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CLINICAL ARTICLE

Orthopedic disease burden in adult patients with symptomatic lumbar scoliosis: results from a prospective multicenter study

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OBJECTIVE Although the health impact of adult symptomatic lumbar scoliosis (ASLS) is substantial, these patients often have other orthopedic problems that have not been previously quantified. The objective of this study was to assess disease burden of other orthopedic conditions in patients with ASLS based on a retrospective review of a prospective multicenter cohort.

METHODS The ASLS-1 study is an NIH-sponsored prospective multicenter study designed to assess operative versus nonoperative treatment for ASLS. Patients were 40–80 years old with ASLS, defined as a lumbar coronal Cobb angle ≥ 30° and Oswestry Disability Index ≥ 20, or Scoliosis Research Society-22 questionnaire score ≤ 4.0 in pain, function, and/or self-image domains. Nonthoracolumbar orthopedic events, defined as fractures and other orthopedic conditions receiving surgical treatment, were assessed from enrollment to the 4-year follow-up.

RESULTS Two hundred eighty-six patients (mean age 60.3 years, 90% women) were enrolled, with 173 operative and 113 nonoperative patients, and 81% with 4-year follow-up data. At a mean (± SD) follow-up of 3.8 ± 0.9 years, 104 nonthoracolumbar orthopedic events were reported, affecting 69 patients (24.1%). The most common events were arthroplasty (n = 38), fracture (n = 25), joint ligament/cartilage repair (n = 13), and cervical decompression/fusion (n = 7). Based on the final adjusted model, patients with a nonthoracolumbar orthopedic event were older (HR 1.44 per decade, 95% CI 1.07–1.94), more likely to have a history of tobacco use (HR 1.63, 95% CI 1.00–2.66), and had worse baseline leg pain scores (HR 1.10, 95% CI 1.01–1.19).

CONCLUSIONS Patients with ASLS have high orthopedic disease burden, with almost 25% having a fracture or nonthoracolumbar orthopedic condition requiring surgical treatment during the mean 3.8 years following enrollment. Comparisons with previous studies suggest that the rate of total knee arthroplasty was considerably greater and the rates of total hip arthroplasty were at least as high in the ASLS-1 cohort compared with the similarly aged general US population. These conditions may further impact health-related quality of life and outcomes assessments of both nonoperative and operative treatment approaches in patients with ASLS.

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KEYWORDS adult; arthroplasty; fracture; orthopedic disease burden; scoliosis; spine deformity; lumbar

Adult spinal deformity (ASD) has many etiologies, including untreated or residual adolescent idiopathic scoliosis, iatrogenic deformities, and degenerative pathologies.[1,2] ASD is highly prevalent, especially among older individuals, affecting up to 68% of those at least 65 years of age.[3,4] When patients are symptomatic, the health impact of ASD can be substantial, with disability scores comparable to those of patients with cancer, diabetes, and heart disease.[5] However, the symptoms and disability of patients with ASD not only derive from their

ABBREVIATIONS ASD = adult spinal deformity; ASLS = adult symptomatic lumbar scoliosis; HR = hazard ratio; NRS = numeric rating scale; ODI = Oswestry Disability Index; PCS = Physical Component Score; PI-LL = pelvic incidence to lumbar lordosis; PRO = patient-reported outcome; PT = pelvic tilt; SAE = serious adverse event; SF-12 = 12-Item Short-Form Health Survey; SRS-22 = Scoliosis Research Society-22; THA = total hip arthroplasty; TKA = total knee arthroplasty.

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spinal pathologies, but also reflect the collective impact of comorbidities and degenerative conditions that accumulate with aging.[6,7]

For many adults with spinal deformity, their spinal disease may be the dominant driver of pain and disability, but other orthopedic conditions may also negatively contribute to health-related quality of life. These other orthopedic conditions can not only impact pain and function, but may also confound the determination of responses to operative and nonoperative treatments. Despite the potential collateral impact of other orthopedic conditions in patients with ASD, the nonthoracolumbar orthopedic disease burden has not been defined in this patient population.

Results of an NIH-funded trial of adult symptomatic lumbar scoliosis (ASLS), the most common form of ASD, have been recently reported.[8] Our objective in the present study was to use this ASLS patient population to assess nonthoracolumbar orthopedic disease burden. In addition, we sought to identify demographic, clinical, and radiographic factors associated with greater nonthoracolumbar orthopedic disease burden in this population.

Methods

Patient Population and Data Collection

The current analysis used data from patients with ASLS who were prospectively enrolled in an NIH-sponsored multicenter trial (ASLS-1) between 2010 and 2014 with the aim of assessing the effectiveness of operative versus nonoperative treatment for ASLS.[8] Nine centers in North America contributed patients and each center received IRB approval for study participation (see *Appendix*).

Enrollment criteria for ASLS-1 were patients 40–80 years old and the presence of ASLS. ASLS was defined as either idiopathic or de novo lumbar scoliosis with a Cobb angle ≥ 30°, and with a Scoliosis Research Society-22 (SRS-22) questionnaire score ≤ 4.0 in the domains of pain, function, and/or self-image, and/or an Oswestry Disability Index (ODI) score ≥ 20. Patients were excluded if they had excessive medical comorbidities, pregnancy, osteoporosis (t-score < –3.0 of the femoral neck), history of a thoracolumbar fusion or thoracolumbar decompression across multiple levels, grade 3–5 spondylolisthesis, congenital spine anomalies, scoliosis of neuromuscular etiology, or were considered to be at high risk of surgical morbidity or failure. Only patients deemed surgical candidates were offered enrollment.

At enrollment, patients willing to be randomized to either operative or nonoperative treatment were entered into the randomized study arm. Enrolled patients who declined randomization were entered into the observational study arm based on their treatment choice (operative or nonoperative). Details of randomization, treatments, and outcomes have been previously reported.[8,9] Because the present study is focused on the development of nonspine orthopedic conditions and is not focused on treatment approach, operative and nonoperative patients in both the observational and randomized arms were included as a single cohort. As part of the baseline and follow-up assessments, each site collected serious adverse events (SAEs). SAEs, as defined by the study sponsor (NIH), were death or any event that was life-threatening, caused significant or permanent disability, resulted in new or prolonged hospitalization, or was unexpected but reasonably related to the treatment intervention.[10] Based on reported SAEs, nonthoracolumbar orthopedic disease events, defined as fracture and orthopedic conditions requiring surgical treatment, were assessed from the time of study enrollment through the 4-year follow-up. Reported events are those collected prospectively from the time of study enrollment and do not include events predating enrollment. The present study focuses on significant orthopedic events (fractures and surgeries) that required hospital admission, because these were the most objectively collected as part of the trial. Except for fractures, which did not all require operative treatment, other nonthoracolumbar orthopedic events that did not require operative treatment were not included in the present analyses. For example, hip arthritis that required no treatment or was treated only with medications or steroid injection was not included, because such conditions can be subjective and were not consistently collected.

Data and Statistical Analysis

Baseline demographic, clinical, and patient-reported outcome (PRO) measures were summarized. Nonthoracolumbar orthopedic events were grouped by type, and the numbers and percentages of patients affected and rates per 100,000 person-years were calculated. Cox regression was used to estimate associations of demographic, clinical, radiographic, and PRO measures with time to a nonthoracolumbar orthopedic event. Bivariate unadjusted models were run, followed by two adjusted models: 1) a preliminary model, including all patient characteristics statistically significantly associated in bivariate models ($p < 0.05$); and 2) a final model, including all patient characteristics associated with p values < 0.10 in the preliminary model. A similar analysis was also performed for comparison of patients who either did or did not undergo an arthroplasty during follow-up. SAS software (version 9.4, SAS Institute) was used for statistical analyses. All statistical tests were two-sided, and a threshold alpha level of 0.05 was used for statistical significance.

Results

Patient Population

The ASLS-1 study included 286 patients: a randomized cohort of 63 patients and an observational cohort of 223 patients. At baseline, 142 patients enrolled with plans for operative treatment and 144 enrolled with plans for nonoperative treatment, based on either randomization in the randomized arm or patient choice in the observational arm. By 4 years, in the combined cohort, 6 patients had crossed over from planned operative to nonoperative treatment, and 40 patients had crossed over from nonoperative to operative treatment. Loss to follow-up/withdrawals were 12/286 (4.2%) at 2 years and 28/286 (9.8%) at 4 years. The overall 4-year follow-up rate was 81% (mean 3.8 ± 0.9 years). The 4-year as-treated cohorts included 173 operative and 113 nonoperative patients. The as-treated operative patients were those who received operative treatment

TABLE 1. Baseline characteristics of 286 patients who received operative or nonoperative treatment for ASLS

Patient Parameter	Value (%)
Mean age ± SD, yrs	60.3 ± 9.3
Mean BMI ± SD, kg/m^2	26.8 ± 5.5
Males	28 (9.8)
Race	
White	268 (93.7)
Black	14 (4.9)
Other	4 (1.4)
Currently working/employed*	171 (59.8)
History of depression/anxiety/psychiatric disorder	88 (30.8)
Substance use	
Current or former tobacco/nicotine use	104 (36.4)
Current or former alcohol/drug use	8 (2.8)
Mean baseline PROs ± SD	
SRS-22 subscore	3.2 ± 0.5
ODI	35.0 ± 15.2
NRS back pain	6.0 ± 2.2
NRS leg pain	3.6 ± 3.0
SF-12 MCS	50.3 ± 11.0
SF-12 PCS	35.2 ± 10.0

MCS = Mental Component Score.
* Includes part-time and full-time homemaker.

at some point during enrollment, including patients who crossed over from nonoperative treatment. The as-treated nonoperative patients were those who only received nonoperative treatments.

Baseline characteristics of the total 286 patients are summarized in Table 1. The mean age was 60.3 years and the majority of patients were women (90%). Almost one-third had a history of depression/anxiety/psychiatric disorder, and 36% were either current or former tobacco/nicotine users. The baseline PRO measures reflect a population with moderate to severe pain and disability (Table 1).

Nonthoracolumbar Orthopedic Procedures and Fractures

A total of 104 nonthoracolumbar orthopedic procedures and fractures were reported at the mean 3.8 ± 0.9 years of follow-up, with 69 patients affected (24.1%), and the overall rate of these events per 100,000 person-years was 9200 (95% CI 7557–11,099; Table 2). The estimated occurrence of these events at 2 years following ASLS intervention was 15.9% (95% CI 11.5%–20.1%) and at 4 years was 24.7% (95% CI 19.3%–29.8%). Thus, the majority of these events occurred within the first 2 years following ASLS intervention, particularly between the 1- and 2-year time points (Fig. 1). Overall, the most common event was arthroplasty. During the 3.8-year follow-up, 29 patients (10.1%) underwent 38 arthroplasties, resulting in a rate of 3362 per 100,000 person-years (95% CI 2419–4563; Table 2). The estimated occurrence of arthroplasty events at 2 years following ASLS intervention was 6.2% (95% CI 3.3%–9.0%) and at 4 years was 10.2% (95% CI 6.5%–13.9%; Fig. 2). Knee arthroplasty was the most common, accounting for two-thirds of the procedures, followed by procedures performed on the shoulder, hip, and hallux (Table 2). A total of 25 orthopedic fractures affected 23 patients (8.0%), with the most common fractures affecting the foot/ankle, patella, shoulder, wrist, and femur. Joint ligament/cartilage repairs were performed in 12 patients (4.2%) and most commonly involved the knee and shoulder. Other less common events included cervical decompression/fusion (n = 7), carpal tunnel release (n = 6), and hammer toe repair (n = 4).

Associations of baseline demographics, radiographic parameters, and PROs and risk of a nonthoracolumbar orthopedic event were estimated (Table 3). In unadjusted analyses, higher risk of an event was observed in patients who were older, not employed, had a greater number of baseline comorbidities, were more likely to have a history of tobacco/nicotine use, had worse sagittal spinal deformity (pelvic tilt [PT] and pelvic incidence to lumbar lordosis [PI-LL] mismatch), and poorer baseline health-related quality of life (leg pain numeric rating scale [NRS] and 12-Item Short-Form Health Survey [SF-12] Physical Component Score [PCS]). On univariate analysis, patients with a thoracic coronal curve > 30° had a lower risk of an event. Adjusted hazard ratios (HRs) are provided for these factors (preliminary model) in Table 3. A final model was generated that included all remaining factors with p values < 0.10 after backward selection from the preliminary model. In the final adjusted model, factors associated with nonthoracolumbar orthopedic events were: greater age (HR 1.44, 95% CI 1.07–1.94), history of tobacco/nicotine use (HR 1.63, 95% CI 1.00–2.66), and greater baseline leg pain NRS score (HR 1.10, 95% CI 1.01–1.19; Table 3). Based on this model, the likelihood of a nonthoracolumbar orthopedic event in this patient population is increased by 44% for each decade increase in age, increased by 63% in those with a history of tobacco/nicotine use, and increased by 10% for each point increase of the baseline leg pain NRS score.

Associations of baseline demographics, radiographic parameters, and PROs with risk of arthroplasty during study enrollment were also estimated (Table 4). Based on the final adjusted model, higher risk of arthroplasty was observed in patients who were of non-White, non-Black race compared to White race ("other," HR 5.37, 95% CI 1.24–23.27), were not working (HR for currently working/employed 0.29, 95% CI 0.13–0.68), and had worse baseline leg pain NRS score (HR 1.29, 95% CI 1.12–1.47; Table 4).

Discussion

The health impact of symptomatic ASD is substantial,[5] but this patient population, which tends to be elderly, may be affected by other health conditions that negatively contribute to health state. Given that ASD is an orthopedic and neurosurgical condition, these patients may also have an increased burden of other orthopedic pathologies. These other orthopedic conditions may confound the ability to accurately assess the specific health impact of spinal deformity and the potential benefits of operative and non-

TABLE 2. Summary of nonthoracolumbar spine orthopedic procedures and fractures occurring among 286 patients within 4 years of enrollment in a study of operative versus nonoperative treatment for ASLS

Procedure/Fracture	No. of Events	No. (%) of Pts Affected	Rate per 100,000 Person-Yrs (95% CI)
Arthroplasty	38	29 (10.1)	3362 (2419–4563)
Knee	25	20 (7.0)	2212 (1466–3212)
Shoulder	6	5 (1.7)	531 (221–1094)
Hip	6	5 (1.7)	531 (221–1094)
Hallux	1	1 (0.3)	88 (8–412)
Fracture	25	23 (8.0)	2212 (1466–3212)
Foot/ankle	9	9 (3.1)	796 (393–1453)
Patella	3	2 (0.7)	265 (73–708)
Shoulder	3	3 (1.0)	265 (73–708)
Wrist	2	2 (0.7)	177 (35–567)
Femur	2	2 (0.7)	177 (35–567)
Cervical	1	1 (0.3)	88 (8–412)
Pelvis	1	1 (0.3)	88 (8–412)
Sacrum	1	1 (0.3)	88 (8–412)
Toe	1	1 (0.3)	88 (8–412)
Tibia	1	1 (0.3)	88 (8–412)
Humerus	1	1 (0.3)	88 (8–412)
Joint ligament/cartilage repair	13	12 (4.2)	1150 (644–1911)
Knee	6	5 (1.7)	531 (221–1094)
Rotator cuff repair	4	4 (1.4)	354 (118–841)
Shoulder, NOS	2	2 (0.7)	177 (35–567)
Elbow	1	1 (0.3)	88 (8–412)
Cervical decompression/fusion	7	7 (2.4)	619 (276–1216)
Carpal tunnel release	6	4 (1.4)	531 (221–1094)
Hammer toe repair	4	4 (1.4)	354 (118–841)
Miscellaneous surgery	6	5 (1.7)	531 (221–1094)
Foot	3	2 (0.7)	265 (73–708)
Wrist/hand/digit	3	3 (1.0)	265 (73–708)
Trigger finger release	2	2 (0.7)	177 (35–567)
Hip dislocation	1	1 (0.3)	88 (8–412)
Hip contracture	1	1 (0.3)	88 (8–412)
Cubital tunnel release	1	1 (0.3)	88 (8–412)
Total	104	69 (24.1)	9200 (7557–11,099)

NOS = not otherwise specified.

operative treatments. The present study assesses the rates of nonthoracolumbar orthopedic events that occurred in a cohort of patients with ASD while enrolled in a prospective multicenter trial that assessed operative and nonoperative treatment for ASLS.

Among 286 patients with ASLS, a total of 104 nonthoracolumbar orthopedic events were reported, with 69 patients (24.1%) affected during a mean of 3.8 ± 0.9 years of study enrollment. Overall, this represents 9200 (95% CI 7557–11,099) events per 100,000 person-years. The present study is the first to report on the nonthoracolumbar orthopedic disease burden in ASD patients; therefore, there are no previous studies for direct comparisons. Several reports have documented the rate of arthroplasty in the US.[11–15] Sloan and colleagues[15] assessed the rates of total hip arthroplasty (THA) and total knee arthroplasty (TKA) in the US in 2014, which is comparable to the 2010–2014 enrollment period of the present study. They reported a TKA rate of 525.3 (95% CI 520.8–529.8) per 100,000 person-years in 2014 among the population aged 55–64 years. The present study population, with a mean age of 60 years, had a TKA rate of 2212 (95% CI 1466–3212) per 100,000 person-years. In the population aged 55–64 years, Sloan et al. reported a rate of THA in 2014 of 273.8 (95% CI 270.4–277.2) per 100,000 person-years. The rate of THA in the present series was 531 (95% CI 221–1094) per 100,000 person-years. Collectively, these comparisons suggest that the rate of TKA was considerably greater in the studied ASLS cohort compared with the similarly aged US general population, and that the rates of THA in

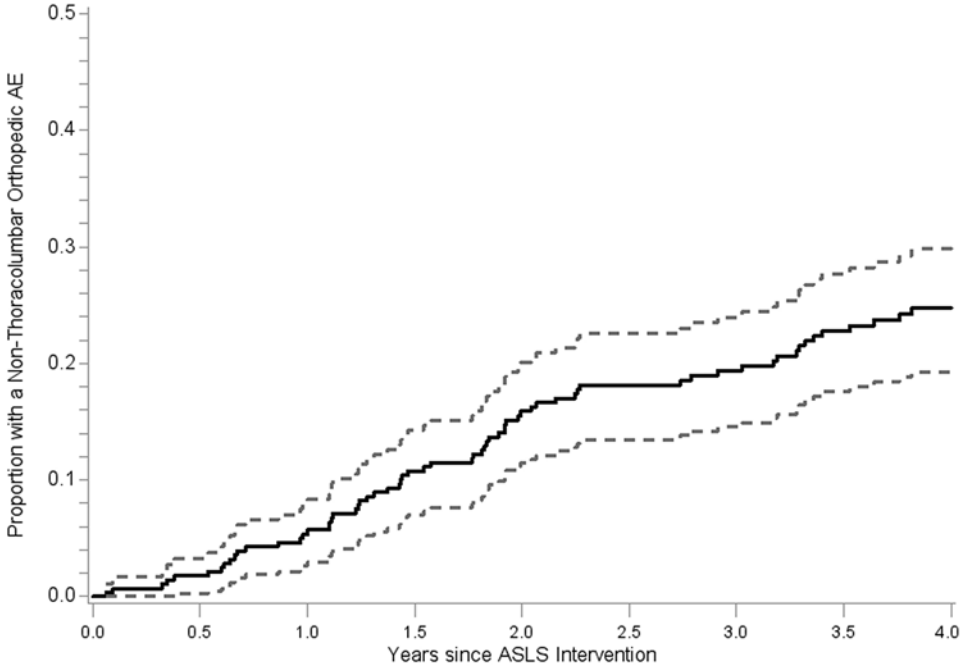

FIG. 1. Cumulative incidence of nonthoracolumbar orthopedic events. The *solid black line* represents an estimate. The *gray dashed lines* represent upper and lower 95% CIs. The 2-year estimate of an adverse event (AE) was 15.9% (95% CI 11.5%–20.1%), and the 4-year estimate was 24.7% (95% CI 19.3%–29.8%).

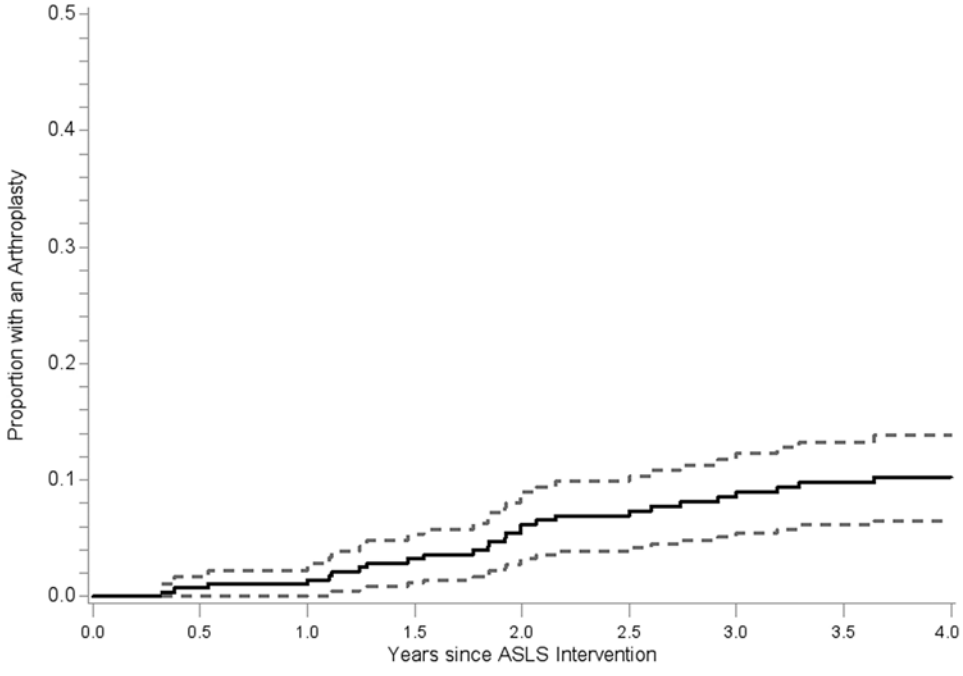

FIG. 2. Cumulative incidence of arthroplasty events. The *solid black line* represents an estimate. The *gray dashed lines* represent upper and lower 95% CIs. The 2-year estimate of an arthroplasty event was 6.2% (95% CI 3.3%–9.0%), and the 4-year estimate was 10.2% (95% CI 6.5%–13.9%).

TABLE 3. Comparison of baseline demographics, radiographic parameters, and PROs of 286 patients with ASLS with and without a nonthoracolumbar orthopedic event

Patient Parameter	Nonthoracolumbar Orthopedic Event			Adjusted HR (95% CI)	
	No, n = 219	Yes, n = 67	HR (95% CI)	Preliminary Model*	Final Model*
Mean age ± SD, yrs, modeled per decade	59.4 ± 9.8	63.3 ± 6.9	**1.57 (1.19–2.06)**	1.35 (0.97–1.88)	**1.44 (1.07–1.94)**
BMI, n (%)					
Underweight/normal	102 (46.6)	26 (38.8)	Ref		
Overweight	51 (23.3)	20 (29.9)	1.16 (0.65–2.07)		
Obese	66 (30.1)	21 (31.3)	1.62 (0.90–2.90)		
Male gender, n (%)	24 (11.0)	4 (6.0)	0.57 (0.21–1.59)		
Race, n (%)					
White	204 (93.2)	64 (95.5)	Ref		
Black	13 (5.9)	1 (1.5)	0.29 (0.04–2.11)		
Other	2 (0.9)	2 (3.0)	2.81 (0.69–11.52)		
Currently working/employed, n (%)†	138 (63.0)	33 (49.3)	**0.58 (0.36–0.94)**	1.01 (0.57–1.78)	
Median no. of baseline comorbidities (IQR)‡	1 (1–2)	2 (1–2)	**1.29 (1.08–1.56)**	1.05 (0.84–1.30)	
Substance use, n (%)					
Current or former tobacco/nicotine use	70 (32.0)	34 (50.8)	**1.94 (1.20–3.13)**	1.60 (0.98–2.62)	**1.63 (1.00–2.66)**
Current or former alcohol/drug use	6 (2.7)	2 (3.0)	1.07 (0.26–4.38)		
Coronal plane					
Mean lumbar Cobb angle ± SD, modeled per 10°	53.7 ± 14.4	50.9 (14.0)	0.85 (0.71–1.02)		
Mean coronal balance (absolute value) ± SD, modeled per 10 mm	22.9 ± 22.4	26.1 (20.9)	1.04 (0.95–1.15)		
Thoracic curve >30°, %	127 (58.0)	29 (43.3)	**0.54 (0.33–0.87)**	0.73 (0.44–1.23)	
Mean global sagittal alignment ± SD, modeled per 10 mm	39.9 ± 37.9	43.4 ± 32.2	1.02 (0.97–1.09)		
Mean PT ± SD, modeled per 10°	23.4 ± 9.9	25.6 ± 8.1	**1.31 (1.02–1.67)**	0.94 (0.64–1.37)	
Mean PI-LL mismatch ± SD, modeled per 10°	15.7 ± 19.2	22.3 ± 15.7	**1.19 (1.05–1.34)**	1.14 (0.94–1.38)	1.12 (0.99–1.28)
Baseline PROs, mean ± SD					
SRS-22 subscore	3.2 ± 0.5	3.1 ± 0.5	0.80 (0.52–1.23)		
ODI, modeled per 10 points	34.1 ± 15.5	37.7 ± 13.7	1.15 (0.99–1.34)		
NRS back pain	5.9 ± 2.2	6.2 ± 2.3	1.06 (0.95–1.18)		
NRS leg pain	3.4 ± 3.0	4.3 ± 3.0	**1.10 (1.02–1.19)**	1.09 (0.99–1.19)	**1.10 (1.01–1.19)**
SF-12 MCS, modeled per 10 points	50.2 ± 10.9	50.7 ± 11.4	1.03 (0.82–1.28)		
SF-12 PCS, modeled per 10 points	36.0 ± 10.3	32.6 ± 8.3	**0.72 (0.56–0.92)**	0.99 (0.97–1.02)	

IQR = interquartile range.

Global sagittal alignment was assessed based on the C7–S1 sagittal vertical axis. Bolded values reflect HRs with 95% CIs that do not cross 1. Note that whether an HR reflects greater or lesser risk of an associated event depends on the directionality of the variable. For example, a greater ODI reflects worse disability, while a greater SF-12 PCS reflects less disability. Missing values included the following: PI-LL mismatch missing for 2 patients with events and 15 patients without; PT missing for 2 patients with an event and 15 patients without; coronal balance and sagittal balance missing for 1 patient without an event.

* The preliminary model includes all the factors with statistically significant associations in the unadjusted models. The final model includes all factors left with p values < 0.10 after backward selection from the preliminary model.

† Includes part-time and full-time homemaker.

‡ Includes autoimmune disease, cancer, cardiac disease, circulatory disorders (artery), circulatory disorders (venous), depression/anxiety/psychiatric disorder history, diabetes, gastrointestinal disease, hypertension, infection history, lung disease/asthma, nervous system disorder, and renal disease.

the study population were at least as high as the similarly aged US general population.

Multiple baseline factors were associated with nonthoracolumbar orthopedic events including older age, history of tobacco/nicotine use, and greater severity of leg pain. The association between greater age and increased orthopedic events is not unexpected, because the most common events observed (arthroplasty, fracture, and joint ligament/cartilage repair) have all been reported to increase with age.[14,16,17] Although leg pain is a common complaint among patients with ASD and not all of the reported orthopedic events were related to the lower extremities, greater severity of leg pain was still significantly associated with the overall occurrence of nonthoracolumbar orthopedic events. Although we assume that the leg pain reported by patients in this study is radicular and related to nerve

TABLE 4. Comparison of baseline demographics, radiographic parameters, and PROs of 286 patients with ASLS with and without an arthroplasty performed

Patient Parameter	Arthroplasty			Adjusted HR (95% CI)*	
	No, n = 257	Yes, n = 29	HR (95% CI)	Preliminary Model	Final Model
Mean age ± SD, yrs, modeled per decade	59.9 ± 9.5	63.7 ± 6.9	**1.62 (1.06–2.48)**	1.16 (0.67–1.99)	
BMI, n (%)					
Underweight/normal	118 (45.9)	10 (34.5)	Ref		
Overweight	61 (23.7)	10 (34.5)	1.31 (0.53–3.23)		
Obese	78 (30.4)	9 (31.0)	2.01 (0.84–4.84)		
Male gender, n (%)	28 (10.9)	0 (0)	—	—	—
Race, n (%)					
White	242 (94.2)	26 (89.7)	Ref	Ref	Ref
Black	13 (5.1)	1 (3.5)	0.78 (0.11–5.76)	0.53 (0.07–4.17)	0.57 (0.08–4.27)
Other	2 (0.8)	2 (6.9)	**8.38 (1.97–35.68)**	**5.18 (1.07–25.08)**	**5.37 (1.24–23.27)**
Currently working/employed, n (%)†	163 (63.4)	8 (27.6)	**0.23 (0.10–0.52)**	**0.34 (0.13–0.88)**	**0.29 (0.13–0.68)**
Median no. of baseline comorbidities (IQR)‡	1 (1–2)	2 (1–3)	**1.44 (1.11–1.87)**	1.02 (0.74–1.39)	
Substance use, n (%)					
Current or former tobacco/nicotine use	88 (34.2)	16 (55.2)	**2.14 (1.03–4.45)**	1.44 (0.65–3.21)	
Current or former alcohol/drug use	7 (2.7)	1 (3.5)	1.15 (0.16–8.44)		
Coronal plane					
Mean lumbar Cobb angle ± SD, modeled per 10°	53.3 ± 14.4	50.6 ± 13.7	0.87 (0.67–1.14)		
Mean coronal balance (absolute value) ± SD, modeled per 10 mm	23.1 ± 21.8	28.8 ± 24.1	1.09 (0.96–1.25)		
Thoracic curve >30°, n (%)	145 (56.4)	11 (37.9)	0.48 (0.23–1.01)		
Mean global sagittal alignment ± SD, modeled per 10 mm	39.6 ± 36.8	51.1 ± 34.1	1.08 (0.99–1.16)		
Mean PT ± SD, modeled per 10°	23.5 ± 9.8	27.6 ± 6.3	**1.56 (1.08–2.25)**	0.93 (0.51–1.69)	
Mean PI-LL mismatch ± SD, modeled per 10°	16.4 ± 19.0	25.5 ± 12.2	**1.27 (1.06–1.53)**	1.20 (0.89–1.61)	1.20 (0.99–1.47)
Baseline PROs, mean ± SD					
SRS-22 subscore	3.2 ± 0.5	3.0 ± 0.6	**0.50 (0.26–0.94)**	1.34 (0.50–3.65)	
ODI, modeled per 10 points	34.0 ± 14.9	43.2 ± 15.5	**1.43 (1.14–1.81)**	1.15 (0.77–1.71)	
NRS back pain	5.9 ± 2.2	6.4 ± 2.3	1.09 (0.92–1.29)		
NRS leg pain	3.4 ± 3.0	5.6 ± 2.2	**1.26 (1.12–1.43)**	**1.26 (1.09–1.45)**	**1.29 (1.12–1.47)**
SF-12 MCS, modeled per 10 points	50.4 ± 10.7	49.1 ± 13.2	0.90 (0.66–1.25)		
SF-12 PCS, modeled per 10 points	35.8 ± 10.1	30.4 ± 8.1	**0.56 (0.37–0.84)**	0.94 (0.50–1.77)	

Global sagittal alignment was assessed based on the C7–S1 sagittal vertical axis. Bolded values reflect HRs with 95% CIs that do not cross 1. Missing values included the following: PI-LL mismatch missing for 1 patient with arthroplasty and 16 patients without; PT missing for 1 patient with arthroplasty and 16 patients without; coronal balance and sagittal balance missing for 1 patient without an arthroplasty.

* The preliminary model includes all the factors with statistically significant associations in the unadjusted models. The final model includes all factors left with p values < 0.10 after backward selection from the preliminary model.

† Includes part-time and full-time homemaker.

‡ Includes autoimmune disease, cancer, cardiac disease, circulatory disorders (artery), circulatory disorders (venous), depression/anxiety/psychiatric disorder history, diabetes, gastrointestinal disease, hypertension, infection history, lung disease/asthma, nervous system disorder, and renal disease.

root compromise, it is possible that for many patients with ASLS the reported leg pain may result at least in part from arthritis of the hips and knees. This suggests that a PRO measure that specifically distinguishes between radicular pain and hip or knee pain may be useful. Even after adjusting for the effects of age and severity of spinal deformity, patients with a history of current or past tobacco/nicotine use had a greater risk of experiencing a nonthoracolumbar orthopedic event during enrollment. Although controversy remains regarding an association between tobacco use and osteoarthritis, recent literature suggests potential direct effects on the proliferation and chondrogenic differentiation of mesenchymal stem cells.[18]

Arthroplasty was the most common nonthoracolumbar orthopedic event affecting the study population during enrollment. Factors associated with these events in the final predictive model included race, employment status, and leg pain. The association between race and risk of nonthoracolumbar orthopedic events should be interpreted cautiously, because the vast majority of patients (93.7%) enrolled in the trial were White, with only 4.9% identifying as Black, and 1.4% reporting a race of "other." In

addition, the broad 95% CIs related to associations with race suggest an imprecise estimate of the HRs. The association between greater leg pain and arthroplasty may reflect added leg pain related to the hip or knee pathology, as noted for the overall model of other orthopedic events. Although this association became stronger when limited to assessment of arthroplasty events (HR 1.29 vs 1.1), it is still likely that the observed greater leg pain is multifactorial and due to a combination of neural compression and degenerative joint disease.

PRO measures are commonly used to assess health status and responses to treatment for many conditions. For ASD, commonly used and reported outcomes measures include the SRS questionnaire (SRS-22r or SRS-30), ODI, SF-12, and more recently, the Patient-Reported Outcomes Measurement Information System (PROMIS).[19–22] The SF-12 and PROMIS are general measures of health status, and the ODI is focused primarily on low-back pain. Although the SRS questionnaire is the only disease-specific outcomes measure widely used for ASD, it was developed primarily for patients with adolescent idiopathic scoliosis and only subsequently validated for use in adults.[23,24] However, there currently exists no disease-specific outcomes measure for ASD. Findings from the present study suggest that the burden of disease from other musculoskeletal conditions should be considered when assessing outcomes based on general health measures and support development of more disease-specific outcomes measures for ASD. Based on current PRO measures used for ASD, it is not possible to directly address the important question of how nonspine orthopedic disease conditions may impact outcomes of patients treated for adult scoliosis. Current outcomes measures also do not permit assessment of whether there is a threshold of nonspine orthopedic disease burden that may preclude effective surgical treatment of scoliosis.

Study Strengths and Limitations

The primary strength of this study is the prospective design, which included directed attention to collection of adverse events that occurred during study enrollment. In addition, the patient population is relatively homogenous, with a focus on ASLS that had not been previously surgically treated and was limited to patients at least 40 years of age. The primary limitation of the present study is the potential that the enrolled patients may not broadly reflect all ASD patients, because study inclusion criteria required that all patients must be candidates for surgical treatment. Thus, the findings may not be generalizable to a patient with symptomatic ASD who is not yet a surgical candidate. Another limitation is the inability to accurately quantify all orthopedic disease burden based on the data collected in the trial. For example, a patient with an arthritic hip or knee that was not surgically treated, or treated with an outpatient procedure during the study interval, would not have been captured. Thus, the nonthoracolumbar orthopedic disease burden defined in this study, although high, is still likely an underestimate of the overall burden. Lastly, it is possible that there may have been differences in healthcare access between the study population and the broader North American population that could confound comparisons.

Conclusions

Patients with ASLS have a high orthopedic disease burden beyond their spinal deformity, with almost 25% having a fracture or orthopedic condition requiring surgical treatment during the mean 3.8 ± 0.9 years following study enrollment. Factors associated with the occurrence of these other orthopedic events include older age, history of tobacco/nicotine use, and greater severity of leg pain at baseline. When evaluating and caring for patients with ASLS, it is important to recognize that these patients will continue to suffer from nonspine orthopedic disease that may require surgical treatment. These conditions may further impact health-related quality of life and impact outcomes assessments of both nonoperative and operative treatment approaches.

Appendix

Sites that contributed patients to the ASLS study were: Washington University School of Medicine, St. Louis, Missouri; University of Virginia Health System, Charlottesville, Virginia; Maryland Spine Center, Baltimore, Maryland; Northwestern University, Chicago, Illinois; Norton Leatherman Spine Center, Louisville, Kentucky; New York University, New York, New York; Hospital for Special Surgery, New York, New York; Hospital du Sacre-Coeur de Montreal, Quebec, Canada; and University Health Network, Toronto Western Hospital, Toronto, Ontario, Canada.

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Disclosures

Dr. Smith reports receiving consultancy fees from Zimmer Biomet, NuVasive, DePuy Synthes, Stryker, Cerapedics, and Carlsmed; receiving royalties from Zimmer Biomet, NuVasive, and Thieme; holding stock in Alphatec and NuVasive; receiving research funding to his institution from DePuy Synthes, International Spine Study Group Foundation (ISSGF), NuVasive, Stryker, and AO Spine; receiving fellowship grant funding to his institution from AO Spine and the Neurosurgery Research and Education Foundation; serving on the editorial boards of *Journal of Neurosurgery: Spine*, *Neurosurgery*, *Operative Neurosurgery*, and *Spine Deformity*; and serving on the Board of Directors of the Scoliosis Research Society (SRS), outside the submitted work. Dr. Shaffrey reports receiving grants from NIH, during the conduct of the study; personal fees from NuVasive, Medtronic, Zimmer Biomet, and SI Bone, outside the submitted work; having direct stock ownership in NuVasive; being a patent holder for Medtronic, NuVasive, and Zimmer Biomet; and receiving royalties from Medtronic and NuVasive. Dr. Kelly reports receiving grants from the NIH and the SRS during the conduct of the study; receiving grants from the Setting Scoliosis Straight Foundation, the ISSGF, and AO Spine, outside the submitted work; support of non–study-related clinical or research effort from DePuy/Synthes Spine; and honoraria from the *Journal of Bone and Joint Surgery*. Dr. Yanik reports receiving grants from the SRS during the conduct of the study; and grants from the NIH, Department of Defense, and Orthopaedic Research and Education Foundation, outside the submitted work. Dr. Lurie reports receiving grants from the NIH and SRS during the conduct of the study; and receiving grants from PCORI and FDA, and personal fees from Spinol and UpToDate, outside the submitted work. Dr. Ames reports receiving personal fees from Stryker, Biomet Zimmer Spine, DePuy Synthes, NuVasive, Next Orthosurgical, Medicrea, Medtronic, Titan Spine, ISSG, *Operative Neurosurgery*, SRS, Global Spinal Analytics, and UCSF, outside the submitted work. Dr. Bess reports being a consultant for K2 Stryker and Mirus; direct stock ownership in Progenerative Medical and Carlsmed; being a patent holder for K2 Stryker and NuVasive; receiving clinical or research support for the study described from the ISSGF; support of non–study-related clinical or research effort from Globus, ISSGF, NuVasive, Medtronic, DePuy Synthes, K2 Stryker, SI Bone, and Seaspine; and receiving royalties from K2 Stryker and NuVasive. Dr. Schwab reports being a consultant to Zimmer Biomet and Medtronic; receiving royalties from Medicrea, Zimmer Biomet, and Medtronic; and being on the executive committee for the ISSG. Dr. Bridwell reports receiving grants from the SRS during the conduct of the study.

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