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ORIGINAL ARTICLE

Pentosidine concentration is associated with degenerative lumbar scoliosis in older women: preliminary results

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Abstract

Purpose Advanced glycation end products (AGEs) have been implicated in the pathogenesis of sarcopenia. The objective of the study was to investigate the prevalence of sarcopenia in degenerative lumbar scoliosis (DLS), and the relationship between biochemical markers including major AGEs, pentosidine, and DLS in older women.

Methods Our study participants were 20 elderly women with idiopathic DLS (mean age 76.4 years, range 56–88). Nineteen age- and sex-matched volunteers (mean age 74.0 years, range 62–86) served as controls. Spinal and femoral BMD of all participants was measured using dual-energy X-ray absorptiometry. We used a bioelectrical impedance analyzer to analyze body composition, including appendicular skeletal muscle mass index [SMI; appendicular lean mass (kg)/(height (m)]^2. SMI < 5.75 was considered diagnostic for sarcopenia. Coronal and sagittal spinal alignments were measured. The following biochemical markers were measured: serum and urinary pentosidine, serum homocysteine, 1,25$(OA)_2$D, and 25(OH)D. The level of each variable was compared between DLS and controls. The relationship between biochemical markers including pentosidine and DLS was examined.

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Results Sarcopenia was observed at a high prevalence in participants with DLS: 50% compared with 15.8% of healthy controls. Height, weight, femoral BMI, appendicular lean mass, total lean mass, and SMI all had significantly lower values in the DLS group. Serum pentosidine was significantly higher for the DLS group compared with controls. Correlations with serum pentosidine revealed a significant positive correlation between lumbar scoliosis, pelvic tilt, and pelvic incidence-lumbar lordosis mismatch, and a significantly negative correlation between thoracic kyphosis ($P < 0.05$).

Conclusions We found that sarcopenia was involved in DLS, and high serum pentosidine levels are associated with severity of coronal and sagittal malalignment in older women, suggesting that high levels of AGEs are a potential biomarker for the progression of lumbar scoliosis and kyphotic deformity. Further studies are needed to clarify the pathogenesis of DLS.

Keywords Degenerative lumbar scoliosis · Sarcopenia · Skeletal muscle · Pentosidine · Homocysteine

Abbreviations

DLS	Degenerative lumbar scoliosis
LS	Lumbar scoliosis
SVA	Sagittal vertical axis
TK	Thoracic kyphosis
LL	Lumbar lordosis
PT	Pelvic tilt
PI	Pelvic incidence
SS	Sacral slope
BIA	Bioelectrical impedance analyzer
DXA	Dual energy X-ray absorptiometry
SMI	Skeletal muscle mass index
BMD	Bone mineral density
AGE	Advanced glycation end product

Introduction

As our society continues to age, more patients develop kyphotic deformities that affect their daily activities. A broad range of associated issues can impact Activities of daily living (ADL) including low back pain due to spinal deformation, back pain, and gait disorders accompanying trunk imbalance, gastroesophageal reflux disease, and esthetic and psychological complaints [1–6]. Various causes of degenerative lumbar scoliosis (DLS) have been reported including: sex, age, osteoporotic vertebral fractures, kyphosis due to deformity, and factors due to spinal surgery, but the disease mechanism is yet to be elucidated [1–6]. Trunk muscles play an important role in the spinal support structure, and paraspinal muscle degeneration has been reported to be related to spinal deformity [7–9]. However, there are no reports on the relationship between trunk and appendicular skeletal muscle mass and spinal deformation.

Sarcopenia is a syndrome characterized by progressive and systemic reduction in skeletal muscle mass. It carries a high risk of becoming bedridden from a fall, and there is great physical and economic loss in an aging society [10–13]. It is believed that sarcopenia results from inactivity, but the mechanism is not entirely clear. Decrease in back strength due to sarcopenia is believed to contribute to the development of DLS.

Eguchi et al. have previously reported that trunk and appendicular skeletal muscle mass were both lower in DLS and low back pain was associated with decrease in appendicular skeletal muscle mass. Regarding relationship between skeletal muscle mass and spinal alignment, appendicular skeletal muscle was related to posterior pelvic tilt, while trunk muscle affected stooped posture, posterior pelvic tilt, lumbar scoliosis, and vertebral rotation. These results indicated that loss of trunk muscle and appendicular muscle, which form the truncal stabilization structure, is thought to be one of the causes of progressive deformation of the spine and low back pain [14].

Advanced glycation end products (AGEs) such as pentosidine are active biomolecules formed by the nonenzymatic covalent binding of sugars with proteins and other molecules [15]. They are formed in high concentrations in diabetes, but also in the physiological organism during aging. AGE cross-links deteriorate the mechanical and biological functions of bone [15, 16]. AGEs have been associated with increased muscle stiffness and reduced whole muscle function. Recent studies suggest that elevated levels of AGEs are independently related to decline in walking abilities, inferior ADL, decreased muscle properties (strength, power, and mass) and increased physical frailty, and may be a contributing risk factor and potential biomarker for decline in motor function [17–19]. Huse et al. demonstrated that nonenzymatic addition of AGEs to the intramuscular connective tissue network may paly a role in the reduction of muscle and physical function with aging [20].

Homocysteine is a sulfur-containing amino acid that is derived from the metabolism of methionine, an essential amino acid [21]. Elevated homocysteine, causing tissue injury by such mechanisms as oxidative stress, is associated with age-related diseases including cardiovascular diseases [22], dementia, and osteoporotic fracture. Homocysteine interferes with collagen cross-linking. Hyperhomocysteinemia reduces bone strength via a reduction of enzymatic cross-links and an increase of nonenzymatic cross-links, pentosidine [16].

The relationship between AGEs and the development of DLS has not been elucidated. We hypothesized that

elevated biochemical markers such as serum and urinary pentosidine indicated an increased risk of developing severe DLS. The aim of this study was to investigate the relationship between biochemical markers such as pentosidine and DLS in older women.

Methods

Participants

Our study consecutive participants were 20 elderly women with DLS (mean age 76.4 years, range 56–88 years) (Table 1). Nineteen age- and sex-matched volunteers (mean age 74.0, range 62–86 years) served as controls (Table 2). Criteria for DLS were lumbar scoliosis > 10° in the coronal plain [2]. Subjects with single or multiple thoracolumbar compression fractures or a history of spinal surgery were excluded.

Spinal alignment in DLS

The frontal view of the lumar spine and the lateral view were photographed in a standing position. Radiographic measurements were made of lumbar scoliosis (LS), sagittal vertical axis (SVA), thoracic kyphosis (TK), lumbar lordosis (LL), pelvic tilt (PT), pelvic incidence (PI), sacral slope (SS), and PI-LL. The LS was measured as the angle between the lower end plate of L1 and the lower end plate of L5 on frontal radiographs. The SVA was measured as the distance from the C7 plumb line to a perpendicular line drawn from the superior posterior end plate of the S1 vertebral body on lateral radiographs. The TK was measured from the upper end plate of T5 to the lower end plate of T12. The LL was measured from the lower end plate of T12 to the upper end plate of S1. The PT was measured as the angle between the vertical line and the line joining the hip axis to the center of the superior end plate of S1. The PI was measured as the angle subtended by a perpendicular line from the upper end plate of S1 and a line connecting the center of the femoral head to the center of the cephalad end plate of S1. The SS was measured as the angle between the superior end plate of S1 and a horizontal line.

DXA

Bone mineral density (BMD) of the left proximal femur and lumbar spine (L2–L4) was measured using dual-energy X-ray absorptiometry (DAX) (Lunar Prodigy, GE Healthcare, WI, USA).

Analysis of skeletal muscle mass

A multifrequency bioelectrical impedance analyzer (BIA), the InBody 720 Biospace device (Biospace Co, Korea), was used according to the manufacturer's guidelines. BIA estimates body composition using the difference of conductivity of the various tissues due to the differences of their biological characteristics. Conductivity is proportional to water content (more specifically to electrolytes). Adipose tissue contains relatively little water compared with other tissues like muscle; therefore, conductivity decreases as body fat increases with relatively high impedance. The volume of body water and fat mass can be calculated by measuring the impedance. In practice, electrodes are placed at eight precise tactile points of the body to achieve a multi-segmental frequency analysis. A total of 30 impedance measurements were obtained using six different frequencies (1, 5, 50, 250, 500, 1000 kHz) for the following five segments of the body: right and left arms, trunk, right and left legs.

Appendicular skeletal muscle mass was calculated as the sum of skeletal muscle mass in the arms and legs, assuming that mass of lean soft tissue is effectively equivalent to skeletal muscle mass. Appendicular skeletal mass index (SMI) was determined as the sum of arm and leg lean mass (kg)/(height (m))^2. The diagnosis of sarcopenia among women was defined as appendicular SMI value < 5.75 kg/m^2, determined using sarcopenia normative data [23].

Biochemical markers

Blood and urinary samples of the participants were collected between the morning and afternoon. The following parameters were measured: serum pentosidine as μg/mL by enzyme-linked immunoassay (ELISA); urinary pentosidine as μg/mg.CRE by ELISA; serum homocysteine as nmol/mL by high performance liquid chromatography; 1,25$(OA)_2$D as pg/mL by radioimmunoassay (RIA); and 25(OH)D as ng/mL by RIA. Serum and urinary pentosidine were measured by the Fushimi Pharmaceutical Co., Kagawa, Japan; homocysteine and 1,25$(OH)_2$D and 25(OH)D were measured by SRL Inc., Tokyo, Japan; and 25(OH)D was measured by the Health Sciences Research Institute East Japan Co., Saitama, Japan.

Statistical analyses

We measured height, weight, BMI, BMD, appendicular lean mass, total lean mass, SMI, sarcopenia prevalence, and biochemical markers in participants in both groups (Table 2). We investigated the correlation between biochemical markers and

Table 1 Patient characteristics

Case	Age	Physical examinations			Spinal alignment								BMD		Skeletal muscle			Biochemical markers				
		Height (m)	Weight (kg)	BMI (kg/m^2)	LS	SVA	TK	LL	PT	PI	SS	PI-LL	Lumbar	Femoral	Total lean mass (kg)	Appendicular lean mass (kg)	SMI (kg/m^2)	Pentosidine (mg/mL)	u-pentosidine (mg/mg.CRE)	Homocysteine (nmol/mL)	1,25(OH)2D (pg/mL)	25(OH)D (ng/mL)
1	79	1.32	45.9	26.34	50	144	5	8	43	65	21	57	1.058	0.815	24.27	10.77	6.18	0.0641	0.0104	6.9	53.2	13
2	88	1.43	43.5	21.27	27		24	17			12		0.965	0.693	24.29	12.39	6.06	0.0856	0.0132	14	68.2	19
3	71	1.51	39.7	17.41	32	88	18	18	34	63	29	45	0.918	0.642	23.78	11.08	4.86	0.0615	0.0291	6.6	60.5	16
4	81	1.56	48.3	19.85	33	83	16	16	47	76	22	60	1.1	0.686	32.01	14.81	6.09	0.061	0.0195	7.7	100.9	15
5	75	1.578	52.1	20.92	29	95	4	− 21	45	47	4	68	1.261	0.929	31.43	15.13	6.08	0.0715	0.0161	7.2	83.9	27
6	73	1.5	53	23.56	18	66	11	11	33	45	16	34	1.156	0.829	26.67	12.47	5.54	0.0747	0.0326	7.6	38.7	18
7	77	1.46	55	25.80	42	151	22	16	39	53	24	37	1.262	0.797	28.87	12.67	5.94	0.0483	0.0179	7.5	75.3	20
8	78	1.43	37.5	18.34	14	194	7	− 56	60	45	− 25	101	1.028	0.922	22.16	10.66	5.21	0.0726	0.0172	12	48.2	14
9	78	1.45	34.5	16.41	45	79	17	1	35	41	5	40	0.73	0.58	19.43	8.53	4.06	0.0627	0.0206	5	74.6	32
10	69	1.45	43.1	20.50	46			22			24		1.007	0.691	24.24	11.54	5.49	0.0892	0.0142	6.1	67.1	26
11	84	1.54	50.4	21.25	29	94	21	35	23	60	36	25	1.487	0.763	28.92	13.92	5.87	0.0641	0.0183	10.2	71.6	32
12	79	1.46	57.7	27.07	10	200	29	− 8	31	40	13	48	1.187	0.737	30.28	13.58	6.37	0.0521	0.0175	13.5	37.3	14
13	56	1.54	57	24.03	57	174	9.8	10	20	59	23	49	1.158	0.842	31.2	14.2	5.99	0.0429	0.0283	8.4	78.5	19
14	75	1.45	44.3	21.07	17	80	46	16	25	32	26	16	0.771	0.642	23.05	10.75	5.11	0.0454	0.0106	7.2	87.6	16
15	80	1.48	36.4	16.62	32	165	33	7	30	44	17	37	0.942	0.641	22.08	10.08	4.60	0.0587	0.0138	7.5	71.4	20
16	67	1.45	39.4	18.74	36	53	41	11	35	40	2	29	1.024	0.612	23.72	11.52	5.48	0.0725	0.0159	10.4	60.2	16
17	74	1.5	43.1	19.16	35	152	3	32	43	83	48	51	0.869	0.612	17.8	12.03	5.35	0.0825	0.1028	11	92	26
18	83	1.47	38.8	17.96	53	85	25	9	27	40	11	31	0.917	0.652	17.8	10.67	4.94	0.0728	0.0285	11.7	40.8	13
19	77	1.54	42.8	18.05	23	51	24	46	31	49	33	3	1.118	0.666	18.5	13.71	5.78	0.0465	0.0158	16.7	28.7	14
20	83	1.53	51.1	21.83	39	178	23	22	35	74	40	52	1.156	0.759	28.23	14.13	6.04	0.0559	0.0191	9.7	71.8	31
Mean ± SD	76.4	1.48	45.68	20.81	33.35	118.4	19.9	10.6	35.3	53.1	19.1	43.5	1.056	0.726	24.94	12.23	5.551	0.0642	0.0231	9.35	65.53	20.05
	± 7.04	± 0.06	± 7.04	± 3.18	± 13.1	± 50.3	± 12.0	± 21.3	± 9.7	± 14.5	± 15.9	± 21.5	± 0.179	± 0.103	± 4.60	± 1.77	± 0.607	± 0.013	± 0.020	± 3.04	± 19.51	± 6.55

Sarcopenia positive (SMI < 5.75)

Table 2 Physical examination, BMD, skeletal mass, and biochemical markers in the patient participants with degenerative lumbar scoliosis and healthy volunteers

	DLS ($n = 20$)	Control ($n = 19$)	P
Physical examinations			
Age	76.4 ± 7.04	74.0 ± 6.14	0.275
Height (m)	1.48 ± 0.06	1.53 ± 0.05	**0.013**
Weight (kg)	45.68 ± 7.04	54.91 ± 6.15	**0.0001**
BMI (kg/m^2)	20.81 ± 3.18	23.61 ± 3.09	**0.008**
Spinal alignment			
Lumbar scoliosis (°)	33.4 ± 13.1	3.3 ± 3.2	**9.1×10^{-12}**
Sagittal vertical axis (mm)	118.4 ± 50.3	34.6 ± 41.8	**1.4×10^{-5}**
Thoracic kyphosis (°)	19.9 ± 12.0	28.4 ± 10.7	**0.04**
Lumbar lordosis (°)	10.6 ± 21.3	36.5 ± 15.2	**0.0002**
Pelvic tilt (°)	35.3 ± 9.7	19.0 ± 9.0	**2.3×10^{-5}**
Pelvic incidence (°)	53.1 ± 14.5	43.0 ± 6.7	**0.018**
Sacral slope (°)	19.1 ± 15.9	27.2 ± 8.9	0.068
PI-LL (°)	45.3 ± 21.5	7.3 ± 17.0	**9.4×10^{-6}**
BMD			
Spine (g/cm^2)	1.056 ± 0.179	1.054 ± 0.159	0.839
Femoral (g/cm^2)	0.726 ± 0.103	0.823 ± 0.094	**0.019**
Skeletal muscle			
Total lean mass (kg)	24.94 ± 4.60	30.53 ± 2.68	**0.00004**
Appendicular lean mass (kg)	12.23 ± 1.77	14.45 ± 1.53	**0.00017**
SMI (kg/m^2) > 5.75	5.551 ± 0.606	6.190 ± 0.549	**0.0014**
Sarcopenia prevalence (%)	50.0	15.8	**0.0235**
Biochemical markers			
Serum Pentosidine (μg/mL) 0.00915–0.0431	0.0642 ± 0.013	0.0540 ± 0.010	**0.0097**
u-Pentosidine (μg/mg.CRE) 0.01942–0.0701	0.0231 ± 0.020	0.0149 ± 0.0039	0.084
Homocysteine (nmol/mL) 4.5–15.3	9.345 ± 3.043	8.821 ± 2.885	0.585
1,25(OH)$_2$D (pg/mL) 20–60	65.53 ± 19.51	67.18 ± 18.77	0.789
25(OH)D (ng/mL) > 20	20.05 ± 6.55	18.47 ± 4.86	0.401

Normal range for each parameter is described in the left column

Bold letters indicate statistically significant pararmeters and values

spinal alignment in all the participants including volunteers (Fig. 1).

Statistical analyses were performed using StatView software (version 5.0). For each variable, differences between groups were evaluated using an unpaired *t* test. Differences in the prevalence of sarcopenia between both groups were evaluated using a Chi-squared test.

Pearson correlation coefficients were calculated to determine the correlation between biochemical markers including pentosidine and homocysteine and spinal variables. All data are expressed as the mean standard ± deviation (SD). $P < 0.05$ was considered significant.

Results

Physical examinations

Height ($P < 0.05$), weight ($P < 0.001$), and BMI ($P < 0.01$) were significantly lower for patients in the DLS group compared with control participants (Table 2).

Spinal alignments

LS ($P < 0.001$), SVA ($P < 0.001$), LL ($P < 0.001$), PT ($P < 0.001$), PI ($P < 0.005$), and PI-LL ($P < 0.001$) were significantly higher, and TK ($P < 0.05$) was significantly lower for the DLS group compared with controls, but there were no significantly differences between the groups for SS ($P = 0.068$) (Table 2).

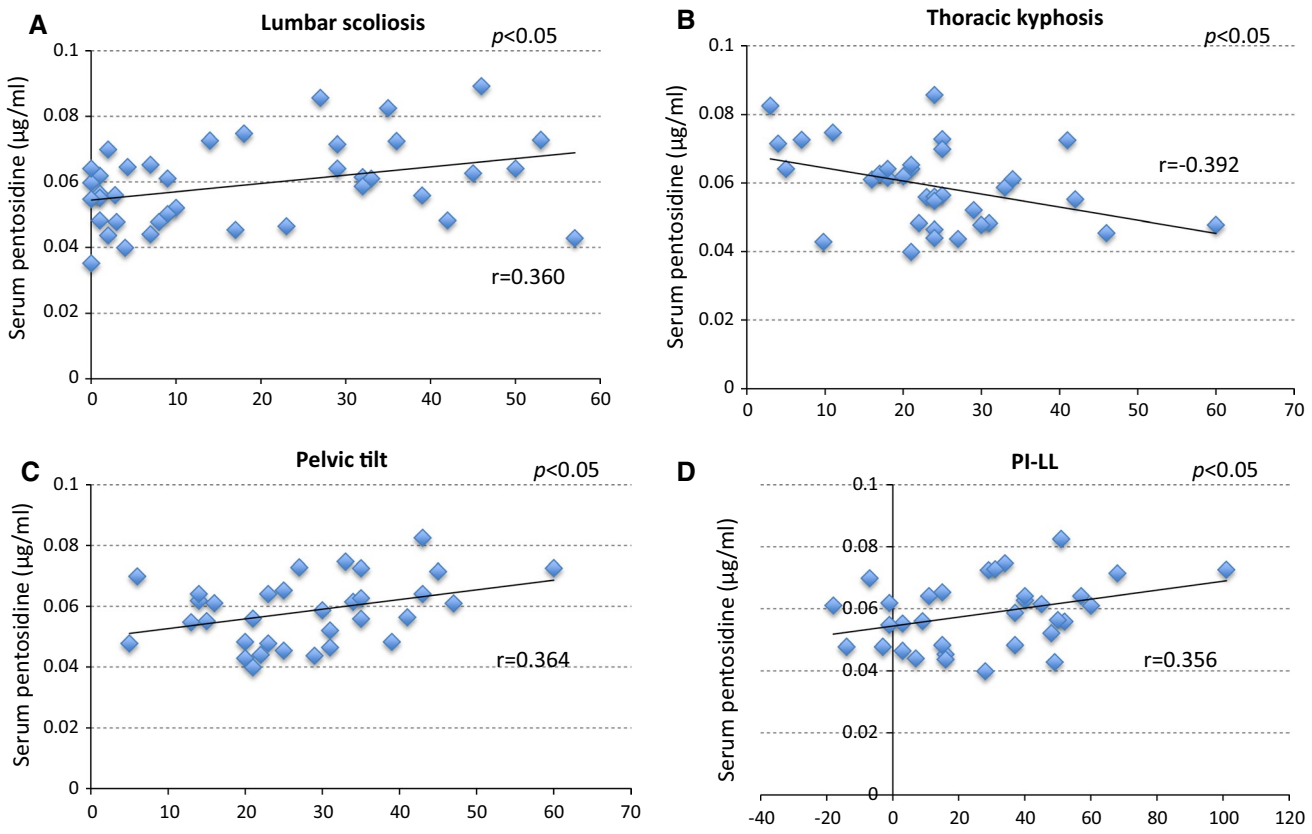

Fig. 1 Correlation of serum pentosidine with spinal alignment: lumbar scoliosis (**a**), thoracic kyphosis (**b**), pelvic tilt (**c**), and PI-LL (**d**). Correlations with serum pentosidine revealed a significant positive correlation between lumbar scoliosis, pelvic tilt, and pelvic incidence-lumbar lordosis mismatch, and a significantly negative correlation between thoracic kyphosis TK ($P < 0.05$)

BMD

Proximal femoral BMD was significantly lower for the DLS group compared with controls ($P < 0.05$), but there were no significantly differences between the groups for spinal BMD (Table 2).

Skeletal muscle mass

The DLS group had significantly lower values for all items of skeletal muscle mass including total lean mass ($P < 0.001$), appendicular lean mass ($P < 0.001$), and SMI ($P < 0.01$). The prevalence of sarcopenia was significantly higher in the DLS group than among matched controls, including 10 out of 20 cases (50.0%), versus 3 out of 19 controls (15.8%) ($P < 0.05$) (Table 2).

Biochemical markers

The levels of serum pentosidine were significantly higher for the DLS group compared to controls ($P < 0.01$). No other variables were significantly different between the groups: urinary pentosidine ($P = 0.084$); homocysteine ($P = 0.585$); $1,25(OA)_2D$ ($P = 0.789$); and 25(OH)D ($P = 0.401$) (Table 2).

Correlation between biochemical markers and spinal alignment

Correlations with serum pentosidine revealed a significant positive correlation between LS ($r = 0.360$, $P < 0.05$), PT ($r = 0.364$, $P < 0.05$), and PI-LL ($r = 0.356$, $P < 0.05$), and a significantly negative correlation between TK ($r = -0.392$, $P < 0.05$) (Fig. 1). Correlations with urinary pentosidine revealed a significant positive correlation between PI ($r = 0.545$, $P < 0.05$) and a significantly negative correlation between TK ($r = -0.397$, $P < 0.05$).

We did not detect correlation of any spinal alignments other than spinal alignment with biochemical markers (Table 3).

Discussion

Reports have been published on research using MRI to assess paraspinal muscle in spinal deformities. Yagi et al.

Table 3 The correlation of spinal alignments with biochemical markers

	LS		SVA		TK		LL		PT		PI		SS		PI-LL	
	r	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value	*r*	*P* value
Serum pentosidine	**0.36**	**0.025**	0.117	0.516	**− 0.392**	**0.024**	− 0.255	0.118	**0.364**	**0.037**	0.227	0.204	− 0.177	0.289	**0.356**	**0.042**
Urinary pentosidine	0.276	0.09	0.225	0.208	**− 0.397**	**0.028***	0.004	0.979	0.232	0.195	**0.545**	**0.001**	0.252	0.122	0.223	0.212
Homocystein	− 0.070	0.67	0.249	0.163	0.125	0.489	− 0.163	0.323	0.160	0.373	0.009	0.960	− 0.184	0.261	0.106	0.556

LS lumbar scoliosis, *SVA* sagittal vertical axis, *TK* thoracic kyphosis, *LL* lumbar lordosis, *PT* pelvic tilt, *PI* pelvic incidence, SS: sacral slope

Bold letters indicate statistically significant pararmeters and values

[7] reported that multifidus and iliopsoas muscle cross-sections were smaller in spinal deformation, and that this correlated with sagittal alignment. A report found fatty degeneration of multifidus muscle on the concave side of degenerative scoliosis [8], while hyperplasia of the multifidus muscle and iliopsoas muscle have been reported regarding the convex side of degenerative scoliosis [9]. Bok et al. reported that decrease in MRI-defined paraspinal muscle volume was significantly associated with kyphotic deformity in patients with ankylosing spondylitis even after multivariate adjustment, hypothesizing that dynamic imbalance between atrophic extensor muscle and relatively preserved psoas muscle was suggested as possible explanations for the causal relationship between muscle degeneration and kyphotic deformity [24].

On the other hand, when Enomoto et al. [25] took surface electromyograms of paravertebral muscle activity, they found that compared to lumbar spinal canal stenosis (LSCS), patients with degenerative lumbar scoliosis (DLS) had high paravertebral muscle activity. Yagi et al. [7] measured appendicular skeletal muscle mass in patients with DLS and LSCS by dual-energy X-ray absorptiometry (DXA) and reported that there was no significant difference between the two groups. However, postoperative measurements were only taken for appendicular weight, and height-corrected SMI values were not considered. Muscle assessment in adult spinal deformity had previously been limited to localized evaluation of appendicular and trunk muscle mass using MRI. How these might relate to sarcopenia has never been investigated until this time.

Sarcopenia is defined as an age-associated loss of skeletal muscle mass and function, and includes a risk of adverse outcomes, such as physical disability and poor quality of life [10, 11]. Sarcopenia is common in older individuals, with a reported prevalence in 60–70 year olds of 5–13% [9]. Miyakoshi et al. [26] reported 20% of Japanese patients with osteoporosis suffer complications because of sarcopenia, while only 10% of healthy individuals have sarcopenia.

Eguchi et al. previously reported that sarcopenia complications were noted in 16% of patients with lumbar canal stenosis and a much higher 46.6% of patients with DLS and both appendicular and trunk skeletal muscle mass was lower in the DLS group [14].

In the present study, appendicular lean mass, total lean mass, and SMI had significantly lower values in the DLS group and a large proportion of the patients with DLS had sarcopenia compared with controls: 50 versus 16%.

The present study shows that serum pentosidine levels were higher in older woman with DLS compared with controls. Serum pentosidine concentration was positively correlated with lumbar scoliosis, pelvic tilt, and pelvic incidence-lumbar lordosis mismatch, and negatively correlated with thoracic kyphosis.

To our knowledge, this is the first study demonstrating biochemical markers such as pentosidine in DLS.

Advanced glycation end products (AGEs) accumulate in various musculoskeletal tissues such as bone [15, 16], intervertebral disc [27, 28], and muscle [20] with increasing age, and adversely affect the biomechanical properties of such structures.

Significantly higher levels of AGEs were reported in patients with osteoporosis, increasing the risk of fractures [29–31]. Serum and bone concentrations of pentosidine were higher in subjects with hip fractures compared with osteoarthritis after adjustment for age, sex, weight, serum creatinine, and diabetes [29]. Serum and urinary pentosidine levels were significantly higher in the patients with fragility distal radius fracture than in the volunteers after adjusting for BMD [30]. Neumann et al. demonstrated that the elevated serum pentosidine levels but not endogenous secretory receptor for AGEs could be a potential biomarker to estimate the individual fracture risk type 1 diabetes [31]. A recent study revealed that plasma pentosidine content showed a significant linear correlation with pentosidine content in cortical bone [32]. These previous studies suggested that serum pentosidine level could be used as a surrogate marker for pentosidine content in bone and utilized to evaluate bone strength. However, Hashidate et al. reported that serum pentosidine levels were not changed by 3 years of treatment with bisphosphonates in osteoporotic women suggesting that serum petosidine may not be an optimal way to evaluate bone quality after bisphosphonate treatment [33].

Regarding relationship between disc degeneration and spinal malalignment in patients with DLS, Bao et al. demonstrated that disc degeneration was strongly correlated with sagittal malalignment such as a more positive SVA, decreased TK and LL [34].

Alterations in concentrations of pyridinoline and pentosidine collagen cross-links occur with intervertebral disc aging and degeneration, which may contribute to the loss of disc integrity and play a role in the pathogenesis of the degenerative process such as degenerative disc disease [27], lumbar spondylosis [35], and scoliosis [28].

High AGE levels are associated with decline in muscle function [17–19].

Serum pentosidine is independent risk factors for loss of muscle mass in postmenopausal women with type 2 diabetes after adjusting for age [19].

AGEs may play a role in sarcopenia through upregulation of inflammation and endothelial dysfunction in the microcirculation of skeletal muscle through the receptor for AGEs, or RAGE [36].

Homocysteine interferes with collagen cross-linking. The enzymatic and nonenzymatic cross-link deterioration induced by hyperhomocysteinemia (HHcy) may accelerate bone fragility [13]. Previous studies have shown that HHcy is associated with muscle weakness and lower body weight. HHcy inhibits satellite cell regenerative capacity and enhances oxidative stress thorough p38 MAPK signaling, proposing a potential risk factor for frailty in the elderly [37].

The pathogenesis of idiopathic DLS has not been elucidated. The present study demonstrates that sarcopenia is associated with DLS and high serum pentosidine levels are associated with severity of coronal and sagittal malalignment in older women, suggesting that levels of AGEs are potential biomarkers for the progression of DLS. Further studies are needed to clarify the mechanism.

The present study has several limitations. (1) The first is that a small number of subjects were investigated, requiring confirmation of our findings in a larger population. (2) The study is cross-sectional and not longitudinal. (3) DXA appears the most reliable tool to evaluate body composition and is considered the criterion standard in clinical practice. BIA may provide a simpler, portative, and less expensive alternative. BIA has a tendency to overestimate muscle mass compared with DXA, but agreement between DXA and BIA is high for lean mass arm and for axial lean mass [38]. In future, results should be compared to DXA measurements of muscle mass. (4) We evaluated only slim Japanese women with low BMI; therefore, the amount of truncal fat is much less likely to affect calculations than it might in a typical western population. (5) DLS patients were shorter and had reduced bodyweight compared to controls, which might have affected results. Further studies are needed to clarify the mechanisms of developing DLS.

Conclusion

We examined the prevalence of sarcopenia in idiopathic DLS and the relationship between biochemical marker, serum pentosidine and DLS. Sarcopenia was recognized in 50% of our participants with DLS, compared with 16% of controls. Serum pentosidine levels were significantly higher in the patients with DLS than in controls. High serum pentosidine levels are associated with severity of coronal and sagittal malalignment in older women, suggesting that high levels of AGEs are a potential biomarker for a progression of lumbar scoliosis and kyphotic deformity. Further studies are needed to clarify the pathogenesis of DLS.

Author contributions YE conducted data collection and data entry, and wrote the manuscript. TT developed data collection. HI and KF participated in the design of the study and performed the statistical analysis. All authors contributed to and approved the final manuscript.

Compliance with ethical standards

Ethics and consent to participate We declare that all protocols involving humans have been approved by the Chiba university Hospital and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. We declare that all participants provided written informed consent before their inclusion in this study.

Conflict of interest The authors declare that they have no competing interests. We did not receive grants or external funding in support of our research or preparation of this manuscript. We did not receive payments or other benefits or a commitment or agreement to provide such benefits from any commercial entities.

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