UNIVERSITY OF TORONTO SPINE PROGRAM

Journal Club

Webinar

Frailty in Spine Disorder and Spine Surgery

September 22, 2020

6:00 PM EST

Accreditation:

This educational event is a self-approved group learning activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada

AGENDA

6:00 PM	Welocme Remarks (**Professpr Michael Fehlings & Professor Albert Yee)**
6:05 PM	**Invited Faculty Presentation** **Jamie Wilson**, University of Nebraska Medical Center *Talk: "Frailty is More Important than Age when Considering Spine Surgery for the Elederly Patient"*
6:20 PM	**Discussion**
6:30 PM	**U of T Spine Fellow Presntations** **Laura Lohkamp** - Assessment of a novel adult cervical deformity frailty index as a component of preoperative risk stratification Frailty syndrome and the use of frailty indices as a preoperative risk stratification tool in spine surgery: a review **Nandan Marathe** - The impact on frailty and sarcopenia on postoperative outcomes in adult spine surgery. A systematic review of the literature - Sarcopenia, but not frailty , predicts early mortality and adverse events after emergent surgery for metastatic disease of the spine **Ohad Einav** - Effect of frailty on Outcome after traumatic spinal cord injury **Julia Bowes** - Association between frailty status and odontoid fractures after traumatic falls: investigation of varying injury mechanisms among 70 elderly odontoid fracture patients
7:15 PM	**Discussion**
7:25-7:30 PM	Wrap up

CO-CHAIRS AND SPEAKERS

U of T SPINE PROGRAM CO-DIRECTORS

Dr. Michael Fehlings is a Professor of Neurosurgery, Co-Director of the Spine Program and Vice Chairman (Research) in the Department of Surgery at the University of Toronto. He holds the Halbert Chair in Neural Repair and Regeneration and combines an active clinical practice in complex spinal surgery at the Toronto Western Hospital with a translationally oriented research program focused on discovering novel treatments for the injured brain and spinal cord. He has authored over 950 peer-reviewed articles (h-index 94) chiefly in the area of central nervous system injury and complex spinal surgery. His work has been featured in Nature, Nature Neuroscience, Science Translational Medicine, Nature Reviews Neurology, JAMA, Lancet Neurology, and the New England Journal of Medicine. Dr. Fehlings has held a number of prominent leadership roles, including current President of the International Neurotrauma Society, the Chair of the AO Foundation Clinical Investigation and Documentation Advisory Committee, past Chair of the AOSpine International Spinal Cord Injury Knowledge Forum, past President of the Cervical Spine Research Society, and leader of several international clinical research trials. Dr. Fehlings is a Fellow of the Royal Society (Canada) and a Fellow of the Canadian Academy of Health Sciences. He has received numerous international recognitions including the Royal College Gold Medal, Olivecrona Award, Ryman Prize, Magnus Medal in Neurosurgery and the Jonas Salk Award.

Dr. Albert Yee is the Holland Bone and Joint Program Chief and the Head of the Division of Orthopaedic Surgery at Sunnybrook Health Sciences Centre, where he holds the Marvin Tile Chair in Orthopaedic Surgery. Dr. Yee is an Orthopaedic Spine Surgeon at Sunnybrook Health Sciences Centre, an Associate Scientist (Physical Sciences Platform) at Sunnybrook Research Institute and a Consultant in Surgical Oncology, Bone Metastasis Clinic, Odette Cancer Centre. He is a Full Professor at the University of Toronto in the Institute of Medical Sciences with a cross appointment in the Institute of Biomaterials and Biomedical Engineering. He is the Vice Chair of Research in the Division of Orthopaedic Surgery and Co-Director of the University of Toronto's Department of Surgery Spine Program. Dr. Yee is

the Past President of the Canadian Orthopaedic Research Society, President of the Canadian Spine Society and Co-Chair of Bone & Joint Canada. He is the Canadian Lead for the Young Investigators Initiative (YII) of Bone & Joint Canada, and the US Bone & Joint Initiative, a grant mentorship and career development program. Dr. Yee has over 100 peer reviewed publications and has received academic honours including the American British Canadian (ABC) International Travelling Fellowship (American Orthopaedic Association / Canadian Orthopaedic Association, 2013), the Charles H. Tator Surgeon-Scientist Mentoring Award (2012), and the Canadian Orthopaedic Foundation J. Edouard Samson Award (2011). Dr. Yee's laboratory focuses on translational orthopaedic research utilizing pre-clinical surgical models to evaluate novel minimally invasive vertebral metastatic therapies (e.g. Photodynamic Therapy, Radiofrequency Ablation). His work has led to first in human clinical trials and FDA approval with commercialization of new minimally invasive spine technology. He has interest in understanding mechanisms of disease in cancer invasiveness to bone with an aim towards identifying potential new promising therapeutic targets.

INVITED FACULTY

Dr. Jamie R. Wilson is a fellowship-trained complex spine surgeon, Assistant Professor of Neurosurgery and Co-Director of the Comprehensive Spine Program at the University of Nebraska Medical Center. He received a BA in physiological sciences, and his MD from St. John's College, University of Oxford in the United Kingdom. After 2 years of clinical academic training at the University of Southampton, he completed his residency in Neurosurgery at Leeds Teaching Hospitals in the North of England, achieving his Fellowship of the Royal College of Surgeons of England (board certified equivalent) in 2017. He has most recently undertaken a 2-year complex spine fellowship at the University of Toronto, Canada.

Dr. Wilson is a clinician scientist with a focus on clinical epidemiology, and the application of machine learning and statistical modelling to registry data. His work to date has focused on improving outcomes and access to care for Geriatric Spine patients, and he is passionate about the use of new technology in the pursuit of improving standards of care in Spine Surgery. He has published over 30 scientific articles,

presented at national and international conferences, won multiple academic awards and has contributed to residency and medical student training programs.

U OF T CITYWIDE SPINE FELLOWS / TRAINEES

Dr. Laura-Nanna Lohkamp completed her Neurosurgery residency at the Charite Berlin, followed by pediatric subspecialisation in Lyon, France and at Sickkids, including 6 months of pediatric ortho spine. Master's degree from International University Dresden/Harvard. Clinical focus: adult and pediatric spine surgery.

Dr. Nandan Marathe completed his Residency in Orthopedic Surgery: Seth GS Medical College and King Edward Memorial Hospital, Mumbai, India, his fellowship in Endoscopic Spine surgery: Daejeon Woori Hospital, Korea, and Indo-American Spine Alliance Fellowship: Indian Spinal Injuries Centre, New Delhi (AOSpine Centre). He is currently a clinical fellow in adult Spine Surgery at Toronto Western Hospital.

Dr. Julia Bowes completed medical school at the University of Calgary followed by Orthopaedic surgery residency at the University of Alberta. Julia is currently in her first year fellowship training at Sunnybrook hospital with a clinical focus of adult spine surgery and a research interest in medical education.

Dr. Ohad Einav completed his residency in Orthopedic surgery at Meir Kfar Saba followed by spine surgery fellowship in Hadera, Israel. He had his Master degree from Masaryk University, Brno. Ohad is currently doing his fellowship training at Sunnybrook Hosptial with focus on adult spine surgery.

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APPENDIX

Articles

Asian Spine Journal
Review Article
Asian Spine J. June 3, 2019 [Epub ahead of print] • https://doi.org/10.31616/asj.2018.0239

Frailty Syndrome and the Use of Frailty Indices as a Preoperative Risk Stratification Tool in Spine Surgery: A Review

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This comprehensive narrative literature review aims to extract studies related to frailty indices and their use in elective spine procedures, as limited studies regarding frailty exist in the spine literature. Most studies are retrospective analyses of prospectively collected databases. Evidence suggests a positive correlation between frailty level and mortality rate, postoperative complication rate, length of stay, and the possibility of discharge to a skilled nursing facility; these correlations have been illustrated across various spine procedures. The leading index is the modified frailty index, which measures 11 deficits. The development of more comprehensive frailty indices, such as the Adult Spinal Deformity Frailty Index, are promising and have high predictive value regarding postoperative complication rate in patients with spinal deformity. However, a frailty index that combines clinical, radiographic, and laboratory measures awaits development. Perhaps, the use of a frailty index in preoperative risk stratification for elective spine procedures could serve multiple purposes, including screening for high-risk patients, enhancement of operative decision making, approximation of complication rate for informed decision making, and refinement of perioperative care. Further prospective studies are warranted to determine clinically meaningful interventions in frail individuals.

Keywords: Frailty; Adverse events; Elective surgical procedure; Spine; Mortality

Introduction

Precise prediction of how patients will tolerate elective spine surgery is a significant challenge for spine surgeons. Historically, surgeons have relied on clinical experience, general assessment of overall health, and American Society of Anesthesiologists (ASA) scores to ascertain the ability of patients to tolerate surgery. Limited tools exist to risk stratify patients during preoperative planning objectively. Reportedly, the United States population continues to age, resulting in more patients undergoing surgery at increasingly advanced ages with higher medical comorbidities [1]. Eventually, the demand for a geriatric risk stratification tool will be driven by market forces as healthcare shifts from a fee-for-service to value-based compensation model. In modern healthcare systems, spine surgeons are expected to face pressure to provide systemic value-based outcomes measures for which reimbursement could be fundamentally tied [2,3].

Previously designed tools, such as the ASA Physical Sta-

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tus Classification System, have been useful in evaluating operative risk and estimating perioperative complications. Nevertheless, the ASA scale has poor inter-rater reliability [4-6] and is limited in its capability to precisely risk stratify patients with mild levels of comorbidity [7,8]. Recent years have witnessed an increased use of the concept of frailty as a predictor of patients' operative risk. Broadly, frailty is defined as an age-related syndrome characterized by declined physiological reserve across multiple organ systems. To date, several studies have reported frailty syndrome to be an independent risk factor for perioperative complications [9-12], while others have reported in specific populations that high frailty index scores are superior to the ASA in estimating mortality and complication rates [8,9,13]. Notably, frailty can be used to help surgeons quantifiably distinguish patients 'physiologic' and chronologic age.

Risk stratification using a frailty index offers a promising tool to identify patients most likely to experience complications to explicate inherent risks of surgery for health professionals, patients, and their families. While several reviews of frailty in surgical patients exist [10,11,14], to the best of our knowledge, this is the first review of frailty related to spine surgery. Hence, this study aims to provide a literature overview as it pertains to the frailty index and elective spine surgery.

Defining Frailty

Broadly, frailty is defined as an age-related syndrome characterized by reduced physiological reserve across multiple organ systems with a resultant diminished resistance to stressors [15] and a decline in the threshold for decompensation [16]. In addition, frailty could overlap with common geriatric syndromes such as sarcopenia, malnutrition, cachexia, functional disability, and multiple comorbidities [10,14]. Frailty syndrome conceptually addresses the distinction between chronological age and physiological age; severely frail patients are not necessarily elderly and not all elderly individuals are frail.

1. Measuring frailty

Two major models of defining frailty are the frailty phenotype and the deficit accumulation model, also known as the frailty index. The frailty phenotype model summarizes the multidimensionality of frailty into the following

Table 1. Comparison of frailty indices found in spine literature

mFI	ASD-FI	CCI
Cerebrovascular problems; respiratory problems; congestive heart failure; myocardial infarction; decreased peripheral pulses; arterial hypertension; cardiac problems; changes in everyday activity; clouding or delirium; history of stroke; history of diabetes mellitus	Documented by physician: >3 medical problems; body mass index (kg/m^2) <18.5 or >30.0; cancer; cardiac disease; currently on disability; depression; diabetes; hypertension; liver disease; lung disease; osteoporosis; peripheral vascular disease; pervious blood clot (deep vein thrombosis/pulmonary embolism/stroke); smoking status Patient–reported (questionnaire); bladder incontinence; bowel incontinence; deteriorating health this year; difficulty climbing 1 flight of stairs; difficulty driving a car; difficulty getting dressed; difficulty getting in/out of bed; difficulty sleeping >6 hours; difficulty walking 91.44 m; difficulty with light activity; feeling downhearted/depressed most of the time; feeling tired most of the time; feeling worn out most of the time; general health (fair/poor); inability to bathe without assistance; inability to cheer up often; inability to do normal work/schoolwork/housework; inability to lift heavy objects; inability to travel >1 hour; inability to walk without assistive device; leg weakness; loss of balance; not in excellent health; personal care dependency; restricted activity level; restricted social life	1-Point clinical conditions: myocardial infarct; congestive heart failure; peripheral vascular disease; cerebrovascular disease; dementia; chronic pulmonary disease; connective tissue disease; ulcer disease; mild liver disease; diabetes 2-Point clinical conditions: hemiplegia; moderate to severe renal disease; diabetes with end organ damage; any tumor; leukemia; lymphoma 3-Point clinical conditions: moderate to severe liver disease 6-Point clinical conditions: metastatic solid tumor; acquired immune deficiency syndrome
mFI=Σdeficits/11 total deficits	ASD-FI=Σdeficits/40 total deficits	CCI=Σpoints
Significantly frail: mFI ≥0.21 to 0.36[a]	Not frail: CD-FI <0.3; frail: CD-FI 0.3–0.5; severely frail: CD-FI >0.5 [34,36,45]	No comorbidities: CCI ≤1; minor comorbidities: CCI 2–3; severely comorbidities: CD-FI ≥4 [46]

mFI, modified frailty index; ASD-FI, Adult Spinal Deformity Frailty Index; CCI, Charlson Comorbidity Index; CD-FI, Cervical Deformity Frailty Index.
[a]Varies by study.

five measures (the Fried Frailty Criteria): unintentional weight loss; grip strength weakness; poor endurance; slow walking speed; and low physical activity; the presence of ≥3 indicates an individual is positive for the frailty phenotype. A study reported these biomarkers as meaningful, as they represent the downward physiologic spiral observed in frailty syndrome [17]. Several studies have proposed using single surrogate measures, such as grip strength or gait speed, as a marker for the frailty phenotype [18-24].

The deficit accumulation model counts the number of deficits in health across multiple organ systems to obtain a single score that is representative of the overall frailty level of patients. Although multiple frailty indices exist, those leading in the spine literature are as follows: modified frailty index (mFI); Charlson Comorbidity Index (CCI); Adult Spinal Deformity Frailty Index (ASD-FI); and Cervical Deformity Frailty Index (CD-FI) [17,25]. Table 1 compares three frailty indices found in the spine literature and lists the deficits measured in each index.

No consensus exists regarding which variables should be used to evaluate the frailty level in spine surgery. While some studies have used the medical history of patients to measure the frailty level, others have used a combination of medical, functional, and laboratory measures to evaluate a frailty score. Given the multifactorial nature of the syndrome, the general consensus is that no single biomarker, taken independently, is adequate for the frailty assessment [15]. Although both frailty index model and frailty phenotype measures have pros and cons, some have inferred that the frailty index model remains the most versatile with wide applicability for both research and clinical use, as it quantifies the concept of frailty [26,27].

2. Prevalence of frailty

The prevalence of frailty varies on the basis of the method used to measure it, the study population, and the threshold used to classify an individual as frail. A cohort study of community-dwelling elderly (age, 64–74 years) using the Fried Frailty Criteria reported the overall frailty prevalence to be 8.5% in females and 4.1% in males [28]. In the geriatric population undergoing general surgery procedures, studies have reported the frailty prevalence to be as high as 40%–50% [29,30]. In the degenerative spine disease (DSD) surgical population, using a threshold of mFI ≥0.27, the prevalence of clinically significant frailty has been reported to be approximately 4%, with frailty syndrome being 2 times as common in individuals aged >65 years [7]. Several frailty studies involving spine procedures reported the percentage of patients with, at least, mild frailty to be 48%–60% [7,8,31-35].

The Use of Frailty Indices in Non-Orthopedic Surgery

The effect of frailty on surgical outcomes has been investigated in non-orthopedic surgical populations. In addition, studies have shown the application of frailty indices to be useful in estimating postoperative mortality [36], complications [29], increased length of stay (LOS) [29], and discharge to a skilled nursing facility (SNF) [36,37]. Several studies have reported that the use of a frailty index exhibits better predictive value than ASA classification regarding 30-day all-cause postoperative mortality, 1-year all-cause mortality, and risk of nursing facility discharge [9,13,36]. Moreover, functional measures of frailty (i.e., ambulation deficits and inability to perform activities of daily living) reportedly predict short-term and mid-term mortality, as well as a multitude of in-hospital morbidities, prolonged LOS, and discharge to SNF, suggesting that preoperative ambulation deficits translate into elevated postoperative risk for pneumonia, re-intubation, prolonged urinary catheterization, and development of urinary tract infection—all of which combined could account for protracted recovery and higher mortality [38].

Frailty and Spine Surgery

Compared with non-orthopedic literature, few studies regarding frailty indices exist in the spine literature. Most of these studies regarding frailty indices are retrospective analyses of prospectively collected databases, in which a frailty index score is retrospectively evaluated using the preoperative medical history to correlate high frailty index scores with the elevated postoperative complication rate.

The evidence indicates that higher levels of frailty correlate with higher risk of mortality, postoperative complications, prolonged hospital LOS, and more probability of discharge to a rehabilitation facility in both general surgery and, precisely, spine surgical populations. The ability of a frailty index to estimate postoperative complications varies on the basis of the study population, invasiveness of the procedure, and index used to measure frailty. Table 2 summarizes pertinent studies in the spine literature, categorizing each study

Table 2. Summary table of literature pertaining to the frailty index and complication rates following elective spine surgery

Reference	Procedure type	Study size/ database	Frailty index	Follow-up period	Study outcomes	Findings	Conclusions
Ali et al. [39] (2016)	All spine surgeries in ACS-NSQIP between 2006–2010	18,294/ACS-NSQIP	mFI: significant frailty, mFI ≥0.27	30 Days	30-Day rates of wound infection, any infection, Clavien-Dindo Class IV complications, and mortality	Found a dose-respond relationship between mFI and complication rate. As mFI increased from 0 to ≥0.27: mortality rate increased 0.1% to 2.3% (p<0.001), Clavien IV complication rate increased 0.8% to 7.1% (p<0.001), wound infection rate increased 1.7% to 4.1% (p<0.001), and overall infection rate increased 8.1% to 24.3% (p<0.001).	mFI score is independent predictor of postoperative morbidity and mortality in this population. Study failed to demonstrate predictive superiority of inferiority of mFI relative to ASA classification system, but mFI score ≥0.27 had greater odds of developing Clavien-Dindo class IV complications compared to ASA.
Shin et al. [8] (2017)	ACDF	6,148/ACS-NSQIP	mFI: significant frailty, mFI ≥0.27	30 Days	30-Day rates of mortality, Clavien-Dindo grade IV complications, any complications, HAC including surgical site infection, UTI, and VTE.	As mFI increased from 0 to ≥0.27: morality rate increased 0.1% to 3.0% (p<0.001), Clavien IV complication rate increased 0.8% to 5.6% (p<0.001), HAC rate increased 1.4% to 4.1% (p=0.003), and total complication rate increased 2.0% to 9.0% (p<0.001). mFI ≥0.27 independently predicts Clavien IV complication rate (OR, 4.67; 95% CI, 2.27–9.62).	mFI score ≥0.27, age >75 yr and ASA class >3 were all found to be independent predictors of Clavien class 4 complications. Rates for all outcome variables assessed increased in a stepwise fashion with increasing mFI for both ACDF and PCF.
Shin et al. [8] (2017)	PCF	817/ACS-NSQIP	mFI: significant frailty, mFI ≥0.36	30 Days	30-Day rates of mortality, Clavien-Dindo grade IV complications, any complications, HAC including surgical site infection, UTI, and VTE.	As mFI increased from 0 to ≥0.36: morality rate increased 0.0% to 10.0% (p<0.001), Clavien IV complication rate increased 0.7% to 20.0% (p<0.001), HAC rate increased 3.1% to 7.7% (p=0.005), and total complication rate increased 4.1% to 35.0% (p<0.001). mFI ≥0.36 independently predicts Clavien IV complication rate (OR, 41.26; 95% CI, 6.62–257.15).	Age >75 yr and ASA class >3 were not found to be independent predictors of class 4 complications.
Medvedev et al. [41] (2016)	PCF	5,627/ACS-NSQIP	Frailty Based Risk Score—comprised of 21 clinical, functional, and laboratory deficits.	30 Days	30-Day rates of major and minor complications, readmission, and reoperation. Major complication defined as those that result in permanent sequelae or reoperation. Minor complications resolved without consequence.	Frailty score was a significant predictor of: 'all complications' (OR, 1.78; 95% CI, 1.61–1.96), readmission (OR, 1.40; 95% CI, 1.22–1.62), prolonged intubation (OR, 2.54; 95% CI, 2.00–3.22), and re-intubation (OR, 2.34; 95% CI, 1.82–3.02).	Frailty score was found to be an independent predictor of reoperation, readmission, intubation related complications, unplanned re-intubation, and all-cause complication rate.

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Table 2. Continued

Reference	Procedure type	Study size/ database	Frailty index	Follow-up period	Study outcomes	Findings	Conclusions
Miller et al. [42] (2018)	Cervical spine deformity surgery	61/ISSG database for adult cervical spine deformity	CD-FI—uses 40 variables found in ISSG cervical deformity database; NF, CD-FI <0.2; frail, CD-FI 0.2–0.4; SF, CD-FI >0.4	≥1 Year	Primary outcome: incidence of major complications, defined as complications that were potentially life-threatening, required reoperation, or created permanent injury. Secondary outcomes: hospital LOS, discharge disposition, and medical/surgical complication rates.	On multivariate logistic regression, odds of major complication were significantly greater for SF patients (OR, 43; 95% CI, 2.7–684) compared with NF patient. Greater frailty associated with greater odds of major complication (OR, 7.6; 95% CI, 1.5–38.4). Institutional discharge and prolonged LOS did not correlate significantly with CD-FI.	Increasing frailty was associated with increasing risk of major complications. Postoperative medical complications were more highly correlated with frailty than were surgical complications. LOS and discharge disposition not related to degree of frailty in this study.
Leven et al. [31] (2016)	ASD surgery	1,001/ACS-NSQIP	mFI: significant frailty, mFI ≥0.27	30 Days	30-Day mortality and complications including pneumonia, sepsis, DVT, PE, wound complications, deep infection, central nervous system complication, sepsis/septic shock, cardiac arrest, acute renal failure, UTI, reoperation.	As mFI increased from 0 to 0.27: mortality increased 0.3% to 10%, complication rate increased 35% to 60%, blood transfusion increased 32% to 55%, and PE/DVT increased 1.3% to 5% (all p<0.01). mFI of ≥0.36 (n=10 patients) correlated with 0% mortality and all-cause complication rate of 50%. Risk stratifying patients using mFI score of ≥0.18 was better predictor of reoperation than patient characteristics of age ≥60 yr and obesity class ≥III.	Patients with higher mFI scores had higher rates of mortality, blood transfusions, PE/DVT, and any postoperative complications (p<0.01). mFI of ≥0.27 shown to be optimal cutoff with respect to several complications, mortality, and reoperation risk.
Miller et al. [32] (2017)	ASD surgery	417/ISSG–ASD prospective patient database	ASD-FI: NF, CD-FI <0.3; frail, CD-FI 0.3–0.5; SF, CD-FI >0.5	≥2 Years	Primary outcome: incidence of major complications, defined as complications that were potentially life-threatening, required reoperation, or created permanent injury. Secondary outcomes: incidence of deep wound infection rate, wound dehiscence incidence, LOS, PJK, pseudo-arthrosis incidence, and reoperation rate.	When compared to NF reference group: frail group had significantly greater odds of any complication (p=0.02), major complication (p=0.006), and prolonged LOS (p<0.001); SF group has significantly greater odds of any complication (p=0.03), major complication (p=0.001), reoperation (p=0.02), prolonged LOS (p<0.001), deep wound infection (p=0.03), wound dehiscence (p=0.02), pseudoarthrosis (p=0.03), and PJK (p=0.02).	After controlling for complexity of procedure, frailty is independently associated with longer LOS and higher overall complication, major complication, and reoperation rates. Increasingly severe frailty is associated with increased postoperative incidence of PJK, pseudo-arthrosis, wound dehiscence, and deep wound infection.
Miller et al. [43] (2018)	ASD surgery	266/ESSG database	ASD-FI (truncated to 36 variables): NF, CD-FI <0.3; frail, CD-FI 0.3–0.5; SF, CD-FI >0.5	≥2 Years	Primary outcome: major perioperative complications, defined as complications that substantially changed expected path to recovery, were potentially life threatening, required reoperation, or caused permanent injury. Secondary outcomes: length of hospital stay, reoperation, PJK, deep wound infection, and surgical/medical complications.	Compared to NF patients, frail and SF patients had higher odds of experiencing a major complication with OR 1.8 (95% CI, 1.0–33), and OR 2.6 (95% CI, 1.3–5.5), respectively. On multivariable analysis SF compared to NF patients had higher odds of developing PJK (OR, 7.0; 95% CI, 1.4–34), wound infection (OR, 9.7; 95% CI, 2.3–41) and reoperation (OR, 3.9; 95% CI, 1.7–8.9). Compared to NF, frail and SF patients had significantly longer hospital LOS.	Measurement of frailty using the ASD-FI in the ESSG database showed that frail and SF patients, compared to non-frail patients, had significantly greater odds of developing a major complication, PJK, deep wound infection, and reoperation. Elevated frailty was associated with longer hospital stays.

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Table 2. Continued

Reference	Procedure type	Study size/ database	Frailty index	Follow-up period	Study outcomes	Findings	Conclusions
Reid et al. [34] (2018)	ASD surgery with ≥4 level instrumented fusion	332/ISSG–ASD database	ASD-FI: NF, CD-FI <0.3; frail, CD-FI 0.3–0.5; SF, CD-FI >0.5	≥2 Years	Postoperative HRQoL scores including ODI scores, SF-36 PCS scores, numeric back pain scores, and numeric leg pain scores; collected at 2 years postoperatively. Primary study outcome was if patients reached SCB for aforementioned scores.	Baseline HRQoL and pain scores were significantly worse in frail patient groups than the non-frail group (p<0.0001). At 2-year follow-up patients in all frailty categories experienced improvement in HRQoL measures. Absolute changes between baseline and postoperative ODI, PCS, and leg pain scores were significantly greater the frail group. Regarding numeric back pain scores, frail and SF patients were less likely to reach SCB than NF patients.	Despite higher preoperative risk stratification scores, increased complication rates, and worse baseline HRQoL scores: frail patients undergoing ASD surgery were more likely to reach SCB for most HRQoL measures following compared to NF Group. SF were least likely to reach SCB for most HRQoL measures.
Yagi et al. [44] (2018)	Surgery for ASD, DS, and LSCS	156 (ASD), 152 (DS), 173 (LSCS)	mFI: NF, mFI=0; pre-frail, mFI <0.21; frail, mFI >0.21 CCI: no comorbidities, CCI £1; minor comorbidities, CCI 2–3; severely comorbidities, CD-FI ≥4	≥2 Years	Primary outcome: postoperative clinical outcomes and complication rate. Secondary outcomes: sagittal alignments and incidence of PJK and failure.	Postoperative ODI scores in ASD subjects deteriorated as mFI increased. In DS and LSCS subjects, clinical outcome scores improved regardless of CCI severity. In ASD surgery, major complication rate significantly increased with increasing mFI (36% in non-frail to 81% in frail group). In DS group, complication rate tended to increase with mFI and CCI, but increase was not significant.	Postsurgical clinical outcomes improved regardless of frailty score for DS and LSCS groups but declined significantly in ASD subjects with elevated frailty scores. Complication rate in ASD surgery worsened with increases in mFI and CCI.
Ondeck et al. [33] (2018)	PLF	16,495/ACS-NSQIP	ASA; mFI; mCCI—truncated version of the CCI	30 Days	30-Day rates of any AE, severe AEs (coma, cardiac arrest, death, DVT, myocardial infarction), minor AEs (acute kidney injury, anemia requiring transfusion, pneumonia, surgical site infection, UTI, dehiscence), infectious AEs, extended hospital LOS, and discharge to higher level of care.	Both ASA and mFI outperformed the mCCI in discriminative ability across all adverse outcomes. ASA and mFI had statistically similar predictive value in 5 of 6 outcomes, but regarding LOS ASA outperformed mFI.	For PLF, the ASA and age have better discriminative abilities for perioperative adverse outcomes than the mFI and the mCCI.
Phan et al. [35] (2017)	Anterior lumbar interbody fusion	3,920/ACS-NSQIP	mFI	30 Days	Death and any postoperative complication within 30 days. Complications categorized into larger cohorts such as: death, pulmonary complications, renal complications, etc. Other outcomes measured include LOS >5 days and return to operating room.	As mFI increased from 0 to 0.27, there was significant stepwise increase in overall complication rate from 10.8% to 32.7%. Risk of any complication increases by odds ratio of 2.4 between mFI of 0 vs. 0.27. High frailty scores significant associated with greater risk of pulmonary complications but no significant association between high mFI score and UTI, VTE, LOS>5 days, return to operating room, nor mortality could be found.	High mFI scores were independently associated with all-cause complication rate and pulmonary complication rate.

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Table 2. Continued

Reference	Procedure type	Study size/ database	Frailty index	Follow-up period	Study outcomes	Findings	Conclusions
Flexman et al. [7] (2016)	DSD	52,671/ACS-NSQIP	mFI: significantly frail: mFI ≥0.27	30 Days	30-Day rates of death and major complications within 30 days (Clavien–Dindo grade ≥2), LOS, and discharge to facility.	The mFI was in independent predictor of 30-day rate of major complications (p<0.0005), infection (p=0.04), prolonged LOS (p<0.0005), discharge to higher level of care (p<0.0005), and death (p=0.05). The OR for death was 1.44 for every 0.1 increase in frailty score.	Frailty is an important predictor of clinically relevant outcomes in patients undergoing surgery for DSD. Also, the need for reoperation due to surgical site infection was strongly predicted by presence of frailty.
Charest-Morin et al. [40] (2018)	Primary elective thoracolumbar surgery for non-complex DSD	102/Spine Adverse Events Severity System ver. 2	mFI: frail, mFI ≥0.21 Sarcopenia measured by NTPA—obtained via computed tomography during preoperative assessment	Not provided	Occurrence of any perioperative AE including, but not limited to, dural tear, instrumentation failure, positioning-related complications; postoperative anemia, cardiac complications, wound infection, delirium, electrolyte abnormalities, pneumonia, neuropathic pain, UTI, and urinary retention. All AEs graded on scale of 1–6, with major events defined as grade 3 or higher. Secondary outcomes include hospital LOS, discharge to facility, and in-hospital mortality.	After controlling for invasiveness of procedure (using Spine Surgical Invasiveness Index, no relationship between NTPA and AEs (adjusted OR, 1.06; 95% CI, 0.91–1.23) nor between mFI and AEs (OR, 0.85 per 0.1 increase in mFI; 95% CI, 0.58–1.24) could be found. mFI, but not NTPA, was associated with increased risk of death (OR, 3.12 per 0.1 increase in mFI score; 95% CI, 1.21–8.03). Neither mFI nor NTPA predicted LOS or discharge to facility.	Both mFI and NTPA were not predictive of AEs, LOS, or discharge to higher level of care. mFI, but not NTPA, predictive of death. Based on relatively low sample size, lack of surgical complexity, and low prevalence of frailty in study population, study is likely underpowered to detect relationship with respect to frailty and rate of AEs.

mFI, modified frailty index; ASA, American Society of Anesthesiologists; ACDF, anterior cervical discectomy and fusion; HAC, hospital acquired conditions; UTI, urinary tract infection; VTE, venous thromboembolism; OR, odds ratio; CI, confidence interval; PCF, posterior cervical fusion; ISSG, International Spine Study Group; CD-FI, Cervical Deformity Frailty Index; NF, not frail; SF, severely frail; LOS, length of stay; ASD, adult spinal deformity; DVT, deep vein thrombosis; PE, pulmonary embolism; ASD-FI, Adult Spinal Deformity Frailty Index; PJK, proximal junctional kyphosis; ESSG, European Spine Study Group; HRQoL, health-related quality of life; ODI, Oswestry Disability Index; SF-36, 36-item Short-Form Health Survey; PCS, Physical Component Summary; SCB, substantial clinical benefit; DS, degenerative spondylolisthesis; LSCS, lumbar spinal canal stenosis; CCI, Charlson Comorbidity Index; AE, adverse event; PLF, posterior lumbar fusion; mCCI, modified Charlson Comorbidity Index; DSD, degenerative spine disease; NTPA, normalized total psoas area.

by the procedure type, and discusses the predictive capacity of the frailty index as it relates to postoperative complications associated with that specific procedure.

1. Postoperative mortality

Multiple studies have reported that increased frailty index scores correlate with postoperative mortality. From the ACS-NSQIP database, increasing mFI scores were found to be an independent predictor of 30-day mortality in the general spine surgery population [39], as well as in patients undergoing anterior cervical discectomy and fusion (ACDF) [8], posterior cervical fusion (PCF) [8], adult spinal deformity (ASD) procedures [31], and procedures for degenerative spine conditions [7]. Charest-Morin et al. [40] reported that the mFI was superior to the presence of sarcopenia in estimating mortality in 102 patients undergoing primary elective surgery for noncomplex DSD. Nevertheless, increased mFI scores did not correlate with increased 30-day mortality rates for patients undergoing anterior lumbar interbody fusion (ALIF) in one study [35].

2. Postoperative complications

Across various spine procedures, increasing frailty index scores correlated with higher rates of all-cause complications. In the ACS-NSQIP dataset, Ali et al. [39] reported a positive correlation between the mFI and the 30-day complication rate in the general spine surgical population; this correlation between the increasing frailty score and the 30-day all-cause complication rate has also been reported in patients undergoing ACDF [8], PCF [8,41], ALIF [35], and ASD surgery [31].

The preoperative stratification of patients into tiered risk categories using a frailty index score could offer a surgeon with a predictive tool for major life-threatening complications; this has been reported in the general spine surgery population [39], as well as in patients undergoing cervical spinal deformity surgery [42] and ASD surgery [32,43,44]. In these studies, individuals were assigned to tiered risk groups based on frailty index threshold values; assignment to a high-risk group was predictive of the postoperative complication rate.

Some studies reported that frailty syndrome correlated with an elevated risk of infection [7,32,39,43] and pulmonary complications [35,41]. Ali et al. [39] reported that in increasing frailty levels markedly elevated both wound infection rate and total postoperative infection rate in the general spine surgery population. Medvedev et al. [41], using a frailty-based risk score comprising of 20 items, reported that frailty index score was an independent predictor of unplanned re-intubation and elevated intubation-related complication rates. In ACS-NSQIP patients undergoing ALIF, Phan et al. [35] reported that elevated mFI correlated with a higher risk of pulmonary complications but not wound complications. These findings corroborated that of non-orthopedic frailty studies that demonstrate how frailty syndrome and deficits in preoperative mobility could translate into increased perioperative pulmonary and infection risk [38].

3. Reoperation rate

Frailty syndrome independently correlates with the reoperation rate in patients undergoing surgery for DSD [7], ASD [31,32,43], and PCF [41], while a study of patients undergoing ALIF failed to establish a marked correlation between the frailty score and the reoperation rate. In patients undergoing surgery for ASD, Leven et al. [31] reported that mFI scores of 0.09 compared with 0.18 exhibited a higher predictive value for reoperation than age >60 years and obesity class >III (body mass index >40 kg/m^2). In DSD surgery, Flexman et al. [7] reported that the need for reoperation because of surgical site infection was robustly estimated by the presence of frailty.

4. Prolonged length of stay, institutional discharge, and readmission

To date, multiple studies of non-orthopedic surgeries have demonstrated a correlation of frailty syndrome with prolonged LOS and elevated risk of institutional discharge [13,29,36-38,45]. In the spine literature, the data are mixed, with conflicting data [7,32,35,40,42,43] on the correlation between frailty syndrome and prolonged LOS or institutional discharge.

Regarding readmission, high frailty-based risk scores correlated with increased 30-day readmission rates in patients undergoing PCF [41]. In ACDF, Phan et al. [46] reported a significant and independent correlation between ASA class 4, cardiac comorbidity, and prior stroke and 30-day rate of hospital admissions; considering several of these factors also correlated with high levels of frailty, future studies investigating readmission and the frailty

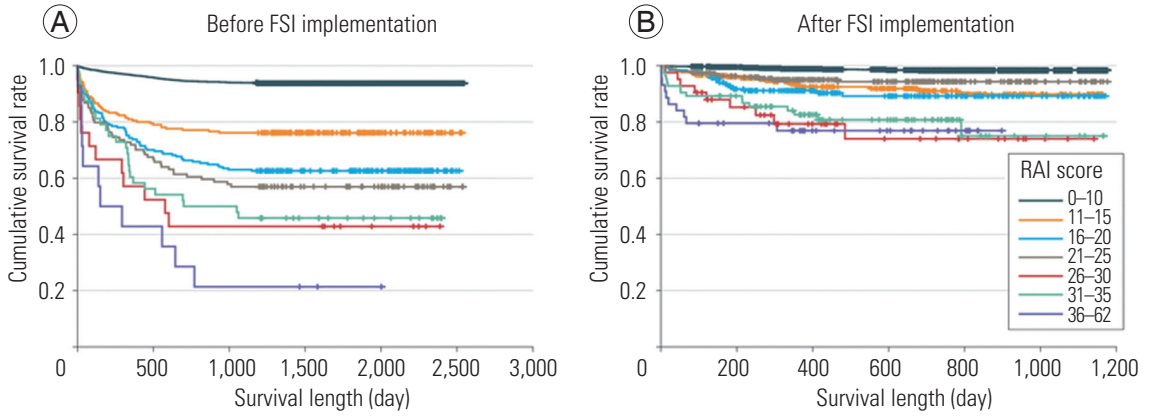
index could yield similar results.

5. Quality of life in patients with adult spinal deformity

In the ASD literature, mixed results exist regarding whether frailty is useful in estimating the odds of functional improvement. A study of patients who underwent ASD surgery reported that the proportion of moderately frail patients to reach substantial clinical benefit (SCB) at the 2-year follow-up was higher than that of non-frail patients regarding several health-related quality of life measures, including the Oswestry Disability Index (ODI), the 36-item Short-Form Health Survey Physical Component Summary score, and numeric leg pain. Reportedly, severely frail patients were least likely to reach SCB [34]. Another study of frailty in ASD surgery did not find this correlation; rather the postsurgical ODI scores declined markedly as frailty and comorbidity level increased [44].

Discussion

In the surgical community, the concept of frailty and the use of the frailty index has been gradually gaining acceptance; it is imperative that spine surgeons recognize the correlation between frailty and perioperative risk in the geriatric population. Overall, the literature indicates that



No. at risk RAI score							
0–10	4,654	4,459	4,377	3,313	1,537	142	0
11–15	210	166	160	107	40	3	0
16–20	214	150	135	105	75	1	0
21–25	114	76	66	45	33	3	0
26–30	21	11	9	9	4	0	0
31–35	48	27	24	15	9	0	0
36–62	14	6	3	2	1	0	0

No. at risk RAI score							
0–10	2,922	2,560	2,027	1,707	1,178	506	0
11–15	340	261	176	139	64	27	0
16–20	192	153	110	83	53	26	0
21–25	254	224	155	125	49	17	0
26–30	42	32	20	13	9	3	0
31–35	84	71	49	35	11	5	0
36–62	44	31	22	18	8	0	0

Fig. 1. The implementation of a FSI at a single medical center resulted in significant improvement in postoperative survival among frail patients. The Kaplan–Meier survival curves of cohorts before (A) and after (B) the FSI implementation. Individuals are stratified into cohorts based on the RAI, a 14-item frailty index. Stratification demonstrates that survival benefit was highest in individuals with the highest levels of frailty. The sample included all 9,153 patients (5,275 before FSI implementation and 3,878 after FSI implementation). Mantel-Cox log rank tests for differences in the survival distribution are as follows (p<0.001 for overall difference before and after FSI implementation). Before FSI implementation, the lowest 2 strata of frailty were different from each other and from all the other strata (all p<0.001). There was no difference between the 16 to 20 and 21 to 25 RAI strata (p=0.31), although the 16 to 20 RAI stratum was different from the highest 3 strata of frailty (all p<0.05). The 21 to 25 RAI stratum was not different from the 26 to 30 (p=0.16) or the 31 to 35 (p=0.24) RAI stratum, but it was different from the 36 to 62 RAI stratum (p=0.004). Although the lines of the highest 3 strata diverge, the differences did not reach statistical significance (all p>0.05); however, this is likely attributable to the low numbers in these RAI strata. After FSI implementation, the lowest frailty stratum was different from all others (p<0.001), but there was no difference between the next RAI strata (e.g., 11–15, 16–20, and 21–25; all p>0.20), although these 3 were different from the top 3 strata (all p<0.03). There was no difference between the top 3 strata (e.g., 26–30, 31–35, and 36–62; all p>0.50), but they were all different from each of the lowest 3 strata (all p<0.05). Hash marks indicate censored data. FSI, Frailty Screening Initiative; RAI, Risk Analysis Index. Reprinted from Hall et al. JAMA Surg 2017;152:233-40, with permission of American Medical Association [47].

increasing levels of frailty, as measured by a frailty index, independently predict the postoperative mortality rate, complication rate, reoperation rate, prolonged LOS, and readmission rate.

Perhaps, a spine-specific frailty index could be a useful objective measure that could serve multiple purposes, including preoperative screening for high-risk patients and estimation of the complication rate for use in multidisciplinary conferences, especially for high-risk ASD patients. Reportedly, preoperative screening using a frailty index, followed by a multidisciplinary review of operative decision making, markedly improves postoperative mortality in elective surgery. Hall et al. [47] reported that the institution of a Frailty Screening Initiative (FSI) in patients undergoing elective surgery led to marked mortality benefit among significantly frail patients, with 30-day, 6-month, and 1-year mortality rates in frail patients falling from 12.2% to 3.8%, 23.9% to 7.7%, and 34.5% to 11.7%, respectively. Fig. 1 presents their Kaplan–Meier survival curve before and after the FSI implementation [47]. In the spine population, elevated frailty index scores have been reported as an independent predictor of surgical complications. Preoperative screening using a frailty index might identify high-risk patients, who subsequently qualify for case discussion in a multidisciplinary conference.

In complex ASD surgeries, the implementation of risk reduction protocols, such as the Seattle Spine Team Protocol, have accounted for decreased complication rates [48,49]. Sethi et al. [49] reported that the combined use of a multidisciplinary spinal surgery conference, a patient education course, dual operating surgeons, a dedicated complex spine anesthesia team, and enhanced intraoperative monitoring of laboratory measurements and vitals, led to a 51% decline in the 30-day complication rate for complex ASD surgery patients. The use of frailty index scores and the consequent estimation of mortality and complication rate could provide clinically pertinent information to the multidisciplinary team. In addition, objective risk stratification scores, such as the Seattle Spine Score for ASD surgery, have exhibited superiority in predictive capacity regarding the 30-day complication rate compared with an expert physician using medical history alone [50]. The frailty index is a conceptually similar model for objectively measuring risk and might benefit spine surgeons in the context of screening for high-risk geriatric patients, enhancing operative decision making, and refining postoperative care.

The spine literature offers limited information on the implementation of a frailty index. To the best of our knowledge, no prospective studies exist regarding frailty and spine surgery [42]. Without prospective data, we are limited in our ability to assess the impact of a frailty diagnosis on operative decisions and perioperative care. In addition, the ACS-NSQIP database studies are limited by 30-day follow-up and might not capture the level of surgical complexity. In ASD surgery patients, controlled for the complexity of the procedure, Miller et al. [32] reported an independent correlation between frailty and complication rate. However, Charest-Morin et al. [40] failed to demonstrate this correlation in DSD surgery.

The current body of literature predominantly uses the mFI, although recent studies have adopted alternative indices such as the CCI, CD-FI, or ASD-FI [32,34,42,44]. The mFI score evaluation is convenient from medical history, but indices that account for a higher number of variables and comprise relevant laboratory or functional measures have enhanced accuracy in measuring the frailty level. No consensus exists in the spine literature regarding which particular frailty index is optimal for risk stratification. Perhaps, a frailty index that combines clinical and medical history information, comorbidities, objective laboratory values, and radiographic parameters, such as the bone density, could be the most robust, predictive, accurate, and useful for spine surgeons.

Specialty-specific indices, such as the Metastatic Spinal Tumor Frailty Index, could predict postoperative outcomes with higher accuracy because of only selecting variables with the highest correlation to poor outcomes. Perhaps, the development of a spine-specific frailty index, which involves radiographic measures and/or relevant laboratory measures, might have improved the correlation between the index score and the complication rate.

Conclusions

In conclusion, currently available frailty indices are adequate in predicting the perioperative complication risk and could be useful in the preoperative screening of geriatric spine patients and guiding surgical management.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Association Between Frailty Status and Odontoid Fractures After Traumatic Falls: Investigation of Varying Injury Mechanisms Among 70 Elderly Odontoid Fracture Patients

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Objectives: To determine significant associations between patient frailty status and odontoid fractures across common traumatic mechanisms of injuries (MOIs) in the elderly.

Design: Retrospective review.

Setting: Single, academic-affiliated hospital with full surgical services.

Patients/Participants: Patients 65 years or older with traumatic odontoid fractures were included.

Intervention: Nonoperative management (soft/hard collar, halo, traction tongs, and Minerva) and/or operative fixation.

Main Outcome Measurements: Modified frailty index (mFI), MOI, concurrent injuries, inpatient length of stay (LOS), reoperation, and mortality rates.

Results: Seventy patients were included (80.6 ± 8.5 years, 60% F, 88% European, 10% Maori/Pacific, 1.4% Asian, Charlson Comorbidity Index 5.3 ± 2.2, mFI 0.21 ± 0.15). The most common MOIs were falls (74.3%), high-speed motor vehicle accidents (MVAs) (17.1%), low-speed MVAs (5.7%), and pedestrian versus car (2.9%). Patients with traumatic falls exhibited significantly higher mFI scores (0.25) compared with low-speed MVAs (0.16), high-speed MVAs (0.08), and pedestrian versus car (0.01) ($P = 0.003$). Twenty-seven patients with odontoid fractures were frail, 33 were prefrail, and 10 were robust. Ninety-two percent of frail patients had a traumatic fall as their MOI, as opposed to 73% of prefrail and 30% of robust patients ($P < 0.001$). Prefrail and frail patients were 4.3 times more likely than robust patients to present with odontoid fractures through traumatic fall [odds ratio (OR): 4.33 (1.47–12.75), $P = 0.008$], and frailty increased likelihood of reoperation [OR: 4.2 (1.2–14.75), $P = 0.025$] and extended LOS [OR: 5.71 (1.05–10.37), $P = 0.017$]. Frail patients had the highest 30-day ($P = 0.017$) and 1-year mortality ($P < 0.001$) compared with other groups.

Conclusion: Patients with traumatic odontoid fractures from falls were significantly more frail in comparison with any other MOIs, with worse short- and long-term outcomes.

Key Words: frailty, odontoid fracture, C2, traumatic falls, ground level, elderly, geriatric

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

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INTRODUCTION

Odontoid fractures are the most common type of cervical spine fractures in the elderly.[1,2] With increasing age, the odontoid base loses bone density relatively faster than the tip or body, placing geriatric patients with already accelerated bone loss at even greater risk.[3] Ground-level falls (GLFs) are especially problematic in this patient population, as they represent the most common mechanism of injury (MOI).[1,4,5] Mortality rates for such injuries have been reported between 24% and 26%.[6,7] Although the surgical management of odontoid fractures has historically been debated in the literature (with more recent studies reporting improved survival among patients treated surgically), assessing the extent of injury and making clinical judgements for such patients remains challenging.[8–10]

Frailty is a relatively new medical concept defined as decreased physiologic reserve and vulnerability to hospitalization.[11] Its value in predicting postoperative outcomes including length of stay (LOS) and other postoperative complications for spine surgery has been consistently presented in the literature.[12–14] The modified frailty index (mFI) is a new rendition, which takes into account various comorbidities to predict patient outcomes.[15] However, little is known of frailty's association with traumatic odontoid fractures, especially with regard to traumatic falls, other MOIs, and susceptibility to multiple fractures.

The purpose of this study was to evaluate the relationship between frailty status and MOI in a population of odontoid fracture patients. In addition, outcome assessments were conducted for LOS, 90-day readmission rates, 30-day mortality, and 1-year mortality. Secondary objectives

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included comparing outcomes for surgical versus nonsurgical management and patterns of concurrent cervical and noncervical injuries. It was hypothesized that increased frailty status would correlate with higher rates of odontoid and concurrent cervical fracture through less dangerous MOIs, namely GLFs.

PATIENTS AND METHODS

A single-center, retrospective review of 70 patients with acute C2 fractures identified through computed tomography imaging between 2010 and 2016 was performed. The hospital is a tertiary referral center serving a population of 920,000 with academic links and complete surgical services available on site, although Level 1 Trauma Center status was not verified for the full duration of this analysis. Available images were obtained from a radiology trauma database and clinical records accessed in an analysis approved by the institution's Clinical Audit Support Unit. Inclusion criteria were patients 65 years of age or older who had traumatic odontoid (C2) fractures with available 30-day and 1-year postoperative data. Patients with pathological fractures secondary to tumor, infection, or metastatic disease were excluded.

Demographics

Age, sex, ethnicity, and admission details were collected from hospital electronic and paper medical records. Medical history including mental and baseline functional status before injury were recorded allowing for calculation of the Charlson Comorbidity Index (CCI) and the mFI.

Modified Frailty Index

The mFI is an 11-item score that divides the number of conditions or functional/mental deficit present by 11, giving an index value between 0 and 1 for the patient to be classified as "robust/nonfrail" with a value of 0, "prefrail" with a value greater than 0 but <0.21, or "frail" with a value of >0.21. The severity of frailty increases as the value of mFI approaches 1. The following 11 factors were used to calculate the mFI: dependent functional status, diabetes mellitus, lung problems, congestive heart failure, myocardial infarction, cardiac problems, hypertension, impaired sensorium, previous transient ischemic events (transient ischemic attack), stroke, and peripheral vascular disease.

Biochemical Markers

Serologic results on admission including lymphocyte count, creatinine, albumin, and hemoglobin levels were collated. Creatinine, albumin, and lymphocyte counts have all been linked to higher risk of malnutrition and are therefore considered to be potential predictors of poor outcome.[16]

Statistical Analysis

Statistical analysis was performed using SPSS software (v23.0; IBM, Armonk, NY, USA). Results are reported as mean ± SD. Analysis of variance with post hoc testing determined differences in the mFI among varying MOIs [falls, low-speed motor vehicle accident (MVA), high-speed MVA, and pedestrian vs. car] and outcome measures (readmission rates, 30-day and 1-year mortality). Forward stepwise logistic regression modeling determined significant predictors of odontoid fractures secondary to traumatic fall among the covariates of age, sex, mFI, CCI, biochemical markers, and concurrent injuries. Logistic regression was also used to determine predictors of poor outcomes after odontoid fractures across frailty groups. P values <0.05 were considered statistically significant.

RESULTS

Demographics

A total of 70 patients with traumatic C2 fractures were included in this study. The mean age at presentation was 80.6 ± 8.5 years, with a range of 65–97 years. Sixty percent were women (N = 42), and the majority identified as European (88.6%) in ethnicity (Table 1).

Mechanism of Injury

The most common MOI was traumatic fall (52 patients, 74.3%), followed by high-speed MVAs (12 patients, 17.1%), low-speed MVAs (4 patients, 5.7%), and pedestrian versus car (2 patients, 2.9%). Patients suffering a traumatic fall had a significantly higher mFI at presentation than high-speed MVAs (0.25 vs. 0.076, $P = 0.003$), low-speed MVAs (0.25 vs. 0.16, $P = 0.003$), and pedestrian versus car (0.25 vs. 0.095, $P = 0.003$). Patients with traumatic falls also exhibited significantly lower lymphocyte counts than other MOIs (1.3 vs. 2.9 vs. 1.5 vs. 1.9, $P = 0.033$), in addition to higher CCI (5.71 vs. 3.0 vs. 3.8) compared with pedestrian versus car and high-speed MVAs, respectively. No differences in hemoglobin ($P = 0.43$), creatinine ($P = 0.69$), or albumin ($P = 0.10$) levels were found between MOIs.

Of the patients sustaining traumatic falls, 16 (30.8%) had concurrent cervical injuries at another level, with 13 patients having concurrent C1 or C1 Jefferson fractures, 2 patients with concurrent C3 fracture, and 1 patient with multilevel fracture. Traumatic fall patients had the highest number, but a similar rate (25%), of concurrent C1 fracture compared with other MOIs such as low-speed MVAs (1 of 4 patients), but this trend did not reach statistical significance ($P = 0.230$). Low-speed and high-speed MVAs had higher rates of concurrent C3 fracture (25% and 16.7%) compared with traumatic fall patients (3.8%), but this trend did not reach statistical significance ($P = 0.212$).

In addition, 3.8% of traumatic fall patients had concurrent noncervical injuries (1 wrist, 1 brain; no pelvis, ribs, tibia/fibula, humerus, radius/ulna, and ankle). Non-GLF MOIs showed significantly higher rates of concurrent noncervical injury, including ribs (50% vs. 0%, $P = 0.001$), pelvis (50% vs. 0%, $P = 0.001$), wrist (50% vs. 1.9%, $P = 0.009$), femur (50% vs. 0%, $P = 0.001$), ankle (25% vs. 0%, $P = 0.019$), and humerus/radius/ulna (33.3% vs. 0%, $P = 0.001$).

Frailty

Twenty-seven patients presenting with odontoid fractures were categorized as "frail," 33 were categorized as

TABLE 1. Baseline Demographics, MOI, Management, and Clinical Outcomes for Odontoid Fracture Patients Stratified by the mFI

	Frailty					
	Robust (N = 10)	Prefrail (N = 33)	Frail (N = 27)	*P*	OR (CI)	*P*
Demographics						
Age (y)	76.3 ± 6.8	78.5 ± 8.7	84.9 ± 7.2	*0.003	1.55 (−1.83 to 4.9)	0.363
Sex (% female)	80%	48%	67%	0.885	0.937 (0.38 to 2.3)	0.888
Hemoglobin (g/dL)	13.1 ± 1.6	12.9 ± 1.4	12.7 ± 2.1	0.813	−25.6 (−63.7 to 12.6)	0.185
Creatinine (mg/dL)	0.79 ± 0.14	0.90 ± 0.23	1.13 ± 0.96	0.206	45.4 (−74.5 to 165.3)	0.452
Albumin (g/dL)	3.68 ± 0.54	3.70 ± 0.51	3.43 ± 0.55	0.150	−11.5 (−23.5 to 0.47)	0.059
Lymphocyte count ($\times 10^9$/L)	1.48 ± 0.68	1.64 ± 0.91	1.3 ± 0.90	0.343	−1.6 (−3.6 to 0.31)	0.097
CCI	3.4 ± 0.7	4.4 ± 1.8	5.3 ± 2.2	*<0.001	9.0 (6.4–11.6)	*<0.001
MOI						
Traumatic fall (N = 52)	30%	73%	92%	*<0.001	4.33 (1.47–12.75)	*0.008
Low-speed MVA (N = 4)	0%	9%	4%	0.932	0.88 (0.14 to 5.64)	0.897
High-speed MVA (N = 12)	60%	15%	4%	*0.001	0.20 (0.05 to 0.78)	*0.020
Pedestrian vs. car (N = 2)	10%	3%	0%	0.199	0.08 (0.01 to 7.13)	0.270
Management						
Surgical (N = 8)	10% (1)	18.2% (6)	3.7% (1)	0.229		
Other nonsurgical (N = 62)	90% (9)	81.8% (27)	96.3% (26)	0.229		
Clinical outcomes						
Inpatient LOS (d)	8.2 ± 4.4	12.7 ± 17	8.5 ± 7	0.363	5.71 (1.05 to 10.37)	*0.017
Readmission (90-day)	0.10 ± 0.3	0.21 ± 0.4	0.44 ± 0.5	*0.017	4.20 (1.20 to 14.75)	*0.025
Mortality (30-day)	0.10 ± 0.3	0.03 ± 0.2	0.3 ± 0.5	*0.014	1.97 (0.38 to 10.12)	0.417
Mortality (1-year)	0.10 ± 0.3	0.15 ± 0.4	0.7 ± 0.5	*<0.001	1.80 (0.40 to 7.94)	0.442
Concurrent cervical injury	20%	33%	30%	0.731	1.19 (0.45 to 3.16)	0.732
C1	0%	54.5%	62.5%	0.347	2.22 (0.52 to 9.41)	0.279
Jefferson	50%	9.1%	12.5%	0.634	0.80 (0.10 to 6.60)	0.836
C3	50%	27.3%	12.5%	0.683	0.37 (0.07 to 1.98)	0.244
Multilevel	0%	9.1%	12.5%	0.838	2.86 (0.16 to 52.54)	0.479
Concurrent noncervical injury						
Ribs	30%	9.1%	3.7%	*0.044	0.52 (0.11 to 2.49)	0.412
Pelvis	20%	9.1%	0%	*0.033	0.17 (0.03 to 1.08)	0.061
Wrist	20%	6.1%	0%	*0.033	0.30 (0.04 to 2.41)	0.257
Femur	0%	6.1%	0%	*0.512	0.55 (0.04 to 76.1)	0.811
Arm/humerus/radius/ulna	20%	9.1%	0%	*0.033	0.25 (0.04 to 1.53)	0.134
Brain	0%	0%	3.7%	*0.244	—	1.000

*Values reached statistical significance to $P < 0.05$.

"prefrail," and 10 were categorized as not frail or "robust." Frail patients were on average older than prefrail or robust patients (84.9 ± 7.2 vs. 78.5 ± 8.7 vs. 76.3 ± 6.8, $P = 0.003$), with a higher baseline CCI (5.3 ± 2.2 vs. 4.4 ± 1.8 vs. 3.4 ± 0.7, $P < 0.001$), but not different in terms of sex, hemoglobin, creatinine, albumin, and lymphocyte count (all $P > 0.05$) (Table 1).

There were significantly more frail patients presenting with odontoid fractures through traumatic falls than prefrail or robust patients (92% vs. 73% vs. 30%, $P < 0.001$). However, more robust patients presented through high-speed MVAs (60% vs. 15% vs. 4%, $P = 0.001$) (Table 1).

After controlling for age, sex, and baseline CCI, patients categorized as "prefrail" or "frail" were 4.3 times more likely than "robust" patients to present with odontoid fractures through traumatic fall [odds ratio (OR): 4.33 (1.47–12.75), $P = 0.008$, R2 = 0.433]. On the other hand, frailty status was inversely related to high-speed MVAs; that is, patients presenting with C2 fractures through high-speed MVAs were 0.2 times as likely to be frail [OR: 0.2 (0.05–0.78), $P = 0.020$].

Increasing frailty status was associated with higher rates of concurrent cervical fractures at the C1 level (frail: 62.5%, prefrail: 54.5%, and robust: 0%, $P = 0.347$) (Table 1).

Operative Versus Nonoperative Management

Eight patients had surgery for their injuries, and 62 patients had nonsurgical interventions. Mean fracture translation and angulation was 2.89 ± 3.2 mm and 15.6 ± 15.5 degrees, respectively. Surgical patients tended to present with greater translation (5.86 mm vs. 2.53 mm, $P = 0.238$) and angulation (24.0 vs. 14.6 degrees, $P = 0.204$) than nonsurgical patients. Controlling for frailty, greater fracture translation was found to be a modest yet significant predictor of surgical treatment [OR: 1.35 (1.01–1.79), $P = 0.043$], whereas greater angulation was not [OR: 1.04 (0.98–1.10), $P = 0.221$].

Increasing frailty was not a significant predictor of greater fracture translation or angulation (all $P > 0.05$), or did surgical and nonsurgical patients differ significantly in frailty scores (0.17 vs. 0.21, $P = 0.520$). Readmission, 30-day mortality, and 1-year mortality rates did not differ significantly between surgical and nonsurgical patients [readmission: 37.5% (3/8) vs. 27.4% (17/62); 30-day mortality: 12.5% (1/8) vs. 14.5% (9/62); and 1-year mortality: 37.5% (3/8) vs. 35.5% (22/62)] (Table 1).

Outcomes

Frail patients with odontoid fractures had higher rates of readmission (for any reason) within 90 days than other groups (0.44 ± 0.5 vs. 0.21 ± 0.4 vs. 0.10 ± 0.3, $P = 0.017$), and increasing frailty status increased the odds of readmission by 4.2 times [OR: 4.2 (1.2–14.75), $P = 0.025$]. In addition, frailty was associated with increased odds of extended inpatient LOS [OR: 5.71 (1.05–10.37), $P = 0.017$]. Frail patients also had the highest mortality rates among prefrail and robust patients at 30-day and 1-year postoperative time points (30-day: 0.3 vs. 0.03 vs. 0.10, $P = 0.017$; 1-year: 0.7 vs. 0.15 vs. 0.10, $P < 0.001$) (Table 1).

DISCUSSION

Traumatic odontoid fractures pose a serious threat to elderly patients older than 65 years, especially those patients prone to GLFs. Frailty measures appear useful instruments for assessing outcome prospects in patients with significant comorbidity.[13–15] Our study found that in a cohort of 70 patients with traumatic odontoid fractures, frailty was an independent predictor for increased odontoid fracture incidence as a result of lower energy MOIs—namely GLFs. Traumatic falls were the most common MOI overall—patients had on average a significantly higher mFI on presentation than for any other MOIs, and increasing frailty status was associated with higher rates of readmission and short- and long-term mortality.

The association of frailty with adverse clinical outcomes has been well documented in the literature. In a prospective study of 100 patients presenting to a Level 1 trauma center for GLFs (mean age of 79.5 years), Joseph et al used a frailty index with 50 preadmission variables to stratify patients into frail or nonfrail groups. Frail patients were found to be 1.8 times more likely than nonfrail patients to present with new fractures and 1.42 times more likely to be discharged to a skilled nursing facility.[17] The majority of this study's fracture type was extremity-based, however, and cervical fractures were not well represented, although they are more common than thoracolumbar. Thus, our data add important clinical relevance to a relative paucity in the literature regarding frailty and cervical spine trauma. Elderly patients who present with odontoid fractures secondary to GLFs are more likely frail than nonfrail, and this distinction is important in guiding management decisions.

Not surprisingly, the most common MOI in our cohort was traumatic GLFs, consistent with other reports noting the majority of C2 fractures in the elderly are sustained during simple falls.[1,4,18–20] This is believed to be age-related relative osteopenia of the upper cervical segments and development of a stiffer subaxial cervical spine.[18] As expected, frail patients in our study were significantly older than prefrail or nonfrail patients, and frail patients had a higher baseline CCI. We accounted for this by controlling for age, sex, and CCI as covariates in our regressions, which invariably found that patients with traumatic C2 fractures secondary to GLFs were 4.33 times more likely to be frail. Age was not found to be a significant independent predictor for GLF odontoid fractures, however, increased CCI was predictive. Lomoschitz et al analyzed a cohort of 225 patients 65–75 years of age or older than 75 years with various MOIs and found that falls from standing height, independent of age, were more likely to have injuries of the upper cervical spine. This finding was contrasted by the fact that relatively younger patients (65–75 years), who were more often injured through high-energy mechanisms (ie, MVA), sustained more cervical injuries at lower cervical regions such as C5 and C6.[21] Such findings suggest that the propensity for upper cervical fractures in patients older than 75 years reflect an accelerated phase of age-related changes in the spine. Our study found that frail patients had the highest rates of concurrent fractures in the upper cervical spine at C1 (62.5%) compared with other groups, in addition to lower rates of other concurrent fractures distal to the cervical spine and in the appendicular skeleton. All frailty groups in this study had an average age older than 75 years, suggesting frailty may have acted as an independent predicator for such differences. Indeed, previous studies have shown frailty to be superior to age in outcome prediction and have suggested frailty to be used as a substitute for age in assessing elderly patients who have experienced traumatic GLFs.[17]

Only a small number of patients underwent surgical intervention in this cohort. It was seen that the mean mFI was marginally lower in the surgical cohort than the nonoperative cohort, although 7 of 8 surgical patients were categorized as either prefrail or frail. In addition, those who were frail were more likely to have concomitant fractures of the atlas. Contemporary management of upper cervical spine fractures must permit early mobilization to reduce the risks associated with prolonged recumbency akin to management of hip fractures in the elderly.[22,23] Frailty status alone should not therefore be seen as an isolated factor on which to decline surgical intervention, but rather one to aid in risk stratification and proper patient counseling.

Frailty was also identified as a predictor for adverse clinical outcomes in our patient population, including extended LOS and higher rates of readmission within 90 days. Frail patients had higher rates of readmission, 30-day mortality, and 1-year mortality than either prefrail or nonfrail groups. Shin et al[15] analyzed 30-day postoperative outcomes for patients undergoing anterior cervical discectomy and fusion or posterior cervical fusion and found a mFI greater than 0.36 to be an independent predictor of grade IV Clavien–Dindo complications and higher rates of mortality. Previous studies have described the controversy regarding surgical versus conservative management of odontoid fractures.[10,24–28] Recently, studies report favorable outcomes in 1-year mortality for surgically treated patients.[5,24,29] Schoenfeld

et al found surgical patients (N = 44) had a 21% 1-year mortality rate as opposed to 36% in nonsurgical patients (N = 112), although mortality rates were similar at 3 months. This suggests that most mortality within the first year is attributable to pre-existing comorbidity.[5] The frailty index helps to quantify perioperative physical reserve and comorbidity burden, adding to a list of tools surgeons can use when making such a complex clinical decision.

This study shares limitations common to many retrospective reviews and, as such, is unable to establish causality between increased frailty and various MOIs for odontoid fractures. Furthermore, because data originated from a single center, interpretation at a broader level may be limited due to relatively small sample size. In addition, most patients presenting with cervical fractures were due to traumatic falls from the ground level, which limits the application of our results to other less common MOIs.

CONCLUSIONS

Traumatic falls in elderly patients, more so than trauma as a result of other higher energy mechanisms, are potentially life-threatening injuries. Patients who presented after a traumatic fall were more likely to be frail than those suffering other injury mechanisms. Frail patients were more likely to have extended hospital stay and readmission within 90 days than nonfrail patients, and these patients had higher 30-day and 1-year mortality rates. This study presents frailty as an important clinical instrument in the management of geriatric odontoid fractures.

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Clinical Study

Sarcopenia, but not frailty, predicts early mortality and adverse events after emergent surgery for metastatic disease of the spine

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Abstract

BACKGROUND CONTEXT: Frailty and sarcopenia variably predict adverse events (AEs) in a number of surgical populations.

PURPOSE: The aim of this study was to investigate the ability of frailty and sarcopenia to independently predict early mortality and AEs following urgent surgery for metastatic disease of the spine.

STUDY DESIGN: A single institution, retrospective cohort study.

PATIENT SAMPLE: One hundred eight patients undergoing urgent surgery for spinal metastases from 2009 to 2015.

OUTCOME MEASURES: The incidence of AEs including 1- and 3-month mortality.

METHODS: Sarcopenia was defined using the L3 Total Psoas Area/Vertebral body Area (L3-TPA/VB) technique on CT. The modified Frailty Index (mFI), Metastatic Frailty Index (MSTFI) and the Bollen prognostic scales were calculated for each patient. Additional data included demographics, tumor type and burden, neurological status, the extent of surgical treatment and the use of radiation-therapy. Spearman correlation test, logistic regression and Kaplan-Meier were used to study the relation between the outcomes measures and potential predictors (L3-TPA/VB, MSTFI, mFI, and the Bollen prognostic scales).

RESULTS: Eighty-five percent of patients had at least one acute AE. Sarcopenia predicted the occurrence of at least one postop AE (L3-TPA/VB, 1.07±0.40 vs. 1.25±0.52; p=.031). Sarcopenia (L3-TPA/VB) and the degree of neurological impairment were predictive of postoperative AE but MFI or MSTFI were not. Sarcopenia predicted 3-month mortality, independent of primary tumor type (L3-TPA/VB: 0.86±0.27 vs. 1.12±0.41; p<.001). Kaplan-Meyer analysis showed L3-TPA/VB and the Bollen Scale to significantly discriminate patient survival.

FDA device/drug status: Not applicable.

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CONCLUSIONS: Sarcopenia, easily measured by the L3-TPA/VB on conventional CT, predicts both early postoperative mortality and adverse events in patients undergoing urgent surgery for spinal metastasis, thus providing a practical tool for timely therapeutic decision-making in this complex patient population.

Keywords: Spinal metastasis; Frailty; Sarcopenia; Spinal surgery; Adverse event; Survival

Introduction

Surgical intervention is a well-established component of the treatment algorithm for spinal metastasis, along with radiation therapy and chemotherapy. Symptomatic spinal cord compression and mechanical instability are the primary surgical indications in the metastatic spine disease population. Surgery can be effective in maintaining a patient's function [1]. With recent advances in minimally invasive techniques, surgical morbidity has been reduced [2–6]. Although these procedures are performed with increasing frequency [7,8], a high rate of adverse events (AEs) has been demonstrated, highlighting the vulnerability of these patients [9]. Metastatic spine disease patients often present with indications for urgent surgery such as progressive neurological deterioration. However, metastatic disease burden and life-expectancy must be weighed against potential functional improvement, although surgical decision-making must be done urgently with often incomplete information. Several mortality predictive scores for spinal metastatic patient have been described with limited success [10–14]. To date, none of these provide any practical guidance in the acute setting, as to the urgency and appropriate extent of surgery.

Frailty denotes a state of weakened reserve against stressors and may occur independent of and out of proportion to chronological age [15,16]. One conceptual model of frailty is the theory of the accumulation of deficits which led to the development of frailty indices including the Modified Frailty Index (mFI) [17] and the Metastatic Spinal Tumor Frailty Index (MSTFI) [18]. Derived from large databases, these indexes have been shown to predict adverse events and mortality following spine surgery [18–21]. Related to this, sarcopenia is defined as a progressive loss of skeletal muscle mass, strength, and power and is one manifestation of frailty [22–30]. In the oncologic population, sarcopenia is commonly referred to as cancer cachexia. In prior studies, sarcopenia has been evaluated in a practical fashion by measuring the total area of the psoas muscle on axial computed tomography (CT) scanning although consensus on the appropriate threshold is lacking. Frailty has been shown to predict adverse outcomes in multiple spinal surgical populations [18,19,21,31,32]. In the metastatic spine disease population, frailty and sarcopenia may be potentially useful tools to guide surgical candidacy, urgency and planning, yet, their usefulness to predict mortality and AEs remains unknown in this challenging population.

The objectives of this study were to determine the relationship among sarcopenia, frailty indices, and the Bollen scale with mortality and acute care AEs in patients undergoing surgery for metastatic disease of the spine. We hypothesized that the newer frailty indices (MFI and MSTFI) and sarcopenia measures would discriminate better in the metastatic spine disease population than the historical Bollen Prognostic Scale.

Material and methods

Study population

We included all consecutive patients with metastatic spinal disease, admitted at a quaternary referral center over 8 years between January 1, 2009 and December 31, 2016 in this retrospective cohort study. The study was approved by the Institutional Research Ethics Board with a waiver for informed consent obtained for each individual patient. We included all patients admitted with a diagnosis of metastatic spine disease who required urgent spine surgery because of progressive neurological deterioration or intractable mechanical pain. Patients were excluded if they were treated nonsurgically, had intradural malignancy, primary neoplasm of the spine, a destructive lesion at the L3 level precluding measurement of the L3-TPA/VB ratio, or if a lumbar CT scan was not available within 6 months of their index admission.

Patient and surgical data

The following data were retrieved from our local prospective spine registry; demographics, American Spinal Injury Association (ASIA) classification, surgical procedures (type of surgery, surgical approach, and duration of surgery), adverse events, and mortality. Data regarding primary tumor site, the use of radiation therapy, frailty, Surgical Invasiveness Index (SII), and sarcopenia measures were extracted from the electronic medical record.

Sarcopenia: Sarcopenia was assessed by measuring the right and left psoas muscle area on the axial image in the middle of the L3 vertebral body on a standard abdominal CT scan obtained within 6 month of the index hospital admission. Measurements were conducted in a semiautomated fashion with manual outlining of muscle borders and L3 vertebral body followed by automated volumetric analysis. The imaging settings were adjusted to −30 and 110 Hounsfield units (HU) to exclude vasculature, bony

structures, and fat infiltration for outlining of the muscle borders. For each patient, we calculated the ratio of the sum of the left and right psoas muscle area divided by the area of the L3 vertebral body (L3-TPA/VBA) as depicted in Figure 1. This measurement technique was previously shown to have good inter-rater reliability [23]. The time-dependent changes in muscle mass in oncologic patients are a well-known phenomenon. To account for that, the effect of sarcopenia on survival was analyzed using the day of imaging (as opposed to the admission day) as a reference point for survival time.

Frailty indexes: Frailty was evaluated with the previously described mFI [33] and the MSFTI [18]. The MFI consists of 11 variables including comorbidities and deficits. The MFI score is calculated as a proportion of the number of reported variables divided by the number of variables assessed. Patients were classified as not frail (mFI=0), pre-frail (mFI>0 and <0.21), and frail (≥0.21) based on previous data defining frailty as an index greater than or equal to 0.21 [33]. The MSTFI is a metastatic spine tumor specific frailty index designed to predict surgical morbidity, mortality and length of hospital stay [18]. The score consists of 9 weighted variables, with a range of 0 to 10, higher score meaning increased frailty. The malnutrition variable was omitted from the score for the current study due to insufficient data.

Bollen prognostic scale (BPS): The BPS is a specific prognostic scale designed to stratify patient survival. The BPS was chosen due to its ease in clinical application and its adaptability to improvement in cancer care over time [11]. The scale classifies patients into 4 prognostic categories (from best to worst prognosis: A, B, C and D) based on 3 clinical variables: clinical profile of the primary tumor, Karnofsky Performance Score [34], and the presence of visceral or brain metastasis [10].

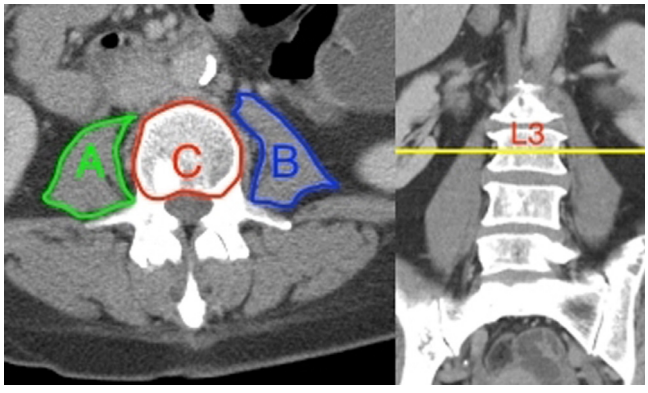

Fig. 1. Measurement technique of psoas surface area. All measurements were made using the surface area measurement tool included in the PACS software. The transverse CT scan cut at the level of the middle of the L3 vertebral body was used to measure area. The L3 Total Psoas Area/ Vertebral Body Area (L3-TPA/VBA) was the sum of the right (A) and left (B) psoas area was divided by the area of the L3 vertebral body.

Postoperative outcomes

Mortality was analyzed 1 and 3 months after the day of admission to hospital (doADM). The time point of reference for calculation of survival was the doADM for all analysis except for L3 Total Psoas Area/ Vertebral Body Area (L3-TPA/VBA) where we used the day of CT-Scan (doCT-S).

AEs were collected using the Spine Adverse Event Severity System (SAVES) V2.0 [35]. SAVES allows systematic prospective collection of postoperative AEs in spinal surgery. Its sensibility to detect an extensive variety of postoperative AEs in various settings and populations of spinal patient was previously demonstrated [9,35–37].

Statistical analysis

Data are summarized as mean (standard deviation) or as median (interquartile range [IQR]). Logistic regression with backward stepwise elimination was used to determine the impact of sarcopenia and frailty on the occurrence of AEs. Spearman Correlation were used to assess the relationship between the number of postop AEs and the different predictors studied (L3-TPA/VBA, Bollen, mFI, MSTFI and SII). Statistical analysis of survival included Kaplan-Meier curves used to determine differences in survival between sarcopenia categories with the Gehan-Breslow-Wilcoxson tests. A two-tailed $p<.05$ was considered statistically significant for all comparisons. All data were analyzed using SPSS (version 24.0 for Mac; IBM, Chicago, Il) and Excel (version 15.2 for Mac; Microsoft, Redmond, WA).

Results

We screened the 271 admissions for spinal metastasis within our database and after elimination of duplicated and repeated admissions we included 169 initial surgical admissions for spinal metastasis. Of these, 61 patients were excluded, leaving 108 patients included in our analysis (Fig. 2). Fifty-three percent were male, and the average age was 61.5 (SD 11.5) years. The most common primary tumor location was breast (22%), followed by lung (17%), and kidney (16%). Thirty-six patients (33%) had solitary vertebral metastasis, 26 (24%) patients had concomitant metastatic node involvement and 46 (43%) had visceral metastases. Detailed demographic data are displayed in Table 1.

Various surgical procedures were performed including 3 anterior cervical decompression and fusions, 6 posterior cervical decompressions with instrumentation, 8 combined (anterior/posterior) cervical procedures, 5 posterior thoracolumbar decompressions without fusion, 43 posterior thoracolumbar decompression and instrumentation and 43 posterior thoracolumbar instrumentation with reconstruction of the anterior column. The mean operative time was 276±125 minutes. The median SII was 19

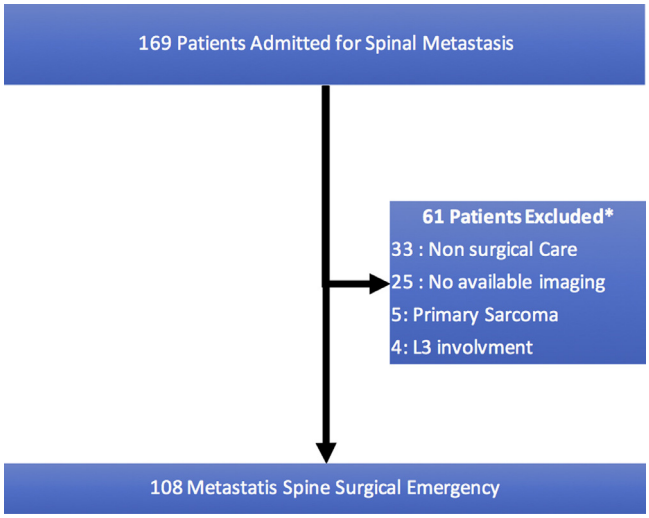

Fig. 2. Flow chart of patients included and excluded in our study. Sixty-one were excluded from the 169 patients considered for inclusion. The exclusion criteria were: patients with no valid CT-Scans, patients with primary tumor of the spine, patients with significant L3 metastatic involvement and patients admitted for non-surgical management of their spinal metastasis. *Six patients had more than one exclusion criteria.

Table 1
Demographic and clinical variables of 108 surgical patients with spinal metastasis

Variable	Included patient	Excluded patient
Gender (male)	57/108 (52.8%)	30/61 (49.2%)
Age (years)	62.5 (35–84)	60.9 (19.3-85.1)
ASIA		
A	0/108 (0.0%)	1/61 (1.6%)
B	2/108 (1.9%)	2/61 (3.3%)
C	14/108 (13.0%)	3/61 (4.9%)
D	43/108 (39.8%)	20/61 (32.8%)
E	49/108 (45.4%)	35/61 (57.4%)
Surgical site		
Cervical	15/108 (13.9%)	5/28 (17.9%)
Thoracic	66/108 (61.1%)	20/28 (71.4%)
Lumbar	25/108 (23.1%)	3/28 (10.7%)
Sacral	2/108 (1.9%)	0
Tumour by group		
Kidney	17/108 (15.7%)	6/61 (9.8%)
Lung	18/108 (16.7%)	11/61 (18.0%)
Breast	24/108 (22.2%)	11/61 (18.0%)
Prostate	13/108 (12.0%)	6/61 (9.8%)
Other	36/108 (33.3%)	27/61 (44.3%)
SII	18.3 (10-27)	N/A
Radiation therapy		
Pre-Op	17/108 (15.7%)	6/28 (21.4%)
Post-Op	56/108 (51.8%)	14/28 (50.0%)
Pre- and postop	9/108 (8.3%)	8/28 (28.6%)
None*	26/108 (24.1%)	1/33 (3.0%)
RT/Non-op	N/A	25/33 (75.8%)
No RT/Non-op	N/A	6/33 (18.2%)

* No radiation therapy during the study period. RT: Radiation Therapy.

Statistical difference between included and excluded patients was always p>0.2 except for radiation therapy distribution (p<.001)

(range 10–27). The median length of hospital stay was 22 days (IQR 12–35).

Adverse events

A total of 287 AEs were observed in 92 patients (85%) with a mean of 2.6 AEs per patient. The most common postoperative AEs were urinary tract infection (41%), electrolyte imbalance (27%), and delirium (23%). Figure 3 displays the incidence of specific AE categories. The distribution of frailty indexes Bollen prognostic categories and sarcopenia are presented in Table 2. Patients who experienced at least 1 AE had a significantly a lower mean L3-TPA/VBA compared with patients who had no AEs (1.07±0.40 vs. 1.25±0.52; p=.031). Conversely, MSTFI, mFI, and Bollen Scale were not significantly associated with having an adverse event AEs (Table 3). L3-TPA/VBA and MFI were significantly correlated with the number of AEs experienced (r_s=−0.292; p=.002 and r_s=0.197; p=.042, respectively) but not the Bollen Scale, MSTFI and SII (Table 4).

Multivariate logistic regression analysis using the backward elimination procedure retained L3-TPA/VBA and preoperative neurological impairment as independent predictors of experiencing one or more AEs (Table 5). MSTFI, mFI, SII, Bollen Score, tumor grade, extent of disease, age, and gender were excluded from the model. For every 1 unit increase in L3-TPA/VBA, the odds of

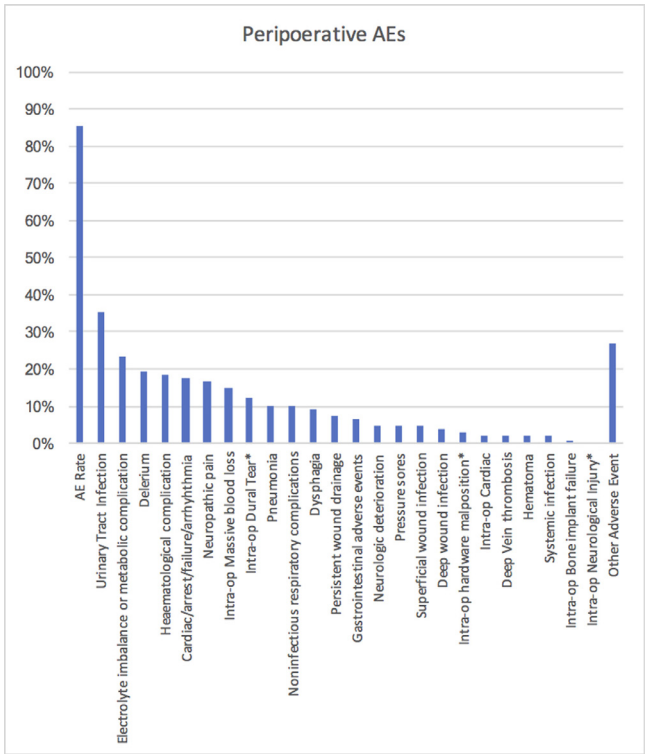

Fig. 3. This bar graph displays global AE rate and clinically relevant AE rate. Intra-operative technical AEs (marked with *) were excluded of our statistical analysis. The category other AEs corresponds to AEs not categorized in the SAVEs form.

Table 2
Distribution of frailty index (mFI, MSTFI) prognostic score (Bollen Categories) and sarcopenia (L3-TPA/VBA) among 108 surgical patients with spinal metastasis

Predictor	108 included patients
MSTFI score	
0	17/108 (15.7%)
1	33/108 (30.6%)
2	21/108 (19.4%)
3	26/108 (24.1%)
MFI	
0	20/108 (18.5%)
0.09	53/108 (49.1%)
0.18	19/108 (17.6%)
0.27	9/108 (8.3%)
0.36	5/108 (4.6%)
0.45	1/108 (0.9%)
Bollen categories	
A	12/108 (11.1%)
B	25/108 (23.1%)
C	43/108 (39.8%)
D	27/108 (25.0%)
L3-TPA/VBA	
Median	0.9294 (0.4849−2.6197)
1rst Quartile	0.7298 (0.4849−0.8072)
2nd Quartile	0.8734 (0.8108−0.9292)
3rd Quartile	1.0788 (0.9297−1.2440)
4rth Quartile	1.5304 (1.2481−2.6197)

Table 4
Bivariate correlation studies between predictive tools and number of postop adverse events

		AE Number
L3-TPA/VBA	r_s	-0.292
	p-value	0.002
Bollen	r_s	0.08
	p-value	0.41
mFI	r_s	0.197
	p-value	0.042
MSTFI	r_s	0.166
	p-value	0.087
SII	r_s	-0.142
	p-value	0.144

L3-TPA/VBA and mFI both showed statistically significant correlation with the number of postoperative adverse events. rs: Spearman correlation coefficient.

Table 5
Logistic regression analysis for postoperative occurrence of adverse events

	95% interval		Odds ratio	p-value
L3-TPA/VBA*	0.09	0.93	0.29	0.037
Neuro Impairment	1.54	11.3	4.17	0.005

* Per 1 unit increase.

MSTFI, mFI, SII, Bollen Score, tumor grade, extent of disease, age and gender were excluded from the model based on lack of significance (p>0.05).

experiencing an adverse event was reduced by 0.29 (95% confidence interval [CI] 0.09−0.93; p=.037). The presence of neurological impairment was associated with an adjusted odds ratio of 4.2 (95% CI 1.5−11.3, p=.005) of having an adverse event.

Mortality

At the time of the study, 42% of the patients were still alive. The overall median survival was 9 (IQR 3.0−23.5) months. L3-TPA/VBA was significantly lower in those who died within 1 month (0.72±0.12 vs. 1.08±0.40; p=.008) and 3 months (0.86±0.27 vs. 1.12±0.41; p<.001) of surgery. Similarly, MSTFI (2.04±0.99 vs. 1.47±1.00; p=.012) and Bollen Prognostic Scale were statistically higher for patients who died within 3 months of surgery (Table 3).

Kaplan-Meier Curves demonstrated differences in cumulative survival when patients were stratified using Bollen Scale (p=.004) and L3-TPA/VBA (p=.04), but not the mFI (p=.399) and MSTFI (p=.096) (Figs. 4 and 5). Further exploratory analysis of L3-TPA/VBA showed that the greatest difference in survival was between the first quartile (1rst quartile of L3-TPA/VBA=0.80712) and the rest (p=.006)

Discussion

Determination of the risk/benefit balance of surgery is a major challenge in the care of metastatic spine disease

Table 3
Comparison of L3-TPA/VBA, MSTFI, MFI, Bollen, and SII Scale values (mean ± SD) among patients based on AEs, 1-month mortality (1m mortality) and 3-month mortality (3m mortality)

	L3-TPA/VBA	MSTFI	MFI	Bollen	SII
AE (n=82)	1.07±0.40	1.62±1.03	0.12±0.10	2.10±0.81	18.2±3.9
No AE (n=26)	1.25±0.52	1.28±1.1	0.09±0.7	2.36±0.81	18.5±3.8
	p=.031	p=.74	p=.11	p=.64	p=.72
1m mortality (n=13)	0.72±0.12	1.85±0.90	0.14±0.07	2.38±0.87	18.3±3.8
>1m mortality (n=95)	1.08±0.40	1.59±1.04	0.12±0.10	2.06±0.80	18.2±3.6
	p=.008	p=.44	p=.12	p=.16	p=.91
3m mortality (n=28)	0.86±0.27	2.04±0.99	0.14±0.09	2.43±0.74	18.1±3.9
>3m mortality (n=80)	1.12±0.41	1.47±1.00	0.11±0.10	1.99±0.81	18.6±3.7
	p<.001	**p=.012**	p=.068	**p=.013**	p=.84

For L3-TPA/VBA, 1-month and 3-month mortality were calculated from the imaging day.

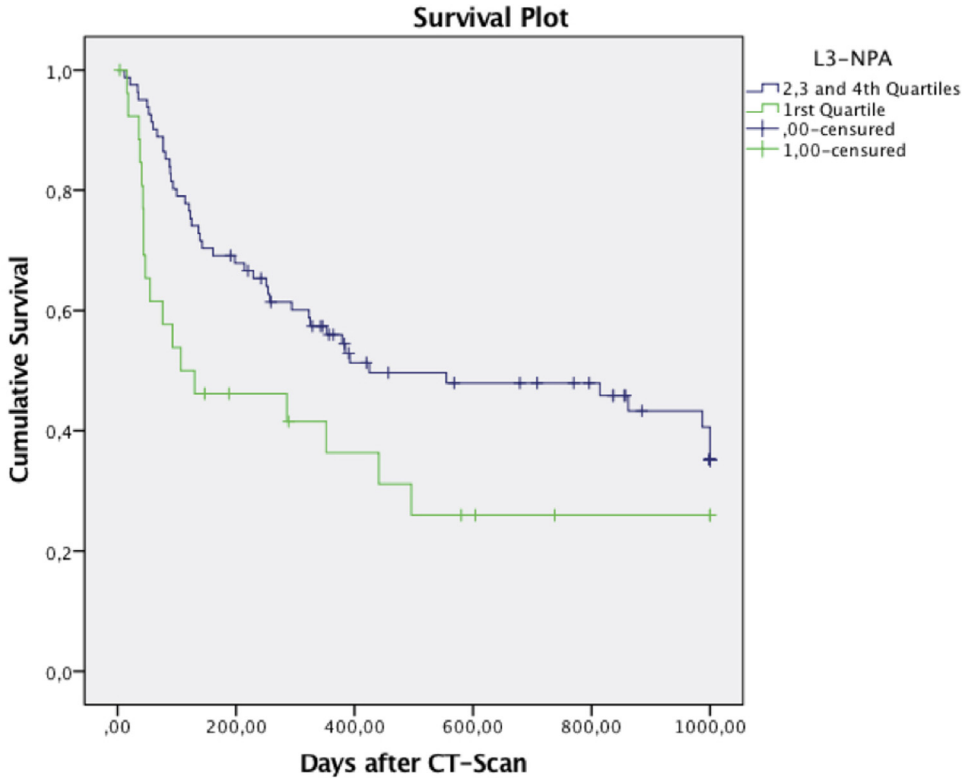

Fig. 4. Kaplan Meier Curves of first psoas quartile (green curve) compared with higher quartiles (blue curve). Survival curves were significantly different (p=0.040), specifically when the first quartile (L3-TPA/VBA<0.81) was compared to the other higher quartiles (p=0.006). There was no difference among the 3 other quartiles.

patients. Surgery is often urgent, usually requiring neural decompression/separation from the tumor mass, and stabilization. The invasiveness of this surgery can be significant, with a high rate of complications. In patients with limited life expectancy, it is critical that we understand the relative risks and benefits to inform clinical decisions. In this study, we evaluated a number of putative predictors of early mortality and AEs in metastatic spine disease patients undergoing urgent surgery. Our results indicate adverse events are common in this population, and that sarcopenia (as assessed using the L3-TPA/VBA ratio) was an independent predictor of experiencing an adverse event, as well as mortality at 1 and 3 months. Similarly, frailty predicted poor outcomes; the mFI independently predicted the total number of adverse events, and the MSTFI was associated with mortality at 3 months. Overall, our study suggests that the L3-TPA/VBA ratio is a clinically useful predictor of early mortality and AES in metastatic spine disease patients undergoing urgent spine surgery.

Previous authors have arbitrarily defined a threshold of 3-months life expectancy for surgical intervention in this population, based on the relative risks and benefits [13,38,39]. Given recent advances in surgical and radiation techniques, this 3-month threshold requires further evaluation. Rapid and sustained improvement in quality of life after spinal surgery for metastasis has been reported in numerous recent series [2–6]. Some authors have recently suggested that a life expectancy of 2 months or even less, would still justify potential surgical benefits of improved quality of life over morbidity and complications [2–4]. Surgical decision making, in conjunction with patient preference, must be informed by accurate life expectancy estimates, anticipated complications, and potential for postoperative improvement in quality of life. Despite recent improvement in this field [40,41], the ability of the clinician to accurately predict life expectancy in patients with metastatic cancer remains challenging, particularly in an urgent setting with incomplete information. Sacropenia, as assessed by a relatively practical tool (L3-TPA/VBA), has the potential to improve risk prediction and informed consent. The Bollen Prognostic Scale was specifically designed to predict mortality and not AEs or quality of life improvement. We confirmed this fact, demonstrating a statistically significant association of the Bollen Scale with survival but not AEs in our study population. The Bollen Prognostic Scale does not capture the impact of postoperative complications. Moreover, in the emergency setting when the primary tumor site is often unknown, the Bollen Scale cannot be applied.

Sarcopenia is associated with functional decline and is a manifestation of frailty in the general population. A growing body of literature, spanning various surgical

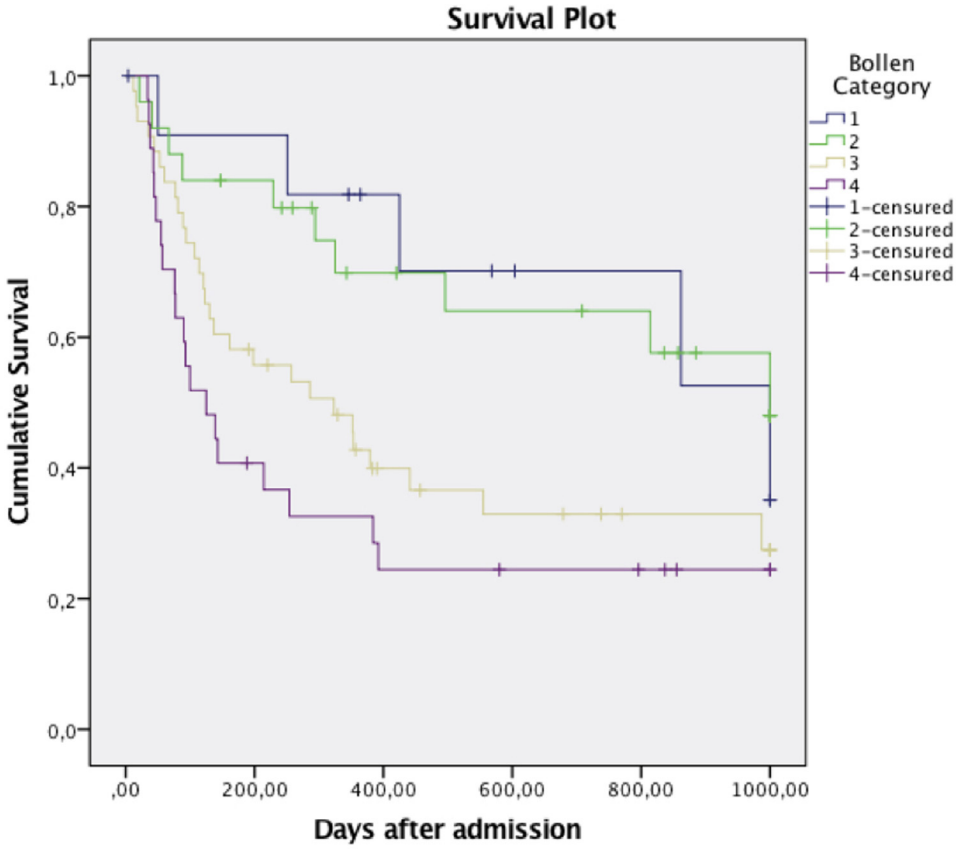

Fig. 5. Kaplan Meier Curves by Bollen Categories. Survival was significantly different between the Bollen Categories (p=.004).

populations, confirms its association with poor clinical outcome [24,25,27,30,42,43]. Previous reports on nononcological spinal surgery populations have shown that morphometric analysis of the psoas could predict complications [44] and mortality [45].

Our results provide new, clinically relevant information to the existing literature regarding the role of sarcopenia on predicting early postoperative outcomes. Gakhar et al. and Zhakaria et al. have previously reported decreased survival with lower psoas size in patients with spinal metastasis [23,45]. In contrast to our study, Zakaria et al. did not examine patients who underwent surgical intervention, but rather those treated with radiation therapy only. Using a measurement technique similar to this study, Gakhar et al. demonstrated an increased 1-year mortality in 86 metastatic spine patients who had the lowest quartile of psoas muscle mass. Our study adds further to these studies as we purposely included medium term survival endpoints (1 and 3 month) given this urgent surgical population. We propose the L3-TPA/VBA ratio as a practical, clinically useful tool to predict one and 3-month survival, with the lowest quartile of L3-TPA/VBA ratio (<0.81) significantly predictive of early mortality and complications.

Previous studies have differed in their methodology for measuring sarcopenia and frailty. Normalizing psoas area to patient height is the most commonly utilized method to measure sarcopenia and account for patient morphology. Accurate measurement of patient height can be challenging in patients confined to bed and can vary with spinal fracture or deformity. Accordingly, we elected to normalize the psoas area using the area of the third lumbar vertebra (L3-TPA/VBA), as this does not require patient mobilization or rely on patient's memory of his own height. Furthermore, this measurement is practical and simultaneously available on the same CT scan slice as the psoas muscle area. This technique has previously been used in the metastatic spine population and has shown good correlation with the conventional NTPA measures (r=0.77; p<0.0001) [23,45].

Most frailty measurement tools are derived from the theory of accumulating deficit popularized by Rockwood et al. [46]. Frailty indexes, like mFI and MSTFI, were designed to identify patients at risk of AE using large nationwide surgical databases and previous studies showed correlation between mFI and postoperative outcomes in various surgical populations [43]. Unlike mFI, MSTFI was not extensively studied in literature but it was specifically designed for the metastatic spinal patient population. For the above reasons, we decided to study both MSTFI and mFI.

We found that the use of mFI might be altered by a ceiling effect in the metastatic spinal population. Using a cutoff of 0.21 for the mFI, only, 14.8% of our population was categorized as frail. Comparatively, 43.5% of our patients

were classified as moderately or severely frail when using MSTFI, suggesting that this frailty measurement is more sensitive and specific to the metastatic spine disease population. Moreover, the clinical use of both these indices might be limited in the emergency setting by the need for extensive medical chart data abstraction for their calculation.

Interestingly, we found no correlation between surgical invasiveness measured with The Spine Surgery Invasiveness Index (SSII) and outcome in this population. SSII was designed to quantify surgical invasiveness in the spinal surgery population [47]. Previous authors have reported a relation between SSII and the occurrence of postop adverse events in trauma and degenerative spine populations [36,48]. Our findings suggested that surgical invasiveness may not play a clinically significant role in this metastatic spinal population, at least not relative to the other putative clinical predictors. Because of the observational nature of our study, an allocation bias of less invasive surgical strategies for higher-risk patients may have minimized any impact of SSII on outcome.

In this study, survival was calculated based from both the day of admission (doADM) and the day of the CT-Scan (doCT-S) from which psoas area was measured. Using admission as the reference point is most commonly used and helps frame the discussion with patients and their families. However, using the doCT-S acquisition reflects more the biological effect of L3-TPA/VBA as it is likely to change with time especially in cancer population [49,50]. This is in keeping with our finding of a stronger correlation between L3-TPA/VBA and survival when using doCT-S rather than doADM. Ideally, a CT scan, allowing psoas measurement, would be performed on the doADM, thus allowing optimal use of this clinically important tool. The results from our study support the use of L3-TPA/VBA as a surrogate of sarcopenia, and a readily available, easily measureable adjunct to help with the complex clinical decision making in the metastatic spine population.

Limitations

A limitation common to studies examining sarcopenia is the lack of a universally accepted definition. Various cut-offs have been proposed in different surgical populations including general surgery, gynecology, and urology. These cut-offs were defined using tertiles or quartiles, with no comment on the normality of sarcopenia in their population, thus limiting the external validity of their findings. Ideally, a cut-off should be determined for a specific clinical purpose such as surgical indication, invasiveness of surgery or prognostication. Ultimately, as part of an informed consent, some patients can still choose to undergo surgery despite knowing the risk of AE or early mortality. We found the greatest increment in mortality between the first and second quartile psoas (cut-off being roughly 0.81) but we do believe this cut-off should be verified in large prospective studies before being applied for clinical decision.

We may have introduced selection bias as 31 patients were excluded from the study because they did not have adequate preoperative imaging including the L3 region.

Lastly, the number of patients included in our study was also relatively small and limited to a single center, therefore our results might not be generalizable to other centers. Our study may have been underpowered to detect relationships between the various predictor variables and outcomes, including the SII.

Conclusions

Sarcopenia, as measured by L3-TPA/VBA, predicted both early mortality and acute care adverse events and patients undergoing urgent surgery for spinal metastases. Although the MSTFI and Bollen scale predicted early mortality in our population, we did not find a significant relationship with other adverse events. Sarcopenia, as measured by L3-TPA/VBA, is practical, readily available, and can inform surgical decision-making prior to urgent surgery where prognostic information may be incomplete. Further research should focus on validating this predictive tool in surgical patients with metastatic disease of the spine.

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An assessment of frailty as a tool for risk stratification in adult spinal deformity surgery

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OBJECTIVE The goal of this study was to analyze the value of an adult spinal deformity frailty index (ASD-FI) in preoperative risk stratification. Preoperative risk assessment is imperative before procedures known to have high complication rates, such as ASD surgery. Frailty has been associated with risk of complications in trauma surgery, and preoperative frailty assessments could improve the accuracy of risk stratification by providing a comprehensive analysis of patient factors that contribute to an increased risk of complications.

METHODS Using 40 variables, the authors calculated frailty scores with a validated method for 417 patients (enrolled between 2010 and 2014) with a minimum 2-year follow-up in an ASD database. On the basis of these scores, the authors categorized patients as not frail (NF) (< 0.3 points), frail (0.3–0.5 points), or severely frail (SF) (> 0.5 points). The correlation between frailty category and incidence of complications was analyzed.

RESULTS The overall mean ASD-FI score was 0.33 (range 0.0–0.8). Compared with NF patients (n = 183), frail patients (n = 158) and SF patients (n = 109) had longer mean hospital stays (1.2 and 1.6 times longer, respectively; $p < 0.001$). The adjusted odds of experiencing a major intraoperative or postoperative complication were higher for frail patients (OR 2.8) and SF patients (4.1) compared with NF patients ($p < 0.01$). For frail and SF patients, respectively, the adjusted odds of developing proximal junctional kyphosis (OR 2.8 and 3.1) were higher than those for NF patients. The SF patients had higher odds of developing pseudarthrosis (OR 13.0), deep wound infection (OR 8.0), and wound dehiscence (OR 13.4) than NF patients ($p < 0.05$), and they had 2.1 times greater odds of reoperation ($p < 0.05$).

CONCLUSIONS Greater patient frailty, as measured by the ASD-FI, was associated with worse outcome in many common quality and value metrics, including greater risk of major complications, proximal junctional kyphosis, pseudarthrosis, deep wound infection, wound dehiscence, reoperation, and longer hospital stay.

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KEY WORDS adult spinal deformity; complications; frailty index; personalized preoperative risk stratification

Frailty is a relatively new medical diagnosis with many contributors that is characterized by reduced physiological function or increased physiological age, which increases an individual's vulnerability to injury. Health tends to deteriorate at different rates for different people, leading to a discrepancy between physiological age and chronological age from a medical standpoint. Frailty assessments have been developed as a way to quantify a person's physiological age.

Although frailty indices were initially developed as

ABBREVIATIONS ASD-FI = adult spinal deformity frailty index; ISSG = International Spine Study Group; LOS = length of hospital stay; NF = not frail; PJK = proximal junctional kyphosis; SF = severely frail; SVA = sagittal vertical axis.

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tools to track physiological aging and predict mortality and self-management ability in nonoperatively treated populations, these indices have recently been shown to be better predictors of perioperative adverse events than chronological age alone.[6,11,12,17] Numerous methods for frailty quantification have been developed and validated.[3,4,7,13,15–18] Searle et al. proposed and validated a method for creating frailty indices by using large, existing patient databases. This step-by-step method was used to create a frailty index (the adult spinal deformity frailty index [ASD-FI]) in this study for use with the existing International Spine Study Group (ISSG) ASD prospective patient database.

This method is based on the concept that the number of deficits in health can be used as a surrogate measure for overall frailty. At least 30 deficits in health, covering areas including mobility, activities of daily living, cognitive function, mood, and medical comorbidities, should be selected to accurately calculate a frailty index. Therefore, variables are not weighted in this model. The deficits selected must meet the following criteria: 1) prevalence increases with age (e.g., heart disease), 2) related to health status (e.g., gray hair would be excluded), and 3) prevalence does not saturate too early (e.g., presbyopia would be disqualified because it is nearly universal by age 55 years). The index is expressed as a ratio of the number of health deficits present to the total number of deficits considered. For example, if 40 deficits were considered and 10 were present, the frailty score would be 10:40 or 0.25. When using this method, the exact variables (deficits in health) included matter less than the number of deficits present. In a series of 1000 iterations, the slope of deficit accumulation (0.03 per year) and the submaximal limit at approximately two-thirds of the deficits tested were insensitive to the precise composition of the index.[18] The frailty index was found to correlate accurately with other objective frailty measures. The key advantage of frailty indices is that they can be created in preexisting patient databases.

Surgery for ASD is known to have high complication rates and therefore warrants thorough preoperative evaluation and risk assessment. Quality and value metrics are increasingly important in the planning of and payment for modern health care delivery and should be based on accurate risk stratification. The development of an index that includes a comprehensive analysis of patient characteristics is important to this risk stratification process. A frailty index quantifies patient physiological reserve comprehensively. This can be used to determine the risk related to operation based only on patient factors and can be used in conjunction with tools examining risk based on surgical invasiveness (e.g., the Adult Spinal Deformity Surgical Invasiveness Index[14]) to personalize risk-benefit discussions with patients and preoperatively determine accurate and appropriate quality and value metric ranges. The purpose of this study was to develop and evaluate the ASD-FI by using an existing ASD database. The ASD-FI was examined for correlation with complication incidence, length of hospital stay (LOS), and reoperation rate to determine the value of incorporating this frailty assessment into preoperative risk stratification. We hypothesized that frailty, as measured by the ASD-FI, would be positively correlated with complication rate and LOS.

Methods

Patient Population

To develop a frailty index, we used a multicenter, prospective database maintained by the ISSG that consists of US patients with ASD. Institutional review board approval for patient inclusion in this database was obtained by each clinical site that contributed data. Each patient provided written informed consent before inclusion in the database. The database inclusion criteria were as follows: surgery for ASD between 2010 and 2014 for scoliosis (major curve ≥ 20°), thoracic kyphosis ≥ 60°, pelvic tilt ≥ 20°, or sagittal vertical axis (SVA) > 5 cm; and age ≥ 18 years. Whereas some previous frailty studies[13,18] have excluded all patients > 60 years old, we chose not to exclude adults on the basis of chronological age because "frailty" can affect surgical outcomes at any age. We included patients with a minimum of 2 years of follow-up.

Development of the ASD-FI

All variables in the ISSG ASD database were reviewed, and those that met criteria for inclusion in the frailty analysis (n = 40), as determined by Searle et al.,[18] were included in the ASD-FI (Table 1). Each variable (i.e., deficit in health) was recorded as a binary variable (e.g., presence vs absence of osteoporosis). The mean score of all deficits was calculated, resulting in a frailty index ranging from 0 to 1 point. Patients with scores of < 0.3 were considered not frail (NF); those with scores of 0.3–0.5 were considered frail; and those with scores of > 0.5 were considered severely frail (SF). These cutoff points were determined on the basis of those used in previous frailty analyses, which were based on risk of mortality curves.[13,18]

Data Analysis

The primary study outcome was incidence of major complications, which were defined as those that were potentially life-threatening, required reoperation, or caused permanent injury, per Glassman et al.[8] Major complications were intraoperative vascular, visceral, or neurological injury; postoperative deep infection; pulmonary embolism; junctional failure; and other similar complications.[9] Secondary outcomes included deep wound infection rate, wound dehiscence incidence, LOS, proximal junctional kyphosis (PJK) incidence, pseudarthrosis incidence, and reoperation rate. This is a retrospective analysis of a prospectively collected database.

Statistical Analysis

All statistical analyses were performed using Small Stata software, version 14.1 (StataCorp LP). First, univariate linear regression (for continuous variables) and logistic regression (for binary variables) of all independent variables were performed, followed by multivariate analysis of all independent variables found to have a p value < 0.3. Variables were eliminated until the maximum supportable number of variables was reached. Mul-

tivariate analyses included surgical invasiveness to assess the independent contribution of frailty to the outcomes of interest.

Results

In the ISSG ASD database, 450 participants had a minimum 2-year follow-up, 417 of whom had adequate data to calculate the ASD-FI (at least 75% [n = 30] of all variables using the method of Searle et al.[18]). The mean ASD-FI score was 0.33 (range 0.0–0.8). One hundred seventy-one patients (41%) were NF, 162 (39%) were frail, and 84 (20%) were SF. There were no significant differences in frailty according to sex or race ($p > 0.05$). Frailty was associated with age, Charlson Comorbidity Index value, and American Society of Anesthesiologists physical status classification score ($p < 0.05$). Patients with greater frailty were significantly more likely to have undergone 3-column osteotomies, to have had a greater number of vertebral levels fused, and to have had decompression, compared with NF patients (Table 2).

Univariate Analysis

All comparisons are made against the reference group of NF patients. On univariate analysis, frail patients had higher odds of having a major complication (OR 2.9, 95% CI 1.7–4.9), as did SF patients (OR 3.5, 95% CI 1.9–6.3) (Table 3). Frail patients had higher odds of experiencing any complication (OR 1.9, 95% CI 1.2–3.1), as did SF patients (OR 2.1, 95% CI 1.2–3.7). The odds of having a reoperation were higher for the SF patients (OR 2.0, 95% CI 1.1–3.7). The SF patients also had higher odds of PJK (OR 2.4, 95% CI 1.0–6.0), wound dehiscence (OR 11, 95% CI 1.2–94), and deep wound infection (OR 4.3, 95% CI 1.0–18).

Univariate analyses of possible confounding preoperative characteristics and surgical factors were performed, and those with p values < 0.3 were included in the multivariate model. These factors included various contributors to surgical invasiveness, such as number of levels fused, performance of osteotomies, operative time, and estimated blood loss. Multivariate models can support inclusion of only a certain number of independent variables, depending on the number of incidences (e.g., the number of major complications in each frailty category). Each multivariate model was reverse-refined to the maximum number of supported independent variables.

Multivariate Analysis

As with the univariate analysis, all comparisons are made against the reference group of NF patients. On multivariate analysis, the odds of having a major complication were higher for frail patients (OR 2.8, 95% CI 1.3–5.9) and SF patients (OR 4.1, 95% CI 1.7–9.6) (Table 4). The odds of having any complication were higher for frail patients (OR 1.8, 95% CI 1.1–3.0) and SF patients (OR 2.1, 95% CI 1.1–3.9). The odds of having a reoperation were higher for frail patients (OR 1.7, 95% CI 1.0–2.9) and SF patients (OR 2.1, 95% CI 1.1–3.9). The odds of experiencing PJK were higher for frail patients (OR 2.8, 95% CI 1.2–6.2) and SF patients (OR 3.1, 95% CI 1.2–8.0). The SF patients

TABLE 1. Factors included in the ASD-FI

Health deficits
Documented by physician
>3 medical problems
Body mass index <18.5 or >30 kg/m^2
Cancer
Cardiac disease
Currently on disability
Depression
Diabetes
Hypertension
Liver disease
Lung disease
Osteoporosis
Peripheral vascular disease
Previous blood clot (deep vein thrombosis/pulmonary embolism/stroke)
Smoking status
Patient-reported (questionnaire, question no.)
Bladder incontinence
Bowel incontinence
Deteriorating health this yr (SF-36v2, 2)
Difficulty climbing 1 flight of stairs (SF-36v2, 3e)
Difficulty driving a car (LSDI, 3)
Difficulty getting dressed (SF-36v2, 3j; LSDI, 1 & 2)
Difficulty getting in/out of bed (LSDI, 6)
Difficulty sleeping >6 hrs (ODI, 7)
Difficulty walking 100 yards (SF-36v2, 3i)
Difficulty w/ light activity (SF-36v2, 3b)
Feeling downhearted/depressed most of the time (SF-36v2, 9f; SRS-22r, 16)
Feeling tired most of the time (SF-36v2, 9i)
Feeling worn out most of the time (SF-36v2, 9g)
General health: fair/poor (SF-36v2, 1)
Inability to bathe w/o assistance (SF-36v2, 3j; LSDI, 8)
Inability to cheer up often (SF-36v2, 9c; SRS-22r, 7)
Inability to do normal work/schoolwork/housework (ODI, 10; SRS-22r, 9 & 12)
Inability to lift heavy objects (SF-36v2, 3c; ODI, 3)
Inability to travel >1 hr (ODI, 9)
Inability to walk w/o assistive device (ODI, 4)
Leg weakness
Loss of balance
Not in excellent health (SF-36v2, 11d)
Personal care dependency (ODI, 2)
Restricted activity level (SRS-22r, 5)
Restricted social life (ODI, 8; SRS-22r, 14 & 18)

LSDI = Lumbar Stiffness Disability Index; ODI = Oswestry Disability Index; SF-36v2 = 36-Item Short-Form Health Survey, version 2; SRS-22r = Scoliosis Research Society-22r questionnaire.

TABLE 2. Characteristics of patients in the ISSG ASD database by frailty status

Characteristic	NF, n = 171		Frail, n = 162		SF, n = 84		p Value
	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	
Age at surgery, yrs	49 (1.3)		61 (1.0)		63 (1.1)		**<0.001***
Female sex		143 (84)		122 (76)		70 (83)	0.15†
Caucasian		139 (81)		146 (89)		93 (75)	0.39†
ASA PSC score							**<0.001***
1		31 (20)		3 (1.9)		1 (1.2)	
2		99 (62)		79 (50)		23 (28)	
3		28 (18)		73 (46)		56 (68)	
4		1 (0.6)		3 (1.9)		2 (2.4)	
Missing		12 (7.0)		4 (2.5)		2 (2.4)	
CCI score							**<0.001***
0		96 (56)		35 (22)		3 (3.6)	
1		36 (21)		40 (25)		16 (19)	
2		25 (15)		47 (29)		14 (17)	
3		11 (6.4)		21 (13)		15 (18)	
4		2 (1.2)		13 (8.0)		13 (16)	
5		0 (0)		2 (1.2)		12 (14)	
6		1 (0.6)		4 (2.5)		5 (6.0)	
7		0 (0)		0 (0)		5 (6.0)	
8		0 (0)		0 (0)		1 (1.2)	
Op time, hrs	6.0 (2.3)		6.8 (2.0)		6.9 (2.2)		**<0.001***
EBL, L	1.4 (1.2)		1.9 (1.9)		2.1 (1.8)		**0.03***
LOS, days	6.8 (2.9)		8.0 (3.9)		10.5 (9.0)		**<0.001***
Procedure							
Interbody fusion		90 (53)		109 (67)		59 (70)	**0.01†**
Decompression		76 (44)		110 (68)		66 (79)	**<0.001†**
3-column osteotomy		19 (11)		40 (35)		27 (44)	**0.001†**
No. of instrumented vertebrae	11 (4.3)		12 (4.2)		12 (4.2)		**0.031***
≤4		16 (9.5)		9 (5.7)		6 (7.1)	
5–8		29 (17)		22 (14)		6 (7.1)	
9–12		69 (41)		69 (43)		43 (51)	
13–16		36 (21)		31 (20)		18 (21)	
≥17		18 (11)		28 (18)		11 (13)	
Major complication		29 (17)		63 (38)		44 (40)	**<0.001†**

ASA = American Society of Anesthesiologists; CCI = Charlson Comorbidity Index; EBL = estimated blood loss; PSC = physical status classification.
Boldface type indicates statistical significance.
* Statistical analysis performed using Kruskal-Wallis H-test.
† Statistical analysis performed using Pearson chi-square test.

also had higher odds than NF patients of experiencing pseudarthrosis (OR 13, 95% CI 1.4–121), wound dehiscence (OR 13.4, 95% CI 1.5–120), and deep wound infection (OR 8.0, 95% CI 1.3–49).

Discussion

We found that frailty is independently associated with higher overall complication, major complication, and reoperation rates. Additionally, increasing frailty was associated with increased incidence of PJK, pseudarthrosis, wound dehiscence, and deep wound infection after ASD surgery. This association persisted in multivariate analyses, emphasizing that the contribution of frailty is independent of the contributions of other factors, like surgical invasiveness. In the modern health care system, complication prediction or preoperative risk stratification is becoming increasingly important for reimbursement based on quality and value metrics. Further refinement of preoperative risk stratification can help develop accurate quality and value metrics. Appropriate quality and value metric ranges should not be computed based simply on a broadly applied admission diagnosis-related group, but instead should be appropriately defined using measures of patient physiological risk and procedural complexity. Currently, comorbidities and other baseline patient char-

TABLE 3. Univariate analysis of outcomes of patients in the ISSG ASD database

Outcome	Frail vs NF			SF vs NF		
	OR	95% CI	p Value	OR	95% CI	p Value
Complication type*						
Deep wound infection	2.9	0.8–11	0.12	4.3	1.0–18	**0.04**
Major	2.9	1.7–4.9	<0.001	3.5	1.9–6.3	**<0.001**
PJK	2.4	1.1–5.3	0.03	2.4	1.0–6.0	0.05
Pseudarthrosis	1.3	0.4–5.0	0.68	3.2	0.9–12	0.08
Wound dehiscence	5.4	0.6–47	0.13	11	1.2–94	**0.03**
Total complications	1.9	1.2–3.1	0.005	2.1	1.2–3.7	**0.01**
Reoperation*	1.6	1.0–2.8	0.07	2.0	1.1–3.7	**0.02**
LOS†	1.2	1.1–1.3	<0.001	1.5	1.4–1.7	**<0.001**

Boldface type indicates statistical significance.
* Statistical analysis performed using univariate logistic regression.
† Statistical analysis performed using univariate Poisson regression.

TABLE 4. Multivariate analysis of outcomes of patients in the ISSG ASD database

Outcomes	OR	95% CI	p Value
Deep wound infection*			0.906
3-column osteotomy	0.4	0.1–1.7	0.20
Frail vs NF	2.4	0.4–15	0.33
Gait imbalance	3.8	0.4–39	0.26
No. of levels fused†	1.2	1.0–1.5	0.05
Op time‡	1.7	1.2–2.5	**0.01**
SF vs NF	8.0	1.3–49	**0.03**
LOS§			
Allograft used	1.1¶	1.1–1.2	**0.001**
Decompression	1.0¶	0.9–1.0	0.18
Frail vs NF	1.2¶	1.1–1.3	**<0.001**
No myelopathic symptoms	1.0¶	0.9–1.1	0.96
SF vs NF	1.6¶	1.4–1.8	**<0.001**
Major complications*			
3-column osteotomy	1.2	0.6–2.4	0.62
BMP used	0.9	0.4–1.7	0.66
Caucasian vs other race	2.2	0.7–7.1	0.17
EBL¶	1.8	1.4–2.2	**<0.001**
Frail vs NF	2.8	1.3–5.9	**0.006**
No. of levels fused†	1.0	0.9–1.1	0.85
SF vs NF	4.1	1.7–9.6	**0.001**
Smoker	0.6	0.2–2.2	0.48
PJK*			
Allograft used	1.5	0.7–3.1	0.33
Frail vs NF	2.8	1.2–6.2	**0.01**
No myelopathic symptoms	1.2	0.5–2.6	0.71
Osteotomy	0.5	0.3–1.1	0.08
SF vs NF	3.1	1.2–8.0	**0.02**
Pseudarthrosis incidence*			
3-column osteotomy	3.2	0.8–13	0.11
Decompression	0.3	0.1–1.1	0.06
EBL**	0.9	0.6–1.4	0.73
Frail vs NF	2.7	0.3–27	0.40
SF vs NF	13.0	1.4–121	**0.03**
Reoperation*			0.369
Allograft used	1.0	0.6–1.7	0.91
BMP used	0.8	0.5–1.2	0.26
Female sex	1.0	0.6–1.8	1.00
Frail vs NF	1.7	1.0–2.9	0.05
SF vs NF	2.1	1.1–3.9	**0.02**
Total complications*			
Caucasian vs other race	0.6	0.3–1.5	0.29
Female sex	2.1	1.2–3.7	**0.01**
Frail vs NF	1.8	1.1–3.0	**0.02**
No myelopathic symptoms	0.8	0.4–1.4	0.39
SF vs NF	2.1	1.1–3.9	**0.03**
Smoker	0.8	0.3–1.6	0.39

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acteristics are not directly included in predictions of LOS and complication rates. This is compounded by the fact that the population is aging, and surgeons are operating on patients who are frailer and have more complications (unpublished data).

Surgeries for ASD are known to have high rates of complications. In the Nationwide Inpatient Sample, the overall complication rate was 49%,[5] whereas in a surgeon-maintained database it was 69% (n = 448).[19] In the surgeon-maintained database, rates were as follows: major complications, 39%; radiographic complications, 21%; neurological complications, 20%; implant-related complications, 16%; and infections, 5.4%. In another study of that same database, the rate of medical complications was 27%.[20] Frailty assessments may assist in accurate prediction of risk after spinal surgery and could be invaluable for clinical management and risk stratification.

Many methods of calculating frailty have been proposed and validated. The 3 broad categories of frailty measures are rule-based definitions, summing of impairments, and operational classifications. The frailty index we used in our study, which is an example of summing of impairments, was developed according to the concept that patients who accumulate physiological deficits faster are more frail.[13] Because no specific parameters, like walking speed, need to be measured, we were able to use data that were collected previously. Given the nature of the prospective, multicenter database of patients with ASD used in our study, the frailty index, as proposed by Searle et al.,[18] was selected as the most appropriate model. However, because frailty assessments have been shown to correlate well, the scores from any frailty assessment would probably have similar predictive power for adverse outcomes and could be used for preoperative risk assessment.

Of note, patients with greater frailty had more severe deformity and underwent more complex surgical procedures. It is impossible to determine from this study wheth-

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TABLE 4. Multivariate analysis of outcomes of patients in the ISSG ASD database

Outcomes	OR	95% CI	p Value
Wound dehiscence*			
Allograft used	1.9	0.5–8.0	0.36
BMP used	0.3	0.1–1.2	0.10
Frail vs NF	6.1	0.7–53	0.10
SF vs NF	13.4	1.5–120	**0.02**

BMP = bone morphogenetic protein.
Boldface type indicates statistical significance.
* Statistical analysis performed using multivariate logistic regression.
† For each additional level fused.
‡ For each additional hour of operative time.
§ Statistical analysis performed using multivariate Poisson regression.
¶ Expressed as correlation coefficient.
** For each additional liter of blood lost.

er frailty, which is often associated with low bone density, muscle atrophy, and deconditioning, leads to greater deformity or whether greater deformity, with its associated difficulty with balance and daily activities, leads to greater frailty. Patients who undergo more complex surgical procedures are also known to have higher complication rates. On multivariate analysis, however, frail patients had greater risk of major complications even when controlling for complexity of the procedure, suggesting that frailty is an independent risk factor. Further research on this topic would be beneficial.

A recent study using the modified frailty index developed by the Canadian Study of Health and Aging to analyze patients who had undergone spine surgery and who were entered in the American College of Surgeons National Surgical Quality Improvement Program database showed a strong association between frailty score and complication incidence.[1] Although this study had a large patient population, the use of large national databases has several recognized limitations. First, the use of current procedural terminology[2] codes to identify patients can lead to inclusion discrepancies and does not allow stratification by surgical invasiveness. Second, complication incidence was analyzed for only 30 days after surgery. Third, large national databases have been shown to underestimate complication rates.[10] Fourth, the modified frailty index has not been shown to be an accurate measurement of frailty, because it includes fewer than the validated number of variables.

Our study was designed to address these limitations in a complementary analysis by monitoring a specific patient population for 2 years after surgery and using a more in-depth and disease-specific frailty analysis, which was performed with a validated frailty assessment tool. Our study creates a stronger argument for the incorporation of the frailty index into preoperative risk stratification. Whereas the National Surgical Quality Improvement Program study was limited by a short follow-up period, a less standardized patient population, lack of data on surgical invasiveness, and a modified frailty index, our study had 2 years of follow-up, used surgeon-maintained data from a patient population in whom diagnosis and extent of deformity were known, had surgical invasiveness data that could be used to control for procedure differences when analyzing complication rates, and used a comprehensive frailty index developed using a validated method. However, whereas our study was representative of only patients with ASD undergoing spinal fusion procedures and a comprehensive frailty index, their study had a larger patient population (all spine patients) and a concise index.

Clinical applicability of this study could be challenging because the frailty measurement tool requires documentation of 40 variables and is not weighted by variable. However, because most of the responses were patient generated, this could be integrated into a clinical setting by asking patients to complete the survey in advance as their routine review of systems. Current research is underway investigating the prospective use of the frailty index in a clinical setting. This tool was developed using a validated methodology from geriatrics literature to create a validated tool for frailty assessment with a strong correlation to other frailty measures. In future studies, weighting of variables and decreasing the number of variables required while maintaining accuracy of the frailty measurement achieved with this tool could be pursued. Because frailty indices were initially developed in the field of geriatrics, radiographic measurements were not included in prior indices and were excluded from the ASD-FI. However, recent literature suggests that some radiographic parameters, such as the SVA, increase with age and are potentially related to health status (2 of the criteria for inclusion in a frailty index). In future research, measurements like the SVA could be incorporated into frailty analyses as additional variables.

Conclusions

The ASD-FI was developed according to a validated protocol using the ISSG ASD database. In this database, frail and SF patients had significantly greater odds of incurring major complications than NF patients, as well as higher rates of reoperation and wound infection. These results support the use of the ASD-FI as a component of preoperative risk assessment that would allow the surgeon to counsel patients more effectively on their risk of adverse outcomes after surgery. In addition, this would allow the surgeon to tailor the invasiveness of the surgery on the basis of an accurate assessment of risk of complications. In conclusion, frailty is strongly associated with risk of complications after surgery, and frailty assessments would make a valuable addition to current preoperative risk assessments.

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Assessment of a Novel Adult Cervical Deformity Frailty Index as a Component of Preoperative Risk Stratification

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■ OBJECTIVE: **To determine the value of a novel adult cervical deformity frailty index (CD-FI) in preoperative risk stratification.**

■ METHODS: **We reviewed a prospective, multicenter database of adults with cervical spine deformity. We selected 40 variables to construct the CD-FI using a validated method. Patients were categorized as not frail (NF) (<0.2), frail (0.2–0.4), or severely frail (SF) (>0.4) according to CD-FI score. We performed multivariate logistic regression to determine the relationships between CD-FI score and incidence of complications, length of hospital stay, and discharge disposition.**

■ RESULTS: **Of 61 patients enrolled from 2009 to 2015 with at least 1 year of follow-up, the mean CD-FI score was 0.26 (range 0.25–0.59). Seventeen patients were categorized as NF, 34 as frail, and 10 as SF. The incidence of major complications increased with greater frailty, with a gamma correlation coefficient of 0.25 (asymptotic standard error, 0.22). The odds of having a major complication were greater for frail patients (odds ratio 4.4; 95% confidence interval 0.6–32) and SF patients (odds ratio 43; 95% confidence interval 2.7–684) compared with NF patients. Greater frailty was associated with a greater incidence of medical complications and had a gamma correlation coefficient of 0.30 (asymptotic standard error, 0.26). Surgical complications, discharge disposition, and length of hospital stay did not correlate significantly with frailty.**

■ CONCLUSIONS: **Greater frailty was associated with greater risk of major complications for patients undergoing cervical spine deformity surgery. The CD-FI may be used to improve the accuracy of preoperative risk stratification and allow for adequate patient counseling.**

INTRODUCTION

Chronological age traditionally is used for preoperative risk assessment; however, recent geriatric research has emphasized that people "age" physiologically at different rates. Consequently, biological age may differ from chronological age. The effect of increased biological age has been described using the term "frailty," which is defined as "a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death."[1] Increased frailty has been

Key words
- Adult spinal deformity surgery
- Cervical spine
- Complications
- Frailty
- Individualization
- Risk stratification

Abbreviations and Acronyms
ASE: Asymptotic standard error
CCI: Charlson Comorbidity Index
CD-FI: Cervical deformity frailty index
CFS: Clinical frailty scale
CI: Confidence interval
NF: Not frail
OR: Odds ratio
SF: Severely frail

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shown to be a better predictor of decline in self-management ability than chronological age alone.[2] Although frailty assessments initially were developed as tools to more accurately track aging and predict mortality in nonoperative populations, they have been identified recently in several studies as a better predictor of adverse events after surgery than chronological age alone.[3-5] As the concept of frailty has developed, numerous frailty calculators have been created, studied extensively, and validated. The frailty index proposed by Mitnitski et al.[6] and Searle et al.[7] was developed to facilitate the application of frailty parameters to existing large databases and has a validated methodology for the creation of database-specific frailty indices.

Cervical spine deformity surgery is known to have a high rate of complications and, as such, adequate preoperative evaluation and risk assessment for patients considering surgical correction are essential. In a prospective database of 78 patients, 44% had at least 1 complication and 24% had at least 1 major complication.[8] In patients who underwent 3-column osteotomy in the cervical spine, the complication rate was even greater (60%), and the reoperation rate was 33%.[9] In addition, quality and value metrics are increasingly important in the planning of and payment for modern health care delivery and are based on adequate risk stratification. The development of an index that includes a more comprehensive analysis of patient characteristics will be critical to this process. Given the predictive value of frailty assessments in the preoperative evaluation of patients for trauma surgery, our goal was to create and evaluate an adult cervical deformity frailty index (CD-FI) using the assessment methods of Searle et al.[7] and an existing cervical spine deformity database. To determine the value of incorporating this frailty assessment into preoperative risk stratification, we examined the CD-FI for correlation with complication rate, length of hospital stay, and discharge disposition. We hypothesized that increasing CD-FI scores would be associated with increased complication rates, longer hospital stays, and discharge to a care facility rather than home.

METHODS

Patient Population

We used a multicenter, prospective database maintained by the International Spine Study Group of U.S. patients with adult cervical spine deformity to develop a frailty index. Institutional review board approval for patient inclusion in this database was obtained by each of the sites that contributed patient information. Each patient signed a consent document before inclusion. Inclusion criteria for patients in this database were the following: surgery between 2009 and 2015 for adult cervical spine deformity defined as cervical scoliosis (C2–C7 major curve angle $\geq 10^\circ$) or cervical kyphosis (C2–C7 major curve angle $>10^\circ$), aged ≥ 18 years, and minimum 1-year follow-up. Although some frailty studies[6,7] have excluded patients aged <60 years, we included all patients because frailty is meant to be a measure of physiologic rather than chronologic age.

Frailty Index Development

All variables in the cervical deformity database were reviewed, and those that met criteria for inclusion in the frailty analysis ($n = 40$), as determined by Searle et al.,[7] were included in the CD-FI (Table 1). Each deficit in health was recorded as a binary variable (e.g., presence vs. absence of osteoporosis). The mean score of all of these deficits was calculated, giving a CD-FI score ranging from 0 to 1 point. Patients with scores <0.2 were considered not frail (NF), those with scores of 0.2–0.4 were considered frail, and those with scores >0.4 were considered severely frail (SF). These ranges were chosen on the basis of precedent in the literature and adjusted to ensure adequate numbers of patients in each category for statistical evaluation.

Data Analysis

The primary study outcome was incidence of major complications. The secondary outcomes were length of hospital stay, discharge disposition, and medical/surgical complication rates. Major complications were defined as complications that were potentially life-threatening, required reoperation, or created permanent injury, as recommended by Glassman et al.[10,11]; these included intraoperative vascular, visceral, or neurologic injury, postoperative deep infection, pulmonary embolisms, and junctional failure.[11] Surgical complications included most intraoperative complications and immediate postoperative complications related to surgical technique/error. Medical complications included those unrelated to surgical technique, including stroke, deep venous thrombosis, pulmonary embolism, pneumonia, and urinary tract infection.

Statistical Analysis

All statistical analyses were performed with Small Stata, version 14.1, software for Mac (StataCorp LP, College Station, Texas, USA). First, univariate linear regression (for continuous variables) and logistic regression (for binary variables) of all independent variables was performed, followed by multivariate analysis of all independent variables found to have $P < 0.3$. Variables were eliminated until the maximum supportable number of variables was reached ($n = 5$).

RESULTS

Baseline Characteristics

Of the 61 patients (37 women) with minimum 1-year follow-up, the mean CD-FI score was 0.26 (range 0.25–0.59). Seventeen patients were categorized as NF, 34 as frail, and 10 as SF. Race, sex, and age were not significantly different among the 3 groups ($P > 0.05$) (Table 2). Surgical procedures, including number of spinal levels fused, surgical approach, use of preoperative traction, and performance of vertebral column osteotomies, were similar for all patients ($P > 0.05$) (Table 2). Operative time, admission to the intensive care unit after surgery, and discharge disposition were also similar among the 3 groups ($P > 0.05$) (Table 2).

Major Complications

The incidence of major complications increased with increasing frailty, with a gamma correlation coefficient of 0.25 (asymptotic standard error [ASE], 0.22) (Figure 1). The unadjusted odds of having a major complication were greater for frail patients (odds ratio [OR] 1.1; 95% confidence interval [CI], 0.3–3.8) and SF patients (OR 2.8; 95% CI, 0.6–14) compared with NF patients;

Table 1. Factors Included in the Adult Cervical Spinal Deformity Frailty Index

Current Health Deficits
Documented by physician
>3 medical problems
Anxiety
Body mass index <18.5 or >30
Cancer
Cardiac disease
Cerebrovascular disease
Currently receiving disability benefits
Dementia
Depression
Diabetes
Liver disease
Lung disease
Neuromuscular disease
Osteoporosis
Pancreatic disease
Rheumatoid arthritis
Smoker
Vascular disease
Venous disease
Unsteady gait
Patient-reported (questionnaire, question no.)
Bladder incontinence
Bowel incontinence
Difficulty driving (NDI, 8)
Difficulty getting dressed (mJOA)
Difficulty reading (LSDI, 4)
Difficulty sleeping >6 hours (LSDI, 9; SWAL-QOL, 9b/d)
Difficulty walking without assistive device (mJOA)
Feeling anxious or depressed most of the time (EQ-5D-3L)
Feeling tired most of the time (SWAL-QOL, 9c)
Feeling weak most of the time (SWAL-QOL, 9a)
Feeling worn out/exhausted most of the time (SWAL-QOL, 9e)
General health <50 (EQ VAS)
Inability to concentrate (LSDI, 6)
Inability to do normal work/schoolwork/housework (NDI, 7)
Inability to engage in normal recreational activity (LSDI, 10)
Inability to lift heavy objects (LSDI, 3)
Inability to perform normal activities (EQ-5D-3L)
Inability to walk (EQ-5D-3L)
Leg weakness
Personal care dependency (LSDI, 2)

NDI, Neck Disability Index; mJOA, modified Japanese Orthopaedic Association scale; LSDI, Lumbar Stiffness Disability Index; SWAL-QOL, Quality of Life in Swallowing Disorders questionnaire; EQ-5D-3L, EuroQol, 5 Dimension, 3 Level; EQ VAS, EuroQol visual analogue scale.

however, these differences were not statistically significant ($P > 0.05$) (Table 3). On multivariate logistic regression (Table 4), the odds of having a major complication were significantly greater for SF patients (OR 43; 95% CI, 2.7–684; $P < 0.01$) compared with NF patients. Overall, greater frailty was associated with greater odds of having a major complication (OR 7.6; 95% CI, 1.5–38.4; $P < 0.02$). A similar analysis was performed with the Charlson Comorbidity Index (CCI). On univariate analysis, the odds of developing a major complication increased by 1.1 for each 1-point increase in CCI score ($P = 0.68$). On multivariate analysis, with each 1-point increase in CCI score, the odds of developing a major complication increased 3.26-fold, but this was not statistically significant ($P = 0.06$). Only 8 patients with CCI scores >1 underwent surgery.

Other Outcomes of Interest

A greater incidence of medical complications correlated with greater frailty and had a gamma correlation coefficient of 0.30 (ASE, 0.26). In contrast, the surgical complications were not correlated with greater frailty (gamma correlation coefficient −0.06; ASE, 0.28) (Figure 1). Approximately 60% of patients in each frailty cohort were discharged to home rather than to an inpatient rehabilitation or skilled nursing facility. Length of hospital stay did not correlate significantly with frailty (Table 2).

DISCUSSION

Although limited by a relatively small sample size, this study revealed a significant correlation between increasing frailty and increasing risk of major complications. Medical complications, as anticipated, were more highly correlated with frailty than were surgical complications. Surprisingly, length of hospital stay and discharge disposition were not correlated with degree of frailty in this study. This could be attributable to inadequate sample size. In addition, length of hospital stay varies substantially by institution, and discharge disposition depends largely on patient insurance and institution, which could have confounded our results.

As the U.S. population ages and surgical techniques improve, the surgical candidate population is also aging, especially in fields such as adult spinal deformity surgery. Many patients evaluated as surgical candidates today are older than those who would have

Table 2. Characteristics of 61 Patients with Adult Cervical Spine Deformity by Frailty Status, International Spine Study Group Adult Spinal Deformity Database

	Not Frail (n = 17)		Frail (n = 34)		Severely Frail (n = 10)		
Characteristic	**Mean (SD)**	**No. (%)**	**Mean (SD)**	**No. (%)**	**Mean (SD)**	**No. (%)**	***P* Value**
Age at surgery, years	58 (2.7)		62 (1.9)		63 (3.6)		0.38*
Female sex (vs. male)		10 (59)		20 (59)		7 (70)	0.80†
White race (vs. other)		17 (100)		32 (94)		8 (80)	0.12†
Body mass index	25 (1.6)		30 (1.4)		33 (2.6)		0.03*
Patient independent at baseline‡		16 (94)		31 (94)§		8 (89)§	0.85†
Procedure							
Operative time, hours	8.1 (1.5)		11 (1.5)		12 (4.8)		0.49*
Estimated blood loss, L	0.6 (0.2)		1.1 (0.2)		1.8 (0.1)		0.91*
Three-column osteotomy		3 (18)		1 (2.9)		0	0.09†
No. of instrumented vertebrae	9.6 (1.4)		8.4 (0.5)		7.7 (0.6)		0.80*
≤4		3 (21)		1 (3.3)		1 (11)	
5–8		3 (21)		18 (60)		5 (56)	
9–12		4 (29)		8 (27)		3 (33)	
≥13		4 (29)		3 (10)		0	
Approach							0.94†
Anterior only		3 (18)		4 (12)		1 (10)	
Posterior only		8 (47)		15 (44)		6 (60)	
Posterior and anterior		6 (35)		15 (44)		3 (30)	
Complications							
Major		6 (35)		13 (38)		6 (60)	0.40†
Medical		3 (18)		7 (21)		4 (40)	0.36†
Surgical		5 (29)		6 (18)		3 (30)	0.54†
Admission to ICU postoperatively		12 (71)		26 (76)		9 (90)	0.51†
Length of hospital stay, d	8.4 (12)		6.9 (7.7)		9.5 (10)		0.66*
Discharge to home		10 (59)		20 (59)		6 (60)	1.00†

SD, standard deviation; ICU, intensive care unit.
*From Kruskal-Wallis H test.
†From Pearson χ^2 test.
‡Patient-reported independence for all activities of daily living.
§Data missing from 1 patient.

been considered appropriate surgical candidates at an earlier time.[12] This changing demographic composition mandates increased attention to the effect of aging on surgical care. Although advanced age has been shown to be a risk factor for complications, longer hospital stays, and overall worse outcomes, many patients who present for surgery may have a much older or younger biological age than their chronological age. This difference in biological age is now being quantified through the concept of frailty.[1-7,13-17] Several studies have shown that greater frailty is predictive of poor postoperative outcomes in the general surgery patient population.[3-5] In addition, frailty has been shown to accelerate the development of sarcopenia, a progressive loss of skeletal muscle mass, strength, and power caused by the adverse neurologic, endocrine, nutritional, and immune components of frailty, which disrupt muscle homeostasis.[14]

Many methods of calculating frailty have been proposed and validated. Physicians are able to choose the method that best works for their patient population. Currently, frailty assessments can be grouped into the following 3 categories: rule-based definitions, summing of impairments, and operational classifications.

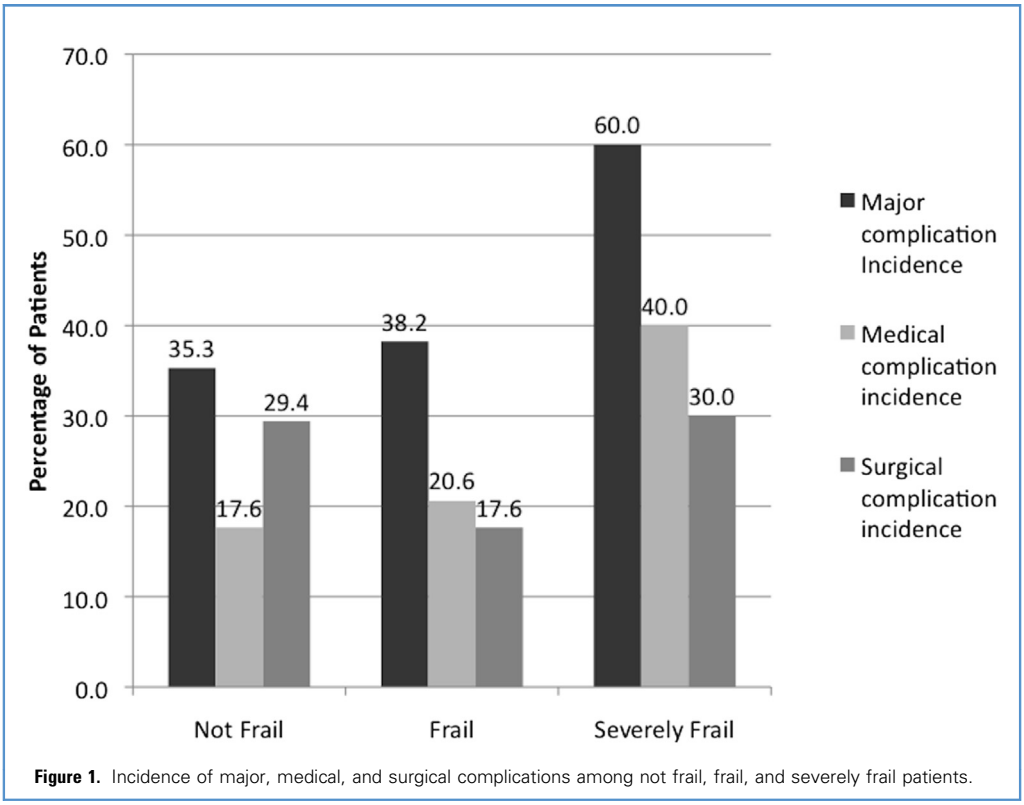

Figure 1. Incidence of major, medical, and surgical complications among not frail, frail, and severely frail patients.

The most commonly used rule-based definition of frailty is the Fried frailty phenotype. Patients must score positively on 3 of the following 5 criteria: unintentional weight loss (≥10 pounds or ≥5% of body weight in the previous year), feeling exhausted, weak grip strength (below the 20th percentile by dynamometer adjusted for sex and body mass index), slow walking speed (below the 20th percentile measured on clinical examination and adjusted for sex and height), and low level of physical activity (patients in the lowest quartile in terms of kilocalories expended per week). Although this phenotype is well researched and validated, the key disadvantages to this model are the necessity to measure grip strength and walking speed in the clinical setting to assess frailty and the exclusive focus on physical frailty without analysis of other systems (i.e., cognition), which also may be affected.[15]

Frailty also can be calculated by summing patient-reported impairments. The frailty index is based on the concept that patients who accumulate physiological deficits faster are frailer. The index is expressed as a ratio of health deficits present to the total number of deficits considered. For example, if 40 deficits were considered and 10 were present, the frailty index would be 10/40 or 0.25.[6] The key advantage of the frailty index is that Searle et al.[7] proposed and validated a method to assess frailty in any existing patient database by creating a frailty index with the following 5 rules: variables whose prevalence increases with age are selected (e.g., heart disease); only variables related to health can be included (e.g., gray hair would be excluded); variables are eliminated if the prevalence saturates too early (e.g., presbyopia would be excluded because it is nearly universal by age 55 years); the variables selected cover a range of systems, including motility, activities of daily living, independence, cognitive function, mood, and comorbidities; and at least 30 distinct variables meeting all these qualifications need to be included. In a series of 1000 iterations, the slope of deficit accumulation (0.03 per year) and the submaximal limit at approximately two-thirds of the deficits tested were insensitive to the precise composition of the index.[7] The frailty phenotype and frailty index have been shown to overlap in their identification of frailty and have notable statistical convergence,[13,16] indicating that the models are comparable in terms of their ability to measure frailty.

Table 3. Univariate Analysis of Complications of 61 Patients with Adult Cervical Spine Deformity, International Spine Study Group Adult Spinal Deformity Database

	Frail vs. Not Frail		Severely Frail vs. Not Frail	
Complication Type	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Major	1.1 (0.3–3.8)	0.84	2.8 (0.6–14)	0.22
Medical	1.2 (0.3–5.4)	0.80	3.1 (0.5–18)	0.21
Surgical	0.5 (0.1–2.0)	0.34	1.0 (0.2–5.7)	0.97

OR, odds ratio; CI, confidence interval.

Table 4. Multivariate Analysis of Major Complication Incidence of 61 Patients with Adult Cervical Spine Deformity, International Spine Study Group Adult Spinal Deformity Database

Variable	OR (95% CI)	*P* Value
Three-column osteotomy	10 (0.4—259)	0.17
Posterior-only approach (vs. other)	2.2 (0.8—5.7)	0.11
Frail (vs. not frail)	4.4 (0.6—32)	0.14
No. of levels fused*	1.3 (1.1—1.7)	0.01
Previous cervical spine surgery	0.2 (0.0—0.9)	0.04
Severely frail (vs. not frail)	43 (2.7—684)	0.01

OR, odds ratio; CI, confidence interval.
*For each additional level fused.

A third category of frailty calculation, termed operational classification, is designed for clinicians with substantial experience evaluating frailty and requires obtaining large amounts of demographic data from patients. Rockwood's operational classification, the Clinical Frailty Scale (CFS), is based on the clinician's judgment of the patient's degree of frailty scored from 1 (very fit: robust, active, energetic) to 7 (severely frail: completely dependent on others for activities of daily living).[17] In a 5-year prospective cohort in which the CFS score was determined at the first visit by family physicians, internists, geriatricians, neurologists, and psychiatrists who had been involved in previous frailty research, the CFS score had a high degree of correlation with the frailty index and frailty phenotype (Pearson coefficient 0.80, $P < 0.01$). However, the physicians scoring the CFS had access to a substantial amount of patient background data and had performed frailty assessments in the past. This type of frailty assessment based on physician judgment may not be as reliable if conducted during routine surgical specialist appointments when there is little time for a thorough assessment of general health and fitness and when the physician has limited experience with other frailty scales. Given the nature of the prospective, multicenter adult cervical spine deformity database used in this study, we selected the frailty index proposed by Searle et al.[7] as the most appropriate model.

Spinal deformity surgery is known to have a high rate of complications. Smith et al.[8] showed that the complication rate in cervical spine deformity surgery was 44% and the rate of major complications was 24%. The authors of this study defined major complications as reported by Glassman et al.[10,11] Quality and value metrics based on preoperative risk stratification are becoming increasingly important for payment for modern health care delivery; therefore, adequate preoperative risk assessment is necessary, especially in fields with high complication rates, such as cervical spine deformity surgery. Although comorbidities are recorded in admission diagnoses, they are not currently accounted for in the standard expected length of hospital stay and anticipated complication rates. Therefore, the development of a new metric that includes a more comprehensive analysis of patient characteristics, such as the CD-FI, is critical to the process of risk stratification. This study showed that the CD-FI score correlated with complication rates. The odds of developing a major complication for SF patients were significantly greater than those of NF patients in our multivariate analysis. The rate of medical complications also was associated with frailty. Given these results, frailty assessment appears to be a valuable component of preoperative risk assessment, which would allow the surgeon to counsel patients more effectively on their risk of adverse outcomes after surgery. By assessing the degree of frailty, the surgeon would be able to inform patients of their degree of risk relative to patients who are not frail. This also would allow the surgeon to modify the invasiveness of the surgery accordingly.

Limitations

This study has several limitations, including a small sample size. The large standard errors and CIs in the multivariate analyses are likely a result of the small sample size. Only 61 patients had at least 1-year follow-up and, of those, only 10 were severely frail. Although this study shows a significant increase in the incidence of major complications with greater frailty, further analysis with additional patients is required to better analyze the effect of frailty on the secondary outcome measures. In addition, patients in this study were undergoing cervical spine deformity surgery. The degree of concordance with patients undergoing cervical spine surgery who do not have cervical deformity has not been studied. Another limitation is that the CD-FI is difficult to use in the clinical setting, given the number of deficits ($n = 40$) needed to calculate the score. In future studies, this model will be adapted to evaluate the validity of a smaller, less cumbersome model that can be used in the clinical setting.

CONCLUSIONS

This study shows an association between frailty and incidence of major complications after adult cervical spine deformity surgery, which is stronger than that between CCI score and major complication incidence. This suggests that using the CD-FI as part of risk stratification may improve predictions of complication rates. Prospective studies are underway to examine the various measurements included in other frailty assessments, such as laboratory values and strength measurements, to determine the most valuable metrics to create a simplified yet equally effective frailty model. Alternatively, during preoperative evaluations by primary care physicians, frailty assessments can easily be conducted during the examination. Frailty indices have been shown to correlate well with the frailty phenotype and CFS; therefore, the score from any frailty assessment would likely have similar predictive power for adverse outcomes and could be used for preoperative risk assessment.

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Review Article

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

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Abstract

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

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

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

FDA device/drug status: Not applicable

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

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Introduction

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

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

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

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

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

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

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

Methodology

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

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

Eligibility criteria

All articles included in our review were published in the English language between January 1st, 1950 and August

21st, 2017 and if they met the following eligibility criteria:

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

Studies were excluded if:

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

Search strategy

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

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

Results

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

Measures identified

Frailty measures

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

Sarcopenia measures

Morphometrics is assessed on axial imaging on CT or MRI imaging modalities to determine psoas muscle area (mm^2) at either the level of L3 or L4 [23–26]. Right and left psoas areas are combined to create the total psoas area (TPA). TPA's can be stratified in tertiles to categorize sarcopenia severity [23,24]. Further normalization of TPA's against Vertebral Body Area (VBA) (mm^2) is an alternative measure when compared by quartiles for identifying sarcopenia [26]. Charest-Morin et al. 2017 standardized psoas areas against patient height (m^2) to create the normalized total psoas area (NTPA) (mm^2/m^2) [25]. Three studies utilizing morphometrics carried out inter-rater observations to ensure accurate collection of musculoskeletal measurements [24–26].

Outcome databases

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

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

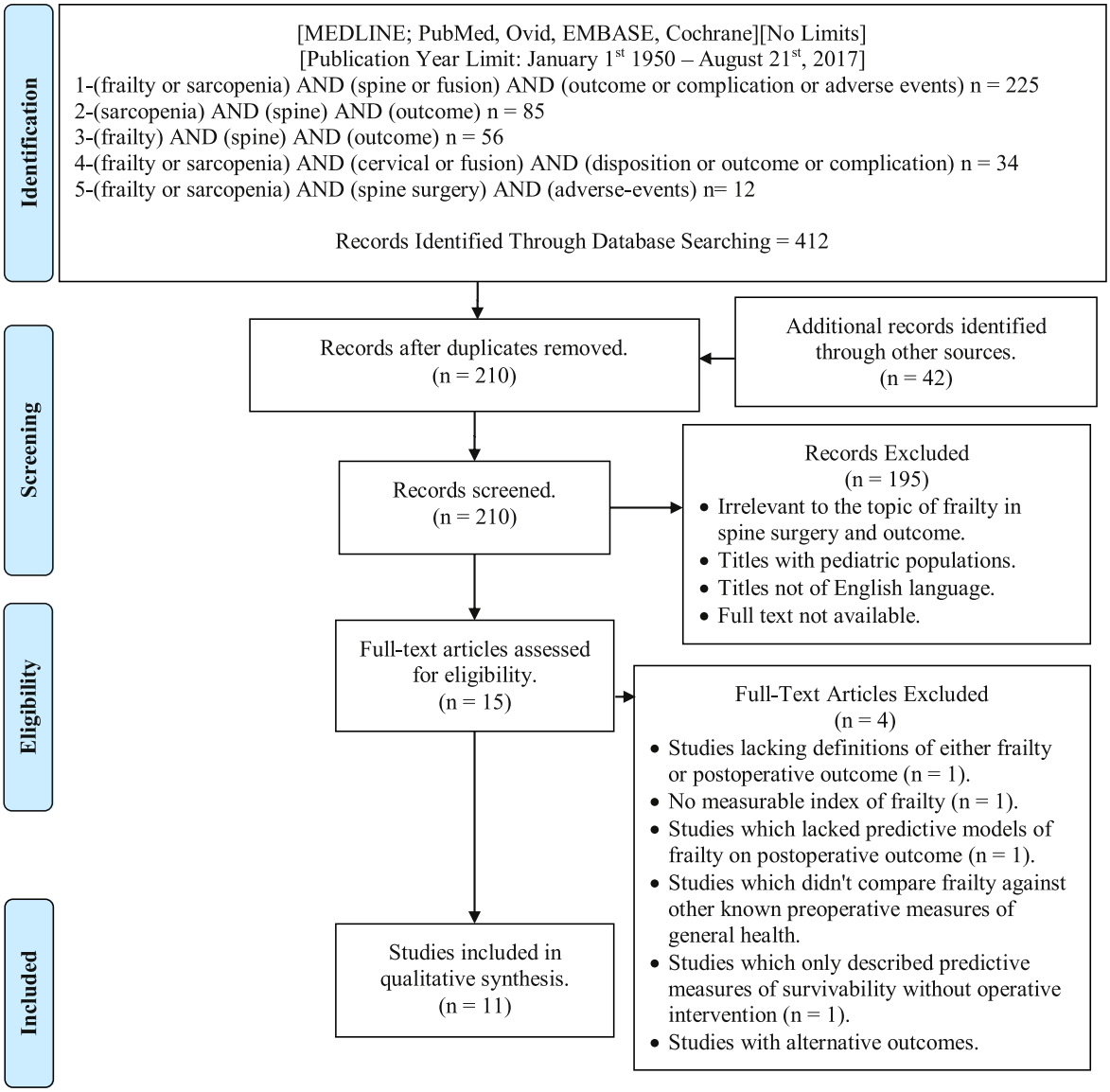

Figure. Electronic search strategy.

demographics, International Classification of Diseases version 9 (ICD-9) codes, Current Procedure Terminology (CPT) codes, medical and surgical data including intraoperative and postoperative complications.

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

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

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

Reported outcomes

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

Frailty studies

We identified seven studies, all retrospective, using clinical measures of frailty to stratify frailty severity and

Table 1
Measures of frailty identified in adult spine surgery literature

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

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

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

Abbreviations: Canadian Study of Health and Aging Frailty Index (CSHA-FI), Modified Frailty Index (mFI), Frailty Basic Score (FBS), Metastatic Spinal Tumor Frailty Index (MSTFI), Adverse Events (AEs), Body Mass Index (BMI)

Table 2
Summary of included studies on frailty and adult spine surgery

Articles	N	Outcome Database	Population /Procedure	Frailty measure	Primary outcomes of study	Adjusted outcomes	Potential bias(es)
Flexman et al. [16]	52,671	ACS-NSQIP	Degenerative spine population /All procedures	mFI	30-Day mortality 30-day morbidity LOS Discharge disposition	30-day mortality OR: 1.44 (95% CI:1.15−1.81 p<.005)* 30-day morbidity OR: 1.15 (95% CI:1.09−1.21 p<.0005) * Increased In-Hospital LOS OR:1.27 (95% CI:1.19−1.35 p<.0005) * Discharge to center of higher care OR: 1.32 (95% CI:1.24−1.40 p<.0005) *	Selection bias Sample bias
Leven et al. [17]	1,001	ACS-NSQIP	Adult spinal deformity/Posterior fusion ≥ 3 levels or anterior fusion ≥4 levels or combined anterior-posterior approach	mFI	30-day mortality 30-day major and minor morbidity 30-day composite AEs	30-day crude mortality rate (%): • mFI score: 0 → ≥0.27=0.3% → 10.0% (P=.001) 30-day major and minor morbidity rate (%): • mFI Score: 0 → ≥ 0.27=35% → 60% (P=.002) 30-day composite adverse event (OR): • mFI 0.09 versus 0: OR 1.7 (95% CI: 1.3−2.2 P<.0001) • mFI ≥ 0.18 versus 0: OR 1.6 (95% CI: 1.1−2.4 P=.010)	Selection bias Sample bias
Ali et al. (18)	18,294	ACS-NSQIP	Not specified/All procedures	mFI	30-day mortality 30-day major and morbidity	30-Day Crude Mortality Rate (%): • mFI Score: 0 → ≥ 0.27 = 0.1% → 2.3% (p<.001) 30-day crude major morbidity rate (%): • mFI Score: 0 → ≥ 0.27=0.8% → 7.1% (p<.001)	Selection bias Sample bias
Phan et al. (19)	3,920	ACS-NSQIP	Degenerative lumbar spine population/ ALIF	mFI	30-day composite AEs 30-day mortality	30-day mortality (OR): • mFI 0.09 versus 0: OR 3.9 (95% CI: 0.4−38.2 p=.996) • mFI 0.18 versus 0: OR 3.1 (95% CI: 0.2−52.4 p=.774) • mFI 0.27 versus 0: OR 19.5 (95% CI: 1.0−387.8 p=.077) 30-Day Composite AEs (OR): • mFI 0.09 versus 0: OR 1.2 (95% CI: 0.9−1.5 p=.063) • mFI 0.18 versus 0: OR 1.4 (95% CI: 1.1−2.0 p=.831) • mFI 0.27 versus 0 OR 2.4 (95% CI: 1.2−4.6 p=.040) In-Hospital LOS > 5 Days (OR): • mFI 0.09 versus 0: OR 1.3 (95% CI: 1.1−1.6 p=.854) • mFI 0.18 versus 0: OR 1.4 (95%CI: 1.1−1.9 p=.590) • mFI 0.27 versus 0: OR 1.7 (95% CI: 0.9−3.3 p=.350)	Selection bias Sample bias Post-Hoc bias
Shin et al. (20)	6,965	ACS-NSQIP	Degenerative cervical spine population /Cervical fusion	mFI	30-day composite AEs 30-day major morbidity	30-day mortality rates (%): • ACDF mFI Score 0 → ≥ 0.27=0.1% → 3.0% (P<.001) • PCF mFI Score 0 → ≥ 0.36=0.0% → 10.0% (P<.001) 30-day composite AEs crude rate (%): • ACDF mFI Score 0 → ≥ 0.27=2.0% → 9.0% (P<.001) • PCF mFI Score 0 → ≥ 0.36=4.1% → 35.0% (P<.001) 30-day major morbidity ACDF Cohort (OR): • mFI 0.09 versus 0: OR 1.34 (95%CI: 0.74−2.41 P=.065)	Selection bias Sample bias

(*continued on next page*)

Table 2 (***Continued***)

Articles	N	Outcome Database	Population /Procedure	Frailty measure	Primary outcomes of study	Adjusted outcomes	Potential bias(es)
						• mFI: 0.18 versus 0: OR 2.15 (95%CI: 1.12−4.12 P=.578) • mFI ≥ 0.27 versus 0: OR 4.67 (95% CI: 2.27−9.62 P<.001) 30-day major morbidity PCF Cohort (OR): • mFI 0.09 versus 0: OR 3.69 (95%CI: 0.75−18.06 P=.185) • mFI 0.18 versus 0: OR 6.10 (95%CI: 1.22−30.41 P=.975) • mFI 0.27 versus 0: OR 9.68 (95%CI: 1.51−61.95 P=.395) • mFI ≥ 0.36 versus 0: OR 41.26 (95% CI: 6.62−257.15 P<.001)	
Medvedev et al. (21)	5,627	ACS-NSQIP	Degenerative and metastatic cervical pathology/PCF or combined ACDF and PCF	FBS	30-day composite AEs	30-day composite AEs OR: 1.78 (95% CI: 1.61−1.96 p<.0001)†	Selection bias Sample bias
De La Garza Ramos et al. (22)	4,583	NIS	Metastatic spine population/All procedures	MSTFI	30-day mortality 30-day minor and major morbidity In-hospital LOS	30-day mortality rate (%): • MSTFI Score of 0 → 5: 1.0% to 9.6% (P<.001) 30-day mortality (OR): • MSTFI Score of 2 versus 0: OR 5.15 (95% CI:2.44−10.86 P<.001) • MSTFI Score of ≥ 3 versus 0: OR 5.74 (95% CI:2.69−12.24 P<.001) 30-day morbidity rate (%): • MSTFI Score of 0 → 7: 6.7% to 100% (P<.001) 30-day morbidity (OR): • MSTFI Score of 1 versus 0: OR: 1.88 (95% CI: 1.33−2.66 P<.001) • MSTFI Score of 2 versus 0: OR: 3.83 (95% CI: 2.71−5.41 P<.001) • MSTFI Score of ≥ 3 versus 0: OR: 6.97 (95% CI: 4.98−9.74 P<.001) In-hospital LOS (Days): • MSTFI Score of 1 versus 0: LOS 3.3±0.4 Days (P<.001) • MSTFI score of 2 versus 0: LOS: 5.6±0.4 Days (P<.001) MSTFI score of ≥ 3 versus 0: LOS 6.4±0.4 Days (P<.001)	Selection bias Sample bias Misclassification bias Ascertainment Bias

* Per 0.10 increase in mFI score.

† Per one unit increase in FBS score.

Abbreviations: American College of Surgeon - National Surgical Quality Improvement Program (ACS-NSQIP), Anterior Lumbar Interbody Fusion (ALIF), Anterior Cervical Discectomy and Fusion (ACDF), Posterior Cervical Fusion (PCF), Posterior Lumbar Interbody Fusion (PLIF), Modifiable Frailty Index (mFI), Frailty Basic Score (FBS), Metastatic Tumor Frailty Index (MSTFI), Length of Stay (LOS), Adverse Events (AEs), Odds Ratio (OR), Confidence Interval (CI); Nationwide Inpatient Sample (NIS) Database

Table 3
Summary of included studies on sarcopenia and adult spine surgery

Articles	N	Outcome Database/ Design	Population/ Procedure	Sarcopenia measure	Primary outcomes of study	Adjusted outcomes	Quality of evidence
Gakhar et al. [26]	86	Single center/ Ambispective	Thoracolumbar procedures for metastatic spine disease	NTPA and TPA/ VB Ratio at L3 on CT scan	1-year mortality	1-year mortality rate‡ • Sarcopenia: 57.1% (p=.02) • NonSarcopenia: 23.8% (p=.02)	Selection bias
Zakaria et al. [23]	395	Single Center HFHS/ Retrospective	Thoracolumbar procedures: laminectomy- lumbar arthrodesis and lumbar interbody arthrodesis	TPA at L4 and Paraspinous at T12 on MRI	90-day composite AEs	90-day composite AEs OR: 1.70 (95% CI:1.04−2.79 p=.035)* • Male OR: 2.42 (95% CI: 1.17−5.01 p=.016)* • Female OR: 1.22 (95% CI: 0.62−2.43 p=.564)*	Measurement bias Sample bias
Bokshan et al. [24]	46	Single center/ Retrospective	Thoracolumbar procedures including scoliosis surgery, fracture, degenerative and infection	TPA at L4 on CT scan	30-day AEs 30-day major and minor morbidity Discharge disposition In-hospital LOS	In-hospital LOS (Days)* • Sarcopenia: 8.1±1.5 (P=.02) • NonSarcopenia: 4.7±0.9 (CI: P=.02) 30-day composite AEs (No.)* • Sarcopenia: 1.2±0.3 (P=.02) • NonSarcopenia: 0.4±0.2 (P=.02) 30-day major morbidity (No.)* • Sarcopenia: 0.3±0.2 (P=.04) • NonSarcopenia 0.03±0.1 (P=0.04) Discharge to center of higher care (Rate)* • Sarcopenia: 81.2% (P=.006) • NonSarcopenia: 43.3% (P=.006)	Selection bias Sample bias
Charest-Morin et al. (25)	102	Single Center SAVES/ Ambispective	Elective noncomplex degenerative lumbar spine procedures	NTPA at L3 on CT scan	30-day composite AEs 30-day mortality Discharge disposition	30-day composite AEs OR: 1.06 (95% CI: 0.91−1.23 P=.45)† 30-day mortality OR: 1.12 (95% CI: 0.83−1.53 P=.47) † Discharge to center of higher care OR: 0.95 (95% CI: 0.76−1.20 P=.70) †	Selection bias Sample bias

* Total Psoas Areas (TPA): Lowest tertile vs. middle and highest TPA tertiles.

† Per 100 mm^2/m^2 in NTPA.

‡ Total Psoas Area (TPA)/Vertebral Body Area (VB) Ratio: Lowest quartile vs. high quartile.

Abbreviations: Length of Stay (LOS), Adverse Events (AEs), Odds Ratio (OR), Confidence Interval (CI). Spine AdVerse Events Severity (SAVES) system; Henry Ford Health System (HFHS), Magnetic Resonance Imaging (MRI), Computed Tomography (CT), Total Psoas Area (TPA), Normalized Total Psoas Area (NTPA), Vertebral Body (VB), Total Psoas Area - Vertebral Body Ratio (TPA/VB)

quantify its predictive effect on postoperative AEs [16–22]. Five articles used mFI while the last two articles used FBS and MSTFI respectively to quantify frailty severity. All studies reported a positive relationship between frailty and its impact on postoperative AEs. Our expert panel determined all seven articles included in this review, which utilized clinical measures of frailty, were a GRADE score of *very low* for their quality of evidence.

30-day postoperative mortality

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

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

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

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

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

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

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

30-day postoperative morbidity and composite AEs

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

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

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

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

Flexman et al. found in patients undergoing all spinal procedures for degenerative spinal conditions, that for every incremental increase in mFI score by 0.10, the likelihood of 30-day postoperative morbidity increased by OR 1.15 (95% CI:1.09– 1.21 p<.0005) after multivariable analysis [16].

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

Likewise, Phan et al. found in patients undergoing ALIF procedures for degenerative spinal conditions, that the frail cohort with mFI scores ≥0.27 were associated with a higher

likelihood 30-day postoperative composite AEs of OR 2.4 (95% CI:1.2–4.6 p=.04) compared to the nonfrail cohort after multivariable analysis [19]. However, within the mild (mFI=0.09) and moderately (mFI=0.18) frail populations, adjusted regression did not demonstrate frailty to be an independent risk factor for experiencing AEs when compared against the nonfrail population [19].

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

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

In-hospital LOS and discharge disposition

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

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

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

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

Bias across frailty studies

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

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

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

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

observed in Phan et al. for the following postoperative AEs of in-hospital LOS and wound complications.

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

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

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

Sarcopenia studies

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

30-day postoperative mortality rates

Only one study by Charest-Morin et al. reported on the association between sarcopenia and its impact on 30-day postoperative mortality [25]. The study did not report a statistically significant increase in 30-day postoperative AEs within the lowest psoas area values [25]. Charest-Morin et al. studied 102 patients undergoing elective surgery for degenerative spine disease and did not identify sarcopenia as an independent risk factor for predicting 30-day postoperative mortality OR: 1.06 (95% CI: 0.91−1.23 P=.45) per 100 mm^2/m^2 in NTPA after multivariable analysis [25].

1-year mortality

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

30-day and 90-day major and minor morbidity

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

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

Similarly, Zakaria et al. studied 395 patients undergoing posterior lumbar interbody fusion (PLIF) procedures for all spinal pathologies. They found patients within the lowest quartile of TPA, as sarcopenic, experienced a higher likelihood of 90-day postoperative AEs OR 1.70 (95% CI: 1.04−2.79 p=.035) when compared against the middle and upper quartiles after multivariable analysis [23]. In the female population of 203 patients, morphometrics was not

associated for predicting 90-day postoperative AEs after adjustment OR 1.22 (95% CI: 0.62–2.43 p=.564) [23]. Conversely, in the male population of 192 patients, an increase of AEs was seen in the lowest quartile of TPA (adjusted odds ratio of OR 2.42 (95% CI: 1.17–5.01 p=.016)) when compared against the middle and upper TPA quartiles [23].

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

In-hospital LOS and discharge disposition

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

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

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

Bias across sarcopenia studies

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

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

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

Discussion

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

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

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

likely reflective of variability in surgical indications and procedures between studies. We believe this is a significant challenge in adapting the use of frailty to different populations in the clinical setting.

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

Recommendations

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

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

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

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

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

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

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

When TPA was normalized against body height (m^2) to form the NTPA (mm^2/m^2) no association with adverse outcome was identified. Possible explanations included that it was a relatively healthy population, surgical intervention(s) were noncomplex spine surgery and a low adverse event rate was observed. Also, it was postulated that underlying degenerative spinal pathology might negatively influence the musculature to avert risk estimation based on this measurement. Such a theory is seen in patients with degenerative scoliosis and degenerative disc disease where psoas areas were atrophied bilaterally or unilaterally on the symptomatic side respectively [31,32].

Recommendations

The TPA is an acceptable form of assessing frailty (*strong recommendation, very low quality of evidence*) in the context of adult spine surgery. The TPA was proven to be a robust measure of frailty by its ability to identify sarcopenic populations amongst the spinal population. As well, TPA reported consistent predictive effects on postoperative AEs. However, the inability to determine cutoff values diagnostic of sarcopenia suggests TPA requires further validation and/or standardization prior to being a gold standard method of assessing frailty.

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

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

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

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

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

Limitations of our study

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

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

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

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

Our study identifies a need for prospective studies which report defined cut-off values for frailty and sarcopenia that are comparable and transferable between different spinal populations. We also recommend future studies to report on common end-points which are comparable and allow for the construction of a meta-analysis. Furthermore, future studies are needed to identify the relationship between

spinal pathology and frailty or sarcopenia in order gain a better understanding of frailty and its predictive effect on postoperative outcomes in the context of spinal surgery.

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

Conclusion

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

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

Supplementary materials

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

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Original Article

Effect of Frailty on Outcome after Traumatic Spinal Cord Injury

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Abstract

Frailty negatively affects outcome in elective spine surgery populations. This study sought to determine the effect of frailty on patient outcome after traumatic spinal cord injury (tSCI).

Patients with tSCI were identified from our prospectively collected database from 2004 to 2016. We examined effect of patient age, admission Total Motor Score (TMS), and Modified Frailty Index (mFI) on adverse events (AEs), acute length of stay (LOS), in-hospital mortality, and discharge destination (home vs. other). Subgroup analysis (for three age groups: <60, 61–75, and 76+ years), and multi-variable analysis was performed to investigate the impact of age, TMS, and mFI on outcome.

For the 634 patients, the mean age was 50.3 years, 77% were male, and falls were the main cause of injury (46.5%). On bivariate analysis, mFI, age at injury, and TMS were predictors of AEs, acute LOS, and in-hospital mortality. After statistical adjustment, mFI was a predictor of LOS ($p = 0.0375$), but not of AEs ($p = 0.1428$) or in-hospital mortality ($p = 0.1245$).

In patients <60 years of age, mFI predicted number of AEs, acute LOS, and in-hospital mortality. In those aged 61–75, TMS predicted AEs, LOS, and mortality. In those 76+ years of age, mFI no longer predicted outcome.

Age, mFI, and TMS on admission are important determinants of outcome in patients with tSCI. mFI predicts outcomes in those <75 years of age only. The inter-relationship of advanced age and decreased physiological reserve is complex in acute tSCI, warranting further study. Identifying frailty in younger patients with tSCI may be useful for peri-operative optimization, risk stratification, and patient counseling.

Keywords: aging; deficit; frailty; prognosis; spinal cord injury

Introduction

In the medical literature, the term frailty is defined as ''a state of decreased physiologic reserve, with increased susceptibility to external stressors.''[1] This concept has previously been identified as independent from chronological age in terms of patient outcomes.[2] Its association with poor outcomes has been demonstrated in multiple settings, from the community dwelling population to the surgical population.[3–10] This relationship appears particularly relevant in patients requiring emergent procedures.[11,12] In a recent systematic review of the spine surgery literature, frailty has been demonstrated to affect post-operative outcomes such as adverse events (AEs), mortality, and length of stay (LOS).[13]

Although the concept of frailty has been largely accepted, its operational definition is less clear. In most of the spinal literature, the Modified Frailty Index (mFI) has been used as a surrogate measure of frailty. The mFI, a simplified version of the Canadian Study of Health and Aging Frailty Index, is based on the theory of ''accumulating deficits.'' The mFI includes 11 variables relating to pre-injury deficits including functional independence and 10 co-morbid medical conditions.[14,15]

To our knowledge, the concept of frailty has never been applied to a newly injured (or acute) traumatic spinal cord injury (tSCI) population. Although typically occurring most frequently in younger males from motor vehicle or sports injury, in tSCI there is an epidemiological shift in the population relating to aging ''baby

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boomers'' that has increased the average age at injury.[16,17] By 2032, the greatest proportion of new tSCI is predicted to be in patients over 70 years of age, with an estimated 46% of the newly injured being over the age of 60 years.[18]

Injuries in the elderly are most often incurred by falls from a standing height, which may be exacerbated by age-related degenerative disc disease. Older individuals are physiologically less able to improve functional recovery even in the presence of neurological recovery,[18–20] with recovery being complicated by a higher rate of pre-existing conditions,[21,22] including degenerative disc disease, and susceptibility to secondary health conditions such as pneumonia and pressure injury.[23,24] The clinical management of older individuals with new tSCI provides a challenge for clinicians, evidenced by a previous study in which older patients were operated on less frequently, and at a longer interval from admission.[16] Whereas clinical decision-making involves a subjective assessment of risk of poor outcomes with consideration of the overall accumulation of deficit, assessment of frailty would assist in clinical decision-making and risk management.

The objectives of this study were therefore to: 1) describe patient characteristics associated with frailty, and 2) examine the effect of frailty on post-operative outcomes in terms of in-hospital mortality, in-hospital LOS, and in-hospital AEs in a cohort of newly injured tSCI patients.

Methods

Study design

Our study is a retrospective cohort of prospectively collected data.

Study population

The analysis cohort comprised individuals with new tSCI admitted for acute care at a Level 1 trauma, quaternary referral center and enrolled in the Rick Hansen Spinal Cord Injury Registry (RHSCIR), a multi-center, Canadian, prospective, observational registry of adults with new tSCI; full details have been described elsewhere.[25] Research Ethics Board (REB) approval was obtained. Study subjects included patients with tSCI injured between 2004 and 2016 who received acute treatment at the study site.

Demographics

Age, gender, and body mass index (BMI) were obtained.

Medical comorbidities

Medical comorbidities at the time of injury were assessed by both the Charlson Comorbidity Index (CCI) and Elixhauser Comorbidity Index (ECI), commonly used indexes that are normally calculated from administrative data codes.[26,27] A total count of comorbidities was also obtained.

Frailty

The mFI as introduced above includes a question regarding functional independence, and the following medical comorbidities: diabetes mellitus, lung problems, congestive heart failure, myocardial infarction, cardiac problems, hypertension, impaired sensorium, prior transient ischemic attack, history of stroke, and peripheral vascular disease. The number of deficits present divided by 11 gives the mFI score, providing an index with a range of 0 to 1. The mFI was calculated by chart review for assessment of functional status, and comorbid conditions as collected in the RHSCIR. Patients were categorized as not frail (mFI = 0), pre-frail (0 <mFI <0.21), and frail (mFI ≥0.21) based on previous data.[28] Comparison of patient groups was also categorized as non-frail (mFI <0.21) and frail (mFI ≥0.21) for analysis purposes.

Injury mechanism

Injury mechanism is ecorded as: assault, fall, sport, transport, or other.[29]

Neurological severity and level

Neurological classification was measured at admission and discharge with the International Standards of Neurological Classification of Spinal Cord Injury (ISNCSCI),[30] including neurological severity (American Spinal Injury Association [ASIA] Impairment Scale [AIS]; A/B/C/D), level of injury (high cervical C1–C4; low cervical C5–T1; thoracic T2–T10; thoracolumbar T11–S5), and Total Motor Score (TMS; out of 100).

Outcome measures

Primary study outcome variables included in-hospital patient mortality, acute hospital LOS, and number of AEs during hospital stay. Secondary outcomes included patient characteristic differences between cohorts and discharge destination (home vs. other). AEs were obtained from the previously validated Spinal AdVerse Events System (SAVES2) database at our institution and is used to identify and record acute care AEs on all spine patients including those with tSCI. AE data are recorded through a rigorous prospective systematic process previously described.[31,32] The top five and total number of AEs from SAVES2 were also explored.

Statistical analysis

Descriptive statistics were used to describe the demographics and injury characteristics of the cohort. Participant characteristics were compared between those deemed as frail and not frail by mFI to determine if there is significant difference between these two groups of participants. The comparison was made using either *t* test or Wilcoxon rank sum test for normally distributed versus non-normally distributed continuous variables, respectively. Comparisons between two categorical variables were assessed using a chi-square test (or Fisher's exact test if the expected cell counts were five or less). Pearson correlations were obtained to examine linear relationship between mFI, age at injury, and TMS at admission with three primary outcomes of interest. Age was selected due to an observed complex relationship between age and mFI, whereas TMS was used to minimize the risk of confounding in terms of patient outcome. These associations were re-examined in multi-variable analysis after adjusting for relevant covariates. Goodness-of-fit tests were performed for all models. Associations with a p-value <0.05 were considered statistically significant. All analyses were performed using SAS software, version 9.4 of the SAS System for Windows© 2013 (SAS Institute, Inc., Cary, NC).

Results

Patient characteristics

A total of 634 patients with tSCI were identified in our database during the study period. The most common mechanism of injury was falls (295, 46.5%). Neurological injury showed AIS Grade A to be the most common (245, 39.1%), followed by AIS D (206, 32.9%), AIS C (123, 19.7%), and AIS B (52, 8.3%). Most patients presented with either high (C1–C4, 237, 37.4%) or low (C5–T1, 230, 36.3%) cervical injuries. The remainder of characteristics are summarized in Table 1.

TABLE 1. PATIENT CHARACTERISTICS FOR THE ANALYSIS COHORT ($N=634$) AND THE FRAIL (MFI >0.21; $N=76$) AND NON-FRAIL (MFI ≤0.21; $N=353$) COHORTS

Variable	*Analysis cohort,* n = *634*	*Frail cohort,* n = *76*	*Non-frail cohort,* n = *353*	P-*value*
Age at injury (years); mean (SD)	50.3 (19.8)	70.6 (11.0)	42.0 (17.5)	**<0.0001**
Male, *n* (%)	488 (77.0)	59 (77.6)	275 (77.9)	0.9587
BMI, mean (SD)	25.2 (4.3)	27.3 (4.2)	24.6 (4.0)	**<0.0001**
Mechanism of injury, *n* (%)				**<0.0001**
Falls	295 (46.5)	56 (73.7)	112 (31.7)	
Transport	160 (25.2)	13 (17.1)	97 (27.5)	
Sports	134 (21.1)	3 (3.9)	113 (32.0)	
Other	45 (7.1)	4 (5.3)	31 (8.8)	
Neurological severity of injury (AIS), *n* (%)				0.2410
A	245 (39.1)	24 (32.0)	156 (44.6)	
B	52 (8.3)	6 (8.0)	27 (7.7)	
C	123 (19.7)	16 (21.3)	61 (17.4)	
D	206 (32.9)	29 (38.7)	106 (30.3)	
Neurological level of injury, *n* (%)				**0.0002**
High cervical (C1-C4)	237 (37.4)	39 (51.3)	116 (32.9)	
Low cervical (C5-T1)	230 (36.3)	30 (39.5)	127 (36.0)	
Thoracolumbar (T2-S5)	167 (26.3)	7 (9.2)	110 (31.2)	
Total Motor Score admission, mean (SD)	46.6 (31.2)	41.8 (30.1)	47.9 (31.5)	0.1529
Charlson Comorbidity Index, mean (SD)	0.6 (1.1)	2.1 (1.4)	0.2 (0.6)	**<0.0001**
Elixhauser Comorbidity Index, mean (SD)	1.0 (1.1)	1.8 (1.2)	0.5 (0.8)	**<0.0001**
mFI, mean (SD)	0.1 (1.1)	0.3 (0.1)	0 (0.0)	**<0.0001**
Count of comorbidities, *n* (%)				**<0.0001**
None	180 (47.4)	1 (2.0)	152 (73.8)	
1–2	155 (40.8)	23 (45.1)	52 (25.2)	
3+	45 (11.8)	27 (52.9)	2 (1.0)	
Top 3 comorbidities; *n* (%)				
Diabetes	52 (13.7)	26 (51.0)	2 (1.0)	**<0.0001**
Osteo/degenerative arthritis	23 (6.1)	3 (5.9)	6 (2.9)	0.3873
Any malignancy	20 (5.3)	7 (13.7)	6 (2.9)	**0.0016**
Top 5 adverse events, *n* (%)				
UTI	273 (43.1)	31 (40.8)	151 (42.8)	0.6576
Pneumonia	267 (42.1)	39 (51.3)	137 (38.8)	**0.0463**
Neuropathic pain	259 (40.9)	29 (38.2)	159 (45.0)	0.2053
Cardiac arrest/failure/arrythmia	143 (22.6)	25 (32.9)	76 (21.5)	**0.0373**
Delirium	136 (21.5)	32 (42.1)	51 (14.4)	**<.0001**

Bold indicates statistical significance.

AIS, American Spinal Injury Association (ASIA) Impairment Scale; BMI, body mass index; IQR, inter-quartile range; mFI, Modified Frailty Index; SD, standard deviation; UTI, urinary tract infection.

Frailty distribution

Table 2 reports frailty status by age group (<60, 61–75, 76+ years); percentage of frail individuals by age group was 2.8%, 27.9%, and 35.6%, respectively. For those aged 61 or older, 30.6% were deemed frail. We noted a complex relationship between frailty and age (Fig. 1). When analyzed as median mFI versus age, peaks were noted for patients aged 61–75, and >75 years. As a result, correlation analysis of variables on outcome was performed according to these age distributions.

TABLE 2. FRAILTY STATUS BY AGE GROUP: FRAIL (MFI >0.21), PRE-FRAIL (0 <MFI <0.21), AND NON-FRAIL (MFI = 0)

Frailty status	*<60 years,* n = *425*	*61–75,* n = *136*	*76+,* n = *73*	*61+,* n = *209*
Non-frail, *n* (%)	302 (71.1)	40 (29.4)	22 (15.1)	51 (24.4)
Pre-frail, *n* (%)	111 (26.1)	58 (42.7)	36 (49.3)	114 (54.7)
Frail, *n* (%)	17 (2.8)	38 (27.9)	26 (35.6)	64 (30.6)

mFI, Modified Frailty Index.

Frailty characteristics

Frail patients were older (mean, 70.6 years [standard deviation (SD), 11.0] vs. mean, 42.0 years [SD, 17.5]; $p<0.0001$), had increased BMI (mean, 27.3 [SD, 4.2] vs. mean, 24.6 [SD, 4.0]; $p<0.0001$), and were more likely to have suffered their injury as a result of a fall versus transport or sports injury ($p<0.0001$). Frail patients had higher incidence of high- and low-cervical injuries versus non-frail patients suffering thoracolumbar injuries ($p<0.0001$). Frail patients also displayed higher accumulation of deficits as per the CCI ($p<0.0001$) and ECI ($p<0.0001$), and as per comorbidity counts ($p<0.0001$). Lastly, frail patients were more likely to have suffered a pneumonia ($p=0.0463$), cardiac arrest/failure/arrythmia ($p=0.0373$), or delirium ($p<0.0001$) during their inpatient stay.

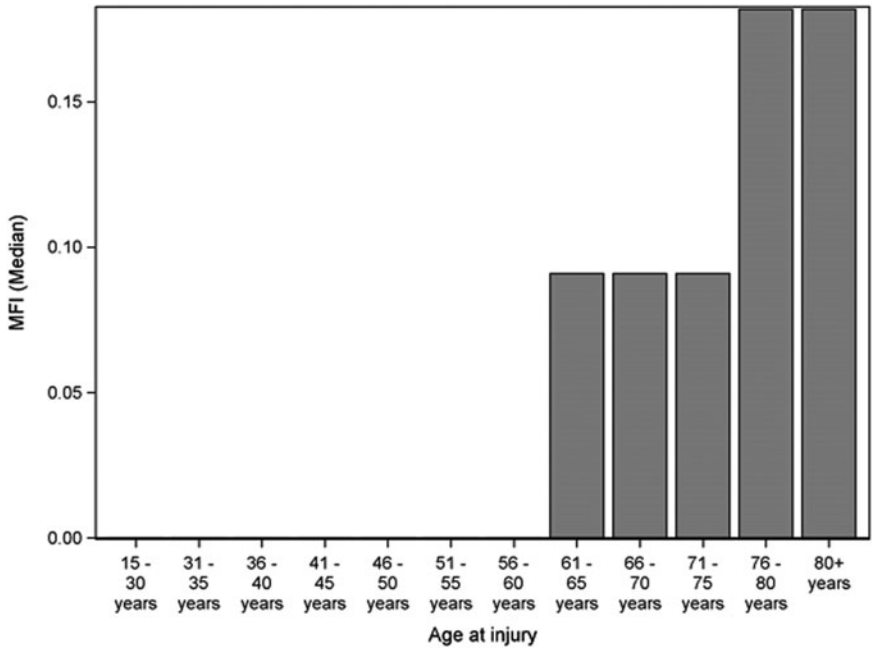

FIG. 1. Relationship between frailty and age at injury. MFI, Modified Frailty Index.

Frailty on post-operative outcomes: Bivariate analysis

mFI was a strong predictor of increased acute LOS (Pearson's $r = 0.163$; $p < 0.0001$), number of AEs ($r = 0.1664$; $p < 0.0001$), and in-hospital mortality ($r = 0.155$; $p < 0.0001$) for the total cohort (Table 3). Age at injury was also significantly correlated with acute LOS ($r = 0.0809$; $p = 0.0418$), number of AEs ($r = 0.0937$; $p = 0.0231$), and in-hospital mortality ($r = 0.2639$; $p < 0.0001$). Lastly, motor score on admission was also predictive of acute LOS ($r = -0.4749$; $p < 0.0001$), number of AEs ($r = -0.3069$; $p < 0.0001$), and in-hospital mortality ($r = -0.2249$; $p < 0.0001$).

Subgroup analysis was then performed on patients aged <60, 61–75, and >75 years to investigate the complex relationship observed between age and frailty (Table 3). In patients aged <60 years, mFI was strongly predictive of acute LOS ($p = 0.0045$), number of AEs ($p = 0.0038$), and in-hospital mortality ($p = 0.0183$). This was also true for motor score on admission, which was predictive of acute LOS ($p < 0.0001$), number of AEs ($p < 0.0001$), and in-hospital mortality ($p = 0.0136$). Age at injury was not predictive of outcomes in this age cohort.

In patients aged 61–75 years, mFI was predictive of acute LOS ($p = 0.0220$), but not predictive of number of AEs or in-hospital mortality. TMS remained predictive of LOS ($p < 0.0001$), number of AEs ($p = 0.0015$), and in-hospital mortality ($p = 0.0296$). Age at time of injury was not predictive of any of the three outcomes.

For patients aged >75 years, age at injury was predictive of acute LOS ($p = 0.0318$) and number of AEs ($p = 0.0009$), but not in-hospital mortality. TMS was predictive of LOS ($p = 0.0427$) and in-hospital mortality ($p < 0.0001$), but not number of AEs. Finally, mFI in this age cohort was not predictive of any outcome measure.

Table 3. Bivariate Analysis of Outcomes for Analysis Cohort ($N = 634$), <60 Years ($N = 425$), 61–75 Years ($N = 136$), and 76+ Years ($N = 73$) Cohorts

		Analysis cohort		*<60 years*		*61-75 years*		*76+ years*	
Independent variable	*Outcome*	*Correlation coefficient*	P-*value*	*Correlation coefficient*	P-*value*	*Correlation coefficient*	P-*value*	*Correlation coefficient*	P-*value*
mFI	Acute LOS	0.1630	**<0.0001**	0.1377	**0.0045**	0.1962	**0.0220**	0.0642	0.5895
	Number of AEs	0.1664	**<0.0001**	0.1452	**0.0038**	0.1565	0.0789	0.1578	0.2056
	In-hospital mortality	0.1550	**<0.0001**	0.1144	**0.0183**	0.0745	0.3886	–0.1321	0.2654
Age at injury	Acute LOS	0.0809	**0.0418**	0.0432	0.3742	0.0431	0.6184	–0.2516	**0.0318**
	Number of AEs	0.0937	**0.0231**	0.0648	0.1988	0.1118	0.2109	–0.3977	**0.0009**
	In-hospital mortality	0.2639	**<0.0001**	0.0083	0.8648	0.1452	0.0916	0.1363	0.2502
Motor score at admission	Acute LOS	–0.4749	**<0.0001**	–0.4770	**<0.0001**	–0.5624	**<0.0001**	–0.2562	**0.0427**
	Number of AEs	–0.3069	**<0.0001**	–0.3538	**<0.0001**	–0.2920	**0.0015**	0.0188	0.8874
	In-hospital mortality	–0.2249	**<0.0001**	–0.1281	**0.0136**	–0.1962	**0.0296**	–0.5181	**<0.0001**

AE, adverse event; LOS, length of stay; mFI, Modified Frailty Index.

Table 4. Multiple Linear Regression Analysis of Acute Length of Stay for the Analysis Cohort ($N=634$)

Parameter	*Estimate*	*Standard error*	*95% confidence intervals*		P-*value*
Intercept	3.9742	0.1048	3.7683	4.1800	<0.0001
Age at injury	0.0000	0.0019	–0.0038	0.0037	0.9832
Motor score at admission	–0.0185	0.0010	–0.0205	–0.0165	**<0.0001**
mFI frail	0.1594	0.1167	–0.0699	0.3887	0.1727
mFI pre-frail	0.1955	0.0771	0.0440	0.3469	**0.0115**
mFI non-frail	Baseline	-	-	-	-

mFI, Modified Frailty Index.

Table 5. Negative Binomial Regression Analysis of Number of Adverse Events for the Analysis Cohort ($N=634$)

Parameter	*Estimate*	*Standard error*	*Wald 95% confidence intervals*		P-*value*
Intercept	1.5154	0.1171	1.2858	1.7449	<0.0001
Age at injury	0.0027	0.0022	–0.0016	0.0069	0.2186
Motor score at admission	–0.0096	0.0013	–0.0120	–0.0071	**<0.0001**
mFI frail	0.2379	0.1260	–0.0091	0.4850	0.0591
mFI pre-frail	0.0201	0.0867	–0.1498	0.1900	0.8166
mFI non-frail	Baseline	-	-	-	-

mFI, Modified Frailty Index.

Frailty on post-operative outcomes: Multi-variable analysis

Previous authors have subdivided patients into not frail (mFI = 0), pre-frail (0 <mFI <0.21), and frail (mFI ≥0.21) categories.[33] A similar division was made for our tSCI cohort, and association with outcome measures was explored.

Acute hospital LOS was significantly different between frailty categories ($p=0.0134$; Table 4) when controlling for the covariates, the mFI was a significant predictor of LOS ($p=0.0375$), with the pre-frail group having a significantly longer LOS ($p=0.0115$) when compared with the non-frail group.

When unadjusted for other covariates, significant differences exist between all three frailty categories ($p=0.0375$) in terms of median number of AEs. After adjusting for age at time of injury and TMS on admission, the mFI was not a significant predictor for number of AEs; however, the frail group tended to be more likely to experience an increased number of AEs compared with the non-frail group ($p=0.0591$) (Table 5).

In-hospital mortality was significantly different between frailty categories ($p<0.0001$), with non-frail patients being more likely to survive. However, in multi-variable analysis, age and motor score at admission were predictors of in-hospital mortality, whereas mFI was not ($p=0.1245$) (Table 6).

Discharge destination was grouped into either discharge home, or discharge to a different destination (e.g., long-term care facility; Table 7). A significantly larger proportion of patients with no frailty were discharged home as compared with other frailty categories ($p=0.0315$). After adjusting for age and motor score on admission mFI was no longer predictive of discharge destination ($p=0.5062$). Of note, TMS at admission is strongly predictive of discharge destination on its own.

Discussion

Our study has identified frailty as a risk factor for poor post-operative outcomes in a tSCI patient population, in keeping with previous findings. First described in an intensive care unit (ICU) setting, Fried and colleagues defined frailty as ''a clinical picture of loss of physiological and cognitive functioning which leaves patients susceptible to significant deterioration often precipitated by relatively minor stressors, such as infection, surgery, or trauma.''[34] With reference to a surgical setting specifically, frailty has been shown to affect post-operative outcomes in multiple specialties,[35,36] disproportionately affecting in-hospital and long-term mortality, and discharge destination.[37]

With regard to spine surgery, most studies have similarly linked frailty and worsened post-operative outcomes, mortality, and discharge disposition.[38,39] Flexman and associates showed higher complication rates, specifically with infection, in a population of elective degenerative spine patients.[33] Ali and co-workers reviewed the 18,294 patients in the National Surgery Quality Improvement Program (NSQIP) database who had undergone spine surgery.[40] Similar to our own work, this group divided the mFI into low (<2.7) and high (≥2.7) categories, and noted a substantial difference in infection (1.7% vs. 4.1%) and mortality (0.1% vs. 2.3%) rates.[40] In an adult spinal deformity population, Miller and colleagues noted increased risk of junctional kyphosis (odds ratio [OR] 2.8), pseudarthrosis (OR 13.0), deep wound infection (OR 8.0), and wound dehiscence (OR 13.4) as compared with non-frail patients.[41] A recent systematic review of the literature found that despite discrepancies in measurement tools, frailty is a consistent predictor of mortality, minor and major morbidity, in-hospital LOS, and discharge disposition in patients undergoing spine surgery.[42]

Traditionally, however, frailty is a concept that has been intimately linked with older age.[43] Bagshaw and associates were among the first groups to note that the prevalence of frailty in younger

Table 6. Multiple Logistic Regression Analysis of In-Hospital Mortality for the Analysis Cohort ($N=634$)

Parameter	*Estimate*	*Standard error*	*Odds ratio*	*95% confidence interval*		P-*value*
Intercept	–6.6591	1.2529	-	-	-	<0.0001
Age at injury	0.0790	0.0190	1.0820	1.0430	1.1230	**<0.0001**
Motor score at admission	–0.0447	0.0106	0.9560	0.9370	0.9760	**<0.0001**
mFI frail	0.9089	0.5917	2.4810	0.7780	7.9130	0.1245
mFI pre-frail	–0.4829	0.6107	0.6170	0.1860	2.0420	0.4291
mFI non-frail	Baseline	-	-	-	-	-

mFI, Modified Frailty Index.

Table 7. Multiple Logistic Regression Analysis of Discharge to Home Including Frailty Status (Frail: mFI >0.21, $N=76$; Non-Frail: mFI ≤0.21, $N=353$) for the Analysis Cohort ($N=634$)

Parameter	*Estimate*	*Standard error*	*Odds ratio*	*95% confidence interval*		P-*value*
Intercept	–6.6305	0.7631	-	-	-	<0.0001
Age at injury	–0.0117	0.00975	0.988	0.970	1.007	0.2306
Motor score at admission	0.0840	0.0088	1.088	1.069	1.107	<0.0001
mFI frail	–0.4093	0.6157	0.664	0.199	2.220	0.5062
mFI pre-frail	–0.5799	0.3700	0.5600	0.271	1.156	0.1171
mFI non-frail	Baseline	-	-	-	-	-

mFI, Modified Frailty Index.

patients is not only underappreciated, but perhaps especially damaging.[44] According to Smart and co-workers, this phenomenon of frailty in the young becomes particularly important in a surgical emergency scenario.[45] Although it is clear that the aging process is a contributor, there are many other patient and environmental factors that can drain physiological reserve in response to stressors.[46]

In our study, frailty was predictive of poor outcome in the entire cohort, but not in the subgroup of the most elderly (≥75 years). As a result, we can conclude that there must exist a more complex relationship between age and frailty than is noted in previous studies. Our work also implies that younger, ''frail'' individuals are likely at particular risk for AEs, complications, and death as compared with their young, non-frail counterparts. In a tSCI population, when an individual is faced with such a devastating injury after reaching a certain age, physiological reserve likely loses its importance.

To our knowledge, no current work has looked at frailty in a tSCI cohort. Of note, our tSCI population had a much higher degree of frailty than other studied populations. In a cohort of patients over the age of 65 years undergoing elective surgery for degenerative conditions of the lumbar spine, modified frailty score was 0.09, with 59.8% being not frail, 20.6% pre-frail, and 19.6% frail.[38] In our cohort of patients over the age of 61 years, 30.6% were frail. When comparing the tSCI population with the elective surgery cohort, despite having a lower age limit of 61 versus 65 years, frailty is 1.5 times more common.[38] This difference is striking, particularly as the main cause of injury is through falls in our cohort, which may occur in more frail individuals. With the increase in the older population, this problem will likely be exacerbated and should be considered in future planning.

Multiple measures of frailty are used in research and published in the literature, and simplified measures such as the mFI and Charlson and Elixhauser comorbidity indexes are not nuanced enough to capture important physiological changes that underpin the multi-dimensional concept of frailty, such as nutritional status, cognitive impairment, and poor performance status.[42] Additionally, cutoff frailty values as used in this and other studies may not apply to tSCI. The insult of the tSCI itself may be so great that it may affect outcomes to a higher degree than values currently used.

The strengths of our study include its large sample and the robust nature of our database. The benefits of the SAVES reporting system have been outlined in our previous work.[47] Data were gathered from a single institution, and may not accurately reflect the experience of other centers. Due to varying definitions, our selection of a threshold value for mFI may not be directly applicable to other published reports.

Conclusions

The link between frailty, the aging process, and poor postoperative outcomes has been well-established through research. When faced with an injury as physiologically taxing as a tSCI, however, the effect of deficit accumulation loses importance. This work will aid in surgical decision-making and risk stratification in tSCI patients. Future efforts should be directed toward the identification of a more accurate tool for measurement of frailty in the elderly, as well as toward finding in a younger population specific risk factors contributing to poor outcomes.

Author Disclosure Statement

No competing financial interests exist.

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