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RANDOMIZED TRIAL

Serious Adverse Events Significantly Reduce Patient-Reported Outcomes at 2-Year Follow-up

Nonoperative, Multicenter, Prospective NIH Study of 105 Patients

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Study Design. This is an analysis of a prospective 2-year study on nonoperative patients enrolled in the Adult Symptomatic Lumbar Scoliosis (ASLS) National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) trial.

Objective. The purpose was to evaluate the impact of serious adverse events (SAEs) on patient-reported outcomes (PROs) in nonoperative management of ASLS as measured by Scoliosis Research Society-22 (SRS-22), Oswestry Disability Index (ODI), and Short Form-12 (SF-12) at 2-year follow-up.

Summary of Background Data. Little is known about PROs in the nonoperative management of ASLS or the prevalence and impact of SAEs on PROs.

Methods. The ASLS trial dataset was analyzed to identify adult lumbar scoliosis patients electively choosing or randomly assigned to nonoperative treatment with minimum 2-year follow-up. Patient data were collected prospectively from 2010 to 2015 as part of NIAMS R01-AR055176–01A2 ''A Multi-Centered Prospective Study of Quality of Life in Adult Scoliosis.'' SAEs were defined as life-threatening medical events, new significant or permanent disability, new or prolonged hospitalization, or death.

Results. One hundred five nonoperative patients were studied to 2-year follow-up. Twenty-seven patients (25.7%) had 42 SAEs; 15 (14.3%) had a SAE during the first year. The SAE group had higher body mass index (29.4 *vs.* 25.2; $P=0.008$) and reported worse SRS-22 Function scores than the non-SAE group at baseline (3.3 *vs.* 3.6; $P=0.024$). At 2-year follow-up, SAE patients experienced less improvement (change) in SRS-22 Self-Image (−0.07 *vs.* 0.26; $P=0.018$) and Mental Health domains (−0.19 *vs.* 0.25; $P=0.002$) than non-SAE patients and had lower SRS-22 Function, Self-Image, Subscore, and SF-12 Mental and Physical component scores (MCS/PCS). Fewer SAE patients reached minimal clinically important difference (MCID) threshold in SRS-22 Mental Health (14.8% *vs.* 43.6%; $P=0.01$).

Conclusion. A high percentage (25.7%) of ASLS patients managed nonoperatively experienced SAEs. Those patients who sustained a SAE had less improvement in reported outcomes.

Key words: adult symptomatic lumbar scoliosis, adverse events, complications, degenerative scoliosis, NIH, nonoperative treatment.

Level of Evidence: 2

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Adult spinal deformity (ASD) remains a challenging and costly condition to treat. Adult scoliosis rates have been estimated to exceed 50% in the population of those over 60 years of age.[1] The natural history of these patients is typically one of gradual functional decline, continued pain, and deterioration in health status.[2] Previous studies have suggested that nonoperative modalities are not effective in improving patient-reported outcomes (PROs) in adult symptomatic lumbar scoliosis (ASLS).[3,4]

Operative management in the older adult population, however, is not benign. Postoperative minor and major complication rates have been reported to exceed 60% and 30%, respectively.[5–10] The magnitude of the surgery, patient comorbidities, advanced age, and lower physiologic reserve have all been implicated as possible reasons for high complication rates.[8,11] In spite of these issues, several studies have demonstrated short- and mid-term clinical benefits to

operative intervention,[12–14] but often compare heterogeneous patient cohorts.

Although multiple studies have demonstrated high complication and adverse events rates after operative intervention for ASLS, to our knowledge, none have examined the adverse event rate in nonoperative ASLS patients. Previous studies comparing operative to nonoperative treatment lack the follow-up[3] to capture adverse events of nonoperative patients for years after initial presentation.

A multicenter, dual-arm study examining operative and nonoperative treatment of ASLS has had a primary aim of investigating the effectiveness of operative *versus* nonoperative treatment for ASLS. Funding was provided by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) for "A Multi-Center Prospective Study of Quality of Life in Adult Scoliosis" - R01AR055176–01A2.[15] Patients participating in the clinical trial for a minimum of 2 years, both operative and nonoperative, were evaluated for the occurrence of all serious adverse events (SAEs). SAE occurrence was defined by this trial as any death, life-threatening event, event that caused significant or permanent disability, or event that led to prolonged or new hospitalization. The purpose of this study was to evaluate the prevalence of SAEs in the nonoperative cohort while evaluating their impact on PROs. We hypothesized that the occurrence of a SAE would negatively influence the effectiveness of nonoperative treatment for ASLS at 2 years follow-up.

MATERIALS AND METHODS

Study Design

A prospective, multicenter series of ASLS patients was evaluated from 2010 to 2015. Patients were enrolled throughout nine centers across the United States and Canada. Patients who met inclusion criteria and agreed to participate chose between a randomized and observational arm. Those desiring to choose their own treatment remained in the observational arm. Both study arms contained an operative and nonoperative cohort. For this study, all ($n = 105$) nonoperative patients (regardless of randomized or observational arm) with 2-year follow-up were included in the analysis. Thirty-two patients crossing over to operative treatment before 2-year follow-up in the nonoperative arm were not studied. Patients were monitored at each enrollment site for the occurrence of SAEs. Monitoring was performed prospectively by each site during follow-up clinical visits at 3, 12, and 24 months. In addition, PROs were completed by mail at 6, 9, 15, 18, and 21 months. Any changes in PRO scores [drop in SRS domain scores of 0.5 or more or increase in Oswestry Disability Index (ODI) of 10 points or greater] resulted in a follow-up call to the patient to determine if an adverse event had occurred. Site monitoring visits were performed annually to review research and clinical charts. SAE details (date of onset, diagnosis, expectedness, relationship to treatment, severity, outcome) were recorded by the enrollment site and reported to the coordinating center for review within 24 hours of discovery. The coordinating center reviewed data and then forwarded to the Data Safety Monitoring Board (DSMB) for review. Institutional Review Board approval was obtained at each participating center.[15]

Patient Population

Patients between the ages of 40 and 80 years and diagnosed with ASLS were eligible for study enrollment. ASLS was defined as an idiopathic or *de novo* lumbar scoliosis with a Cobb measurement $\geq 30^{\circ}$. Symptomatic was defined as a Scoliosis Research Society (SRS)-22 score ≤ 4.0 in the domains of Pain, Function, and/or Self-Image and/or ODI score of ≥ 20. Age and diagnosis categories were defined as such because the majority of patients presenting with symptomatic ASD have idiopathic or *de novo* scoliosis. Idiopathic implies progression of pre-existent teenage scoliosis and *de novo* represents patients who have no history of scoliosis as adolescents, but then develop a deformity as an adult. In general, patients younger than 40 years do not typically have the degenerative changes and comorbidities that make the decision to operate more challenging. Also, patients 81 years or older were not eligible for inclusion, as most providers would not recommend surgical procedures for this age group due to increased risk of perioperative morbidity and mortality. All patients, regardless of treatment arm, were considered reasonable operative candidates at the time of enrollment. Patients with excessive medical comorbidities, pregnancy, osteoporosis (defined by femoral neck dual-energy X-ray absorptiometry t-score < -3.0), previous thoracolumbar fusion, multilevel thoracolumbar decompression, high-grade spondylolisthesis, congenital spine anomalies, neuromuscular scoliosis, and a high risk of operative failure or morbidity were not enrolled in the study.

At enrollment, data regarding patient demographics, comorbidities, and disease severity were captured. Our analysis included basic patient demographic information (age, gender, race), job/working status (defined as full or part-time work outside the home), health wellness characteristics [body mass index (BMI)/obesity, alcohol use, smoking status], medical comorbidities (such as cardiac, lung, circulatory, endocrine, renal, gastrointestinal), and other disorders. A history of medically diagnosed psychiatric disorders, including depression and anxiety, was collected from physician and patient questionnaires, and grouped for dichotomous analysis. Standard baseline radiographic measurements were recorded. Consideration was given to stratification of continuous variables such as patient age, but background analysis revealed that no differences existed among cohorts.

Outcomes

PROs, as measured by the SRS-22, ODI, and SF-12, at 2-year follow-up were the primary outcomes. The reproducibility of PROs has been previously validated, and determined to not require additional separate internal validation.[3,16,17] SAEs were considered for analysis regardless

of their relatedness to the spine pathology or treatment modality. All SAEs within the 2-year follow-up period were reviewed and subcategorized by the most significant related intervention or sequela and grouped according to diagnostic category.

Analysis

Patients meeting inclusion criteria were compared on the basis of the occurrence of any SAE during 2 years following enrollment. Inferential statistics were used to compare baseline patient characteristics between those with and without a SAE. Radiographic measurements underwent independent evaluation by two experienced readers: a spinal surgeon (not otherwise involved in the study clinically or academically) and the clinical trial research nurse. Each reader performed two independent reads (separated by several weeks). The four reads were compared using intraclass correlation-coefficients (ICCs) for both intra- and interobserver reliability and the results demonstrated very high reliability.[18] With the exception of T2-T5 coronal measurements (kappa = 0.71), all ICCs ranged from k = 0.90 to k = 0.99.

Standard statistical tests, including Chi-square for categorical variables and Student *t* test for continuous variables and analysis of variance (ANOVA), were performed. Baseline and 2-year PRO scores and changes in PRO scores were compared between cohorts. Multivariate logistic regression analysis was used to test the influence of baseline characteristics on the occurrence of SAEs. All variables with $P < 0.05$ from the univariate analysis were included in the multivariate model. Model discrimination was measured as the c-index/c-statistic. The c-index is a measure of goodness of fit for binary outcomes in a logistic regression model; values over 0.7[17] indicate a good model, where those above 0.8 indicate a strong model. The number of patients from each cohort achieving a minimal clinically important difference (MCID) for SRS-22, ODI, and SF-12 scores were compared. MCID PRO thresholds were determined based on previous work: SRS-22 (0.4), ODI (10), SF-12 (5).[19–21] All statistical analyses were performed using SAS software (version 9.4; SAS Institute, Cary, NC). The level of significance for all univariate and multivariate analysis was set at $P < 0.05$.

RESULTS

One hundred five patients were studied to 2-year follow-up. Eight patients who withdrew before completing 2-year follow-up were not studied. During the 2 years, 27 patients (25.7%) had 42 SAEs (Table 1). Ten (9.5%) of the 27 patients experienced multiple SAEs. Fifteen (14.3%) patients had a SAE during the first year. Over one-third of 27 SAE patients experienced at least two events during the follow-up period. Nearly 90% of these patients had associated hospitalization. The most common reason for an event was operative intervention related to a progressive medical condition not related to the patient's spinal deformity. Other musculoskeletal (major joint arthritis, cervical myelopathy/radiculopathy, rotator cuff disease; 25.9%), cardiac (14.8%), gastrointestinal (18.5%), and genitourinary (14.8%) events were the top diagnostic categories of SAEs (Table 1). Four of the 42 SAEs were directly related to the patient's spinal deformity, namely side effects of medications (non-steroidal anti-inflammatory drugs).

TABLE 1. Summary of Nonoperative Cohort Experiencing a Serious Adverse Event over 2 yrs

Number of Serious Adverse Events	(N) Patients	Percent
1 event	17	63.0
2 events	7	25.9
3 events	2	7.4
4 events	1	3.7
Total	27	100.0
Highest event intervention/Sequele		
Death	0	0.0
Emergency room visit	2	7.4
Hospitalization	7	25.9
Surgery (urgent)	5	18.5
Surgery (elective)	12	44.4
Unknown	1	3.7
Total	27	100.0
Diagnostic category		
Cardiac	4	14.8
Gastrointestinal	5	18.5
Genitourinary	4	14.8
Musculoskeletal	7	25.9
Oncologic	2	7.4
Neurologic	3	11.1
Respiratory	1	3.7
Unknown	1	3.7
Total	27	100.0

Demographics were similar between SAE and non-SAE cohorts based on age (60.1 *vs.* 63.5 years, $P = 0.24$) and gender (14.8% *vs.* 6.4% males, $P = 0.24$). Slightly more nonwhite patients ($P = 0.022$) and nonworking patients ($P = 0.015$) had a SAE (Table 2). The prevalence of wellness habits (alcohol use, smoking history, $P > 0.5$) and comorbidities, such as cardiac, respiratory, vascular, renal, psychiatric, and oncologic disease (all $P > 0.25$) did not differ between cohorts. Those experiencing a SAE had a higher BMI (29.4 *vs.* 25.2, $P = 0.008$) (Table 2). When BMI was stratified by range (<30, 30–40, and >40), this statistical association persisted ($P = 0.014$). Both cohorts had the same number of obese (nine) and morbidly obese (two) patients, but there was a higher percentage of patients with BMI 30 to 40 and >40 in the SAE group. In the multivariate logistic regression model, BMI remained a significant predictor of SAE, with a c-index of 0.702. A higher BMI was associated with the occurrence of SAEs [odds ratio (OR) 3.408, 95% confidence interval (95% CI): 1.301–8.930)].

TABLE 2. Comparison of Baseline Case Characteristics of Nonoperative ASLS Patients with and Without a Serious Adverse Event

Patient Demographics	Overall (n = 105)	No SAE (n = 78)	SAE (n = 27)	*P*
	Mean (sd)	Mean (sd)	Mean (sd)	
Age, yrs	61.5 (10.0)	60.8 (10.5)	63.5 (8.0)	0.236
BMI	26.3 (6.2)	25.2 (5.4)	29.4 (7.3)	0.008
	%	%	%	
Gender: Males	8.6	6.4	14.8	0.231
Race				0.022
White	89.4	92.2	81.5	
Black	7.7	7.8	7.4	
Other	2.9	0.0	11.1	
Work status (Yes %)	63.8	70.5	44.4	0.015
Baseline comorbidities				
Alcohol/drugs	1.0	1.3	0.0	1.000
Autoimmune	3.8	2.6	7.4	0.272
Cancer	22.9	23.1	22.2	0.927
Cardiac disease	7.6	7.7	7.4	1.000
Circulatory disorders, arterial	1.0	0.0	3.7	0.257
Circulatory disorders, venous	2.9	2.6	3.7	1.000
Diabetes mellitus	2.9	2.6	3.7	1.000
Gastrointestinal (ulcer, stomach)	11.4	12.8	7.4	0.727
Hypertension	37.1	35.9	40.7	0.654
Infection history	4.8	3.9	7.4	0.601
Lung disease/Asthma	13.3	12.8	14.8	0.752
Nervous system disorders	0.0	0.0	0.0	1.000
Obesity	46.7	39.7	66.7	0.016
Psychiatric	21.9	19.2	29.6	0.260
Renal disease	1.0	1.3	0.0	1.000
Smoking	14.3	14.1	14.8	1.000
Coronal plane	Mean (sd)	Mean (sd)	Mean (sd)	
Thoracic Cobb, °	47.4 (13.0)	47.3 (13.9)	47.5 (9.2)	0.978
Lumbar Cobb, °	49.2 (11.8)	48.2 (10.3)	52.0 (15.2)	0.236
Fractional Cobb, °	21.1 (8.8)	20.6 (8.1)	22.6 (10.5)	0.298
Coronal balance, mm	20.4 (16.5)	19.9 (15.7)	21.8 (18.7)	0.605
Thoracic curve >30° (%)	50.5	53.9	40.7	0.240
Sagittal plane				
Sagittal balance, mm	37.8 (30.3)	35.3 (31.0)	44.9 (27.6)	0.157
Pelvic incidence, °	55.7 (13.2)	54.4 (12.3)	59.2 (15.0)	0.110
Sacral slope, °	33.7 (11.3)	33.5 (11.2)	34.2 (11.7)	0.780
Pelvic tilt, °	22.9 (9.6)	22.0 (9.1)	25.2 (10.7)	0.153
PI minus LL mismatch	17.5 (13.9)	16.9 (13.7)	19.1 (14.6)	0.484
ASLS treatment history	%	%	%	
Pharmacological	91.4	93.6	85.2	0.231
Physical therapy	81.0	82.1	77.8	0.626
Spine injection, s	16.2	15.4	18.5	0.703

ASLS indicates adult symptomatic lumbar scoliosis; BMI, body mass index; LL, lumbar lordosis; PI, pelvic incidence; SAE, serious adverse event; sd, standard deviation.

Overall, patients with and without a SAE were similar in terms of radiographic parameters and previous treatment (Table 2). Coronal thoracic, lumbar (48.2° *vs.* 52.0°, $P = 0.24$), and fractional lumbar Cobb measurements were similar between non-SAE and SAE cohorts. Likewise, in the sagittal plane, overall sagittal alignment (C7 sagittal vertical axis), pelvic incidence (PI), lumbar lordosis (LL), pelvic tilt, and PI-LL mismatch did not differ (all $P > 0.23$) (Table 2). Both SAE and non-SAE patients had similar types and rates of nonoperative treatment, including medications, physical therapy, and spine injections (Table 2).

TABLE 3. Comparison of Patient-Reported Outcomes in Nonoperative ASD Patients with and Without a Serious Adverse Event in 2 yrs

	Patient-Reported Outcomes			
	All (n = 105)	No SAE (n = 78)	SAE (n = 27)	
	Mean (sd)	Mean (sd)	Mean (sd)	*P*
Index visit				
SRS-22 Pain	3.05 (0.63)	3.12 (0.59)	2.86 (0.72)	0.062
SRS-22 Function	3.47 (0.59)	3.55 (0.58)	3.25 (0.57)	0.024
SRS-22 Self Image	3.15 (0.66)	3.18 (0.69)	3.08 (0.57)	0.516
SRS-22 Mental Health	3.74 (0.72)	3.70 (0.71)	3.85 (0.73)	0.332
SRS-22 Subscore	3.35 (0.46)	3.39 (0.45)	3.26 (0.48)	0.226
ODI	30.00 (13.78)	28.85 (13.10)	33.33 (15.37)	0.146
SF-12 MCS	51.16 (10.81)	51.52 (10.76)	50.13 (11.07)	0.566
SF-12 PCS	37.87 (10.30)	38.93 (10.63)	34.82 (8.75)	0.074
2-yr follow-up				
SRS-22 Pain 2-yr	3.46 (0.62)	3.47 (0.59)	3.42 (0.67)	0.734
SRS-22 Function 2-yr	3.55 (0.66)	3.65 (0.61)	3.27 (0.71)	0.009
SRS-22 Self Image 2-yr	3.33 (0.74)	3.44 (0.61)	3.01 (0.96)	0.034
SRS-22 Mental Health 1-yr	3.88 (0.68)	3.95 (0.64)	3.66 (0.76)	0.054
SRS-22 Subscore 2-yr	3.55 (0.54)	3.63 (0.48)	3.34 (0.66)	0.042
ODI 2-yr	27.28 (14.87)	26.43 (14.33)	29.70 (16.37)	0.327
SF-12 MCS 2-yr	51.97 (10.67)	53.22 (10.36)	48.41 (10.93)	0.044
SF-12 PCS 2-yr	39.56 (11.35)	40.88 (10.59)	35.79 (12.73)	0.044
2-yr PRO change				
Change in SRS-22 Pain	0.40 (0.58)	0.35 (0.55)	0.56 (0.65)	0.098
Change in SRS-22 Function	0.08 (0.43)	0.10 (0.40)	0.01 (0.51)	0.378
Change in SRS-22 Self Image	0.18 (0.64)	0.26 (0.60)	(−)0.07 (0.71)*	0.018
Change in SRS-22 Mental Health	0.14 (0.66)	0.25 (0.65)	(−)0.19 (0.56)*	0.002
Change in SRS-22 Subscore	0.20 (0.38)	0.24 (0.33)	0.08 (0.47)	0.104
Change in ODI	(−)2.72 (9.46)	(−)2.41 (9.52)	(−)3.62 (9.37)	0.569
Change in SF-12 MCS	0.78 (11.84)	1.66 (12.07)	(−)1.71 (10.97)*	0.205
Change in SF-12 PCS	1.52 (9.65)	1.72 (9.35)	0.97 (10.63)	0.731

*A deterioration from baseline.

ASD indicates adult spinal deformity; MCS, Mental Component Score; ODI, Oswsetry Disability Index; PCS, Physical Component Score; SAE, serious adverse event; sd, standard deviation; SRS, Scoliosis Research Society.

The SAE group reported worse SRS Function than the non-SAE group at baseline (3.25 *vs.* 3.55, $P = 0.024$). There were no statistical differences in the other baseline SRS-22, ODI, or SF-12 scores (Table 3).

At 2-year follow-up, patients experiencing a SAE had less improvement (change) in SRS-22 Self-Image (mean difference = 0.34, 95% CI: 0.22–0.46, $P = 0.018$) and Mental Health (0.45, 95% CI: 0.33 *vs.* 0.57, $P = 0.002$) domain scores than the non-SAE group. Furthermore, at 2 years, SAE patients had lower SRS Function (mean diff = 0.38, 95% CI: 0.26–0.50, $P = 0.009$) and Self-Image (0.43, 95% CI: 0.30–0.57, $P = 0.034$), SRS Subscore (0.29, 95% CI: 0.19–0.39, $P = 0.042$), SF-12 MCS (4.81, 95% CI: 2.80–6.82, $P = 0.044$), and SF-12 PCS (5.01, 95% CI: 2.95–7.23, $P = 0.044$) than those without a SAE at 2-year follow-up (Table 3). Finally, significantly fewer patients with a SAE (14.8% *vs.* 43.6%, $P = 0.01$) reached MCID for the SRS Mental Health domain (Table 4).

DISCUSSION

This study examines the influence adverse events have on PROs over 2 years using the nonoperative cohort in our NIAMS-funded study on ASLS. Overall, we found that over one-quarter of patients experienced a SAE by 2 years. Most of these SAEs were related to interventions for progressive medical conditions not related to the spinal deformity and were associated with lower PROs at 2-year follow-up than for those patients without a SAE.

The first objective of this study was to identify the prevalence of SAEs in the nonoperative arm of the NIH ASLS study. Nearly 15% of patients had a SAE at 1 year and 25% at 2 years following study enrollment. Even if not choosing surgery, patients should realize that concomitant conditions may arise and these conditions may have a negative effect on PROs.

Several progressive arthritic conditions treated operatively met study criteria for SAEs, though were unrelated to the nonoperative management of ASLS. Within the nonoperative cohort, major joint arthritis and cervical

TABLE 4. Percentage of Patients who Reached a Minimal Clinically Important Difference (MCID) from Baseline to 2 yrs

	All (n = 105)	No SAE (n = 78)	SAE (n = 27)	*P*
SRS-22 Pain (%)	54.3	50.0	66.7	0.134
SRS-22 Function (%)	26.7	25.6	29.6	0.686
SRS-22 Self Image (%)	32.4	35.9	22.2	0.191
SRS-22 Mental Health (%)	36.2	43.6	14.8	0.010
SRS-22 Subscore (%)	29.5	30.8	25.9	0.634
Oswestry Disability Index (%)	9.5	10.3	7.4	1.000
SF-12 Mental Component Score (%)	31.4	34.6	22.2	0.217
SF-12 Physical Component Score (%)	34.3	32.1	40.7	0.437

MCID thresholds: SRS-22 (0.4), ODI (10), SF-12 (5).[17]
SAE indicates serious adverse event; SRS, Scoliosis Research Society.

myelopathy treated operatively accounted for nearly one-third of the SAEs during the 2-year follow-up period. In ASLS patients, both spinal stenosis and lower extremity joint arthritis may be an additional source of pain and dysfunction, which negatively affect PROs regardless of ASLS treatment choice.

From the list of patient demographics, comorbidities, radiographic, and treatment factors, few had any association with the development of a SAE. In both the univariate and multivariate logistic regression analysis, obesity was associated with SAE occurrence. The influence of obesity has been widely reported as a risk factor for the development of other medical conditions, such as cardiac disease and major joint arthritis.[22] Obesity is also a well-accepted risk factor for operative complications.[11,23] Given the necessity for all patients to be considered operative candidates, there was a low prevalence of more severe comorbidities, such as diabetes (3%).

The occurrence of a SAE was associated with a negative change in SRS-22 Self-Image and Mental Health domains from baseline to 2-year follow-up. We assume that the SRS-22 Self-Image result is not related to the patient's spinal deformity, as this parameter did not change over the 2-year follow-up period. The non-SAE cohort had positive and statistically significant improvements in many SRS PROs.

When analyzing the absolute values of 2-year PRO scores, patients not experiencing a SAE had significantly higher SRS Subscore and Function and Self-Image domains and SF-12 MCS/PCS scores than their counterparts with no SAE. Scheer *et al*.[7] reviewed the effect of complications (minor, major, reoperation) on 2-year outcomes following ASD surgery and found any complication negatively influenced mental recovery and reoperation also impacted overall satisfaction.

Most patients failed to meet PRO-specific MCID thresholds. The only PRO for which more than 50% of patients reached a MCID threshold was SRS Pain (Table 4). For SRS Mental Health, 43.6% without a SAE reached MCID, while only 14.8% of patients with a SAE reached the MCID threshold of 0.4.[19] These findings are consistent with a multitude of studies.[3,24] Slobodyanyuk *et al*.[4] showed only 24% of patients treated nonoperatively had clinical improvement at 1 year.

The data collected throughout the NIH ASLS trial represent a very complete series of patients with ASLS considered for operative treatment. Our 2-year follow-up rate in the nonoperative cohort was 93%, the highest reported. A previous multicenter study reported the outcomes of nonoperative ASLS patients with a 2-year follow-up rate of 45%.[3] A more recent study from Liu *et al*.[25] used a registry to identify patient factors associated with clinical improvement in nonoperative treatment. Complete 2-year follow-up was only available in 215 of 371 patients (58%).

Our study, however, is not without limitation. The study inclusion criteria were restricted to patients with ASLS. Patients with other scoliosis etiologies or previous fusion surgeries were excluded, and thus, our results cannot necessarily be applied to all pathologies evaluated by ASD surgeons. Furthermore, this study does not include analysis of the 32 patients that crossed over into the operative arm before 2-year follow-up. Presumably, these would be patients with the lowest baseline PROs. Thus, the reported changes in the nonoperative cohort PROs at 2 years may be somewhat positively skewed. Given the number of PROs analyzed, further statistical work, such as a regression analysis, could not be reasonably performed for each scenario. Finally, patients from both the randomized and observational cohorts were included in the analysis, potentially introducing selection bias in the observational patients.

CONCLUSION

The prevalence of SAEs in the nonoperative cohort of the NIAMS-funded study on ASLS was over 25% (27/105) at 2 years. The occurrence of SAEs impacted many PROs at 2 years, most noticeably patient mental health. In the context of an operative treatment option with significant risks and resource utilization, these findings highlight the importance of understanding the high baseline rate of adverse events within the aging, adult deformity population. Surgeons should set expectations to patients, hospitals, and policymakers that, regardless of treatment chosen, the

natural history of patients suffering from ASLS includes SAEs unrelated to their spine and detrimental to PROs.

➢ Key Points

- ❑ Over 25% of patients undergoing nonoperative treatment for adult symptomatic lumbar scoliosis experienced a serious adverse event over 2 years.
- ❑ The most common reason for an adverse event was operative intervention related to a progressive medical condition not related to the patient's spinal deformity.
- ❑ Patients experiencing a SAE had less improvement in SRS-22 Self-Image and Mental Health domains at 2 years follow-up and fewer SAE patients reached the minimal clinically important difference (MCID) threshold in SRS-22 Mental Health.

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