The Spine Journal 20 (2020) 1276–1285

Clinical Study

Probability of severe frailty development among operative and nonoperative adult spinal deformity patients: an actuarial survivorship analysis over a 3-year period

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FDA device/drug status: Not applicable.

Author disclosures: ***PGP:*** Consulting:Medicrea, SpineWave; Speaking and/or Teaching Arrangements: Zimmer Biomet; Scientific Advisory Board/Other Office: Allosource; Grants: Cervical spine Research Society. ***FAS:*** Nothing to disclose. ***CAB***: Nothing to disclose. ***SRH:*** Nothing to disclose. ***KEP:*** Nothing to disclose. ***SN:*** Noting to disclose. ***AEB:*** Nothing to disclose. ***BJ-F:*** Nothing to disclose. ***WA:*** Nothing to disclose. ***CO:*** Nothing to disclose. ***VL:*** Stock Ownership: Nemaris; Consulting: Globus Medical; Speaking and/or Teaching Arrangements: Depuy, K2M; Scientific Advisory Board/Other Office: International Spine Study Group; Scoliosis Research Society; Research Support (Investigator Salary, Staff/Materials)^: Depuy, Medtronic, Nuvasive, Stryker. ***RL:*** Nothing to disclose. ***JSS:*** Royalties: Zimmer Biomet; Consulting: Nuvasive, K2M, Allosource, Cerapedics; Scientific Advisory Board/Other Office: Cervical Spine Research Society, Neurosurgery, Operative Neurosurgery. ***AHD:*** Royalties: Springer; Consulting: Stryker, EOS, Spineart, Orthofix, Trans1; Research Support (Investigator Salary, Staff/Materials)^: Orthofix. ***BGL:*** Nothing to disclose. ***HJK:*** Nothing to disclose. ***JSU***: Nothing to disclose. ***RKE:*** Royalties: Globus Medical; Stock Ownership: Nuvasive, Seaspine, Spine Innovation, Carevature, DiFusion, Alphatec, Inviuty; Consulting: Aesculap, K2M, NuVasive, Seaspine, SI-Bone, Spine Innovation, Titan; Research Support (Investigator Salary, Staff/Materials)^: Scripps Clinic Medical Group. ***DKH***: Nothing to disclose. ***EOK:*** Consulting: DePuy, Styker; Speaking and/or Teaching Arrangements: AOSpine, K2M; Research Support (Investigator Salary, Staff/Materials)^: AOSpine. ***DCB:*** Royalties: DePuy; Consulting: DePuy; Board of Directors: Spine Deformity; Scientific Advisory Board/Other Office: Scoliosos Research Society; Research Support (Investigator Salary, Staff/Materials)^: DePuy, Bioventus, Pfizer. ***RAAH:*** Royalties: DePuy, Globus Medical, SeaSpine; Consulting: DePuy, Globus Medical, Medtronic; Speaking and/or Teaching Arrangements: DePuy, Globus Medical, Orthofix, Inc; Board of Directors: American Orthopaedic Association, Cervical Spine Research Society, International Spine Study Group, North American Spine Society, Scoliosis Research Society, Western Ortho Assn.; Research Support (Investigator Salary, Staff/Materials)^: DePuy, Misonix. ***FJS:*** DePuy, A Johnson & Johnson Company: Research support Globus Medical: Paid consultant; Paid presenter or speaker K2M: IP royalties; Paid consultant; Paid presenter or speaker Medicrea: Paid consultant Medtronic: Paid consultant Medtronic Sofamor Danek: IP royalties; Paid presenter or speaker Nuvasive: Research support Scoliosis Research Society: Board or committee member spine deformity: Editorial or governing board Stryker: Research support VP of International Spine Society Group (ISSG): Board or committee member Zimmer: IP royalties; Paid consultant; Paid presenter or speaker. ***CIS:*** Royalties: Medtronic, Nuvasive, Zimmer Biomet; Stock Ownership: Nvasive; Consulting: Biomet Spine, Nuvasive, Zimmer Biomet, Stryker; Speaking and/or Teaching Arrangements: Medtronic, Nuvasive; Board of Directors: Spine Deformity; Scientific Advisory Board/Other Office: AANS, Cervical SpineResearch Society, Spine; Research Support (Investigator Salary, Staff/Materials)^: Research Support (Investigator Salary, Staff/Materials)^: DePuy, Globus Medical, Medtronic, Neurosurgery RRC. ***CPA:*** Royalties: Stryker, Biomet Spine, Next Orthosurgical, NuVasive; Consulting: DePuy, K2M, Medicrea, Stryker. ***SB:*** Royalties: Pioneer Spine; Consulting: Allosource, DePuy, EOS, K2M, Medtronic, Misonix; Scientific Advisory Board/Other Office: North American Spine Society, Scoliosis Research Society; Research Support (Investigator Salary, Staff/Materials)^: Allosource, Bionet Spine, DePuy, EOS, K2M, Medtronic, NuVasive, OrthoFix.

Disclosure of funding related to current work: The International Spine Study Group (ISSG) is funded through research grants from DePuy Synthes and individual donations.

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https://doi.org/10.1016/j.spinee.2020.04.010

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Received 12 June 2019; revised 31 March 2020; accepted 10 April 2020

Abstract

BACKGROUND: Little is known of how frailty, a dynamic measure of physiological age, progresses relative to age or disability status. Operative treatment of adult spinal deformity (ASD) may play a role in frailty remediation and maintenance.

PURPOSE: Compare frailty status, severe frailty development, and factors influencing severe frailty development among ASD patients undergoing operative or nonoperative treatment.

DESIGN: Retrospective review with maximum follow-up of 3 years.

SETTING: Prospective, multicenter, ASD database.

PARTICIPANTS: Patients were consecutively enrolled from 13 participating centers. Inclusion criteria: ≥18 years undergoing either operative or nonoperative treatment for ASD, exclusion criteria: spinal deformity of neuromuscular etiology, presence of active infection, or malignancy. The mean age of the participants analyzed were 54.9 for the operative cohort and 55.0 for the nonoperative cohort.

OUTCOMES MEASURES: Frailty status, severe frailty development, and factors influencing severe frailty development.

METHODS: ASD patients (coronal scoliosis ≥20°, sagittal vertical axis (SVA) ≥5 cm, Pelvic Tilt (PT) ≥25°, or thoracic kyphosis ≥60°) >18 y/o, with Base Line (BL) frailty scores were included. Frailty was scored from 0 to 1 (not frail: <0.3, frail 0.3−0.5, severe frailty >0.5) through the use of ASD-frailty index (FI) which has been validated using the International Spine Study Group (ISSG) ASD database, European Spine Study Group ASD database, and the Scoli-RISK-1 Patient Database. The ISSG is funded through research grants from DePuy Synthes and individual donations and supported the current work. Operative (Op) and Nonoperative (Non-Op) patients were propensity matched. T-tests compared frailty among treatment groups and BL, 1, 2, and ≥3 years. An actuarial Kaplan-Meier survivorship analysis with log-rank (Mantel-Cox) test, adjusting for patients lost to follow-up, determined probability of severe frailty development. Multivariate Cox Regressions gauged the effect of sagittal malalignment, patient and surgical details on severe frailty development.

RESULTS: The analysis includes 472 patients (236 Op, 236 Non-Op) selected by propensity score matching from a cohort of 1,172. Demographics and comorbidities were similar between groups (p>.05). Op exhibited decreased frailty at all follow-up intervals compared with BL (BL: 0.22 vs Y1: 0.18; Y2: 0.16; Y3: 0.15, all p<.001). Non-Op displayed similar frailty from BL to 2Y follow up, and increased frailty at 3Y follow up (0.23 vs 0.25, p=.014). Compared with Non-Op, Op had lower frailty at 1Y (0.18 vs 0.24), 2Y (0.16 vs 0.23), and 3Y (0.15 vs 0.25; all p<.001). Cumulative probability of maintaining nonsevere frailty was (Op: 97.7%, Non-Op: 94.5%) at 1Y, (Op: 95.1%, Non-Op: 90.4%) at 2Y, and (Op: 95.1%, Non-Op: 89.1%) at ≥3Y, (p=.018). Among all patients, baseline depression (hazard ratio: 2.688[1.172−6.167], p=.020), Numeric Rating Scale (NRS) back pain scores (HR: 1.247 [1.012−1.537], p=.039), and nonoperative treatment (HR: 2.785[1.167−6.659], p=.021) predicted severe frailty development with having a HR>1.0 and p value<.05. Among operative patients, 6-week postoperative residual SVA malalignment (SRS-Schwab SVA+modifier) (HR: 15.034[1.922−116.940], p=.010) predicted severe frailty development indicated by having a HR>1.0 and p value <.05.

CONCLUSIONS: Non-Op patients were more likely to develop severe frailty, and at a quicker rate. Baseline depression, increased NRS back pain scores, nonoperative treatment, and postoperative sagittal malalignment at 6-week follow-up significantly predicted severe frailty development. Operative intervention and postoperative sagittal balance appear to play significant roles in frailty remediation and maintenance in ASD patients. Frailty is one factor, in a multifactorial conservation, that may be considered when determining operative or nonoperative values for ASD patients. Operating before the onset of severe frailty, may result in a lower complication risk and better long-term clinical outcomes.

Keywords: Frailty; Adult spinal deformity; Kaplan-Meier; Hazard ratio; Cox regression; Severe frailty; Operative; Nonoperative; Depression

Introduction

Frailty, a dynamic measure of physiological age associated with increased vulnerability to adverse health effects, has increasingly gained attention over the past decade. To quantify frailty, a number of groups have developed frailty indices that tally patient health deficits, allowing for the stratification of patients into categories such as "not frail," "frail," or " severely frail" states based on corresponding mortality risk curves [1–3]. While frailty indices have successfully been used to predict increased susceptibility to falls, hospitalization, and mortality, researchers have also used frailty indices as an improved method of preoperative risk stratification [4–11].

Recent research has highlighted the risks of major complications, advanced morbidity and mortality when treating severely frail patients. Within normative elderly populations, severely frail individuals have been demonstrated to have a 4.3-fold increased risk of unplanned hospitalization and 5.0-fold increased risk of mortality by 1 year [6]. In surgical populations, severely frail patients have been shown to have as high as a 29.1-fold increased postoperative mortality risk following cytoreduction surgery [12], and increased odds of any major or intraoperative complication, deep wound infection, longer length of stay, and pseudarthrosis for adult spinal deformity (ASD) patients, relative to not frail patients [9]. To date, it remains unclear whether operative intervention at a nonfrail or frail state can remediate or slow the development of frailty.

As the relationships between frailty status, severe frailty development, and factors influencing severe frailty development among ASD patients have yet to be characterized, this investigation aimed to compare frailty status, severe frailty development, and factors that influence severe frailty development in ASD patients undergoing operative and nonoperative treatment.

Methods

Study design

This study is a retrospective review of a prospective, multicenter ASD database.

Data source

Patients were consecutively enrolled from 13 participating centers across the United States from 2008 to 2017. Institutional Review Board Approval and informed patient consent were obtained at each site before enrollment. Database inclusion criteria: patients ≥18 years undergoing either operative or nonoperative treatment for ASD, defined as: coronal Cobb angle ≥20°, sagittal vertical axis (SVA) ≥5 cm, pelvic tilt (PT) ≥25° and/or thoracic kyphosis >60°. Database exclusion criteria were patients with spinal deformity of neuromuscular etiology, presence of active infection, or malignancy.

Data collection

Patient demographic and clinical data collected for this study were age, sex, body mass index, comorbidity status, comorbidity severity (Charlson Comorbidity Index [CCI]), and baseline Numeric Rating Scale (NRS) back pain scores. Surgical data included surgical approach, operative time (Op time), estimated blood loss, techniques used, and length of stay.

Full length free-standing lateral spine radiographs were used to assess patients at baseline, 6-week (Operative patients only), 1-, 2-, and 3-year follow-up intervals. Radiographs were analyzed using SpineView (ENSAM, Laboratory of Biomechanics, Paris, France) software as previously published [13,14]. Spinopelvic radiographic parameters assessed included PT, pelvic incidence minus lumbar lordosis (PI–LL), and S1 sacral slope. Global sagittal alignment parameters assessed included SVA (C7-S1 SVA). Regional alignment was assessed using T1 pelvic angle (T1PA).

Frailty assessment

Frailty was assessed with the Miller et al ASD frailty index (ASD-FI) [1]. Standard frailty indices, which count the number of health deficits a given patient has, assign each deficit an equal "weight," typically 0 or 1 indicating the absence or presence of a deficit. The ASD-FI includes 42 binary variables relating to both objective and subjectively reported mental, physical, and functional health (Table 1) [9]. The mean score of all deficits is calculated, resulting in a frailty score ranging from 0 to 1. Patients with scores <0.3 are considered not frail, scores of 0.3–0.5 are considered frail, and scores ≥0.5 are considered severely frail. The ASD-FI has been validated using the ISSG ASD database, ESSG ASD database, and the Scoli-RISK-1 Patient Database [9,15,16].

Study inclusion criteria

Operative and nonoperative ASD patients with baseline ASD-FI scores were included for analysis.

Statistical analysis

Analysis performed using SPSS (v23.0, Armonk, NY, USA). Patients were stratified by treatment type: Op and Non-Op, and propensity score matched by variables showing significant variance between treatment groups (baseline age, gender, CCI, frailty status (ASD-FI), smoking status, drug/alcohol abuse status, depression, psychological disease, and NRS back pain scores). propensity score matched uses logistic regression to simulate a randomization process, permitting group comparisons [17]. Descriptive and chi-square analyses assessed variations in demographic and categorical variables (including individual comorbidities and SRS-Schwab deformity severity modifiers [18]) between Op and Non-Op groups at baseline, 1-, 2-, and ≥3-year follow-up visits. Independent and

Table 1
Adult spinal deformity frailty index component variables

ASD-FI score component variables *(Miller et al 2017)*	
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
	>3 medical problems
Patient reported outcome measures	Bladder incontinence
	Bowel incontinence
	Deteriorating health this year (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 h (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, and 12)
	Inability to lift heavy objects (SF-36v2, 3c; ODI, 3)
	Inability to travel >1 h (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, and 18)

*SF-36, Short Form 36 Questionnaire, LSDI, lumbar spine disability index, ODI, Oswestry disability index, SRS-22, Scoliosis Research Society 22 Questionnaire.

paired samples *t*- -tests compared continuous variables between treatment groups at BL and follow-up intervals. An actuarial Kaplan-Meier survivorship analysis, adjusting for patients lost to follow-up, determined probability of severe frailty development at all follow-up intervals. Log-rank (Mantel-Cox) analysis determined significant variance in survivorship analysis probabilities between Op and Non-Op. Multivariate Cox Regressions gauged the effect of sagittal alignment, patient and surgical details on severe frailty development utilizing hazard ratios (HR).

Source of funding

The present study group is funded through research grants from DePuy Synthes and individual donations, and supported the current work.

Results

Baseline demographics and clinical comparison of operative and nonoperative ASD patients

One thousand one hundred and seventy ASD patients (844 Op, 326 Non-Op) met inclusion criteria. After propensity score matching patients by baseline age, CCI, ASD-FI, smoking status, drug/alcohol abuse, depression, psychological disease, and NRS back pain scores, 472 patients (236 Op, 236 Non-Op) were included for analysis. Age (Op: 54.9 vs Non-Op:5 5.0, p=.913), gender (woman: 81.8% vs 85.2%), body mass index (25.5 vs 26.3, p=.086), CCI (1.25 vs 1.19, p=.615), race (p=.891), smoking status (9.3% vs 11.9%, p=.370), history of drug/alcohol abuse (0.4% vs 0.8%, p=.562), depression (19.1% vs 21.6%, p=.493), psychological disorders (4.2% vs 4.2%, p=1.0), NRS back pain scores (5.72 vs 5.62, p=.686), overall comorbidity prevalence (30.5% vs 32.2%, p=.617), and all individual comorbidities did not differ between operative and nonoperative cohorts (Table 2).

Surgical details of operative ASD patients

The frequency of operative ASD patients that were presented with a history of prior spinal surgery was 35.5% (83.78 of total 236 patients). Overall, about 0.4% of the 236 operative patients underwent an anterior only approach, 69.8% of the operative cohort underwent a posterior only approach, and 30.2% of the Op patients received a combined approach. Patients that received staged procedures 17.8% of patients underwent staged procedures. The overall rates of surgical decompression and osteotomy were 51.3% and 61.4%, respectively (55.5% Smith Peterson, 10.6% pedicle subtraction, 0.8% corpectomy, 3.8% vertebral column resection, 66.1% 3-column osteotomy). Mean construct length was 11.0±4.3 levels, operative time was 356.1±142.2 minutes, and estimated blood loss was 1370.3±1322.4 mL. Mean inpatient length of stay was 7.11±3.6 days. (Table 3).

Table 2
Baseline demographics and clinical assessment of propensity score-matched adult spinal deformity patients undergoing operative and nonoperative treatments

	Operative (n=236)	Nonoperative (n=236)	p value
Age	54.9	55.0	.913
Gender (female)	81.8%	85.2%	.321
Race			.891
White	93.2%	90.9%	
Black	3.6%	4.1%	
Hispanic	1.4%	2.3%	
Asian	1.4%	2.3%	
Other	0.5%	0.5%	
BMI	25.5	26.3	.086
Smoking status (yes)	9.3%	11.9%	.370
History of drug/alcohol abuse	0.4%	0.8%	.562
CCI	1.25	1.19	.615
NRS back pain	5.72	5.62	.686
Any comorbidity	30.5%	32.2%	.617
Anemia	12.7%	8.5%	.135
Arthritis	30.1%	24.6%	.179
Depression	19.1%	21.6%	.493
Diabetes	5.5%	5.5%	1.00
Heart disease	11.0%	8.1%	.273
Hypertension	26.7%	27.5%	.836
Kidney disease	1.7%	0.8%	.411
Liver disease	0.8%	1.7%	.411
Lung disease	3.4%	5.9%	.190
Neurologic disorder	2.5%	1.3%	.313
Osteoporosis	11.4%	12.7%	.672
Perivascular disease	0.8%	2.5%	.154
Psychological disorder	4.2%	4.2%	1.0

Radiographic deformity comparison of operative and nonoperative ASD patients

Operative and nonoperative patients presented with similar S1 sacral slope (33.1° vs 33.5°, p=.702), PT (21.4° vs 21.5°, p=.906), PI−LL (10.1° vs 7.7°, p=.171), and T1PA (18.3° vs 17.4°), despite operative patients presenting with significantly greater SVA malalignment (42.3 mm vs 26.0 mm, p=.021). Operative and nonoperative patients also presented with similar SRS-Schwab classification coronal curvature types (p=.177), PT deformity modifiers (Moderate(+): 34.2% vs 34.3%, Severe(++): 20.2% vs 18.3%; p=.862), PI−LL modifiers (+: 19.7% vs 17.8%, ++: 27.6%% vs 23.5%; p=.416), moderate SVA modifiers (22.1% vs 21.4%, p=.739) and different rates of severe SVA modifiers (19.9% vs 10.7%, p<.001).

At the first postoperative study interval (6 weeks), operative patients showed superior PT (Op: 18.6 vs Non-Op: 21.5, p=.003), PI−LL (1.7 vs 7.7), T1PA (14.2 vs 17.4), and similar SVA alignment (18.6 vs 21.5, p=.120) relative to nonoperative patients' baseline alignment values. Operative patients also showed lower rates of SRS-Schwab classification coronal curvature (20.1% vs 74.2%, p<.001), severe PT modifiers (11.1% vs 18.3%, p=.007), severe PI−LL modifiers (9.8% vs 23.5%, p<.001), as well as similar moderate and severe SVA modifier rates (p=.163).

Table 3
Surgical details of operative adult spinal deformity patients

Surgical metric	Mean or frequency (%)
History of prior spine surgery	35.5%
Approach	
Anterior only	0.4%
Posterior only	69.8%
Combined	30.2%
Staged procedure	17.8%
Any decompression	51.3%
Any osteotomy	66.9%
Smith Peterson	55.5%
Pedicle subtraction	10.6%
Corpectomy	0.8%
Vertebral column resection	3.8%
3 Column osteotomy	66.1%
Levels fused	11.0±4.3
Operative time (minutes)	356.1±142.2
Estimated blood loss (EBL) (ccs)	1370.3±1322.4
Inpatient length of stay (LOS)	7.11±3.6

While 6-week postoperative alignment values remained consistent through 3-year follow-up for operative patients (all p>.05), nonoperative patients experienced deterioration of SVA alignment by 3-year follow-up (BL: 26.0 mm vs Y3:37.4 mm, p<.001). All 472 (236 Op, 236 Non-Op) patients that were used to create the Sagittal Radiographic baseline parameters for the Operative and Nonoperative groups were also followed up in Y1, Y2, and Y3 for ASD alignment measurements. Nonoperative patients showed higher rates of SRS-Schwab classification coronal curvatures (Op: 18.1% vs Non-Op:78.7%, p<.001), SVA modifiers (+:12.8% vs 32.9%, p<.001; ++: 9.6% vs 13.9%, p=.037), and PI−LL modifiers (+:13.7% vs 19.0%, p<.001) by 3-year follow-up (Table 4).

Comparison of frailty status among operative and nonoperative ASD patients

At baseline, operative and nonoperative patients presented with similar ASD-FI scores, falling within the "not frail" range (0.22 vs 0.23, p=.642). From baseline to 1-year, operative patients improved in ASD-FI score (BL: 0.22 vs Y1:0.18, p<.001), as did nonoperative patients (BL: 0.23 vs 0.24, p<.001). Operative patient ASD-FI scores continued to improve through 3-year follow-up (BL: 0.22 vs Y1:0.18 vs Y2:0.16 vs Y3:0.15, p<.001) while nonoperative patient ASD-FI scores were similar through 2-year follow-up (BL: 0.23 vs 1Y:0.24, p=.391; BL: 0.23 vs 2Y:0.23. p=.832) and declined by 3-year follow-up (BL: 0.23 vs Y3:0.25, p=.041, Fig. 1).

Probabilities and patient factors predictive of severe frailty development among operative and nonoperative ASD patients

Kaplan-Meier survivorship analysis determined Operative patients to have a 97.7% cumulative probability of

Table 4
Sagittal radiographic alignment of operative and nonoperative adult spinal deformity patients over a 3-year interval

Sagittal radiographic parameters		Operative	Nonoperative	p value
Baseline	S1SS (°)	33.1	33.5	.702
	PT (°)	21.4	21.5	.906
	PI–LL (°)	10.1	7.7	.171
	C7-S1 SVA (mm)	42.3	26.0	**.021**
	T1PA (°)	18.3	17.4	.435
6-Week Post-Op (Op) vs baseline (Non-Op)	S1SS (°)	35.5	33.5	**.035**
	PT (°)	18.6	21.5	**.003**
	PI–LL (°)	1.7	7.7	**<.001**
	C7-S1 SVA (mm)	18.6	26.0	.120
	T1PA (°)	14.2	17.4	**.002**
1-Year	S1SS (°)	35.2	34.5	.509
	PT (°)	18.9	21.5	**.010**
	PI–LL (°)	0.68	8.5	**<.001**
	C7-S1 SVA (mm)	13.4	32.7	**<.001**
	T1PA (°)	14.1	18.0	**<.001**
2-Year	S1SS (°)	34.4	34.1	.797
	PT (°)	19.0	21.5	**.037**
	PI–LL (°)	0.33	8.4	**<.001**
	C7-S1 SVA (mm)	11.4	30.4	**.002**
	T1PA (°)	13.9	17.6	**.005**
≥3-Year	S1SS (°)	33.8	32.9	.592
	PT (°)	19.9	22.1	.121
	PI–LL (°)	1.5	9.5	**.002**
	C7-S1 SVA (mm)	14.2	37.4	**.007**
	T1PA (°)	14.9	18.5	**.020**

Bolded values represent a signficant p-value (<0.050).

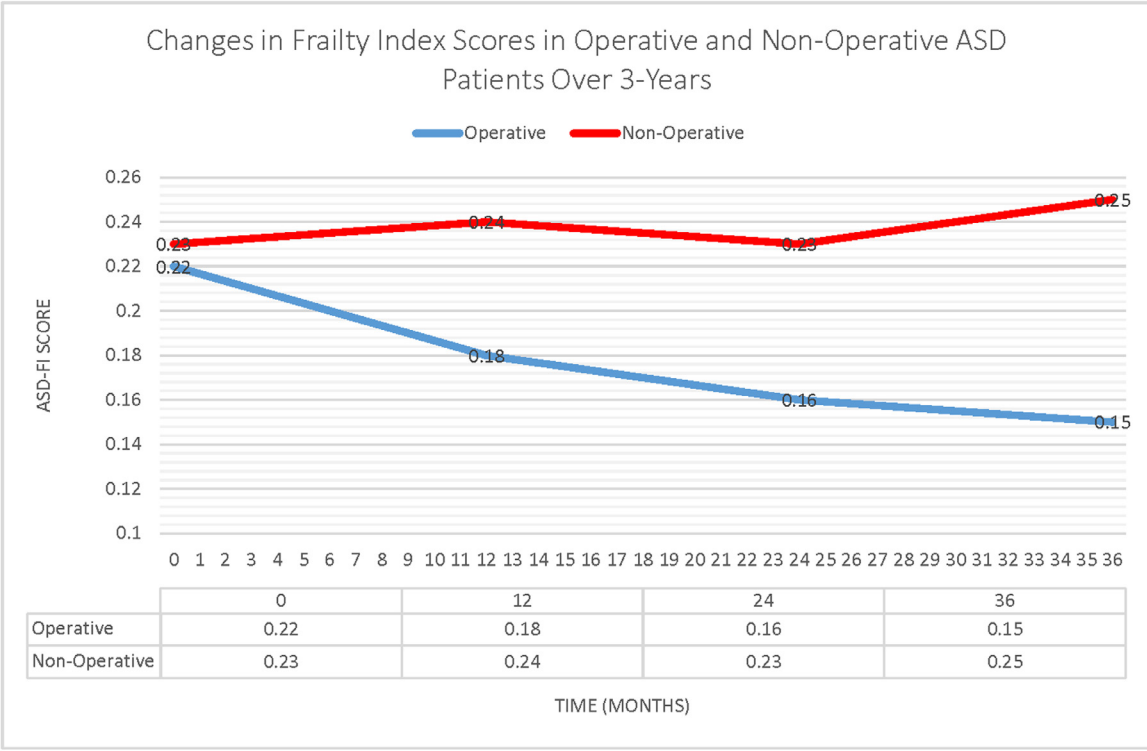

Fig. 1. Frailty assessment of operative and nonoperative adult spinal deformity patients over a 3-year interval.

maintaining nonsevere frailty status by 1-year follow-up, 95.1% by 2-year follow-up, and 95.1% by 3-year follow-up. Nonoperative patients were determined to have a 94.5% cumulative probability of maintaining nonsevere frailty status by 1-year follow-up, 90.4% by 2-year follow-up, and 89.1% by 3-year follow-up (Fig. 2). Nonoperative patients

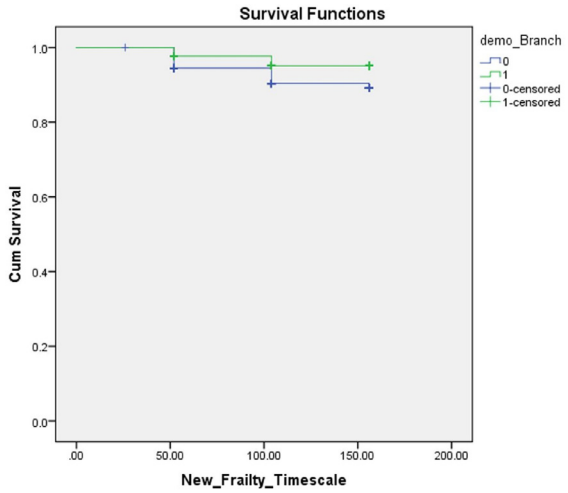

Fig. 2. Kaplan-Meier survivorship analysis and log-rank mantel-cox comparison assessing probabilities of nonsevere frailty maintenance in operative and nonoperative ASD patients.

were more likely to develop frailty, and at a quicker rate compared with operative patients (Log-rank Mantel-Cox test p value:.043).

Two multivariate cox regression analyses assessed the relationship between baseline patient factors and severe frailty development, as well as the relationship between surgical details and immediate 6-week postoperative sagittal alignment on severe frailty development for operative patients, using HR.

The first analysis, adjusting for baseline age, gender, CCI, smoking status, drug/alcohol abuse, depression, psychological disease, osteoporosis, SVA, pelvic tilt, PI–LL, coronal curvature type, NRS back pain scores, and treatment arm (operative/nonoperative) into the regression equation, determined depression (HR: 2.688[1.172–6.167], p=.020), NRS back pain scores (HR: 1.247[1.012–1.537], p=.039), and nonoperative treatment (HR: 2.785[1.167–6.659], p=.021) to be the greatest predictors of severe frailty development. Smoking (HR: 1.837[0.651–5.185], p=.205) and Drug/Alcohol abuse (HR: 3.783[0.360–39.802], p=.268) were also associated with severe frailty development, although both predictors failed to reach significance.

The second analysis, adjusting for depression, NRS back pain, levels fused, inpatient length of stay, SRS-Schwab pelvic tilt, SVA, and PI–LL modifiers into the regression equation, determined moderate residual SVA malalignment (postoperative residual SRS-Schwab SVA+modifier) to the be greatest and only significant predictor of severe frailty development (HR: 15.034[1.922–116.940], p=.010) for operative ASD patients. Depression (HR: 2.422[0.502–11.675], p=.270), postoperative residual severe SRS-Schwab SVA modifiers (HR: 7.8[1.72–353.190], p=.290), and postoperative residual severe SRS-Schwab PI–LL modifiers (HR: 2.876[0.109–75.961], p=.527) also strongly influenced severe frailty development, although failing to reach significance (Table 5).

Discussion

As the population continues to age, the risk for developing degenerative orthopedic conditions has increased, with recent years showing record rates of spinal fusion, total hip and knee arthroplasty procedures [19,20]. While frailty has only recently been used in orthopedic research, recent efforts have pushed for a greater understanding of patient frailty and how it relates to a given condition's prognosis [21–23]. Recent research highlights the dire outcomes associated with severely frail patients. For analyses of degenerative orthopedic conditions, studying frailty over an extended period of time may shed more light on appropriate operative indications, who is most likely to benefit from surgery, and whether frailty progression should be taken into account for treatment decision-making.

Following 236 operative and 236 nonoperative propensity-score matched ASD patients over a 3-year period, we found surgical ASD patients showed progressively improving ASD-FI scores across all follow-up visits. On average, operative patients started out not frail (ASD-FI 0.22) and ended up not frail at Y3 (ASD-FI 0.15). Similarly, nonoperative patients started out not frail (ASD-FI 0.23) and ended up not frail at Y3 (ASD-FI 0.25). However, nonoperative patients ASD-FI scores at Y3 showed to be inferior to those at baseline (BL: 0.22 vs Y3:0.15, p<.001). Operative patients not only improved in our study, but also progressively improved in frailty at each follow-up visit. Operative patients also ended with average ASD-FI scores of 0.15, falling within the normative frailty range for community dwelling elderly adult populations [1]. This result suggests that operative intervention for ASD patients may help remediate patient decline into increased frailty

Kaplan-Meier analysis similarly demonstrated that nonoperative patients show higher cumulative probability of developing severe frailty at all follow-up time-points over the 3-year period, relative to patients undergoing operative treatment. Multivariate cox regression—adjusting for baseline demographic, clinical and radiographic patient characteristics—determined baseline depression (HR: 2.688 [1.172–6.167], p=.020), NRS back pain scores (HR: 1.247 [1.012–1.537], p=.039), and nonoperative treatment (HR: 2.785[1.167–6.659], p=.021) as key drivers of severe frailty development. While nonoperative treatment displayed the largest effect with a 2.8-fold increased risk of severe frailty development, depression and perceived pain scores (NRS Back) also displayed large effects of 2.7-fold and 1.3-fold increased risks, respectively. These findings are consistent with previous literature that highlight the relationship between cognition, mood, and frailty [24]. Chronic pain is well documented to significantly alter the brain's neurochemistry, resulting in a reduction of grey matter, and deleterious effects to cognitive and emotional decision-making [25,26]. Individuals with impaired cognitive abilities, as well as those with major depression, have both been shown to express increased inflammatory

Table 5
Cox regression analysis determining influence of varying factors on severe frailty development utilizing hazard ratios

Model 1: Influence of baseline demographics, clinical status, radiographic alignment, and treatment status on severe frailty development		
Covariates in the equation	Adjusted hazard ratio[95% confidence interval]	p value
Age	1.005[0.971−1.041]	.770
Gender	1.423[0.442−4.579]	.554
CCI	1.119[0.803−1.559]	.508
Smoking status (Yes)	1.837[0.651−5.185]	.205
Drug/alcohol abuse	3.783[0.360−39.802]	.268
Depression	2.688[1.172−6.167]	**.020**
Psychological disorder	0.814[0.166−4.002]	.800
Osteoporosis	0.873[0.262−2.907]	.824
Sagittal alignment parameters		
Pelvic tilt	0.985[0.917−1.057]	.673
SVA	1.003[0.995−1.011]	.460
PI−LL	1.016[0.972−1.011]	.481
Coronal curvature type		
None (reference point)		
Thoracic	1.325[0.422−4.159]	.630
Lumbar	0.990[0.111−8.823]	.993
Double	1.019[0.358−2.896]	.972
NRS back pain score	1.247[1.012−1.537]	**.039**
Nonoperative treatment	2.785[1.167−6.649]	**.021**
Model 2: Influence of postoperative residual sagittal malalignment on severe frailty development among operative ASD patients, adjusting for baseline depression, NRS back scores, levels fused and inpatient length of stay		
Covariates in the equation	Adjusted hazard ratio [95% confidence interval]	p value
Depression	2.422[0.502−11.675]	.270
NRS back pain	1.497[0.932−2.404]	.095
Levels fused	1.279[0.974−1.681]	.077
Inpatient length of stay	1.048[0.845−1.301]	.668
SRS-Schwab PT modifier		
+	0.925[0.079−10.774]	.950
++	0.161[0.004−6.306]	.329
SRS-Schwab SVA modifier		
+	15.034[1.922−116.940]	**.010**
++	7.8[1.72−353.190]	.290
SRS-Schwab PI−LL modifier		
+	0.513[0.021−12.686]	.683
++	2.876[0.109−75.961]	.527

cytokine levels, abnormalities, and associations with future dementia development [27−31]. As chronic systemic inflammation is theorized to play a core role in frailty pathogenesis [24,32,33], chronic depression and pain secondary to deformity may predict systemic decline and worsening frailty status.

Our analysis showed little relationship between radiographic alignment and severe frailty development, suggesting that the longevity of symptomatic deformity and associated chronic exhaustion may pose as a greater risk for frailty progression than the physical degree of deformity. For operative ASD patients, multivariate cox regression determined 6-week postoperative residual SVA malalignment (SRS-Schwab +modifier) as the only significant predictor of severe frailty development (HR: 15.034[1.922−116.940], p=.010). This further suggests that failure to correct global alignment to a neutral position may prolong physiologic exhaustion, resulting in the development of progressive frailty.

While the multicenter database used in this analysis offers an increased generalizability and clinical applicability, an increased potential for error at the data entry level may exist. Because this was a retrospective study and all data points were recorded by various institutions, there is a lack of understanding of how patients were selected for surgical intervention as well as if there were any confounding variables that impacted a patient's frailty status. Reasons for surgical intervention were based upon discretion of the surgeons. Variations in radiographic protocol may also exist between enrollment sites, potentially limiting conclusions that can be drawn from radiographic measurements. Additionally, while propensity score matching reduces the potential for confounding variability between treatment groups, operative and nonoperative patients were not matched for baseline deformity severity to maintain statistical power and minimize sample selection bias. There is a limitation in the possibility of frailty differences being related to the differences in SVA.

Given the findings presented within this study, frailty status may be another data point that can be factored into the multifactorial conversation about decision-making for ASD patients, as well as degenerative diseases that generate significant pain and disability. Frailty, currently used as a preoperative risk stratification tool, also offers value as a dynamic outcome measure when assessed temporally. Furthermore, given the significant mortality and unplanned hospitalization risks associated with severe frailty, physicians should consider severe frailty development as a potential deleterious long-term consequence of nonoperative treatment for ASD patients. A recent study by Reid and colleagues has also determined severely frail ASD patients to be least likely to reach substantial clinical benefit across multiple outcome measures, when compared with frail and nonfrail patients [21]. The utility of this data should be further analyzed in order to establish optimal timing of surgery in conjunction with frailty status to identify the best long-term clinical outcome.

Conclusion

This study compared 236 operative and 236 nonoperative propensity matched ASD patients over a 3-year period. By 3-year follow-up, nonoperative patients showed inferior frailty scores compared with baseline. Nonoperative patients were also more likely to develop severe frailty, and at a quicker rate, relative to operative patients. Baseline depression, increased NRS back pain scores, and nonoperative treatment were all associated with severe frailty development, with nonoperative treatment showing the strongest relationship with severe frailty. For operative patients, residual sagittal malalignment following surgery was the greatest predictor of severe frailty development. These results suggest that operative intervention and postoperative achievement of sagittal alignment may play a significant role in frailty remediation, preventing frailty progression.

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