 5,627 patients undergoing cervical fusion procedures for either degenerative or metastatic disease of the spine. They found frail patients were at a higher likelihood of 30-day postoperative composite AEs of OR 1.78 (95% CI: 1.61–1.96 P < .0001) after multivariable analysis compared to the nonfrail population [21].

Likewise, Phan et al. found in patients undergoing ALIF procedures for degenerative spinal conditions, that the frail cohort with mFI scores ≥0.27 were associated with a higher
likelihood 30-day postoperative composite AEs of OR 2.4 (95% CI: 1.2–4.6 p=.04) compared to the nonfrail cohort after multivariable analysis [19]. However, within the mild (mFI=0.09) and moderately (mFI=0.18) frail populations, adjusted regression did not demonstrate frailty to be an independent risk factor for experiencing AEs when compared against the nonfrail population [19].

In terms of adjusted odds, Shin et al. reported that frail patients in the ACDF cohort were at a higher likelihood of 30-day postoperative morbidity of OR 4.67 (95% CI: 2.27–9.62 P<.001) when compared to the nonfrail cohort [20]. Interestingly, they found the PCF cohort of frail patients were associated with higher odds of OR 41.26 (95% CI: 6.62–257.15 P<.001) [20]. However, when comparing mildly and moderately frail patients to the nonfrail population, they found no increase in the odds of 30-day postoperative morbidity [20]. All outcomes were reported on after multivariable analysis.

De la Garza et al. found increased MSTFI scores were associated with higher likelihood of 30-day postoperative morbidity in the mild, moderate and severely frail patients undergoing spinal surgery for metastatic oncological disease of the spine. They reported odd ratios of: OR 1.88 (95% CI: 1.33–2.66), OR 3.83 (95% CI: 2.71–5.41) and OR 6.97 (95% CI: 4.98–9.74) respectively after multivariable analysis [22]. A statistically significant difference in morbidity rate was found after multivariable analysis when they compared against the frail and nonfrail cohorts (P<.001) [22]. Increased MSTFI scores from 0 to 7 were associated with higher complication rates of 6.7% to 100% (P<.001) [22].

### In-hospital LOS and discharge disposition

Three studies included in our review reported on the relationship between frailty and its impact on longer in-hospital LOS and discharge to a center of higher care [16, 19,22]. Only two studies by Flexman et al. and De la Garza et al. reported a relationship between frailty and its impact on longer in-hospital LOS and discharge to a center of higher care [16,22]. Phan et al. did not report such a finding (19).

Flexman et al. found incremental increases in mFI scores of 0.10 were associated with an adjusted odds ratio of prolonged in-hospital LOS and discharge to a higher care facility of OR 1.27 (95% CI:1.19–1.35) and OR 1.32 (95% CI:1.24–1.40) respectively (p<.0005) after multivariable analysis [16].

De la Garza et al. found patients with metastatic oncological disease of the spine undergoing any spinal surgical intervention that frail patients of the mild, moderate and severe cohorts were associated with a longer average in-hospital LOS of 0.3±0.4 days, 5.6±0.4 days and 6.4±0.4 days (P<.001) respectively when compared against the nonfrail patients after multivariable analysis [22].

In contrast, Phan et al. did not find patients undergoing ALIF procedures for degenerative spinal conditions to be at increased likelihood of in-hospital LOS ≥5 days when the mildly, moderately and severely frail cohorts were compared against the nonfrail population. They reported insignificant odds ratio of OR 1.3 (95% CI: 1.1–1.6 p=.854), OR 1.4 (95% CI: 1.1–1.9 p=.590) and OR 1.7 (95% CI: 0.9–3.3 p=.350) after multivariable analysis, respectively [19].

### Bias across frailty studies

Our reviewers identified selection bias as a potential confounding factor influencing the outcome of all studies using the ACS-NSQIP database. This database only records post-operative AEs within a 30-day postoperative window suggesting that some postoperative AEs may have missed which could potentially influence the impact of frailty on postoperative outcome. Also, all studies utilizing multivariable logistic regression contain a sample bias as study candidates with incomplete information are removed from the analysis. This implies the odds ratio is calculated on patients with complete profiles who may not be reflective of the target population. Another common bias to all studies utilizing clinical markers of frailty is related to the use of specific cut-off values to determine the mild, moderate, and severe frail populations. These cut-off values are still largely arbitrary and are not currently defined in the literature. This implies that the definition of frail patients is different in each study population that may affect the external validity of their findings.

In regards to the individual studies, Flexman et al. indicated within the study population chosen that there was a tremendous increase in the number of cases included in the ACS-NSQIP database from 2006 to 2012 (414 to 20,205 procedures) [16]. This suggests a selection bias due to a possible change in surgical indication thus increasing enrolment rates of patients within the database which may not be representative of the target population.

Multiple biases were identified in Phan et al. which could influence the interpretation of their results. The study population chosen for the study was exclusive to only patients undergoing ALIF procedures thus restricting the applicability of the results to other populations of spine surgery [19]. Furthermore, a large number of statistical tests were performed in such a way which could lead to increased risk of α-type error. When conducting multiple statistical analyses, a p<.05 is not sufficiently strict to determine a statistically significant effect and the alpha level should have been consequently lowered.

Also, several inconsistencies were identified in the odds ratios,CIs, and p-values reported. The authors reported that mild (mFI 0.09 vs. 0), moderate (mFI 0.18 vs. 0), and severely (mFI 0.27 vs. 0) frail cohorts were not associated with increased LOS with associated odds ratios of OR 1.3 (95% CI: 1.1–1.6 p=.854), OR 1.4 (95% CI: 1.1–1.9 p=.590), and OR 1.7 (95% CI: 0.9–3.3 p=.350) respectively [19]. However, if a CI of 95% is reported for a ratio estimate, by definition, the estimate must exclude 1.0 for the p-value to be less than .05. This definition was not
observed in Phan et al. for the following postoperative AEs of in-hospital LOS and wound complications.

After discussing this issue with the authors of the paper and reviewing their statistics, a selection bias resulting in a non-normalized population distribution for the variable in question(s), was responsible for the inconsistencies reported. The authors agreed that mild frailty (mFI=0.09) is not an independent risk factor for wound-related complications as is any mFI score for increased in-hospital LOS.

Shin et al. studied a specific population of patients exclusively undergoing cervical procedures only which consequently restricts the applicability of the reported outcomes to different populations of patients undergoing spinal surgery [20].

The study by De la Garza et al. contained several biases potentially influencing the applicability and validity of their results. Firstly, the population studied consisted of patients with metastatic cancer to the spine [22]. This group of patients may affect the internal validity of the results as they are inherently more vulnerable to additional injury and comorbidity. As a result, there is a higher likelihood that the impact of frailty on postoperative AEs will be higher and more significant. Also, because the population studied is specific to metastatic disease of the spine, the applicability of these results to other surgical populations is limited. Secondly, a misclassification is present as the MSTFI is not a valid measure of frailty since it includes a treatment variable (emergent vs. elective admission, corpectomy, and spinal fusion, anterior or combined approach) that is dependent on changing and consequently, it can affect postoperative outcome independent of frailty [22]. Lastly, an ascertainment bias is present as patients selected for MSTFI validation were from the ACS-NSQIP database, and there is no description to confirm this. As a result, this can influence the predictive effect of MSTFI on postoperative AEs because this population is limited to the ACS-NSQIP variables which may not be reflective of the metastatic disease population.

Sarcopenia studies

Our review identified four studies reporting the association between sarcopenia and its impact on postoperative AEs [23–26]. NTPA was used to quantify sarcopenia severity in two studies while the remaining two studies utilized TPA. One study by Charest-Morin et al. used TPA and/or VB in combination with NTPA [25] and one other study by Zakaria et al. used paraspinous muscle area in conjunction with TPA [23]. Only three studies reported a positive outcome between sarcopenia and its impact on postoperative AEs [23,24,26]. Our review panel determined all four articles included in this review, which assessed sarcopenia, were a GRADE score of very low for their quality of evidence.

30-day postoperative mortality rates

Only one study by Charest-Morin et al. reported on the association between sarcopenia and its impact on 30-day postoperative mortality [25]. The study did not report a statistically significant increase in 30-day postoperative AEs within the lowest psoas area values [25]. Charest-Morin et al. studied 102 patients undergoing elective surgery for degenerative spine disease and did not identify sarcopenia as an independent risk factor for predicting 30-day postoperative mortality OR: 1.06 (95% CI: 0.91–1.23 P=.45) per 100 mm²/m² in NTPA after multivariable analysis [25].

1-year mortality

Only one study by Gakhar et al. reported on the association between sarcopenia and its impact on 1-year mortality and subsequently the study reported a positive outcome [26]. Gakhar et al. studied 86 patients and identified sarcopenic patients requiring decompressive spine surgery for metastatic cancer within the lowest quartile of TPA and/or VBA ratios that were associated with higher mortality rates of 23.8% compared with the highest quartile of 57.1% (p=.02), respectively [26]. They identified a median muscle mass, reported in arbitrary units, of 1.95 (Interquartile Range (IQR) 1.54 –2.29) was associated with patients who died by the 1-year follow up mark compared with a median muscle of 2.26 (IQR 1.70 –2.67) for those who were alive 1-year postoperatively (p=.05) [26].

30-day and 90-day major and minor morbidity

Two studies by Bokshan et al. and Zakaria et al. included in our systematic review reported an association between sarcopenia and 30-day postoperative AEs in addition with 90-day postoperative composite AEs respectively [23,24]. Only one study by Charest-Morin et al. reported an association between sarcopenia and its impact on 30-day postoperative composite AEs [25].

Bokshan et al. studied 46 patients undergoing thoracolumbar procedures for scoliosis, trauma, degeneration, and infection. They reported patient TPAs within lowest tertile as sarcopenic, experienced a greater number of postoperative AEs within a 30-day postoperative window (0.3±0.2 AEs (P=.04)) compared with the nonsarcopenic population (0.03±0.1 AEs (P=.04)) [24]. They also found patients within the lowest TPA tertile experienced a greater number of 30-day composite postoperative AEs (1.2±0.3 AEs (P=.02)) in comparison to nonsarcopenic group of the middle and highest TPA tertiles (0.4±0.2 AEs (P=.02)) [24]. Their results were not adjusted for potential confounders.

Similarly, Zakaria et al. studied 395 patients undergoing posterior lumbar interbody fusion (PLIF) procedures for all spinal pathologies. They found patients within the lowest quartile of TPA, as sarcopenic, experienced a higher likelihood of 90-day postoperative AEs OR 1.70 (95% CI: 1.04–2.79 p=.035) when compared against the middle and upper quartiles after multivariable analysis [23]. In the female population of 203 patients, morphometrics was not
associated for predicting 90-day postoperative AEs after
adjustment OR 1.22 (95% CI: 0.62–2.43 p=.564) [23].
Conversely, in the male population of 192 patients, an increase
of AEs was seen in the lowest quartile of TPA (adjusted
odds ratio of OR 2.42 (95% CI: 1.17–5.01 p=.016)) when
compared against the middle and upper TPA quartiles [23].

In contrast Charest-Morin et al. did not find sarcopenic
patients undergoing spine surgery for degenerative lumbar
spine disease to be at higher odds of 30-day postoperative
composite AEs OR: 1.06 (95% CI: 0.91–1.23 p=.45) when
compared against nonsarcopenic patients assessed with the
NTPA ratio after multivariable analysis [25].

In-hospital LOS and discharge disposition
Two studies reported on the association between sarcopi-
ena and postoperative in-hospital LOS and the impact on
discharge to a center of higher care. The first study by
Bokshan et al. identified an association between sarcopenia and
increased in-hospital LOS [24] while the second study by
Charest-Morin et al. did not find any relation [25].

Bokshan et al. reported patients requiring thoracolumbar
spinal surgery for scoliosis, trauma, degenerative spine
disease, and infection, that those identified as sarcopenic
within the lowest tertile of TPA experienced a longer dura-
tion of in-hospital LOS of 8.1±1.5 days (P=.02) compared
with the middle and highest TPA tertiles of 4.7±0.9 days
(P=.02) [24]. Sarcopenic patients within the lowest tertile
were also associated with higher rates of disposition to a
center of higher care 81.2% (P=.006) compared with the
nonsarcopenic cohort 43.3% (P=.006) [24]. However, no
adjusted analysis was performed.

In contrast, Charest-Morin et al. did not find sarcopenic
patients undergoing elective spinal surgery to be at higher
likelihood of discharge to a center of higher care compared
with nonsarcopenic patients OR: 0.95 (95% CI: 0.76–1.20
P=.70) when using the NTPA after multivariable analysis
[25].

Bias across sarcopenia studies
Our reviewers identified selection bias as a potential
influencing factor affecting studies assessing 30-day post-
operative outcomes as this inherently applies AEs may
have been missed which could affect the impact of sarcope-
nia on postoperative outcome. Also, all studies utilizing
multivariable logistic regression contain a sample bias as
study candidates with incomplete information are removed
from the analysis. This implies the odds ratio is calculated
on patients with complete profiles who may not be reflect-
ive of the target population. Furthermore, three studies did
not define the external variable of surgical invasiveness
within their study population which would affect the pre-
dictive effect on experiencing postoperative AEs and there-
fore the external validity of their results.

In regards to the individual studies, we identified Zakaria
et al. to contain an additional measurement bias [23]. The
psosas area measure was not adjusted for the body surface
area or height. This may be cofounding factor because the
female population had a lower tertile of psosas area but was
not associated with a significant odds ratio despite the pop-
ulation experiencing a higher number of AEs.

Gakhar et al. was identified to contain a selection bias.
First, they only included patients who obtained a CT scan
within one week of their surgery and were followed up for
one year [26]. However, the authors did not identify how
many patients with metastatic disease of the spine failed to
fill this criterion and therefore it is difficult to assess the
external validity of the study. Furthermore, the population
studied creates a bias as these patients with metastatic dis-
tease to the spine are inherently at a higher risk of experienc-
ing greater mortality and morbidity. As a result, this
increases the predictive effect of sarcopenia and limits the
applicability of these results to other areas of spinal surgery.

Discussion
Frailty and sarcopenia have been previously recognized
as independent risk factors for postoperative AEs in elderly
patients undergoing surgical intervention [8,9]. In the context
of adult spine surgery, the relationship between baseline
frailty and sarcopenia with postoperative outcomes has only
recently been explored. Our review identified seven studies
that implicitly assessed the impact of frailty on postoperative
AEs. Although the exact definition of frailty varied between
studies, the concept (a decline in multiple physiological
reserves causing an inability to respond to provoked stress)
consistently was associated with an increased risk of postop-
erative complications after surgery. This also included
increased in-hospital LOS, early postdischarge mortality,
and discharge to an escalated level of care.

1a) What is the most appropriate clinical frailty measure
for spine surgery to predict adverse postoperative
outcomes?

Our review identified mFI as the most viable current
option for assessing, quantifying, and stratifying frailty
severity in patients undergoing spine surgery. The mFI is a
scoring index designed to assess frailty based on the theory
of deficit accumulation described by Rockwood et al. [2,4].
Amongst the multiple frailty measures examined, mFI was
the most commonly used. It was easily applied to an exten-
sive surgical database such as ACS-NSQIP and proved to be
a robust measure of frailty in determining its impact on post-
operative outcomes. Although the mFI has proven to be a
useful research tool, its clinical applicability remains unclear,
and much remains to be determined regarding issues such as
validity, reliability, upper and lower thresholds, and ceiling
effects. Probably of most immediate importance is the need
to identify clinically useful cutoffs that would allow deline-
ation between frail and nonfrail patients, thus impacting clin-
cal decision making such as appropriateness for surgery. In
the studies we examined, the various cut-offs proposed were
likely reflective of variability in surgical indications and procedures between studies. We believe this is a significant challenge in adapting the use of frailty to different populations in the clinical setting.

Alternatives to the mFI we identified were the FBS and MSTFI. The FBS was used by Medvedev et al. and maps a greater number of patient health variables [21]. However, the FBS is not validated for spinal surgery and the original article describing its construct for vascular surgery cannot be retrieved. The MSTFI developed by De La Garza et al. is specific to patients with metastatic disease of the spine [22]. In such a population, deficit accumulation is most likely secondary to the burden of the neoplastic disease. The MSTFI includes components related to the surgical approach and emergency status and not only patient health and/or physiological factors. Conceptually surgical characteristics, such as the spinal surgical invasiveness index, should not be part of the frailty measurement because they are influenced by the physiological reserve and spinal pathology of the patient. While surgical invasiveness is a known risk factor for the development of AEs, such as surgical site infection, we believe it should be assessed independently from frailty or sarcopenia.

Recommendations

The mFI is the most appropriate measurement tool for assessing frailty (strong recommendation, low quality of evidence) in the context of adult spine surgery. Our recommendation is based on multiple factors. First, mFI is an externally validated measure of frailty that has been well reported in the spinal population with consistent predictive effects. Second, mFI has proven to be applicable to multiple different spinal populations (degenerative vs. traumatic) of varying size (small vs. large cohorts) in identifying frailty as an independent risk factor for postoperative AEs. The mFI can also be easily amalgamated into clinical practice as it requires no training.

We do not recommend FBS (strong recommendation, very low quality of evidence) as a tool for assessing frailty in the context of adult spine surgery due to a lack of documented construct, an absence of external validity, and limited use in the spine surgery literature.

Lastly, MSTFI may be an appropriate measure of frailty (strong recommendation, very low quality of evidence) in the context of the spinal metastasis population. The MSTFI may not be generalizable to other spinal populations as it was constructed and externally validated based on this population. The MSTFI, also, incorporates a treatment variable (surgical invasiveness based on approach) which is an important factor that should be taken into consideration as it serves as an independent risk factor for predicting postoperative outcome within the oncological spine population [29].

1b) What is the best measurement technique for sarcopenia in spine surgery to predict adverse postoperative outcomes?

Sarcopenia has proven to be a significant independent risk factor in predicting adverse outcome in both medical and surgical specialties [12, 13]. In the context of spine surgery, multiple measurement techniques were described for identifying the sarcopenic population. Our study identified three studies which reported sarcopenia as an independent risk factor associated with adverse postoperative outcome [23,24,26]. In contrast, neither Charest-Morin et al. nor Zakaria et al. were able to identify such a relationship in the degenerative spine and female populations respectively. These contrasting results likely reflect the fact that there is no consensus on the appropriate diagnostic values for identifying and determining the sarcopenic population [7, 30]. In the study by Charest-Morin et al., the findings indicate that sarcopenia, when defined using the NTPA, likely does not exert a significant impact on a population of relatively healthy patients undergoing simple surgical procedures of the spine.

In the studies reviewed, TPA was assessed at either the L3 or L4 level and then distributed into tertiles to determine the sarcopenic population [23,24,26]. Using tertiles to define sarcopenia requires a normally distributed population. However, the normality of the distribution was unspecified in three studies [23,24,26] and not observed in Charest-Morin et al. [25]. Zakaria et al. later suggested that the use of tertiles or quartiles to identify the sarcopenic population was not reliable in assessing sarcopenia [23].

Other methods of assessing sarcopenia may have more advantages in the spine surgery population. Gakhar et al. proposed using a TPA and/or VBA ratio to increase the sensitivity in patients with metastatic spine disease [11,26]. Clinically, TPA and/or VBA ratio can easily be applied to available pre-operative imaging. Such a measure may be important when considering surgical intervention in the emergency oncological spine population where a high rate of AEs is known [29]. Zakaria et al. 2016 later demonstrated that the lowest tertile of TPA and/or VB was a strong predictor of mortality in nonoperative patients with metastatic disease to the spine (HR 1.43, 95% CI 1.05–1.94, p=.025) [11]. Despite a strong association, the overall consistency of TPA and/or VB in a nonmetastatic population has yet to be proven.

When TPA was normalized against body height (m²) to form the NTPA (mm²/m²) no association with adverse outcome was identified. Possible explanations included that it was a relatively healthy population, surgical intervention(s) were noncomplex spine surgery and a low adverse event rate was observed. Also, it was postulated that underlying degenerative spinal pathology might negatively influence the musculature to avert risk estimation based on this measurement. Such a theory is seen in patients with degenerative scoliosis and degenerative disc disease where psosas areas were atrophied bilaterally or unilaterally on the symptomatic side respectively [31,32].
The TPA is an acceptable form of assessing frailty (strong recommendation, very low quality of evidence) in the context of adult spine surgery. The TPA was proven to be a robust measure of frailty by its ability to identify sarcopenic populations amongst the spinal population. As well, TPA reported consistent predictive effects on postoperative AEs. However, the inability to determine cutoff values diagnostic of sarcopenia suggests TPA requires further validation and/or standardization prior to being a gold standard method of assessing frailty.

The TPA and/or VB is an acceptable form of assessing frailty (strong recommendation, very low quality of evidence). Our recommendation is because the TPA and/or VB was a robust measure of frailty by identifying sarcopenic populations between oncological and nononcological spinal populations. As well, the TPA and/or VB consistently predicted postoperative AEs within these populations. This suggests the TPA and/or VB maybe a comparable measure across different spinal populations that can accurately predict postoperative AEs. Though the inability to determine cutoff values diagnostic of sarcopenia suggests TPA and/or VB requires further standardization.

We do not recommend the use of NTPA (weak recommendation, very low quality of evidence). This is due to the lack of repeat studies utilizing NTPA as a measure of sarcopenia and determining its predictive effect on postoperative AEs.

2) In which spinal surgery population(s) does frailty and/or sarcopenia have the most clinically significant role?

We recommend that, in the population(s) undergoing either thoracolumbar or cervical procedures for degenerative spinal pathology, frailty or sarcopenia is an appropriate risk factor in predicting postoperative AEs (strong recommendation, very low quality of evidence). The mFI and TPA have been the most consistent measures of frailty and sarcopenia associated with predicting AEs including 30-day morbidity and/or mortality and composite outcomes, increased in-hospital LOS and discharge to a center of higher care in this population. Precaution should be taken when applying such outcomes that are most responsive to frailty, to different spinal populations since the severity and type of spinal pathology may play an underlying role in the predictive effect. Precaution is also warranted in healthy populations as a ceiling effect can be observed with frailty and sarcopenia measures.

We suggest that MSTFI or TPA and/or VB ratio plays a clinically significant role in the metastatic spinal population (strong recommendation, very low quality of evidence). The MSTFI, as a measure of frailty, was explicitly designed for such a population to predict postoperative AEs. Regarding sarcopenia, the TPA and/or VB ratio demonstrated to be the most significant in predicting the occurrence of AEs and mortality in this population. Gakhar et al. and Zakaria et al. both demonstrated TPA and/or VB was associated with predicting mortality in a surgical and nonsurgical population respectively [11,26].

Limitations of our study

The limitations of this systematic review are related to the nature of the original articles. A significant limitation is the absence of clear cut-off values. Cut-off values to define either sarcopenia or frailty are still largely arbitrary and may be variable depending on the population studied. Also, these cut-off values may not be necessarily comparable and transferable between different spinal populations as the type of spinal pathology may influence frailty or sarcopenia severity and thereby its predictive effect.

Frailty and sarcopenia should not be interpreted as dichotomous variables but rather continuous variables of overall health. As a result, this interpretation creates difficulty in identifying precise thresholds and comparing frailty or sarcopenia severity between different studies. Also, this variability is even more pronounced in the sarcopenia literature where the optimal measurement method is unknown and the research on this specific subject is just emerging in spine surgery. Furthermore, various endpoint outcomes were reported making comparability difficult and limiting this study to a systematic review instead of a meta-analysis. As well the lack of explicit methodology for composing predictive models of frailty within each study added to poor comparability between studies.

The second limitation of this review is the studies included were specific to the spine population that is widely heterogeneous and makes the direct comparison of studies difficult. The impact of frailty and/or sarcopenia on postoperative outcomes is certainly dependent on the surgical magnitude and pathology of the patient population (degenerative, deformity, oncology, etc.). As a result, these variables will inherently play a role in dictating postoperative outcomes and are likely to serve as independent risk factors.

The last limitation of this study is the applicability of such measures in a clinical context. The lack of prospective studies utilizing frailty tools in clinical practice has resulted in these measures only being studied in a research or theoretical context. Specifically, the use of tertiles and quartiles to define sarcopenic populations is potentially an unreliable measure in clinical practice where multiple factors (physician skill, access to imaging modalities, etc.) may influence its applicability and possibly the predictive effect.

Our study identifies a need for prospective studies which report defined cut-off values for frailty and sarcopenia that are comparable and transferable between different spinal populations. We also recommend future studies to report on common end-points which are comparable and allow for the construction of a meta-analysis. Furthermore, future studies are needed to identify the relationship between...
spinal pathology and frailty or sarcopenia in order gain a better understanding of frailty and its predictive effect on postoperative outcomes in the context of spinal surgery.

Potential biases in our review include publication bias and citation bias. The use of two independent reviewers minimized these biases by providing a clear methodology and reporting both significant and insignificant findings. This provided a framework to avoid the inclusion of frequently and/or easily found articles within the review. Secondly, it allowed for better reporting on the articles included.

**Conclusion**

This systematic review identified eleven studies, seven utilizing frailty measure, and four assessing sarcopenia, which evaluated the impact of frailty and sarcopenia on postoperative outcomes. Frailty and sarcopenia were both independent risk factors associated with increased likelihood of postoperative complications including mortality, morbidity, in-hospital LOS, and discharge disposition. The mFI was the most commonly applied measure of frailty, but in terms of sarcopenia, due to a lack of cutoff values and heterogeneity between studies, there was no consensus on the most appropriate measure. Despite this, the relationship between sarcopenia and postoperative outcomes was equivocal.

Frailty and sarcopenia should be recognized as dynamic markers reflective of overall health due to change. Appropriate patient selection using validated tools for frailty and sarcopenia in the context of spine surgery may one day provide an opportunity to conservatively intervene as an attempt to improve the nutritional status, muscular strength, and general health. These tools may also one day provide guidance on patient-specific surgical approaches to reduce surgical invasiveness when risk is excessive. Most importantly these factors may play a vital role in the process of informed consent and patient education. However, due to variation between measures of frailty and sarcopenia and poor reporting on common end-points, this review highlights the need for future prospective studies to determine their clinical application.

**Supplementary materials**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.spinee.2018.07.008.

**References**


