The Measurements of Frailty and Their Possible Application to Spinal Conditions. A Systematic Review

Eryck Moskven (eryckmoskven@rcsi.ie)
The University of British Columbia https://orcid.org/0000-0002-7329-2564
Raphaële Charest-Morin
The University of British Columbia
Alana M. Flexman
The University of British Columbia
John T. Street
The University of British Columbia

Research

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Abstract

Background: Frailty is associated with an increased risk of postoperative adverse events (AEs) within the surgical spine population. Multiple frailty tools have been reported in the surgical spine literature. However, the applicability of these tools remains unclear. The primary objective of this systematic review is to appraise the construct, feasibility, objectivity, and clinimetric properties of frailty tools reported in the surgical spine literature. Secondary objectives included determining the applicability and the most sensitive surgical spine population for each tool.

Methods: This systematic review was registered with PROSPERO: CRD42019109045. Publications from January 1950 to December 2020 were identified by a comprehensive search of PubMed, Ovid, Embase, and Cochrane, supplemented by manual screening. Studies reporting and validating a frailty tool in the surgical spine population with a measurable outcome were included. Each tool and its respective clinimetric properties were evaluated using validated criteria and definitions. The applicability of each tool and its most sensitive surgical spine population was determined by panel consensus. Bias was assessed using the Newcastle-Ottawa Scale.

Results: 47 studies were included in the final qualitative analysis. A total of 14 separate frailty tools were identified, in which nine tools assessed frailty according to the cumulative deficit definition, while four instruments utilized phenotypic or weighted frailty models. One instrument assessed frailty according to the comprehensive geriatric assessment (CGA) model. Twelve measures were validated as risk stratification tools for predicting postoperative AEs, while one tool investigated the effect of spine surgery on postoperative frailty trajectory. The modified frailty index (mFI), 5-item mFI, adult spinal deformity frailty index (ASD-FI), FRAIL Scale, and CGA had the most positive ratings for clinimetric properties assessed.

Conclusions: The assessment of frailty is important in the surgical decision-making process. Cumulative deficit and weighted frailty instruments are appropriate risk stratification tools. Phenotypic tools are sensitive for capturing the relationship between spinal pathology, spine surgery, and prehabilitation on frailty trajectory. CGA instruments are appropriate screening tools for identifying health deficits susceptible to improvement and guiding optimization strategies. Studies are needed to determine whether spine surgery and prehabilitation are effective interventions to reverse frailty.

Introduction

Concurrent with the ageing population, the number of elderly patients with comorbidities presenting to surgeons for surgical consideration is increasing [1]. This is concerning as these patients undergoing surgery are at an increased risk of postoperative adverse events (AEs) [1, 2]. This increased vulnerability was initially thought to be due to the effects of ageing and comorbidity burden. Recent evidence suggests that frailty imparts a substantial risk to the development of adverse outcomes [1–5]. Frailty is a syndrome characterized by the age-associated decline in physiological reserve and reduced resilience to stressors resulting in adverse health outcomes [6, 7]. The concept of frailty and its impact on health outcomes has been well validated in the geriatric literature. This relationship has only been recently investigated within the surgical spine population, with evidence identifying that frailty is significantly associated with postoperative AEs [8].

Unfortunately, there is no standardized tool for assessing frailty due to the heterogeneity of the syndrome and the multiple systems affected. Two main models have been described to help operationalize frailty tools in a standardized and specific manner. The phenotypic model, described by Fried *et al*, conceptualizes frailty as a biological syndrome resulting from the age-associated decline across multiple physiological systems [6]. The frailty index (FI), proposed by Rockwood *et al*, conceptualizes frailty as a lifelong accumulation of age-related deficits [9]. Frailty occurs when a certain threshold of age-related deficits is reached and overwhelms the physiological reserve [9]. Several other surrogate markers for frailty have been described, such as sarcopenia. Defined as the progressive loss of skeletal muscle mass, strength, and power, sarcopenia can be the effect of musculoskeletal ageing, but it is not specific to frailty [10]. Similarly, sarcopenia is associated with adverse postoperative outcomes following spine surgery in the adult surgical spine population [8]. Unfortunately, the optimal tool for assessing frailty in patients with spinal disease is unknown. This is due to the diversity of frailty tools reported in the spine literature, the interaction between underlying spine disease and frailty, and the unknown clinical applicability of these measures.

There is increasing recognition that frailty is a dynamic marker of health susceptible to optimization and reversibility [11, 12]. This is an important consideration as spine disease is a significant risk factor for developing frailty [13]. Clinical features characteristic of spinal disability such as reduced physical activity, poor endurance, and slow walking speed overlap with phenotypic features of frailty. Timely spine surgery may be pivotal in improving frailty and reducing long-term mortality, disability, and morbidity. Consequently, if spinal disease incurs a greater degree of frailty, prolonged surgical wait-times may increase the risk of adverse health outcomes. Current frailty measures reported in the surgical spine literature may be valuable risk stratification tools. However, it is unknown whether these tools are sensitive to capturing the relationship and effect of spinal pathology and surgical intervention on frailty.

Since frailty measures may be important tools in surgical spine practice, our main objective sought to identify and appraise the construct, feasibility and objectivity of frailty tools currently reported in the surgical spine literature. Our secondary objectives included assessing the clinimetric properties and determining the clinical applicability of each frailty measure as a risk stratification or frailty trajectory tool; and determining the most sensitive surgical spine population(s) to each frailty tool.

Methodology

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [14]. The PRISMA checklist can be found in the supplemental information. The protocol was registered with PROSPERO international prospective register for systematic reviews [15]: registration number CRD42019109045.

Eligibility Criteria

As this systematic review aims to appraise the validity of the frailty tools reported in the surgical spine literature, a broad eligibility criteria was developed to capture all possible articles. Selected studies consisted of full-text articles published in the English language between January 1st, 1950 and December 30th, 2020 that met the following eligibility criteria.

1. Population: adult spine population undergoing spine surgery (age ≥ 18 years).
2. Intervention/indicator: utilization of a frailty tool with a stated methodological design.
3. Comparison: n/a.
4. Outcome: postoperative AEs (mortality, morbidity, prolonged postoperative length of stay (LOS), and adverse discharge disposition), postoperative functional outcome, or change in postoperative frailty status.
5. Study design: randomized controlled trials, case-series, cohort (retrospective, prospective, and ambispective), and cross-sectional studies.

Exclusion criteria included studies reporting non-adult (age < 18 years of age) populations; studies published in a non-English language; studies reporting a frailty tool in a non-surgical spine population; studies that did not describe or provide a reference to the methodological design of the frailty measure; review articles; abstracts without a published article; letters; and editorials.

Search Strategy

The search for relevant literature was conducted in the PubMed, EMBASE, Ovid, and Cochrane databases by two independent reviewers (E.M. and R.C-M). Search strategies were individually tailored to the requirements of the specific database. All search strategies included the following search terms of *"frailty", "screening tool", "geriatric assessment", "spine", "surgery", "psychometric properties", "clinimetric properties", "validity"*, and *"reliability."* Broad search terms were uniformly decided upon to capture all possible articles reporting the use of a frailty measure in the surgical spine population. *Figure-1* depicts an example of the search terminology applied in the PubMed database. Preliminary restrictions such as the English Language, full text, and human study only were subsequently applied. The reference lists of all full-text articles were manually screened to ensure the inclusion of all relevant studies.

Study Identification

Once the preliminary literature search was complete, duplicate entries were removed, and the remainder of publications were subjected to four tiers of review by two independent reviewers (E.M. and R.C-M.). The titles were initially screened for relevance by the two reviewers. Next, the abstracts of all relevant titles were reviewed against the inclusion and exclusion criteria. A third author (J.S.) was available to adjudicate if any disagreement between the two reviewers occurred. Full-text articles of all included studies were evaluated according to the inclusion and exclusion criteria. Finally, bibliographies of all included articles were reviewed for relevant references, which were subjected to the inclusions and exclusion criteria and, if selected, they underwent full review. The selection process produced a list of full-text publications reporting frailty tools within the surgical spine literature.

Data Abstraction and Analysis

Since the objective of this systematic review is to evaluate the applicability of frailty measures in the surgical spine population as risk stratification tools or frailty trajectory measures, a qualitative analysis of the results was undertaken. A meta-analysis was not possible due to the heterogeneity of the frailty tools reported, the lack of standardized outcomes reported across the included literature, and the diversity of individual components or subscales within each frailty tool.

Each frailty measure identified in the selected studies was firstly categorized based on its operational definition and then deconstructed into its components. Components were categorized as either subscales or individual items. Subscales were defined as the constitution of individual items within the frailty measure used to assess a specific component of the frailty syndrome. Individual items were defined as a measure, question, clinical symptom, clinical sign, or health deficit that does not constituent to any set of items and assesses a specific aspect of the frailty syndrome. *Appendix-1* depicts the breakdown of each frailty measure reported in the surgical spine literature.

Evaluation of each frailty tool, and its associated items and subscales, was conducted by two authors (E.M. and R.C-M.) using defined criteria formulated to assess the objectivity, feasibility, and clinimetric properties. In the absence of a previously defined precedent on objectivity, feasibility, validity, or reliability, these criteria were defined in practical terms by a panel of spine surgeons and anaesthesiologists with prior publications and knowledge in this field. Objectivity was defined as the assessment of an item or subscale that was not subjective to the bias, personal judgement, or cultural background of patients, their families or healthcare providers [16]. Feasibility was defined as an item or subscale that is easily obtainable from a standard spine history, physical examination, medical record, and routine laboratory tests without the need for special equipment [16]. Clinimetric properties (validity, reliability, responsiveness, and floor and ceiling effect) were evaluated using a validated set of quality appraisal definitions established by the Consensus-based Standards for Health Measurement Instruments (COSMIN) [17–19]. Any discrepancies were resolved by reaching a consensus between the authors or adjudication with a third reviewer (J.S.). *Appendix-2* demonstrates the qualitative assessment of each of the clinimetric properties.

Methodological evaluation and bias assessment of the included studies was performed independently by the two lead authors (E.M. and R.C-M.) using either The Cochran Risk of Bias tools for randomized control trials (RCTs) [20] or the Newcastle-Ottawa Scale (NOS) for non-randomized studies [21]. The NOS contains three sections: population, inter-group comparability, and outcomes assessment that are divided into a total of eight items. Each item is given either a negative score of 0 (unclear, high risk of bias) or a positive score of 1 (clear, low risk of bias). Only inter-group comparability can be given a positive score of 2 at most. The total NOS score ranges from 0–9, whereby a lower score indicates a higher risk of bias, and a higher score indicates a lower risk of bias. Additionally, the quality of evidence for each included study was evaluated using a 5-point scale derived from the Oxford Centre for Evidence-Based Medicine *(Appendix-3)*[22]. Any disagreements between the two lead reviewers were resolved by either panel consensus between all authors or adjudication by a third author (J.S.).

Finally, all authors participated in a panel evaluation to determine the clinical applicability of each frailty tool for either risk stratification or capturing the relationship between spinal pathology and surgical intervention on frailty trajectory. This was determined by reviewing the clinimetric properties assessed and whether the components for each frailty tool were modifiable or non-modifiable. The authors also determined the spine population(s) most sensitive for each frailty tool. This evaluation is important given the heterogeneity of the spine population, whereby different spinal pathologies impart different effects on frailty.

Results

The literature search retrieved a total of 8,268 publications, from which 43 were retained, along with four additional articles found in the authors' libraries or bibliographies of reviewed full-text articles (*Figure-2*). 47 studies were included in the final analysis and extraction of data [23–69].

Study Characteristics

Of the 47 included studies, frailty tools were reported in the following spine populations: degenerative disease, complex adult spinal deformity, oncology, trauma, and cervical fusion *(Table-1)*. The remaining studies reported a frailty measure within the spondylodiscitis, anterior lumbar interbody fusion (ALIF), thoracolumbar instrumentation, or vertebral tuberculosis population. Several studies did not specify a specific spine population. Overall, most included studies were retrospective in design, utilized an age inclusion criteria of eighteen years of age or greater (age ≥ 18 years), and reported postoperative AEs as the primary outcome of interest. A comprehensive summary of the study characteristics including study design, age inclusion criteria, outcome of interest, and outcome measure is outlined in *Table-1*.

Prevalence of Frailty

Significant differences in frailty prevalence were observed between different surgical spine populations due to the frailty tool used, the effect of underlying spinal pathology on frailty, and the cutoff values applied to stratify the study population into robust, pre-frail, and frail cohorts. A comprehensive summary of the frailty prevalence reported amongst the included studies and between different populations is outlined in *Table-1*. Frailty prevalence could not be calculated or identified from several studies due to insufficient information/data or the lack of cutoff values stratifying the population into robust, pre-frail, and frail cohorts. Overall, the prevalence of frailty was higher in the complex adult spinal deformity population.

Characteristics of Frailty Tools

The selected studies yielded 14 frailty tools representing the combination of 357 individual items designed to assess frailty domains *(Table-1, Table-2)*. Five subscales were identified *(Appendix-1)*. The total number of components (individual items) reported in a single frailty tool ranged from 5 to 109.

Nine of the 14 frailty tools operationalized frailty according to the accumulation of deficit model (*Table-2*). All nine of these frailty measures utilized a dichotomous scale to evaluate the presence or absence of deficits. Four measures calculated frailty as a ratio (n/t) of the sum of deficits present in the model (n) divided by the total number of deficits evaluated (t). Five tools calculated frailty as a whole number by the sum of deficits present within the model.

Of the 47 studies reporting a cumulative deficit model, the modified frailty index (mFI) was the most reported frailty tool in 26 studies (55.3%), followed by the 5-item mFI in six studies (12.8%), adult spinal deformity frailty index (ASD-FI) in five studies (10.6%), cervical deformity frailty index (CD-FI) in three studies (6.4%), and the metastatic spinal tumour frailty index (MSTFI) in three studies (6.4%). The modified cervical deformity frailty index (mCD-FI), primary spinal tumour frailty index (PSTFI), frailty based score (FBS), and the modified frailty score (MFS) were the least reported cumulative deficit measures *(Table-1 and Table-2)*.

Of the 26 studies utilizing the mFI, 15 studies reported predefined cutoff values to stratify the study population into robust, pre-frail, or frail cohorts, while the remaining 10 studies reported a continuous dose-response ratio *(Table-2)*. Only one study reported both predefined mFI cutoff values and a continuous dose-response ratio [42]. Similarly, predefined robust, pre-frail, and frail values were reported by all studies using the 5-item mFI *(Table-2)*. All studies utilizing the ASD-FI reported predefined cutoff values to stratify patients into robust, frail and severely frail cohorts *(Table-2)*. Predefined MSTFI values were reported in two studies to stratify patients into mild, moderate and severely frail MSTFI scores *(Table-2)*. One study reported the MSTFI as a continuous score [36]. Studies reporting the CD-FI applied predefined values to stratify patients into robust, frail and severely frail cohorts or non-frail and frail cohorts. Predefined values were applied in the studies reporting the mCD-FI and PSTFI. The studies reporting the FBS and the MFS did not use cutoff values.

The FRAIL Scale and Fried Phenotype measures are ordinal scores containing items operationalized according to the phenotypic frailty model *(Table-2)*. Frailty is calculated based on the sum of the items present within each tool. Predefined robust, pre-frail and frail cutoff values were reported by the studies utilizing these measures. The Hospital Frailty Risk Score (HFRS) and Risk Analysis Index (RAI) operationalized frailty according to a weighted scale system. Components are derived from either the phenotypic, cumulative deficit, or comprehensive geriatric assessment (CGA) frailty models. The HFRS and RAI use predefined values to stratify the study population into robust, pre-frail, frail or severely frail cohorts. Lastly, one study operationalized frailty according to the CGA model. The CGA examines frailty using validated subscales with predefined values to identify the presence of the frailty domain. The CGA calculates frailty on an ordinal scale, and a predefined criterion identifies the frailty syndrome *(Table-2)*.

The most common frailty domains assessed were comorbidity status (93%), function (86%), nutrition and weight (79%), cognition (50%), and mood and mental health (43%). Domains of energy, strength, fall risk, and continency were assessed in 36% of included measures. Laboratory features and social support were assessed in 29% of measures, while general health and polypharmacy were assessed in 14%. Clinical symptoms/signs, vision or hearing impairment, living status, and slow gait speed were assessed in 7% of measures. Two tools included non-frailty domains such as surgical approach and tumor-specific radiographic features. None of the frailty tools assessed the domains of care goals, advanced directives, sexual function, dentition, or spirituality. Ten of the frailty tools identified were validated for use in a clinical context. The remaining four were validated for use in either a clinical or community context *(Table-2)*. Special equipment or training was reported for three of the frailty tools. It should be noted that no publication or study reported the time to complete each measure.

Predictors of Outcome

Of the 14 frailty tools, 13 were evaluated as predictors of postoperative AEs or postoperative functional outcomes *(Table-2)*. Only one of the tools investigated the effect of spine surgery on postoperative frailty trajectory *(Table-2)*. The remaining tool was not appropriately evaluated for predicting postoperative outcomes. *Appendix-2* contains a detailed summary of the predictive validity for each frailty tool.

Modified Frailty Index (mFI)

Of the 26 studies reporting the use of the mFI, the validity as a risk stratification tool for predicting postoperative AEs was assessed in 23 studies using appropriate statistical methodology. Within the degenerative spine population undergoing complex primary elective spine surgery, the mFI significantly and independently predicted postoperative AEs including mortality, major and minor morbidity, prolonged postoperative LOS, adverse discharge disposition, and unplanned readmission and reoperation *(Appendix-2)*. Further receiver operator characteristic (ROC) analysis identified acceptable sensitivity for the mFI to predict postoperative AEs within this patient population *(Appendix-2)*. However, in the degenerative spine population undergoing non-complex spine surgery, the mFI was not a significant or sensitive predictor of postoperative AEs *(Appendix-2)*.

Within the complex adult spinal deformity population, the mFI significantly and independently predicted postoperative AEs including mortality, major and minor morbidity, and hardware/implant complications with excellent sensitivity after ROC analysis *(Appendix-2)*. Limited studies assessed the validity of the mFI as a risk stratification tool for predicting postoperative AEs in the spine trauma population *(Appendix-2)*. Initial validation demonstrated that the mFI weakly predicted postoperative AEs following surgical stabilization of thoracolumbar fractures *(Appendix-2)*. Further validation demonstrated that the mFI did not predict postoperative AEs including mortality, adverse discharge disposition, or prolonged postoperative LOS following complex spine surgery for traumatic spinal cord injury (tSCI) *(Appendix-2)*.

Similarly, in the spine tumor population undergoing complex spine surgery, limited studies and conflicting evidence limit the validity of the mFI as a risk stratification tool for predicting postoperative AEs. Initial validation demonstrated that the mFI weakly predicted 30-day postoperative mortality and prolonged postoperative LOS with poor sensitivity *(Appendix-2)*. Further validation identified that the mFI was not predictive of postoperative AEs including morbidity, mortality, and prolonged postoperative LOS *(Appendix-2)*.

Within several unique spine populations, such as patients with spondylodiscitis or undergoing cervical fusion and anterior lumbar interbody fusion (ALIF), the mFI weakly predicted postoperative AEs including mortality and major morbidity *(Appendix-2)*. When validated in several non-specific surgical spine populations, the mFI significantly predicted postoperative AEs including major complications, mortality, postoperative surgical site infection, and prolonged postoperative LOS *(Appendix-2)*.

Finally, pre-frail and frail mFI scores were significantly associated with lower 2-year postoperative functional and symptomatic scores following spine surgery for complex adult spinal deformity *(Appendix-2)*. However, the mFI was not associated with any differences in 2-year postoperative radiographic outcomes *(Appendix-2)*. Similarly, pre-frail and frail mFI scores were not associated with differences in 2-year postoperative functional and symptomatic outcomes in the degenerative spine population *(Appendix-2)*.

Adult Spinal Deformity Frailty Index (ASD-FI)

Of the five studies reporting the ASD-FI, three evaluated its validity as a risk stratification tool for predicting postoperative AEs while two studies assessed the association between ASD-FI and postoperative functional outcomes in the complex adult spinal deformity population. As a risk stratification tool, the ASD-FI significantly predicted postoperative AEs including major complications, prolonged postoperative LOS and reoperation *(Appendix-2)*. Baseline preoperative ASD-FI scores significantly correlated with preoperative functional disability and 2-year postoperative functional outcomes *(Appendix-2)*. Lastly, mild and severely frail ASD-FI scores were associated with worse baseline spinopelvic radiographic parameters including C7-S1 Sagittal Vertical Axis (SVA), Pelvic Incidence – Lumbar Lordosis (PI-LL) mismatch, and Pelvic Tilt (PT) *(Appendix-2)*. Mild and severely frail ASD-FI scores were only weakly associated with significant differences in 3-year postoperative C7-S1 SVA *(Appendix-2)*. Regarding functional outcomes, mild and severely frail ASD-FI scores were only associated with differences in standardized 1-year and 3-year postoperative functional outcomes *(Appendix-2)*. When analyzing for change in postoperative functional outcome, the ASD-FI was only associated with improvements in 1-year and 3-year postoperative Scoliosis Research Society – 22 (SRS-22) scores *(Appendix-2)*.

Metastatic Spinal Tumour Frailty Index (MSTFI)

All studies reporting the MSTFI assessed its validity as a risk stratification tool for predicting postoperative AEs within the metastatic spinal tumor population. Initial validation identified that the MSTFI significantly predicted postoperative major AEs and mortality with moderate discrimination and sensitivity *(Appendix-2)*. Mild, moderate and severely frail MSTFI scores were also associated with significant differences in postoperative LOS *(Appendix-2)*. However, further external validation identified that the MSTFI is not a predictor of postoperative AEs including mortality, major complications or prolonged postoperative LOS *(Appendix-2)*. Further ROC analysis demonstrated poor sensitivity of the MSTFI to predict postoperative major AEs and overestimation of the MSTFI to predict postoperative in-hospital mortality *(Appendix-2)*.

5-item Modified Frailty Index (5-item mFI)

All studies reporting the 5-item mFI assessed its validity as a risk stratification tool for predicting postoperative AEs. Within the degenerative population undergoing primary elective complex cervical and lumbar spine surgery, the 5-item mFI significantly predicted postoperative AEs including mortality, major and minor AEs, adverse postoperative discharge disposition, prolonged postoperative LOS, and unplanned postoperative readmission and reoperation *(Appendix-2)*. Further ROC analysis demonstrated good to excellent sensitivity of the 5-item mFI to predict postoperative AEs *(Appendix-2)*. However, in the degenerative population undergoing non-complex lumbar spine surgery, the 5-item mFI did not significantly predict postoperative AEs *(Appendix-2)*. When applied within the complex adult spinal deformity, the 5-item mFI significantly predicted postoperative AEs including major AEs and hardware-related complications *(Appendix-2)*.

Cervical Deformity Frailty Index (CD-FI)

Two studies assessed the validity of the CD-FI as a risk stratification tool for predicting postoperative AEs within the adult cervical deformity population undergoing complex spine surgery. The remaining studies assessed the effect of spine surgery on postoperative frailty trajectory or the association between CD-FI and postoperative radiographic and functional outcomes *(Appendix-2)*. As a risk stratification tool, only severely frail CD-FI scores predicted 2-year postoperative major AEs *(Appendix-2)*. Frail CD-FI scores were not significantly predictive of 2-year postoperative major AEs *(Appendix-2)*.

In regards to postoperative frailty trajectory, initial validation identified that spine surgery for cervical spine deformity significantly improved 1-year postoperative CD-FI scores *(Appendix-2)*. Postoperative improvements in weakness, anxiety, driving, fatigue, exhaustion, concentration, recreation, activity, mobility, and depression were the most significant factors associated with improvement in postoperative frailty trajectory *(Appendix-2)*. Improvement in baseline to 1-year postoperative spinopelvic radiographic parameters was also associated with significant improvements in 1-year postoperative frailty *(Appendix-2)*. After further analysis, successful spine surgery and improvement in exhaustion were the two variables most predictive of 1-year postoperative improvement in frailty *(Appendix-2).*

The CD-FI was significantly associated with worse preoperative function and symptom scores in frail patients with cervical spine deformity awaiting spine surgery *(Appendix-2)*. In terms of baseline radiographic parameters, frail CD-FI scores were associated with worse Sagittal Vertical Axis (SVA) alignment than the non-frail cohort *(Appendix-2)*. However, there was no significant difference in either 3-month or 1-year postoperative radiographic changes between frail and non-frail CD-FI score cohorts *(Appendix-2)*. The CD-FI was associated with significant differences in standardized 1-year postoperative functional and symptomatic outcomes including the Neck Disability Index (NDI), modified Japanese Orthopedic Association (mJOA) and EuroQol – 5D (EQ5D) scores between non-frail and frail patients *(Appendix-2)*. Following unadjusted analysis, the CD-FI was only associated with significant improvements in 1-year postoperative EQ5D scores *(Appendix-2)*.

Modified Cervical Deformity Frailty Index (mCD-FI)

The validity of the mCD-FI as a risk stratification tool was assessed by one study in the cervical deformity population. Initial validation demonstrated that only severely frail mCD-FI scores predicted postoperative mortality *(Appendix-2)*. Further analysis did not identify the same association for frail mCD-FI scores *(Appendix-2)*.

Primary Spinal Tumour Frailty Index (PSTFI)

The validity of the PSTFI as a risk stratification tool was assessed by one study in the primary spinal tumour population. Initial validation identified that the PSTFI predicted postoperative major AEs with moderate sensitivity after ROC analysis *(Appendix-2)*. However, external validation identified only severely frail PSTFI scores weakly predicted 30-day postoperative AEs with poor sensitivity after ROC analysis *(Appendix-2)*.

Frailty Based Score (FBS)

Only one study assessed the validity of the FBS as a risk stratification tool within the cervical fusion population. Initial validation identified that the FBS significantly predicted any 30-day postoperative AEs, including unplanned readmission and unplanned reoperation with moderate discrimination and sensitivity *(Appendix-2)*.

FRAIL Scale

Two studies assessed the validity of the FRAIL Scale as a risk stratification tool for predicting adverse postoperative cognitive and functional recovery. Within the degenerative population undergoing complex and non-complex cervical and lumbar spine surgery, the FRAIL Scale significantly predicted a reduced likelihood of 3-month postoperative functional recovery in the frail cohort *(Appendix-2)*. The FRAIL Scale did not predict 3-month postoperative cognitive recovery or 3-day postoperative functional recovery *(Appendix-2)*. Further external validation in a non-specific population undergoing elective spine surgery identified that the FRAIL Scale significantly postoperative delirium in the frail cohort *(Appendix-2).*

Fried Frailty Phenotype Measure

The validity of the Fried Phenotype as a risk stratification tool for predicting postoperative AEs was assessed by one study within the thoracolumbar degenerative and deformity population. Initial validation identified that the Fried Phenotype did not predict six-week postoperative AEs including major AEs and adverse postoperative discharge disposition *(Appendix-2)*. The Fried Phenotype did not also predict postoperative unplanned readmission or prolonged postoperative LOS *(Appendix-2)*.

Hospital Frailty Risk Score (HFRS)

Only one study assessed the validity of the HFRS as a risk stratification tool for predicting postoperative AEs within the degenerative spine population. Initial validation demonstrated that moderate and severely frail scores predicted postoperative admission to critical care, the total incidence of postoperative AEs, adverse postoperative discharge disposition, postoperative unplanned readmission or emergency department visit, prolonged postoperative LOS and increased direct costs *(Appendix-2)*. Further ROC analysis with the inclusion of the HFRS identified a greater sensitivity to predict postoperative AEs *(Appendix-2)*.

Risk Analysis Index (RAI)

The validity of the RAI as a risk stratification tool for predicting postoperative AEs was assessed by one study within a non-specific surgical spine population. Initial validation identified that pre-frail and frail RAI scores were significantly associated with a higher rate of postoperative readmission, mortality, and longer postoperative LOS compared to non-frail scores *(Appendix-2)*. Pre-frail and frail RAI scores had a higher critical care admission rate than non-frail scores, but this did not reach statistical significance *(Appendix-2)*. Further analysis observed that pre-frail and frail RAI scores significantly predicted 1-year postoperative mortality *(Appendix-2)*.

Comprehensive Geriatric Assessment (CGA)

The validity of the CGA as a risk stratification tool for predicting postoperative AEs was assessed by one study within the degenerative population undergoing non-complex and complex lumbar spine surgery. Initial validation demonstrated that the CGA significantly predicted 30-day postoperative AEs including minor and major AEs *(Appendix-2)*. Further analysis identified that the CGA predicted a greater likelihood of 30-day postoperative major and minors AEs in the complex fusion cohort *(Appendix-2)*.

Modified Frailty Score (MFS)

Lastly, one study reported the association between the MFS and postoperative AEs in the vertebral tuberculosis population *(Appendix-2)*. Initial observation demonstrated that the value of the MFS was significantly higher in the 30-day postoperative mortality cohort than the survival cohort *(Appendix-2)*. However, the authors did not perform any formal analysis establishing the predictive validity of the MFS.

Clinimetric Properties, Objectivity, Feasibility, and Applicability

Predictive validity was the most commonly assessed clinimetric properties across all the included studies *(Table-3, Appendix-2)*. Content and concurrent validity, responsiveness, and reliability were the second most assessed clinimetric properties. The mFI, ASD-FI, 5-item mFI, FRAIL Scale, and CGA had the most positive ratings. None of the instruments identified had positive ratings for all the clinimetric properties. The MFS was the only instrument without any rating since none of the clinimetric properties were assessed. *Appendix-2* summarizes the evidence evaluating the clinimetric properties of the frailty tools within the surgical spine literature. A more comprehensive summary of this evaluation is described in *Table-3*.

The mFI, FRAIL Scale, mCD-FI, 5-item mFI, MSTFI, FBS, MFS, RAI, and CGA were all clinically feasible tools *(Table-3)*. Of these, the mFI, mCD-FI, 5-item mFI, MSTFI, MFS, RAI, and CGA were objective tools. The remaining measures were neither feasible nor objective. Nine of the 14 frailty tools are only applicable as risk stratification tools *(Table-3)*. This is due to the non-modifiable constructs of these measures that cannot capture clinical changes in frailty or the initial validation of these instruments as risk stratification tools. The FRAIL Scale, Fried Phenotype, ASD-FI, and CD-FI are applicable as either risk stratification tools or frailty trajectory tools. The constructs of these measures contain modifiable items sensitive to improvement. Only one frailty tool identified is not clinically applicable due to an absence of information assessing any clinimetric property.

Assessment of Methodological Quality

A summary of the bias assessment is presented in *Figure-3*. The NOS score of the included studies ranged from 5–9. The most common sources of bias included absent follow-up time [24, 26, 27, 33, 35, 36, 45, 53, 56, 62, 64, 69], inadequate follow-up of cohorts [24, 36, 37, 44, 46, 47, 51, 52, 55, 67, 69], not adjusting for confounding factors within the statistical model [25, 26, 31, 32, 37, 40, 43, 44, 46, 51, 54, 56, 62–64, 67, 69], and poor representation of the cohort [26, 32, 37, 44, 45, 47, 50, 51, 55, 63, 67–69]. Less common sources of bias included poor ascertainment of the exposure and outcome data [45–47, 67], insufficient follow-times for outcome(s) to occur [46], and inadequate demonstration that the outcome was not present at the start of the study [31, 46, 51, 52, 55]. Most of the studies scored 2–3 on the Quality Rating Scale as they were either retrospective or prospective cohort studies *(Appendix-4)*.

Discussion

Although not necessarily synonymous with ageing, the prevalence of frailty is increasing in the surgical spine population [1, 70]. This is concerning as frail patients undergoing spine surgery are at an increased risk of adverse postoperative outcomes [8]. Accordingly, the assessment of frailty is an important factor in the surgical decision-making process regarding surgical risk, invasiveness, and timing. However, the applicability of these instruments as risk stratification or frailty trajectory tools is unknown. This is due to the heterogeneity and lack of consensus with frailty tools currently reported and the effect of underlying spine disease on frailty.

Similar reviews assessing the clinimetric properties and applicability of frailty tools have been completed in different contexts [16, 18, 71, 72]. To our knowledge, this review is the first to evaluate the objectivity, feasibility, applicability, and sensitivity of frailty tools reported in the surgical spine literature. Additionally, this systematic review is the first that has rigorously evaluated the clinimetric properties of frailty tools reported in the surgical spine literature using a validated set of qualitative criteria and definitions. One of the most important outcomes identified in our review is that although most tools were predictive of postoperative outcomes, many lacked formal evaluation of important clinimetric properties. Additionally, several frailty measures were not objective or clinically feasible. This was due to items (subjective questions) or techniques (lengthy questionnaires) common to these measures that cannot be reliably or reasonably completed in clinical practice.

Risk Stratification Tools

The mFI, developed and validated by Velanovich *et al*, was constructed by matching 11 variables found within the National Surgical Quality Improvement Program (NSQIP) database to those within the 70-item Canadian Study of Health and Aging frailty index (CSHA-FI) [73]. Since its development, the mFI has been extensively validated as a risk stratification tool for predicting postoperative AEs across the surgical literature [74]. In recent years, an increase in the missing proportion of variables required to calculate the mFI has raised concern about its validity as a risk stratification tool [75]. To overcome this, Chimukangara *et al* identified the top five most reported mFI variables within the NSQIP database, condensing the mFI into the 5-item mFI [76]. Across the surgical literature, the 5-item mFI is recognized as a valid risk stratification tool for predicting postoperative AEs [76–78].

Within the degenerative and deformity populations undergoing complex spine surgery, the mFI and 5-item mFI are sensitive risk stratification tools for predicting postoperative AEs. These tools have been validated using a robust study methodology in large cohorts with accurate, precise and reproducible risk estimates. Additionally, the mFI and 5-item mFI are reliable tools given the high degree of concordance between their respective frailty tiers. Lastly, since few deficits are required to assess frailty, both tools are easily applicable without the need for an extensive chart review, special tests or training.

The mFI is not a sensitive risk stratification tool in the non-complex degenerative, tumor, or trauma spine populations due to conflicting evidence, poor study methodology, and construct limitations of the mFI. Since the mFI is mainly composed of deficits that assess comorbidity status, it is not sensitive for assessing the multiple systems affected by frailty. Consequently, in healthy patients with little to no comorbidities undergoing spine surgery, the mFI is significantly underpowered as a risk stratification tool [24, 27]. In the tumor population, the construct does not account for the physiological effects of metastatic disease, such as tumour burden and adjunctive therapy. These factors influence underlying physiological reserve and confound the relationship between frailty and postoperative AEs [35, 36, 79]. Within the thoracolumbar trauma population, poor study design and insufficient evidence limit the validity of the mFI as a risk stratification tool. Finally, in the tSCI population, the magnitude of the injury, patient age, and total motor score on admission overpowers any association between the mFI and postoperative AEs [33].

The constructs of the mFI and 5-item mFI significantly deviate from the general multisystem concept of frailty. A valid frailty index must contain 30–40 deficits in which each deficit covers a range of systems, is associated with overall health status, increases in prevalence with age, and cannot saturate early [80]. Frailty indices containing few deficits, such as the mFI and 5-item mFI, are prone to instability and imprecise index estimates [80]. Furthermore, during the design of the mFI and 5-item mFI, the reduction of frailty deficits from the 70-item CHSA-FI was performed without analysis of convergent validity [81]. This raises concern as to whether the mFI and 5-item mFI are of the same degree of construct as the CHSA-FI. Lastly, the non-modifiable constructs of the mFI and 5-item mFI limit the sensitivity of these frailty tools to capture clinical changes. Yagi *et al* identified that despite optimization of each mFI factor, no significant reduction in postoperative AEs was observed when compared against the non-frail cohort [30]. Therefore, the mFI and 5-item mFI are applicable as risk stratification tools only.

The ASD-FI, developed by Miller *et al*, was constructed using variables within the International Spine Study Group (ISSG) database that met the frailty index inclusion criteria [48]. Cutoff values were then applied to stratify the population into robust, frail, and severely frail cohorts. Since its development, the ASD-FI has demonstrated to be a valid risk stratification tool for predicting postoperative AEs within the complex adult spinal deformity population. The ASD-FI also has several strengths as a risk stratification tool compared to the mFI and 5-item mFI. The ASD-FI was developed using a standard methodology for creating accurate and precise frailty indexes [50]. The ASD-FI is also a more sensitive frailty tool as it evaluates a greater number of health domains within the frailty syndrome. The ASD-FI has also been extensively validated within the complex adult spinal deformity population as a risk stratification tool. In a series of studies by Miller *et al*, the ASD-FI reliably predicted 2-year postoperative AEs in external and internal validation cohorts [48–50]. The mFI and 5-item mFI were validated in either a large national cohort with limited follow-up periods, underestimated complication rates and missing patient variables; or in small cohorts where patient age, lifestyle, and ethnicity impact surgical outcomes [28, 29]. However, the number of deficits required to calculate the ASD-FI makes it clinically unfeasible. Given this, the mFI and 5-item mFI are more appropriate risk stratification frailty tools in the adult spinal deformity population.

The CD-FI was developed in the same fashion as the ASD-FI for use in the cervical deformity population as a risk stratification tool [80]. Passias *et al* further condensed the CD-FI to a 15-item mCD-FI by identifying the health deficits most predictive of the overall CD-FI score [56]. The CD-FI and mCD-FI were internally validated as risk stratification tools in the cervical deformity population [53, 55, 56]. However, it is unknown whether these measures are valid or sensitive risk stratification tools for predicting postoperative AEs or functional outcomes. This is due to the lack of external validation studies, conflicting evidence, and poor methodological design of the current validation study [55].

As the ASD-FI and CD-FI contain several modifiable frailty deficits that overlap with clinical features of spinal disease, these measures are sensitive to capturing the effect of spine surgery on postoperative frailty trajectory. Segreto *et al* identified a significant reduction in 1-year postoperative CD-FI scores following spine surgery for cervical deformity [54]. However, responsiveness was evaluated by a *t*-test that only compares differences in the score. This methodology does not assess the validity of the score change in relation to the CD-FI construct to capture responsiveness. Accordingly, the ASD-FI and CD-FI are more appropriate risk stratification tools given the lack of literature assessing the responsiveness of these measures.

Although the ASD-FI, CD-FI, and mCD-FI are promising frailty tools, some concerns may limit the applicability of these tools. Firstly, the cutoff values chosen to stratify frailty severity were determined without any formal analysis. The health deficits included within these tools were also derived from questionnaires commonly utilized in spine practice. Consequently, the ASD-FI, CD-FI, mCD-FI may overestimate frailty and the associated predicted risk. Additionally, no formal sensitivity analysis has been performed assessing the performance of these measures against other frailty tools. Lastly, the need to acquire all 42 deficits to calculate the ASD-FI and CD-FI significantly hinders the clinical applicability of these tools.

The MSTFI and PSTFI were constructed as risk stratification tools for the metastatic and primary spine tumor populations [62, 64]. De la Garza Ramos *et al* constructed the MSTFI by identifying patient recorded variables within a national multicenter database that had the greatest independent effect for predicting postoperative AEs [62]. Nine variables were identified to construct the MSTFI, and cutoff scores were applied to stratify patients into robust, mild, moderate, and severe frail cohorts. The PSTFI was developed using items within the MSTFI, except those pertaining to surgical approach [64]. Cutoff values were similarly applied to stratify patients according to frailty severity.

Within the metastatic spine tumor population, both the mFI and MSTFI demonstrated significant heterogeneity and difficulty in predicting postoperative AEs [34, 62, 63]. Initial validation by De la Garza Ramos *et al* suggested the MSTFI was an appropriate risk stratification tool [62]. However, external validation by Massaad *et al* identified that the predicted outcomes stratified by MSTFI severity were not consistent with those reported in the initial validation study [63]. The authors observed that the MSTFI overestimated the risk of postoperative AEs for severely frail patients while underestimating the risk for mildly frail patients [63]. Bourassa-Moreau *et al* observed that neither the mFI nor MSTFI were associated or predictive of postoperative AEs [36]. Consequently, given the heterogeneity and inconsistency, no recommendation can be made as to whether the mFI or MSTFI are appropriate risk stratification tools for this spine population. This highlights the challenge of defining and quantifying frailty in the metastatic spine tumour population. Further efforts are required to improve the determination of frailty in this specific surgical cohort.

Similarly, determining the most sensitive frailty tool for the primary spine tumour population is difficult. Our review observed that the mFI and PSTFI weakly predict postoperative AEs with large confidence estimates and relatively poor sensitivity. Additionally, patients with primary spine tumors are often younger and less likely to have comorbidities or present with clinical features of frailty. Consequently, comorbidity-based frailty tools such as the mFI or PSTFI are not sensitive for evaluating frailty within this population. Additionally, since the PSTFI is derived from the MSTFI, it is poorly sensitive for assessing frailty in the primary spinal tumour population.

As frailty tools, the construct of the MSTFI and PSTFI are not designed to evaluate frailty. The MSTFI and PSTFI contain surgical, radiographic, and laboratory items that are not sensitive or specific to frailty. The limited number of deficits within these frailty tools is also problematic. It increases the potential for imprecise index estimates, and when applied to small healthy cohorts, the lack of deficits significantly reduces the ability to detect a relationship with adverse outcomes [36]. The cutoff values applied to stratify frailty severity were also chosen without any formal assessment. Finally, given the non-modifiable constructs of these measures, the MSTFI and PSTFI are only applicable as risk stratification tools. The need for medical imaging or extensive chart review may hinder these measures' feasibility due to extensive time requirements.

Similar to the mFI and the 5-item mFI, the FBS was constructed using commonly reported variables within the NSQIP database [82]. The FBS was initially validated as a risk stratification tool for the vascular surgery population [82]. Medvedev *et al* further validated its use as a risk-stratification tool in the surgical spine population to predict postoperative AEs [65]. However, the clinical applicability of the FBS and its most sensitive surgical spine population cannot be determined for several reasons. The FBS was validated in a heterogeneous cohort without any formal analysis adjusted for cervical pathology. Consequently, it is unknown whether the FBS is more sensitive to a subtype of cervical spine pathology. The FBS has also not been externally validated, raising concern about its validity as a risk stratification tool. Finally, due to its non-modifiable construct, the FBS is only applicable as a risk stratification tool.

The modified frailty score (MFS) is a 19-item frailty index validated by Patel *et al* for predicting mortality in the orthogeriatric population [69, 83]. It was constructed by including 19 of the 70 deficits within the CSHA-FI [83]. The MFS is associated with higher rates of 30-day postoperative mortality following spine surgery for tuberculous spondylodiscitis [69]. However, no formal analysis was performed to evaluate its predictive validity, limiting its applicability as a risk stratification tool. Many clinimetric properties of the MFS have also not been assessed. The 19 deficits included from the 70-item CHSA-FI were arbitrarily chosen without any formal analysis of convergent validity. Despite these limitations, the MFS assesses a greater number of frailty domains than other deficit accumulation measures reported in the surgical spine literature. Accordingly, the MFS is a more sensitive frailty tool in healthy populations and is less prone to instability and poor index estimates.

The Hospital Frailty Risk Score (HFRS) is a validated risk stratification tool that incorporates administrative coding into the assessment of frailty. Initially constructed by Gilbert *et al* [84], the HFRS contains 109-items health-deficits derived from International Classification of Disease – 10 (ICD-10) codes collected upon admission to hospital. The HFRS can be calculated from routinely collected data within electronic medical records without the need for extensive chart review. The HFRS demonstrated to be a valid risk stratification tool for predicting postoperative AEs following spine surgery for degenerative spine conditions. Similar studies validating the HFRS in non-spine surgical populations have demonstrated equivocal or superior findings for the HFRS to predict postoperative AEs [85]. Given this, the HFRS is a sensitive risk stratification tool in the degenerative spine population. However, the technological requirements needed to use the HFRS may limit its applicability.

As a frailty tool, the HFRS differs from traditional deficit accumulation tools reported in the literature. The HFRS is calculated from ICD-10 codes, which are individually scored based on the prevalence of the health deficit and individual association with adverse health outcomes. Accordingly, the HFRS is a more reliable and accurate tool as the estimated risk is adjusted for the health deficits that contribute to frailty. However, many of its clinimetric properties have not been formally assessed. Gilbert *et al* acknowledged difficulties designing the HFRS from ICD-10 coded data as these health-deficits do not capture the multisystem and dynamic progression of frailty [84]. Consequently, the predictive abilities of the HFRS may be overstated compared to other frailty tools that capture the dynamic features of frailty such as functional states, phenotypic characteristics, caregiver support and fluctuations influenced by acute illnesses. Additionally, given its design and primary application as a risk stratification tool, its role as a frailty trajectory tool is significantly limited.

The Risk Analysis Index (RAI), constructed by Hall *et al*, is a 14-item questionnaire designed for assessing frailty in surgical patients [86]. It is recognized as a valid risk stratification tool for predicting postoperative AEs and identifying patients requiring preoperative optimization within the elderly surgical population [87]. Within the surgical spine population, pre-frail and frail RAI scores were associated with adverse postoperative outcomes. However, multiple limitations are present within the validation study. Many of the postoperative outcomes studied occurred at an exceeding low frequency, likely creating a type 2 statistical error that underpowered the predictive validity of the RAI. A selection bias further compromises the validity of the RAI as Agarwal *et al* failed to report the number of patients with complete or missing RAI and outcome data [67]. Additionally, the statistical analysis did not adjust for confounding patient and operative variables. Given these limitations, no recommendation can be made regarding whether the RAI is a sensitive risk stratification tool within the surgical spine population as further validation studies are needed.

Similar to the HFRS, the RAI differs from traditional frailty tools. Using predefined criteria, the RAI assesses multiple frailty domains to create a weighted score representative of the patient's frailty state. The content of the RAI is more sensitive for assessing frailty as it is adapted from the previously validated Minimum Data Set (MDS) Mortality Risk Index-Revised (MMRI-R) [86]. Additionally, the RAI uses a defined set of items and a standardized scoring system to eliminate potential inter-rater bias or error amongst users. As the RAI has only been recently investigated in the surgical spine population, many of its clinimetric properties remain unknown. Further investigation is ultimately warranted to determine its validity and reliability in the surgical spine population. Lastly, given that the RAI is validated as a perioperative risk stratification tool, its role as a frailty trajectory tool is limited despite a modifiable construct.

Lastly, the Comprehensive Geriatric Assessment (CGA) tool assesses frailty based on a multidisciplinary approach for optimizing, coordinating and integrating geriatric care. The CGA evaluates the frailty domains of function, cognition, mood and mental health, nutrition, comorbidity status, polypharmacy, and social health using validated subscales. The CGA is validated as both a risk stratification tool and an instrument for guiding preoperative optimization of frail patients [88]. Within the spine population, Chang *et al* recently validated the CGA as a risk stratification tool for predicting postoperative AEs in elderly patients after lumbar spine surgery for degenerative disease [68]. Despite a relatively small population, the study had a robust study methodology with strict inclusion criteria to assess the predictive validity of the CGA. The components of the CGA also had defined values for each frailty component evaluated from either the original articles or subsequent validation study [68]. However, the criterion to define frailty was chosen arbitrarily without formal sensitivity or construct validation. The sample population was also relatively heterogeneous, raising concern for type II error and a lack of statistical power. Despite these limitations, the CGA is a valid and sensitive risk stratification tool for predicting postoperative AEs within the degenerative lumbar spine population.

As a frailty tool, the CGA is highly sensitive for assessing and quantify frailty. Given its construct, the CGA differs from previously discussed frailty tools that contain non-validated or arbitrary content to evaluate and define frailty. The CGA may be a valuable screening tool to help guide perioperative optimization of frail patients undergoing surgical intervention. CGA targeted optimization has improved functional outcomes and reduced mortality in the community and hospital-dwelling frail population [89, 90]. Furthermore, the CGA may be sensitive to capturing the relationship between spinal disease and frailty as it contains components susceptible to improvement following spine surgery. Despite these strengths, the CGA lacks standardized content, delivery, and interpretation, potentially limiting cross-population validity and reliability [91]. Further studies are warranted to establish its clinimetric properties and determine the validity, reliability, and responsiveness in the surgical spine population.

Frailty Trajectory Tools

The FRAIL (fatigue, resistance, ambulation, illness, and weight loss) Scale is a validated five-item frailty tool developed by the International Academy on Nutrition and Ageing Task Force [92, 93]. The conceptual foundations are heavily rooted in the phenotypic frailty model as four of the items (fatigue, resistance, ambulation, and weight loss) are derived from it. Validated cutoff values are used to stratify scores into robust, pre-frail, and frail patients. Since its conceptualization, the FRAIL Scale has proven to be a reliable and valid frailty tool for identifying elderly patients at an increased risk of adverse health outcomes [94]. Based on our review, the FRAIL Scale predicted a lower likelihood of postoperative functional return and a higher risk of postoperative delirium in patients undergoing elective spine surgery for degenerative disease. These findings are important considering spine surgery aims to improve functional outcomes back to baseline or surpass them. Failure to return to, or surpass baseline function is concerning as spine surgery is associated with significant risks. Given this, the FRAIL Scale may be a valuable tool in the decision-making process to identify patients requiring timely surgical intervention or preoperative optimization.

The Fried Phenotype is a five-item frailty tool developed by Fried *et al* [6]. Constructed and validated by Fried *et al*, the tool assesses five items including weight loss, weakness (strength), exhaustion (endurance), slowness (gait speed), and low physical activity (kilocalories) [6]. Validated cut off-values are used to stratify scores into robust, pre-frail, and frail patients [6]. Since its initial validation, the Fried Phenotype is recognized as a reliable, valid, diagnostic, and sensitive assessment tool for identifying frail patients at an increased risk of early disability, morbidity, and mortality [70, 95]. Interestingly, our review identified that the Fried Phenotype did not predict postoperative AEs within the thoracolumbar population undergoing elective spine surgery for degenerative or deformity spine conditions. This may have been due to several factors. Firstly, the cohort size of the validation population was relatively small, therefore increasing the risk of potential bias' and reducing the statistical power of the risk estimates. The relationship between the Fried Phenotype and postoperative AEs may have also been confounded by the Timed Up and Go (TUG) test. As a test of physical impairment, the TUG inherently captures phenotypic elements of frailty, therefore confounding the relationship between the Fried phenotype and postoperative AEs.

Of the frailty tools identified in our review, the FRAIL Scale and Fried Phenotype are the most sensitive for capturing the impact of spinal pathology and surgical intervention on frailty trajectory. The underpinning phenotypic construct overlaps with those clinical features of disability and weakness associated with spinal disease [13]. Given this, if spine surgery aims to improve functional outcomes, the modifiable construct of the Fried Phenotype and FRAIL Scale are sensitive to capturing changes in frailty trajectory. Although this relationship has not been studied in spine literature, both the Fried Phenotype and FRAIL Scale have been observed as responsive tools for capturing changes in frailty trajectory [72].

The FRAIL Scale and Fried Phenotype are also potentially useful assessment tools for screening and tracking responsiveness to frailty targeted preoperative rehabilitation [96]. Over the past several years, prehabilitation has gained popularity in the literature as a means of preoperatively optimizing patients' health to improve postoperative outcomes [97]. Rudimentary in their composition, mode of administration and outcome measure, preliminary evidence suggests these programs may reduce the risk of postoperative AEs [97]. Although no program has been described in the spine literature, tailored preoperative physiotherapy improves and maintains postoperative functional outcomes in patients with degenerative lumbar spine disorders [98]. Considering the relationship between degenerative lumbar disease and frailty, preoperative optimization of frailty may be critical in improving outcomes following spine surgery.

Though, developing a frailty-targeted prehabilitation program is challenging due to the uniqueness of health-deficits to each patient. The CGA may overcome this challenge as it is a powerful screening tool for identifying health deficits susceptible to optimization and tailoring multidisciplinary interventions. Initial studies investigating CGA and frailty targeted prehabilitation with nutrition and exercise interventions have found mild phenotypic and functional improvements in hospitalized and community-dwelling geriatric patients [88, 90, 99, 100]. However, it is unknown whether these improvements significantly reduce adverse outcomes, especially in the surgical context. Studies are ultimately needed to determine the most effective method of identifying susceptible health-deficits and clarifying the composition, mode of administration, and clinical efficacy of prehabilitation programs.

Future Directions

Since the assessment of frailty in the surgical spine setting may be important in the clinical decision-making process, we must be confident that the assessment tools used are sensitive, reliable, and validated. The evaluation of clinimetric properties is also essential as it clarifies what constitutes a good clinical measure. Most of the frailty tools identified in this review lacked prospective external validation and formal evaluation of clinimetric properties. Future studies should focus on the prospective validation of these frailty tools to reaffirm their validity and applicability as reliable risk stratification tools. Prospective studies are also needed to determine the validity of other well-established frailty tools for predicting postoperative AEs. Measures such as the Clinical Frailty Scale (CFS) or the Edmonton Frail Scale (EFS) are validated risk stratification tools for predicting postoperative AEs among geriatric patients undergoing major elective surgery [101, 102].

Further studies are also needed to investigate the relationship between spine disease, surgical intervention, and frailty. Given that symptomatic spine disease is a risk factor for frailty, timely spine surgery may be an effective intervention to reverse frailty and reduce adverse health outcomes. Inversely, if spinal disease incurs a greater risk of frailty, the likelihood of adverse health outcomes is inherently increased for patients waiting for spine surgery. Validating this relationship with phenotypic tools may better identify patients requiring timely surgery.

Unfortunately, limited evidence has investigated the concept of frailty reversibility. Consequently, it is known whether a specific threshold of reversible health deficits is required to significantly reduce the risk of adverse health outcomes. It is also unknown whether a therapeutic limit exists whereby the number of reversible frailty deficits becomes saturated and no longer imparts a reduction in the risk of long-term mortality and disability. Finally, it is unclear if the concept of frailty reversibility is validated for specific operational definitions of frailty. Future studies are needed to investigate these concerns and determine whether prehabilitation and spine surgery are effective interventions in reversing frailty and reducing adverse health outcomes in patients with spinal disease.

Strengths and Limitations

This review contains several strengths and limitations. The literature search used a broad search terminology to identify all possible studies reporting a frailty tool in the surgical spine population. The use of two independent reviewers during the literature search and study identification phases reduces the likelihood of possible biases such as selection bias, publication bias, and competing interests. The approach to tool evaluation was also structured and well defined. A validated set of qualitative appraisal criteria was used to evaluate and transparently report the clinimetric properties for each frailty tool. Lastly, the recommendations suggested were determined by panel consensus. This methodology reduces any potential biases or competing interests.

Despite these strengths, our review has several limitations. Some of the definitions utilized in this study, especially those on feasibility, applicability, and objectivity, have not necessarily been validated. To reduce bias and subjectivity, we identified previously published definitions as a guide for formulating the criteria used in this review. Use of search limitations such as "English Language" and "Full-text only" may also reduce the scope of articles we could capture. Consequently, this review may under-report the frailty tools currently studied within the surgical spine literature.

Another limitation was the inability to include frailty tools reported in patient populations with neurological features similar to the surgical spine population. Inclusion of such articles would have allowed us to appraise a greater range of frailty tools. However, the studies identified during the initial design of this review defined populations by underlying diagnosis, not clinical features. This resulted in study populations with heterogeneous neurological features that are not comparable or relevant to those clinical features within the surgical spine population. Given this poor cross-population comparability, the methodology of this review was re-drafted to exclude these studies as it would have reduced the strength of our analysis and recommendations.

Conclusion

Frailty measures within surgical spine practice are important tools in the surgical-decision making process regarding risk stratification, timely surgical intervention, and prehabilitation. Fourteen frailty tools were identified across the surgical spine literature, with most validated as risk stratification tools for predicting postoperative AEs. Although most measures were feasible and objective, many lacked assessment of multiple clinimetric properties. Instruments derived from the cumulative deficit and weighted frailty models containing non-modifiable constructs are the most appropriate risk stratification tools. Phenotypic frailty tools are the most sensitive for capturing the relationship between spinal disease, spine surgery, and prehabilitation on frailty trajectory. The CGA is an effective screening instrument for identifying health-deficits susceptible to improvement through tailored preoperative optimization programs. Studies are needed to investigate whether spine surgery or prehabilitation are effective interventions in reversing frailty, improving longitudinal health outcomes and reducing the risk of postoperative AEs in patients with spine disease. Finally, studies are needed to formally evaluate the clinimetric properties of the frailty tools within the surgical spine population.

Declarations

1. *Ethics Approval and Consent to Participation*

Not Applicable.

2. *Consent for Publication*

Not Applicable.

3. *Availability of Data and Materials*

All relevant data extracted from the studies included within the review can be found in *Appendix-2*, MoskvenSupplementalData2.docx.

4. *Competing Interests*

The authors declare that they have no competing interests.

5. *Funding*

The authors declare that no funding was received during the design, collection, analysis and interpretation of data and writing of the manuscript.

6. *Author's Contributions*

EM was involved in the conception and design; acquisition, analysis, and interpretation of data; and drafting of the manuscript. R.C-M was involved in the conception and design; acquisition, analysis, and interpretation of data; and drafting of the manuscript. AMF was involved in the conception and design; drafting of the manuscript; and critical revision of the manuscript for important intellectual content. JTS was involved in the conception and design; supervision; and critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript for submission.

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References

1. Partridge JS, Harari D, Dhesi JK. Frailty in the older surgical patient: a review. Age Ageing. 2012;41(2):142-7.
2. Lin HS, Watts JN, Peel NM, Hubbard RE. Frailty and post-operative outcomes in older surgical patients: a systematic review. BMC Geriatr. 2016;16(1):157.
3. De Saint-Hubert M, Schoevaerdts D, Cornette P, D'Hoore W, Boland B, Swine C. Predicting functional adverse outcomes in hospitalized older patients: A systematic review of screening tools. J Nutr Health Aging. 2010;14(5):394-9.
4. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a Predictor of Surgical Outcomes in Older Patients. Journal of the American College of Surgeons. 2010;210(6):901-8.
5. Hubbard RE, Peel NM, Samanta M, Gray LC, Mitnitski A, Rockwood K. Frailty status at admission to hospital predicts multiple adverse outcomes. Age Ageing. 2017;46(5):801-6.
6. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in Older Adults: Evidence for a Phenotype. Journal of Gerontology: MEDICAL SCIENCES. 2001;563(3):M146–M57.
7. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173(5):489-95.
8. Moskven E, Bourassa-Moreau E, Charest-Morin R, Flexman A, Street J. The impact of frailty and sarcopenia on postoperative outcomes in adult spine surgery. A systematic review of the literature. Spine J. 2018;18(12):2354-69.
9. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. ScientificWorldJournal. 2001;1:323-36.
10. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31.
11. Jadczak AD, Makwana N, Luscombe-Marsh N, Visvanathan R, Schultz TJ. Effectiveness of exercise interventions on physical function in community-dwelling frail older people: an umbrella review of systematic reviews. JBI Database of Systematic Reviews and Implementation Reports. 2018;16(3).
12. de Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millan-Calenti JC. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. BMC Geriatr. 2015;15:154.
13. Kim H-J, Park S, Park S-H, Lee JH, Chang B-S, Lee C-K, et al. The prevalence and impact of frailty in patients with symptomatic lumbar spinal stenosis. European Spine Journal. 2019;28(1):46-54.
14. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535.
15. Booth A, Clarke M, Ghersi D, Moher D, Petticrew M, Stewart L. Establishing a minimum dataset for prospective registration of systematic reviews: an international consultation. PLoS One. 2011;6(11):e27319.
16. McDonald VS, Thompson KA, Lewis PR, Sise CB, Sise MJ, Shackford SR. Frailty in trauma: A systematic review of the surgical literature for clinical assessment tools. J Trauma Acute Care Surg. 2016;80(5):824-34.

17. Mokkink LB, Prinsen CAC, Bouter LM, Vet HCWd, Terwee CB. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) and how to select an outcome measurement instrument. Braz J Phys Ther. 2016;20(2):105-13.
18. de Vries NM, Staal JB, van Ravensberg CD, Hobbelen JS, Olde Rikkert MG, Nijhuis-van der Sanden MW. Outcome instruments to measure frailty: a systematic review. Ageing Res Rev. 2011;10(1):104-14.
19. Terwee CB, Bot SDM, de Boer MR, van der Windt DAWM, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. Journal of Clinical Epidemiology. 2007;60(1):34-42.
20. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane Handbook for Systematic Reviews of Interventions. 2nd ed. Chichester (UK): John Wiley & Sons; 2019.
21. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses 2019 [Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
22. Group. OLoEW. The Oxford Levels of Evidence 2: Oxford Centre for Evidence-Based Medicine; [Available from: https://www.cebm.net/index.aspx?o=5653.
23. Flexman AM, Charest-Morin R, Stobart L, Street J, Ryerson CJ. Frailty and postoperative outcomes in patients undergoing surgery for degenerative spine disease. Spine J. 2016;16(11):1315-23.
24. Charest-Morin R, Street J, Zhang H, Roughead T, Ailon T, Boyd M, et al. Frailty and sarcopenia do not predict adverse events in an elderly population undergoing non-complex primary elective surgery for degenerative conditions of the lumbar spine. The Spine Journal. 2018;18(2):245-54.
25. Ondeck NT, Bohl DD, Bovonratwet P, McLynn RP, Cui JJ, Shultz BN, et al. Discriminative ability of commonly used indices to predict adverse outcomes after poster lumbar fusion: a comparison of demographics, ASA, the modified Charlson Comorbidity Index, and the modified Frailty Index. The Spine Journal. 2018;18(1):44-52.
26. Xu W, Zhang XM, Ke T, Cai HR, Gao X. Modified Frailty Index and Body Mass Index as Predictors of Adverse Surgical Outcomes in Degenerative Spinal Disease. Turk Neurosurg. 2018;28(6):897-903.
27. Sun W, Lu S, Kong C, Li Z, Wang P, Zhang S. Frailty and Post-Operative Outcomes in the Older Patients Undergoing Elective Posterior Thoracolumbar Fusion Surgery. Clinical interventions in aging. 2020;15:1141-50.
28. Leven DM, Lee NJ, Kothari P, Steinberger J, Guzman J, Skovrlj B, et al. Frailty Index Is a Significant Predictor of Complications and Mortality After Surgery for Adult Spinal Deformity. Spine (Phila Pa 1976). 2016;41(23):E1394-E401.
29. Yagi M, Hosogane N, Fujita N, Okada E, Tsuji O, Nagoshi N, et al. Predictive model for major complications 2 years after corrective spine surgery for adult spinal deformity. European Spine Journal. 2019;28(1):180-7.
30. Yagi M, Michikawa T, Hosogane N, Fujita N, Okada E, Suzuki S, et al. Treatment for Frailty Does Not Improve Complication Rates in Corrective Surgery for Adult Spinal Deformity. Spine (Phila Pa 1976). 2019;44(10):723-31.
31. Yagi M, Fujita N, Okada E, Tsuji O, Nagoshi N, Tsuji T, et al. Impact of Frailty and Comorbidities on Surgical Outcomes and Complications in Adult Spinal Disorders. Spine (Phila Pa 1976). 2018;43(18):1259-67.
32. Kessler RA, De la Garza Ramos R, Purvis TE, Ahmed AK, Goodwin CR, Sciubba DM, et al. Impact of frailty on complications in patients with thoracic and thoracolumbar spinal fracture. Clinical Neurology and Neurosurgery. 2018;169:161-5.
33. Banaszek D, Inglis T, Marion TE, Charest-Morin R, Moskven E, Rivers CS, et al. The Effect of Frailty on Outcome after Traumatic Spinal Cord Injury. Journal of Neurotrauma. 2019.
34. Lakomkin N, Zuckerman SL, Stannard B, Montejo J, Sussman ES, Virojanapa J, et al. Preoperative Risk Stratification in Spine Tumor Surgery: A Comparison of the Modified Charlson Index, Frailty Index, and ASA Score. Spine. 2019;44(13).
35. Raphaële C-M, Alana MF, Shreya S, Charles GF, John TS, Michael CB, et al. Perioperative adverse events following surgery for primary bone tumors of the spine and en bloc resection for metastases. Journal of Neurosurgery: Spine SPI. 2019:1-8.
36. Bourassa-Moreau É, Versteeg A, Moskven E, Charest-Morin R, Flexman A, Ailon T, et al. Sarcopenia, but not frailty predicts early mortality and adverse events after emergent surgery for metastatic disease of the spine. The Spine Journal. 2019.
37. Alas H, Fernando H, Baker JF, Brown AE, Bortz C, Naessig S, et al. Comparative outcomes of operative relative to medical management of spondylodiscitis accounting for frailty status at presentation. Journal of Clinical Neuroscience. 2020;75:134-8.
38. Shin JI, Kothari P, Phan K, Kim JS, Leven D, Lee NJ, et al. Frailty Index as a Predictor of Adverse Postoperative Outcomes in Patients Undergoing Cervical Spinal Fusion. Spine (Phila Pa 1976). 2017;42(5):304-10.
39. Phan K, Kim JS, Lee NJ, Somani S, Di Capua J, Kothari P, et al. Frailty is associated with morbidity in adults undergoing elective anterior lumbar interbody fusion (ALIF) surgery. The Spine Journal. 2017;17(4):538-44.
40. Rushna A, Jason MS, David RN, Heath JA, Ilan R. Use of the modified frailty index to predict 30-day morbidity and mortality from spine surgery. Journal of Neurosurgery: Spine SPI. 2016;25(4):537-41.
41. Kweh B, Lee H, Tan T, O'Donohoe T, Mathew J, Fitzgerald M, et al. Spinal Surgery in Patients Aged 80 Years and Older: Risk Stratification Using the Modified Frailty Index. Global Spine Journal. 2020:2192568220914877.
42. Kweh BTS, Lee HQ, Tan T, Tew KS, Leong R, Fitzgerald M, et al. Risk Stratification of Elderly Patients Undergoing Spinal Surgery Using the Modified Frailty Index. Global Spine Journal. 2021:2192568221999650.
43. Azizkhanian I, Rothbaum M, Alcantara R, Ballinger Z, Cho E, Dore S, et al. Demographics and Outcomes of Interhospital Neurosurgical Transfer Patients Undergoing Spine Surgery. World Neurosurgery. 2020;144:e221-e6.
44. Kim J-Y, Park IS, Kang D-H, Lee Y-S, Kim K-T, Hong SJ. Prediction of Risk Factors after Spine Surgery in Patients Aged >75 Years Using the Modified Frailty Index. J Korean Neurosurg Soc. 2020;63(6):827-33.

45. Rothrock RJ, Steinberger JM, Badgery H, Hecht AC, Cho SK, Caridi JM, et al. Frailty status as a predictor of 3-month cognitive and functional recovery following spinal surgery: a prospective pilot study. Spine J. 2019;19(1):104-12.
46. Susano MJ, Grasfield RH, Friese M, Rosner B, Crosby G, Bader AM, et al. Brief Preoperative Screening for Frailty and Cognitive Impairment Predicts Delirium after Spine Surgery. Anesthesiology. 2020;133(6):1184-91.
47. Komodikis G, Gannamani V, Neppala S, Li M, Merli GJ, Harrop JS. Usefulness of Timed Up and Go (TUG) Test for Prediction of Adverse Outcomes in Patients Undergoing Thoracolumbar Spine Surgery. Neurosurgery. 2020;86(3):E273-E80.
48. Miller EK, Neuman BJ, Jain A, Daniels AH, Ailon T, Sciubba DM, et al. An assessment of frailty as a tool for risk stratification in adult spinal deformity surgery. Neurosurg Focus. 2017;43(6):E3.
49. Miller EK, Vila-Casademunt A, Neuman BJ, Sciubba DM, Kebaish KM, Smith JS, et al. External validation of the adult spinal deformity (ASD) frailty index (ASD-FI). Eur Spine J. 2018;27(9):2331-8.
50. Miller EK, Lenke LG, Neuman BJ, Sciubba DM, Kebaish KM, Smith JS, et al. External Validation of the Adult Spinal Deformity (ASD) Frailty Index (ASD-FI) in the Scoli-RISK-1 Patient Database. Spine (Phila Pa 1976). 2018;43(20):1426-31.
51. Reid DBC, Daniels AH, Ailon T, Miller E, Sciubba DM, Smith JS, et al. Frailty and Health-Related Quality of Life Improvement Following Adult Spinal Deformity Surgery. World Neurosurg. 2018;112:e548-e54.
52. Pierce KE, Passias PG, Alas H, Brown AE, Bortz CA, Lafage R, et al. Does Patient Frailty Status Influence Recovery Following Spinal Fusion for Adult Spinal Deformity?: An Analysis of Patients With 3-Year Follow-up. Spine. 2020;45(7).
53. Miller EK, Ailon T, Neuman BJ, Klineberg EO, Mundis GM, Jr., Sciubba DM, et al. Assessment of a Novel Adult Cervical Deformity Frailty Index as a Component of Preoperative Risk Stratification. World Neurosurg. 2018;109:e800-e6.
54. Segreto FA, Passias PG, Brown AE, Horn SR, Bortz CA, Pierce KE, et al. The Influence of Surgical Intervention and Sagittal Alignment on Frailty in Adult Cervical Deformity. Operative Neurosurgery. 2020;18(6):583-9.
55. Pierce KE, Passias PG, Daniels AH, Lafage R, Ahmad W, Naessig S, et al. Baseline Frailty Status Influences Recovery Patterns and Outcomes Following Alignment Correction of Cervical Deformity. Neurosurgery. 2021.
56. Passias PG, Bortz CA, Segreto FA, Horn SR, Lafage R, Lafage V, et al. Development of a Modified Cervical Deformity Frailty Index: A Streamlined Clinical Tool for Preoperative Risk Stratification. Spine (Phila Pa 1976). 2019;44(3):169-76.
57. Weaver DJ, Malik AT, Jain N, Yu E, Kim J, Khan SN. The Modified 5-Item Frailty Index: A Concise and Useful Tool for Assessing the Impact of Frailty on Postoperative Morbidity Following Elective Posterior Lumbar Fusions. World Neurosurg. 2019.
58. Kang T, Park SY, Lee JS, Lee SH, Park JH, Suh SW. Predicting postoperative complications in patients undergoing lumbar spinal fusion by using the modified five-item frailty index and nutritional status. The Bone & Joint Journal. 2020;102-B(12):1717-22.
59. Zreik J, Alvi MA, Yolcu YU, Sebastian AS, Freedman BA, Bydon M. Utility of the 5-Item Modified Frailty Index for Predicting Adverse Outcomes Following Elective Anterior Cervical Discectomy and Fusion. World Neurosurgery. 2020.
60. Wilson JRF, Badhiwala JH, Moghaddamjou A, Yee A, Wilson JR, Fehlings MG. Frailty Is a Better Predictor than Age of Mortality and Perioperative Complications after Surgery for Degenerative Cervical Myelopathy: An Analysis of 41,369 Patients from the NSQIP Database 2010-2018. J Clin Med. 2020;9(11):3491.
61. Yagi M, Michikawa T, Hosogane N, Fujita N, Okada E, Suzuki S, et al. The 5-Item Modified Frailty Index Is Predictive of Severe Adverse Events in Patients Undergoing Surgery for Adult Spinal Deformity. Spine. 2019;44(18).
62. De la Garza Ramos R, Goodwin CR, Jain A, Abu-Bonsrah N, Fisher CG, Bettegowda C, et al. Development of a Metastatic Spinal Tumor Frailty Index (MSTFI) Using a Nationwide Database and Its Association with Inpatient Morbidity, Mortality, and Length of Stay After Spine Surgery. World Neurosurg. 2016;95:548-55 e4.
63. Elie M, Natalie W, Muhamed H, Shalin SP, Mitchell SF, Ali K, et al. Performance assessment of the metastatic spinal tumor frailty index using machine learning algorithms: limitations and future directions. Neurosurgical Focus FOC. 2021;50(5):E5.
64. Ahmed AK, Goodwin CR, De la Garza-Ramos R, Kim RC, Abu-Bonsrah N, Xu R, et al. Predicting Short-Term Outcome After Surgery for Primary Spinal Tumors Based on Patient Frailty. World Neurosurg. 2017;108:393-8.
65. Medvedev G, Wang C, Cyriac M, Amdur R, O'Brien J. Complications, Readmissions, and Reoperations in Posterior Cervical Fusion. Spine (Phila Pa 1976). 2016;41(19):1477-83.
66. Hannah TC, Neifert SN, Caridi JM, Martini ML, Lamb C, Rothrock RJ, et al. Utility of the Hospital Frailty Risk Score for Predicting Adverse Outcomes in Degenerative Spine Surgery Cohorts. Neurosurgery. 2020;87(6):1223-30.
67. Agarwal N, Goldschmidt E, Taylor T, Roy S, Dunn SCA, Bilderback A, et al. Impact of Frailty on Outcomes Following Spine Surgery: A Prospective Cohort Analysis of 668 Patients. Neurosurgery. 2021;88(3):552-7.
68. Chang SY, Son J, Park S-M, Chang B-S, Lee C-K, Kim H. Predictive Value of Comprehensive Geriatric Assessment on Early Postoperative Complications Following Lumbar Spinal Stenosis Surgery: A Prospective Cohort Study. Spine. 2020;45(21).
69. Shah K, Kothari M, Nene A. Role of Frailty Scoring in the Assessment of Perioperative Mortality in Surgical Management of Tuberculous Spondylodiscitis in the Elderly. Global Spine J. 2018;8(7):698-702.
70. Cooper Z, Rogers SO, Jr., Ngo L, Guess J, Schmitt E, Jones RN, et al. Comparison of Frailty Measures as Predictors of Outcomes After Orthopedic Surgery. J Am Geriatr Soc. 2016;64(12):2464-71.
71. Darvall JN, Gregorevic KJ, Story DA, Hubbard RE, Lim WK. Frailty indexes in perioperative and critical care: A systematic review. Arch Gerontol Geriatr. 2018;79:88-96.

72. Faller JW, Pereira DDN, de Souza S, Nampo FK, Orlandi FS, Matumoto S. Instruments for the detection of frailty syndrome in older adults: A systematic review. PLoS One. 2019;14(4):e0216166.
73. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. J Surg Res. 2013;183(1):104-10.
74. Panayi AC, Orkaby AR, Sakthivel D, Endo Y, Varon D, Roh D, et al. Impact of frailty on outcomes in surgical patients: A systematic review and meta-analysis. Am J Surg. 2018.
75. Passias PG, Bortz CA, Pierce KE, Segreto FA, Horn SR, Vasquez-Montes D, et al. Decreased rates of 30-day perioperative complications following ASD-corrective surgery: A modified Clavien analysis of 3300 patients from 2010 to 2014. Journal of Clinical Neuroscience. 2019;61:147-52.
76. Chimukangara M, Helm MC, Frelich MJ, Bosler ME, Rein LE, Szabo A, et al. A 5-item frailty index based on NSQIP data correlates with outcomes following paraesophageal hernia repair. Surg Endosc. 2017;31(6):2509-19.
77. Segal DN, Wilson JM, Staley C, Michael KW. The 5-Item Modified Frailty Index Is Predictive of 30-Day Postoperative Complications in Patients Undergoing Kyphoplasty Vertebral Augmentation. World Neurosurg. 2018;116:e225-e31.
78. Chen SY, Stem M, Cerullo M, Gearhart SL, Safar B, Fang SH, et al. The Effect of Frailty Index on Early Outcomes after Combined Colorectal and Liver Resections. Journal of Gastrointestinal Surgery. 2018;22(4):640-9.
79. Buettner S, Wagner D, Kim Y, Margonis GA, Makary MA, Wilson A, et al. Inclusion of Sarcopenia Outperforms the Modified Frailty Index in Predicting 1-Year Mortality among 1,326 Patients Undergoing Gastrointestinal Surgery for a Malignant Indication. Journal of the American College of Surgeons. 2016;222(4):397-407.e2.
80. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. BMC Geriatr. 2008;8(1):24.
81. Flaatten H, Clegg A. Frailty: we need valid and reliable tools in critical care. Intensive Care Medicine. 2018;44(11):1973-5.
82. Nemshah YS, Amdur R, Ashby B, Nguyen B-N, Mazhari R, Neville R, et al. A NOVEL FRAILTY BASED VASCULAR RISK SCORE FOR PREDICTION OF POOR OUTCOMES IN PERIPHERAL VASCULAR INTERVENTION. Journal of the American College of Cardiology. 2014;63(12 Supplement):A2033.
83. Patel KV, Brennan KL, Brennan ML, Jupiter DC, Shar A, Davis ML. Association of a modified frailty index with mortality after femoral neck fracture in patients aged 60 years and older. Clin Orthop Relat Res. 2014;472(3):1010-7.
84. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet. 2018;391(10132):1775-82.
85. Meyer M, Parik L, Greimel F, Renkawitz T, Grifka J, Weber M. Hospital Frailty Risk Score Outperforms Current Risk Stratification Models in Primary Total Hip and Knee Arthroplasty. The Journal of Arthroplasty. 2020.
86. Hall DE, Arya S, Schmid KK, Blaser C, Carlson MA, Bailey TL, et al. Development and Initial Validation of the Risk Analysis Index for Measuring Frailty in Surgical PopulationsRisk Analysis Index and Measuring Frailty in Surgical PopulationsRisk Analysis Index and Measuring Frailty in Surgical Populations. JAMA Surgery. 2017;152(2):175-82.
87. van der Windt DJ, Bou-Samra P, Dadashzadeh ER, Chen X, Varley PR, Tsung A. Preoperative risk analysis index for frailty predicts short-term outcomes after hepatopancreatobiliary surgery. HPB (Oxford). 2018;20(12):1181-8.
88. Eamer G, Taheri A, Chen SS, Daviduck Q, Chambers T, Shi X, et al. Comprehensive geriatric assessment for older people admitted to a surgical service. Cochrane Database Syst Rev. 2018;1(1):CD012485-CD.
89. Tikkanen P, Lönnroos E, Sipilä S, Nykänen I, Sulkava R, Hartikainen S. Effects of comprehensive geriatric assessment-based individually targeted interventions on mobility of pre-frail and frail community-dwelling older people. Geriatrics & Gerontology International. 2015;15(1):80-8.
90. Grigoryan KV, Javedan H, Rudolph JL. Orthogeriatric care models and outcomes in hip fracture patients: a systematic review and meta-analysis. Journal of orthopaedic trauma. 2014;28(3):e49-e55.
91. Lee H, Lee E, Jang IY. Frailty and Comprehensive Geriatric Assessment. J Korean Med Sci. 2020;35(3):e16-e.
92. van Kan GA, Rolland YM, Morley JE, Vellas B. Frailty: Toward a Clinical Definition. Journal of the American Medical Directors Association. 2008;9(2):71-2.
93. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging. 2012;16(7):601-8.
94. Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: A review. Eur J Intern Med. 2016;31:3-10.
95. Chang S-F, Lin P-L. Frail phenotype and mortality prediction: A systematic review and meta-analysis of prospective cohort studies. International Journal of Nursing Studies. 2015;52(8):1362-74.
96. Alvarez-Nebreda ML, Bentov N, Urman RD, Setia S, Huang JC, Pfeifer K, et al. Recommendations for Preoperative Management of Frailty from the Society for Perioperative Assessment and Quality Improvement (SPAQI). J Clin Anesth. 2018;47:33-42.
97. Hughes MJ, Hackney RJ, Lamb PJ, Wigmore SJ, Christopher Deans DA, Skipworth RJE. Prehabilitation Before Major Abdominal Surgery: A Systematic Review and Meta-analysis. World Journal of Surgery. 2019;43(7):1661-8.
98. Fors M, Enthoven P, Abbott A, Öberg B. Effects of pre-surgery physiotherapy on walking ability and lower extremity strength in patients with degenerative lumbar spine disorder: Secondary outcomes of the PREPARE randomised controlled trial. BMC Musculoskeletal Disorders. 2019;20(1):468.
99. Kim H, Suzuki T, Kim M, Kojima N, Ota N, Shimotoyodome A, et al. Effects of exercise and milk fat globule membrane (MFGM) supplementation on body composition, physical function, and hematological parameters in community-dwelling frail Japanese women: a randomized double blind, placebo-controlled, follow-up trial. PloS one. 2015;10(2):e0116256-e.

100. Li C-M, Chen C-Y, Li C-Y, Wang W-D, Wu S-C. The effectiveness of a comprehensive geriatric assessment intervention program for frailty in community-dwelling older people: a randomized, controlled trial. Archives of Gerontology and Geriatrics. 2010;50:S39-S42.
101. McIsaac DI, Taljaard M, Bryson GL, Beaulé PE, Gagné S, Hamilton G, et al. Frailty as a Predictor of Death or New Disability After Surgery: A Prospective Cohort Study. Annals of Surgery. 2020;271(2).
102. Han B, Li Q, Chen X. Effects of the frailty phenotype on post-operative complications in older surgical patients: a systematic review and meta-analysis. BMC Geriatr. 2019;19(1):141-.

Tables

TABLE-1 Characteristic of Studies Reporting a Frailty Tool in a Surgical Spine Population

Study	Year	Spine Study Population	Study Design	Age Criteria	Frailty Measure	Database	Follow Up Time	Cohort Size	Frailty Prevalence	Outcomes Studied
Flexman *et al* [23]	2016	Degenerative spine disease	Ambispective cohort	Age ≥ 18 years	mFI	ACS-NSQIP	30-days	53,145	4.0%	Postoperative major AEs and mortality, prolonged postoperative LOS, and adverse discharge disposition.
Charest-Morin *et al* [24]	2018	Degenerative spine disease	Ambispective cohort	Age ≥ 65 years	mFI	SAVES	Not specified	102	19.6%	Any postoperative AEs, prolonged postoperative LOS, adverse discharge disposition, and in-hospital postoperative mortality.
Ondeck *et al* [25]	2018	Degenerative spine disease	Ambispective cohort	Not specified	mFI	ACS-NSQIP	30-days	16,496	Not reported	Postoperative major AEs, any postoperative AEs, prolonged postoperative LOS, and adverse discharge disposition.
Xu *et al* [26]	2018	Degenerative spine disease	Retrospective cohort	Age ≥ 18 years	mFI	Unicenter database	Not specified	1,970	3.0%	Postoperative major AEs, prolonged postoperative LOS, and adverse discharge disposition.
Sun *et al* [27]	2020	Degenerative spine disease	Retrospective cohort	Age ≥ 65 years	mFI	Unicenter database	Not specified	426	15.5%	Postoperative major AEs, any postoperative AEs, and adverse discharge disposition.
Leven *et al* [28]	2016	Complex adult spinal deformity	Retrospective cohort	Age ≥ 18 years	mFI	ACS-NSQIP	30-days	1001	Not reported	Postoperative major AEs and postoperative mortality.
Yagi *et al* [29]	2019	Complex adult spinal deformity	Retrospective cohort	Age ≥ 50 years	mFI	Multicenter database	2-years	170	Not reported	Postoperative major AEs.
Yagi *et al* [30]	2019	Complex adult spinal deformity	Retrospective cohort	Age ≥ 21 years	mFI	Multicenter database	2-years	240	7.0%	Postoperative major AEs including surgical, neurological, and hardware related complications.
Yagi *et al* [31]	2018	Degenerative spine disease and adult spinal deformity	Retrospective cohort	Age ≥ 50 years	mFI	Multicenter database	2-years	481	4.0%	Postoperative functional and symptomatic patient reported outcomes.
Kessler [32]	2018	Thoracolumbar trauma	Ambispective cohort	Age ≥ 18 years	mFI	ACS-NSQIP	30-days	189	18.0%	Postoperative major AEs.
Banaszek *et al* [33]	2019	Traumatic spinal cord	Ambispective cohort	Not specified	mFI	SAVES	Not specified	634	17.2%	Any postoperative

		injury								AEs, in-hospital mortality, prolonged postoperative LOS, and adverse-discharge disposition.
Lakomkin *et al*[34]	2018	Spinal tumors	Ambispective cohort	Not specified	mFI	ACS-NSQIP	30-days	2,170	Not reported	Postoperative major and minor AEs, postoperative mortality, and prolonged postoperative LOS.
Charest-Morin *et al*[35]	2019	Metastatic spinal tumors	Ambispective cohort	Not specified	mFI	SAVES	Not specified	113	Not reported	Any postoperative AEs, prolonged postoperative LOS, unplanned reoperation and in-hospital mortality.
Bourassa-Moreau *et al*[36]	2019	Metastatic spinal tumors	Ambispective cohort	Not specified	mFI	SAVES	3-months	108	14.8%	Any postoperative AEs, 1-month and 3-month postoperative mortality.
					MSTFI				43.6%[d]	
Alas *et al*[37]	2020	Spondylodiscitis	Retrospective cohort	Age ≥ 18 years	mFI	Unicenter database	1-year	116	Not reported.	Postoperative ICU admission and 1-year postoperative mortality.
Shin *et al*[38]	2017	Cervical spine fusion	Ambispective cohort	Age ≥ 18 years	mFI	ACS-NSQIP	30-days	6,965	Not reported	Postoperative major AEs, any postoperative AEs, and postoperative mortality.
Phan *et al*[39]	2017	ALIF	Ambispective cohort	Age ≥ 18 years	mFI	ACS-NSQIP	30-days	3,920	Not reported	Postoperative major AEs, postoperative mortality, prolonged postoperative LOS, and unplanned reoperation during same admission.
Rushna *et al*[40]	2016	Not specified	Ambispective cohort	Age ≥ 18 years	mFI	ACS-NSQIP	30-days	18,294	Not reported	Postoperative major AEs and any postoperative AEs.
Kweh *et al*[41]	2020	Not specified	Ambispective cohort	Age ≥ 80 years	mFI	Unicenter database	6-months	115	Not reported	Postoperative major AEs and postoperative mortality.
Kweh *et al*[42]	2021	Not specified	Ambispective cohort	Age ≥ 65 years	mFI	Unicenter database	6-months	348	27.5%	Postoperative major AEs and postoperative mortality.
Azizkhanian *et al*[43]	2020	Not specified	Retrospective cohort	Age ≥ 18 years	mFI	Unicenter database	Not specified	671	Not reported	Postoperative major AEs and admitted by inter-hospital transfer (IFT).
Kim *et al*[44]	2020	Thoracolumbar instrumentation	Retrospective cohort	Age ≥ 75years	mFI	Unicentre database	6-months	138	31.9%	Postoperative major AEs and postoperative mortality.

Rothrock *et al*[45]	2019	Degenerative spine disease	Prospective cohort	Age ≥ 65 years	FRAIL Scale	Unicenter database	3-months	87	18.0%	Postoperative cognitive and functional recovery to baseline.
Susano *et al*[46]	2020	Not specified	Prospective cohort	Age ≥ 70 years	FRAIL Scale	Unicenter database	Not specified	219	24%	Postoperative delirium, any postoperative AEs, prolonged postoperative LOS, and adverse discharge disposition.
Komodikis *et al*[47]	2019	Degenerative spine disease and adult spinal deformity	Prospective cohort	Not specified	Fried Phenotype	Unicenter database	6-weeks	103	54.9%	Postoperative major AEs, prolonged postoperative LOS, adverse discharge disposition and unplanned postoperative readmission.
Miller *et al*[48]	2017	Complex adult spinal deformity	Retrospective cohort	Age ≥ 18 years	ASD-FI	ISSG	2-years	417	38.8% 20.1%[c]	Postoperative major AEs, any postoperative AEs, prolonged postoperative LOS, and unplanned postoperative reoperation.
Miller *et al*[49]	2018	Complex adult spinal deformity	Retrospective cohort	Age ≥ 18 years	ASD-FI	ESSG	2-years	266	33.8% 15.4%[c]	Postoperative major AEs, any postoperative AEs, prolonged postoperative LOS, and unplanned postoperative reoperation.
TABLE-1 Characteristic of Studies Reporting a Frailty Tool in a Surgical Spine Population Continued										
Miller *et al*[50]	2018	Complex adult spinal deformity	Retrospective cohort	Age ≥ 18 years	ASD-FI	Scoli-RISK-1	2-years	267	38.6% 22.1%[c]	Postoperative major AEs, any postoperative AEs, and prolonged postoperative LOS.
Reid *et al*[51]	2018	Complex adult spinal deformity	Retrospective cohort	Age ≥ 18 years	ASD-FI	Multicenter database	2-years	332	52.7% 6.6%[c]	Postoperative functional and symptomatic patient reported outcomes.
Pierce *et al*[52]	2019	Complex adult spinal deformity	Retrospective cohort	Not specified	ASD-FI	ISSG	3-years	191	40.8% 15.6%[c]	Postoperative functional and symptomatic patient reported outcomes.
Miller *et al*[53]	2018	Cervical adult spinal deformity	Retrospective cohort	Age ≥ 18 years	CD-FI	ISSG	2-years	61	55.7% 16.4%[c]	Postoperative major AEs, prolonged postoperative LOS, and adverse discharge disposition.
Segreto *et al*[54]	2020	Cervical adult spinal deformity	Retrospective cohort	Age ≥ 18 years	CD-FI	Multicenter database	1-year	138	Not reported	Postoperative major and

										minor AEs, postoperative clinical outcomes, and change in postoperative frailty status.
Pierce *et al*[55]	2021	Cervical adult spinal deformity	Retrospective cohort	Age ≥ 18 years	CD-FI	ISSG	1-year	106	47.2%	Postoperative functional and symptomatic patient reported outcomes.
Passias *et al*[56]	2019	Cervical adult spinal deformity	Retrospective cohort	Age ≥ 18 years	mCD-FI	Multicenter database	Not specified	121	46.3% 5.8%[c]	Postoperative mortality and postoperative functional and symptomatic patient reported outcomes.
Weaver *et al*[57]	2019	Degenerative spine disease	Ambispective cohort	Not specified	5-item mFI	ACS-NSQIP	30-days	23,516	19.1%	Postoperative major AEs, postoperative mortality, adverse discharge disposition, and postoperative readmission.
Kang *et al*[58]	2020	Degenerative spine disease	Retrospective cohort	Age ≥ 50 years	5-item mFI mFI	Unicenter database	30-days	584	24.1% Not reported	Postoperative major AEs.
Zreik *et al*[59]	2020	Degenerative spine disease	Ambispective cohort	Not specified	5-item mFI	ACS-NSQIP	30-days	23,754	15.8%	Postoperative major AEs, unplanned postoperative readmission, and adverse discharge disposition.
Wilson *et al*[60]	2020	Degenerative spine disease	Ambispective cohort	Not specified	5-item mFI mFI	ACS-NSQIP	30-days	41,369	16% 3%[c] 19% 4%[c]	Postoperative major AEs and mortality, unplanned postoperative readmission and reoperation, prolonged postoperative LOS and adverse discharge disposition.
Yagi *et al*[61]	2019	Complex adult spinal deformity	Retrospective cohort	Age ≥ 21 years	5-item mFI mFI	Multicenter database	2-years	281	12% 7%	Postoperative major AEs including surgical, neurological, and hardware related complications, and postoperative severe AEs.
De la Garza Ramos *et al*[62]	2016	Metastatic spinal tumors	Retrospective cohort	Age ≥ 18 years	MSTFI	Multicenter database	Not specified	4,583	40.1%[a] 24.7%[b] 18.0%[c]	Postoperative major AEs, postoperative mortality, and prolonged postoperative LOS.
Massaad *et al*[63]	2021	Metastatic spinal tumors	Retrospective cohort	Age ≥ 18 years	MSTFI	Unicenter database	30-days	479	23.2%[a] 33.8%[b] 36.5%[c]	Postoperative major AEs, postoperative mortality, and prolonged

										postoperative LOS.
Ahmed *et al* 64	2017	Primary spinal tumors	Retrospective cohort	Not specified	PSTFI	Multicenter database	Not specified	1,589	20.1%[a] 6.0%[b] 2.2%[c]	Postoperative major AEs
Medvedev *et al* 65	2016	Posterior cervical fusion only	Ambispective cohort	Age ≥ 18 years	FBS	ACS-NSQIP	30-days	5,627	Not reported	Postoperative major AEs, unplanned postoperative readmission, and unplanned postoperative reoperation.
Hannah *et al* 66	2020	Degenerative spine disease	Retrospective cohort	Not specified	HFRS	Unicenter database	3-months	11,754	88.3%[a] 11.3%[b] 0.14%[d]	Postoperative AEs, prolonged postoperative LOS, adverse discharge disposition, postoperative ICU stay, and postoperative unplanned readmission.
Agarwal *et al* 67	2021	Not specified	Prospective cohort	Age ≥ 18 years	RAI	Unicenter database	1-year	668	8.5%	Postoperative mortality, readmission, admission to ICU, and prolonged postoperative LOS.
Chang *et al* 68	2020	Degenerative spine disease	Prospective cohort	Age ≥ 65 years	CGA	Unicenter database	30-days	261	9.6%	Postoperative major and minor AEs.
					mFI				14.2%	
					5-item mFI				32.6%	
Shah *et al* 69	2018	Vertebral tuberculosis	Retrospective case-series	Age ≥ 70 years	MFS	Unicenter database	30-days	26	Not reported	Postoperative mortality, prolonged postoperative LOS, and prolonged postoperative ICU stay.

a, mildly frail; b, moderately frail; c, severely frail; d, combined moderately and severely frail populations.

Abbreviations: adverse events (AEs); length of stay (LOS); modified Frailty Index (mFI); metastatic spinal tumour frailty index (MSTFI); adult spinal deformity frailty index (ASD-FI); cervical deformity frailty index (CD-FI); modified cervical deformity frailty index (mCD-FI); 5-item modified frailty index (5-item mFI); primary spinal tumour frailty index (PSTFI); frailty base score (FBS); modified frailty score (MFS); American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP); Spine Adverse Events Severity System (SAVES); Internal Spine Study Group (ISSG); European Spine Study Group (ESSG); intensive care unit (ICU); Timed Get Up and Go (TUG); Short Form – 36 (SF-36); visual analogue scale (VAS), Scoliosis Research Society – 22 (SRS-22); Oswestry Disability Index (ODI); Postoperative Quality of Recovery Scale (PQRS); Confusion Assessment Method (CAM); EuroQol – 5 Dimension (EQ-5D); Neck Disability Index (NDI); modified Japanese Orthopaedic Association (mJOA); neck disability index (NDI); numeric rating scale (NRS); Hospital Frailty Risk Score (HFRS); Risk Analysis Index (RAI); comprehensive geriatric assessment (CGA); anterior lumbar interbody fusion (ALIF).

TABLE-2 Frailty Tool Characteristics Reported in the Surgical Spine Literature

Frailty Tool	Ref.	Validation Author	Operational Definition	# of Items	Component Domains	Cut Off Values	Setting	Special Tools	Training	Outcome
mFI	23-44, 58, 60, 61, 68	Velanovich *et al* [73]	Accumulation of deficits - dichotomous scale. Range: 0-1	11	Comorbidity, cognition, and function.	-mFI of 0 (non-frail); mFI > 0 and < 0.21 (pre-frail); mFI > 0.21 frail [30, 31]. -mFI of 0 (non-frail) mFI > 0 and < 0.21 (pre-frail); mFI ≥ 0.21 (frail) [23, 24, 26, 27, 29, 33, 35, 36]. -mFI of 0 (non-frail); mFI > 0 and < 0.27 (pre-frail); mFI ≥ 0.27 (frail) [44, 61]. -mFI ≥ 0.27 (frail) [32, 42, 68]. -mFI of 0 (non-frail); mFI of 0.09 (pre-frail); mFI of 0.18 (frail); and mFI ≥ 0.27 (severely frail) [60]. -Continuous dose-response ratio, no cutoff values specified [25, 28, 34, 37-43, 58].	Hospital	No	No	Postoperative major AEs; postoperative mortality; prolonged postoperative LOS; adverse discharge disposition; postoperative unplanned reoperation or readmission.
ASD-FI	48-52	Miller *et al* [48]	Accumulation of deficits - dichotomous scale. Range: 0-1	40-42	Comorbidity, function,, mood and mental health, energy, strength, nutrition and weight, falls risk, social support, and general health.	ASD-FI of 0 (non-frail); ASD-FI of 0.3-0.5 (frail); ASD-FI > 0.5 (severely frail) [48-52].	Hospital	No	No	Postoperative major AEs; postoperative mortality; postoperative functional and symptomatic outcomes.
5-Item mFI	57-61	Chimukangar *et al* [76]	Accumulation of deficits - dichotomous scale. Range: 0-5	5	Comorbidity and function.	-5-item mFI of 0 (non-frail); 5-item mFI of 1 (pre-frail); 5-item mFI ≥ 2 (frail) [57-59, 61, 68]. -5-item mFI of 0 (non-frail); 5-item mFI of 1 (pre-frail); 5-item mFI of 2 (frail) and 5-item mFI ≥ 3 (severely frail) [60].	Hospital	No	No	Postoperative major AEs; postoperative mortality; prolonged postoperative LOS; adverse discharge disposition; unplanned postoperative readmission or reoperation.
MSTFI	36, 62, 63	De la Garza Ramos *et al* [62]	Accumulation of deficits - dichotomous scale. Range:0-9	9	Comorbidity, surgical approach, laboratory, and nutrition.	-MSTFI of 0 (non-frail); MSTFI of 1 (mild frailty); MSTFI of 2 (moderate frailty); MSTFI ≥ 3 (severely frail) [62, 63].	Hospital	No	No	Postoperative major AEs; postoperative prolonged LOS.

						- Continuous dose-response ratio, no cutoff values specified [36].				
PSTFI	64	Ahmed *et al*[64]	Accumulation of deficits - dichotomous scale. Range:0-9	9	Comorbidity, radiographic features, laboratory, and nutrition.	PSTFI of 0 (non-frail); PSTFI of 1 (mild frailty); PSTFI of 2 (moderate frailty); PSTFI ≥ 3 (severely frail) [64].	Hospital	Yes	No	Postoperative major AEs.
CD-FI	53-55	Miller *et al*[53]	Accumulation of deficits - dichotomous scale. Range: 0-1	40-42	Comorbidity, function, mood and mental health, energy, strength, nutrition and weight, cognition, falls risk, social support, and general health.	-CD-FI of 0 (non-frail); CD-FI of 0.2-0.4 (frail); CD-FI > 0.4 (severely frail) [53, 54]. -CD-FI < 0.3 (non-frail) and CD-FI > 0.3 (frail) [55].	Hospital	No	No	Postoperative major AEs; postoperative mortality; postoperative symptomatic and function outcome; postoperative frailty trajectory.
mCD-FI	56	Passias *et al*[56]	Accumulation of deficits - dichotomous scale. Range: 0-1	15	Comorbidity, function, mental health and mood, energy, strength, nutrition and weight, and falls risk.	mCD-FI of 0 (non-frail); mCD-FI of 0.3-0.5 (frail); mCD-FI > 0.5 (severely frail) [56].	Hospital	No	No	Postoperative mortality; prolonged postoperative LOS.
FBS	65	Medvedev *et al*[65]	Accumulation of deficits - dichotomous scale. Range: 0-20	20	Comorbidity, nutrition and weight, function, cognition, laboratory, medication, and clinical features.	Continuous dose-response ratio, no cutoff values specified [65].	Hospital	No	No	Postoperative major AEs; postoperative unplanned readmission or reoperation.
MFS	69	Shah *et al*[69]	Accumulation of deficits - dichotomous scale. Range: 0-19	19	Comorbidity, cognition, mood and mental health, falls risk, and function.	Continuous dose-response ratio, no cutoff values specified [69].	Hospital	No	No	Postoperative mortality.
FRAIL Scale	45, 46	van Kan *et al*[92, 93]	Phenotype - ordinal scale. Range: 0-5	5	Energy (fatigue), strength (resistance), function (ambulation), comorbidity (illness), and weight and nutrition (weight loss).	Score 0 (robust); score 1-2 (pre-frail); score 3-5 (frail) [45].	Hospital and community	No	No	Postoperative delirium; postoperative cognitive and functional recovery.
Fried Frailty Phenotype	47	Fried *et al*[6]	Phenotype - ordinal scale. Range: 0-5	5	Weight loss, weakness (strength), exhaustion (endurance), slowness (gait speed), and low physical activity (kilocalories).	Score 0 (robust); score 1-2 (pre-frail); score 3-5 (frail) [47].	Hospital and community	Yes	Yes	Postoperative major AEs; prolonged postoperative LOS; adverse discharge disposition; unplanned reoperation.
HFRS	66	Gilbert *et al*[84]	Weighted instrument - dichotomous scale with weighted score.	109	Comorbidity, falls risk, cognition, mood and mental health, function, laboratory findings, nutrition and weight, and social support.	HFRS of 0-5 (low risk frailty); HFRS of 5-15 (moderate risk frailty); and HFRS of > 15 (high risk frailty) [66].	Hospital and community	Yes	Yes	Postoperative major AEs; unplanned readmission; prolonged postoperative LOS; and average direct costs.
RAI	67	Hall *et al*[86]	Weighted instrument - ordinal scale with weighted score.	14	Comorbidity, function, social support, nutrition and weight, and cognition.	RAI of 0-29 (robust/non-frail); RAI of 30-36 (pre-frail); RAI of ≥ 37 (frail) [67].	Hospital and community	No	No	Postoperative readmission, mortality, and prolonged postoperative LOS.

			Range: 0-81							
CGA	68	Chang *et al* [68]	CGA instrument - ordinal scale. Range: 0-6	54	Function, comorbidity, cognition, mood and mental health, nutrition, and polypharmacy.	CGA score of ≥ 3 (frail) [68].	Hospital	No	No	Postoperative minor and major AEs.

Abbreviations: adverse-events (AEs); modified Frailty Index (mFI); metastatic spinal tumour frailty index (MSTFI); adult spinal deformity frailty index (ASD-FI); cervical deformity frailty index (CD-FI); modified cervical deformity frailty index (mCD-FI); 5-item modified frailty index (5-item mFI); primary spinal tumour frailty index (PSTFI); frailty based score (FBS); modified frailty score (MFS); length of stay (LOS); Hospital Frailty Risk Score (HFRS); Risk Analysis Index (RAI); comprehensive geriatric assessment (CGA).

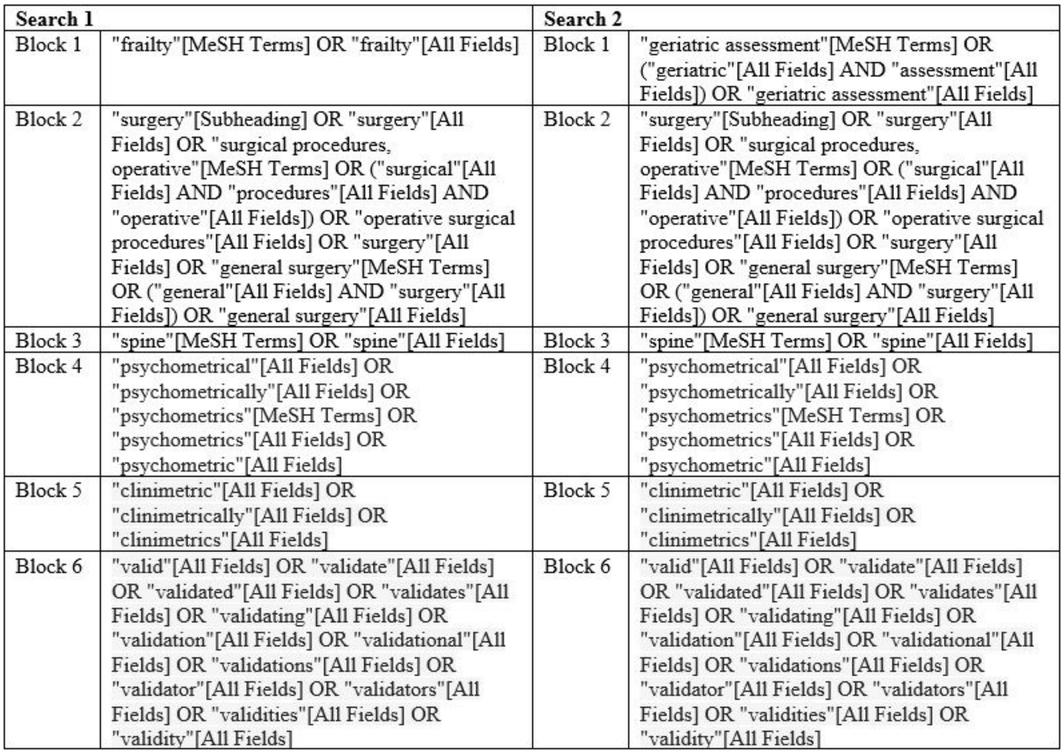
TABLE-3 Clinimetric Properties and Applicability of Frailty Tools in the Surgical Spine Literature

Frailty Tool	Reliability	Validity				Responsiveness	Feasible	Objective	Clinical Applicability	Sensitive Population(s)
		Construct Validity	Content Validity	Predictive Validity	Concurrent Validity					
mFI	+	0	?	+[a,b]	+[a,b]	?	Yes	Yes	Risk stratification	Degenerative spine disease Adult spinal deformity
ASD-FI	0	0	+	+[b]	0	0	No	No	Risk stratification or frailty trajectory	Adult spinal deformity
CD-FI	0	0	+	?	0	?	No	No	Risk stratification or frailty trajectory	Cannot determine
mCD-FI	0	?	?	?	0	0	Yes	Yes	Risk stratification	Cannot determine
5-Item mFI	+	?	?	+[a,b]	+[a,b]	0	Yes	Yes	Risk stratification	Degenerative spine disease Adult spinal deformity
MSTFI	0	0	-	?	0	0	Yes	Yes	Risk stratification	Cannot determine
PSTFI	0	0	-	?	0	0	No	Yes	Risk stratification	Cannot determine
FBS	0	0	?	+	0	0	Yes	Yes	Risk stratification	Cannot determine
MFS	0	0	0	?	0	0	Yes	Yes	Not applicable	Cannot determine
FRAIL Scale	0	0	+	+[a]	0	0	Yes	No	Risk stratification or frailty trajectory	Degenerative spine disease
Fried Phenotype	0	?	+	?	0	0	No	Yes	Risk stratification or frailty trajectory	Cannot determine
HFRS	0	0	?	+[a]	0	0	No	Yes	Risk stratification	Degenerative spine disease
RAI	0	0	?	?	0	0	Yes	Yes	Risk stratification	Cannot determine
CGA	0	0	+	+[a]	?	0	Yes	Yes	Risk stratification	Degenerative spine disease

+, convincing arguments or evidence that the measure has met the respective clinimetric criteria/definition; -, convincing arguments or evidence that the measure has not met the respective clinimetric criteria/definition; ?, unknown due to poor methodological quality, doubtful design, or non-convincing arguments; 0, clinimetric property not assessed or no information available; a, degenerative spine population; b, complex adult spinal deformity population.

Abbreviations: modified Frailty Index (mFI); metastatic spinal tumour frailty index (MSTFI); adult spinal deformity frailty index (ASD-FI); cervical deformity frailty index (CD-FI); modified cervical deformity frailty index (mCD-FI); 5-item modified frailty index (5-item mFI); primary spinal tumour frailty index (PSTFI); frailty base score (FBS); modified frailty scale (MFS); Hospital Frailty Risk Score (HFRS); Risk Analysis Index (RAI); Comprehensive Geriatric Assessment (CGA).

Figures



Search 1		Search 2	
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Block 2	"surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "surgery"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields]	Block 2	"surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "surgery"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields]
Block 3	"spine"[MeSH Terms] OR "spine"[All Fields]	Block 3	"spine"[MeSH Terms] OR "spine"[All Fields]
Block 4	"psychometrical"[All Fields] OR "psychometrically"[All Fields] OR "psychometrics"[MeSH Terms] OR "psychometrics"[All Fields] OR "psychometric"[All Fields]	Block 4	"psychometrical"[All Fields] OR "psychometrically"[All Fields] OR "psychometrics"[MeSH Terms] OR "psychometrics"[All Fields] OR "psychometric"[All Fields]
Block 5	"clinimetric"[All Fields] OR "clinimetrically"[All Fields] OR "clinimetrics"[All Fields]	Block 5	"clinimetric"[All Fields] OR "clinimetrically"[All Fields] OR "clinimetrics"[All Fields]
Block 6	"valid"[All Fields] OR "validate"[All Fields] OR "validated"[All Fields] OR "validates"[All Fields] OR "validating"[All Fields] OR "validation"[All Fields] OR "validational"[All Fields] OR "validations"[All Fields] OR "validator"[All Fields] OR "validators"[All Fields] OR "validities"[All Fields] OR "validity"[All Fields]	Block 6	"valid"[All Fields] OR "validate"[All Fields] OR "validated"[All Fields] OR "validates"[All Fields] OR "validating"[All Fields] OR "validation"[All Fields] OR "validational"[All Fields] OR "validations"[All Fields] OR "validator"[All Fields] OR "validators"[All Fields] OR "validities"[All Fields] OR "validity"[All Fields]

Figure 1

Example of MEDLINE PubMed Search Terminology – Blocks were combined: Block 1 AND (Block 2 OR Block 3 OR Block 4 OR Block 5 OR Block 6).

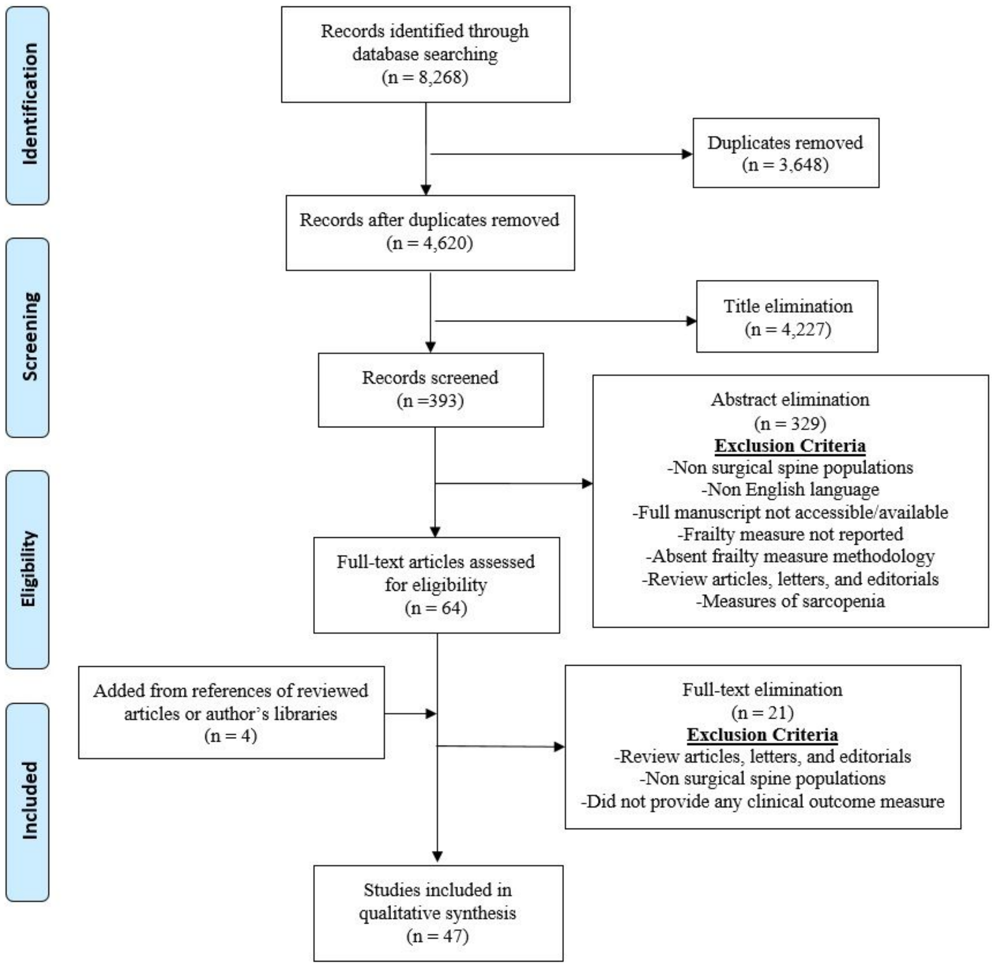

Figure 2

Flow Diagram of Included and Excluded Articles

	Selection				Comparability	Outcome		
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes occur	Adequacy of follow up of cohorts
Flexman *et al* 2016 [23]	+	+	+	+	++	+	+	+
Charest-Morin *et al* 2018 [24]	+	+	+	+	++	+	?	-
Ondeck *et al* 2018 [25]	+	+	+	+	+	+	+	+
Xu *et al* 2018 [26]	?	+	+	+	+	+	?	+
Sun *et al* 2020 [27]	+	+	+	+	++	+	?	+
Leven *et al* 2016 [28]	+	+	+	+	++	+	+	+
Yagi *et al* 2019 [29]	+	+	+	+	++	+	+	+
Yagi *et al* 2019 [30]	+	+	+	+	++	+	+	+
Yagi *et al* 2018 [31]	+	+	+	-	+	+	+	+
Kessler *et al* 2019 [32]	-	+	+	+	+	+	+	+
Banaszek *et al* 2019 [33]	+	+	+	+	++	+	?	+
Lakomkin *et al* 2018 [34]	+	+	+	+	++	+	+	+
Charest-Morin *et al* 2019 [35]	+	+	+	+	++	+	?	+
Bourassa-Moreau *et al* 2019 [36]	+	+	+	+	++	+	?	-
Alas *et al* 2020 [37]	-	+	+	+	+	+	+	-
Shin *et al* 2017 [38]	+	+	+	+	++	+	+	+
Phan *et al* 2017 [39]	+	+	+	+	++	+	+	+
Rushna *et al* 2016 [40]	+	+	+	+	+	+	+	+
Kweh *et al* 2021 [41]	+	+	+	+	++	+	+	+
Kweh *et al* 2021 [42]	+	+	+	+	++	+	+	+
Azizkhanian *et al* 2020 [43]	+	+	+	+	+	+	+	+
Kim *et al* 2020 [44]	?	+	+	+	+	+	+	?
Rothrock *et al* 2019 [45]	?	+	-	+	++	-	?	+
Susano *et al* 2020 [46]	+	+	?	-	+	-	-	-
Komodikis *et al* 2020 [47]	?	+	+	+	++	-	+	-
Miller *et al* 2017 [48]	+	+	+	+	++	+	+	+
Miller *et al* 2018 [49]	+	+	+	+	++	+	+	+
Miller *et al* 2018 [50]	?	+	+	+	++	+	+	+
Reid *et al* 2018 [51]	?	+	+	-	+	+	+	-
Pierce *et al* 2020 [52]	+	+	+	-	++	+	+	?
Miller *et al* 2018 [53]	+	+	+	+	++	+	?	+
Segreto *et al* 2020 [54]	+	+	+	+	+	+	+	+
Pierce *et al* 2021 [55]	-	+	+	-	+	+	+	?
Passias *et al* 2019 [56]	+	+	+	+	+	+	?	+
Weaver *et al* 2019 [57]	+	+	+	+	++	+	+	+
Kang *et al* 2020 [58]	+	+	+	+	++	+	+	+
Zreik *et al* 2021 [59]	+	+	+	+	++	+	+	+
Wilson *et al* 2020 [60]	+	+	+	+	++	+	+	+
Yagi *et al* 2019 [61]	+	+	+	+	++	+	+	+
De la Garza-Ramos *et al* 2016 [62]	+	+	+	+	+	+	?	+
Massaad *et al* 2021 [63]	?	+	+	+	+	+	+	+
Ahmed *et al* 2017 [64]	+	+	+	+	+	+	?	+
Medvedev *et al* 2016 [65]	+	+	+	+	++	+	+	+
Hannah *et al* 2020 [66]	+	+	+	+	++	+	+	+
Agarwal *et al* 2021 [67]	?	+	+	+	+	?	+	?
Chang *et al* 2020 [68]	?	+	+	+	++	+	+	+
Shah *et al* [69]	-	+	+	+	+	+	?	?

Figure 3

Bias Assessment of Included Studies

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- MoskvenSupplementalData1.docx
- MoskvenSupplementalData2.docx