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Aorta Movement in Patients With Scoliosis After Posterior Surgery

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Study Design. Retrospective analysis.

Objective. To evaluate movement of the aorta in patients with scoliosis who have undergone the posterior correction and fusion.

Summary of Background Data. Surgeons check preoperative imaging for pedicle screw placement, but past analyses indicated that the aorta shifts after scoliosis surgery. Few studies, however, evaluated the aorta movement in detail.

Methods. A total of 22 patients with a right thoracic curve underwent posterior instrumentation and fusion. The average age at surgery was 17.2 years. The average of the preoperative Cobb angle was 65.2° which decreased to 20.0°.

Computed-tomographic data were analyzed by multiplanar reconstruction. In our coordinate system, the middle of the base of the left superior facet was set as the origin and a line connecting the middle points of both bases of the superior facets was defined as the X-axis. We defined the angle and the distance to describe the aorta position and analyzed the movement of the aorta relative to the spine. Deformity parameters were examined to determine their correlation with the aorta parameters.

We simulated variable pedicle screw placement and defined a warning pedicle when the aorta enters the expected area of the screw and examined them in 24 scenarios.

Results. The aorta moved 4.7 ± 3.0 mm on an average. The aorta had a tendency to migrate in the anteromedial direction and this movement correlated with preoperative apical vertebral translation, preoperative sagittal alignment, and change of sagittal alignment. The ratio of warning pedicles at the middle thoracic level (T7–T9) increased after deformity correction.

Conclusion. The aorta moved anteromedially relative to the spine after the posterior correction and the risk of the aorta by a pedicle screw increased by correction of the deformity at the middle thoracic spine. Surgeons are recommended to anticipate the aorta movement in the surgical planning.

Key words: scoliosis, pedicle screw, aorta, computed tomography. **Spine 2010;35:E1571–E1576**

Posterior correction and fusion by instrumentation is popular in the deformity surgery and pedicle screws have been the dominant anchors for the last decade. However, several authors[1–3] reported a possible risk of aorta injury by a pedicle screw. Although surgeons use preoperative radiographic imaging in placing pedicle screws to prevent the aorta containment, the aorta may move after surgical correction of the spinal deformity. Few analyses of the movement of this organ after posterior surgery have been reported. The purpose of the present study was to evaluate the aorta movement after the posterior correction and fusion in scoliosis surgery.

Materials and Methods

A total of 37 patients with scoliosis underwent posterior instrumentation and fusion at the University Hospital between 2005 and 2007 and 22 patients with a right thoracic curve were included in this study. Scoliosis was idiopathic in 18 patients, Chiari-syrinx in 2, multiple epiphyseal dysplasia in 1, and Noonan syndrome in 1. A total of 15 patients were excluded: 5 patients with congenital scoliosis, 4 with idiopathic scoliosis with no thoracic curve, 3 with Marfan syndrome who might have had abnormal vascular movement, 2 with idiopathic scoliosis with left thoracic curve, and 1 with tubular sclerosis with left thoracic curve. Patient age at surgery was 10 to 29 (mean, 17.2) years old and 18 were women and 4 were men. Lenke's classification of scoliosis was type 1 in 8 patients, type 2 in 5, type 3 in 1, type 4 in 4, type 5 in 1, and type 6 in 3. The preoperative Cobb angle averaged 65.2° ± 11.6° (range, 50°–88°) and corrected to 36.3° ± 12.0° (range, 18°–70°) on bending films, and to 26.6° ± 10.0° (range, 13°–44°) on fulcrum-bending films.[4] The apex vertebra of the thoracic curve ranged from T5–T10 (T5:1, T7:2, T8:6, T9:5, T10:8). All patients were treated by posterior correction and fusion by pedicle screw instrumentation. The average number of instrumented vertebrae was 12.2 ± 1.6 (9–16 vertebrae). Postoperative Cobb angle averaged 20.0° ± 7.7° (range, 11°–39°) and correction rate was 69.6% ± 8.5% (53%–83.1%). Cincinnati correction index[5] was 1.74 ± 0.57 (0.95–3.38) and Fulcrum bending correction index[6] was 1.18 ± 0.16 (0.78–1.48).

The patients were evaluated by computed tomography (CT) before and after surgery. Preoperative examination was for the computer-assisted placement of pedicle screws and the postoperative one was to confirm the location of pedicle screws. There was no need to replace any screw. The preoperative CT was obtained from the upper thoracic to the lower lumbar spine with a width of 1.25 mm as directed by a naviga-

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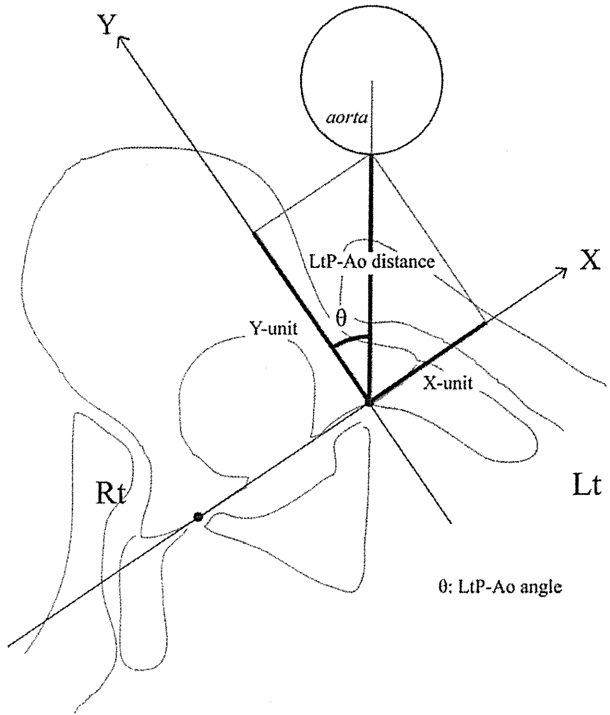

Figure 1. Aorta parameters. The origin is set in the middle of the base of the left superior facet. A line connecting the 2 middle points of both bases of the superior facets is defined as X-axis. LtP-Ao distance indicates the left pedicle-aorta distance; LtP-Ao angle, the left pedicle-aorta angle.

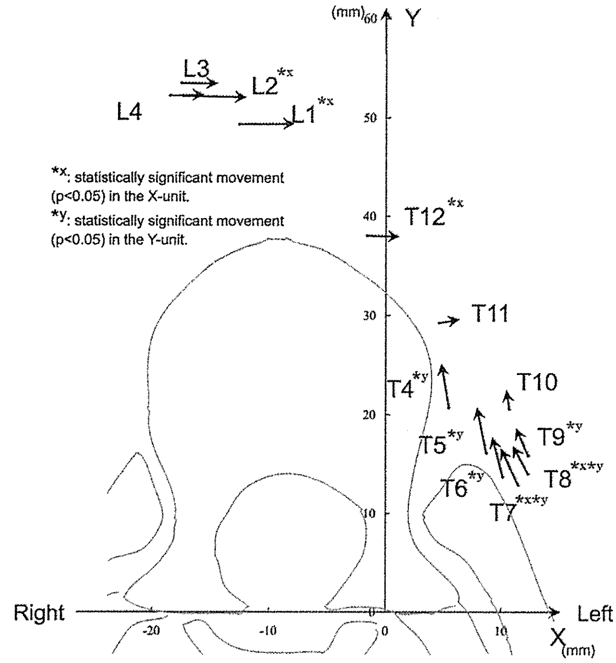

Figure 2. The aorta movement relative to the spine before and after posterior correction and fusion in our Cartesian coordinate system. The aorta moved to the anterior direction at the upper and middle thoracic levels and to the medial direction at the lower thoracic and lumbar levels.

tion protocol, and the postoperative CT was obtained with a helical scan and developed with a width of 1.00 mm less than 2 weeks after surgery. All Digital Imaging and Communication in Medicine data were transferred to a personal computer and analyzed by Digital Imaging and Communication in Medicine or DICOM software (ExaView LITE: Ziosoft, Tokyo, Japan). In the present study, we used our original Cartesian coordinate system and measured parameters describing the location of the aorta from T4 to L4 of the 22 patients. We selected the middle of the base of the left superior facet as the point of origin of this coordinate system (Figure 1) because the most probable threat to the aorta is by a pedicle screw on the left side at the thoracic spine. A line connecting the 2 middle points of both bases of the superior facets was defined as the X-axis; the Y-axis is determined to be parallel to the upper endplate of each vertebral body. The angle formed by the Y-axis and a line connecting the origin and the center of the aorta was defined as the left pedicle-aorta (LtP-Ao) angle and length of a line connecting the origin and the edge of the aorta as the LtP-Ao distance. Two parameters and the X- and Y-units of the LtP-Ao distance at 240 vertebral bodies were measured pre- and postsurgery after excluding vertebrae with incomplete data. From the repeatability test from our previous study,[7] interclass corre-

Table 1. Aorta Parameters Before and After Surgery

		LtAo-Angle (deg)			LtAo-Distance (mm)			
Level	n	Preop	Postop	Change	Preop	Postop	Change	Movement (mm)
T4	6	22.3 ± 30.9 (−6 to 65)	16.2 ± 24.6 (−18 to 55)	−4.1 ± 13.0 (−28 to 9)	22.0 ± 8.4 (11 to 32)	25.8 ± 8.3 (14 to 39)	3.6 ± 3.1* (−1 to 8)	5.9 ± 4.2 (1 to 12)
T5	20	30.8 ± 21.0 (−1 to 78)	23.8 ± 18.0 (−10 to 67)	−7.2 ± 8.9* (−23 to 12)	19.9 ± 4.7 (12 to 32)	23.6 ± 6.0 (14 to 37)	4.3 ± 3.7* (−1 to 14)	5.4 ± 2.9 (1 to 13)
T6	22	37.3 ± 16.8 (9 to 74)	30.2 ± 14.2 (3 to 59)	−7.1 ± 9.1* (−22 to 8)	18.1 ± 3.7 (13 to 28)	20.7 ± 5.0 (11 to 33)	2.6 ± 2.7* (−2 to 9)	4.6 ± 2.7 (1 to 13)
T7	22	42.3 ± 14.0 (17 to 74)	32.6 ± 11.4 (12 to 59)	−10.0 ± 7.7* (−22 to 3)	17.9 ± 3.7 (12 to 26)	19.7 ± 4.5 (12 to 33)	1.9 ± 2.6* (−3 to 7)	4.1 ± 2.6 (0 to 9)
T8	22	42.4 ± 11.1 (16 to 65)	34.5 ± 8.5 (20 to 55)	−7.9 ± 7.1* (−20 to 4)	19.2 ± 4.3 (13 to 30)	20.2 ± 3.7 (14 to 29)	1.0 ± 2.6 (−6 to 4)	3.9 ± 2.1 (1 to 8)
T9	22	39.2 ± 11.5 (13 to 53)	32.5 ± 8.8 (9 to 46)	−6.8 ± 7.0* (−23 to 7)	20.8 ± 4.9 (14 to 32)	21.8 ± 4.2 (16 to 31)	1.0 ± 2.4 (−6 to 5)	3.8 ± 2.2 (1 to 9)
T10	22	29.9 ± 14.1 (−13 to 51)	27.1 ± 10.3 (0 to 49)	−2.7 ± 7.5 (−15 to 13)	24.1 ± 6.3 (15 to 36)	25.0 ± 5.2 (17 to 34)	0.9 ± 3.2 (−5 to 6)	4.3 ± 2.8 (0 to 10)
T11	22	13.0 ± 20.4 (−46 to 44)	13.9 ± 13.6 (−21 to 37)	0.8 ± 10.0 (−17 to 25)	31.8 ± 8.0 (19 to 46)	31.3 ± 6.7 (20 to 43)	−0.5 ± 3.1 (−7 to 4)	5.1 ± 4.4 (0 to 19)
T12	21	0.4 ± 16.2 (−26 to 28)	3.7 ± 13.2 (−18 to 34)	3.3 ± 6.4* (−10 to 13)	39.4 ± 8.1 (25 to 52)	38.2 ± 7.4 (25 to 55)	−1.0 ± 2.5 (−7 to 4)	5.0 ± 3.0 (1 to 10)
L1	21	−12.6 ± 14.1 (−36 to 13)	−8.0 ± 10.6 (−29 to 9)	4.8 ± 5.5* (−8 to 12)	50.3 ± 6.8 (36 to 63)	49.0 ± 6.2 (39 to 59)	−1.5 ± 3.3* (−7 to 6)	6.0 ± 3.1 (1 to 13)
L2	21	−16.0 ± 10.3 (−38 to 2)	−12.0 ± 8.8 (−28 to 3)	4.1 ± 4.6* (−3 to 14)	54.5 ± 4.5 (44 to 61)	52.8 ± 4.4 (44 to 61)	−1.6 ± 1.5* (−7 to 2)	5.2 ± 3.2 (2 to 14)
L3	14	−17.6 ± 5.2 (−27 to −10)	−14.0 ± 5.3 (−23 to −5)	2.6 ± 4.0* (−4 to 8)	55.4 ± 4.5 (47 to 63)	54.4 ± 4.3 (48 to 62)	−1.0 ± 2.9 (−5 to 4)	4.4 ± 2.6 (1 to 8)
L4	5	−19.6 ± 5.9 (−28 to −12)	−17.0 ± 4.6 (−25 to −13)	2.4 ± 3.0 (−1 to 7)	53.2 ± 3.3 (48 to 57)	53.2 ± 4.7 (48 to 59)	0.0 ± 3.1 (−3 to 4)	3.9 ± 2.0 (2 to 7)
Total	240	17.9 ± 27.4 (−46 to 78)	15.4 ± 21.6 (−29 to 67)	−2.5 ± 9.1 (−28 to 25)	31.3 ± 15.3 (11 to 63)	31.9 ± 13.9 (11 to 62)	0.7 ± 3.3 (−7 to 14)	4.8 ± 3.2 (0 to 20)

*$P < 0.01$.

LtAo-Angle indicates left pedicle-aorta angle; LtAo-Distance, left pedicle-aorta distance; Preop, preoperative; Postop, postoperative.

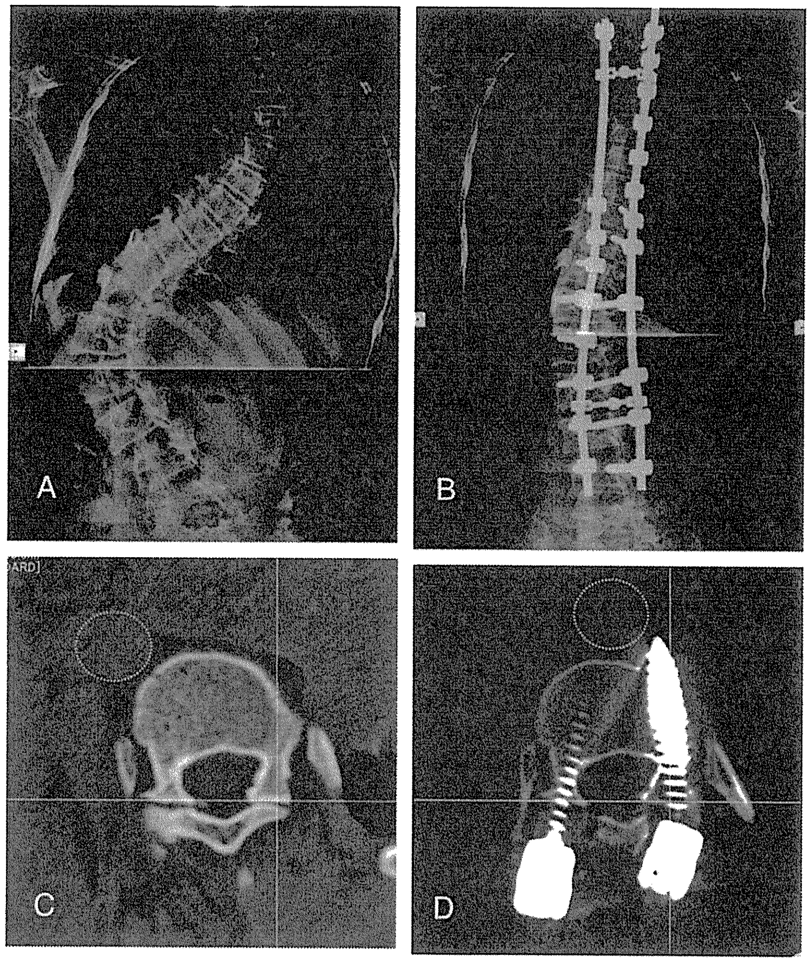

Figure 3. **A**, Standing anteroposterior spinal radiograph of a 14-year-old girl with a 69° right thoracic curve and 88° left lumbar curve. She had only 11 thoracic vertebrae (no T12) and the apical vertebral translation was 69.5 mm. She had had foraminal magnum decompression and duroplasty 16 months before spinal surgery. **B**, Standing coronal radiograph 2 weeks after segmental pedicle screw instrumentation from T2 to L4 demonstrating thoracic curve correction to 19° and lumbar curve correction to 25°. The apical vertebral translation decreased to 30.1 mm. **C**, Preoperative computed tomography by multiplanar reconstruction at T11. The aorta (dotted circle) located in front of the right side of the vertebral body. **D**, Postoperative computed tomography adjusted by multiplanar reconstruction to match the preoperative imaging. The aorta (dotted circle) had moved 19.5 mm to the bicortical pedicle screw of the left side.

lation coefficients were 0.922 to 0.957 in the intraobserver measurement and 0.896 to 0.929 (0.864–0.961) in the interobserver measurement.

We analyzed the movement of the aorta relative to the spine in each level. To determine the relationship between the thoracic main curve and thoracic coronal/sagittal alignment, we selected patients who had their main curve in the thoracic spine. In the 17 selected patients, we measured the Cobb angle and the apical vertebral translations (AVT) of the main curve, and the sagittal alignment (the Cobb angle at T5–T12) before and after surgery. These deformity parameters were examined for their correlation, with the maximum movement of the aorta in the main thoracic curve. Statistical analysis was performed by SPSS 17.0 (SPSS Inc., Chicago, IL).

We simulated placement of the pedicle screw with a direction different from the ideal trajectory. Sensitivity analysis was performed by varying the direction error and the length of the screw independently. The direction error started from 10° up to 30° with 10° increments (3 scenarios). The length of the screw started from 25 to 40 mm with increments of 5 mm (4 scenarios). Therefore, we set up total of 24 scenarios in the preoperative or postoperative state. We defined a warning pedicle as being when the aorta enters the expected area of the screw. Ratio between the number of warning pedicles and the number of the examined pedicles at 1 spine level was calculated from T4 to L4 in every scenario.

Results

The LtP-Ao angle changed significantly from T5 to T9 and from T12 to L3 (t test, $P < 0.01$) (Table 1), whereas the LtP-Ao distance changed significantly from T4–T7, L1 and L2. The average of the aorta movement in the examined 240 vertebrae was 4.7 ± 3.0 mm. The aorta moved more than 10 mm in 14 vertebrae (5.8%), and had a tendency to migrate in the anteromedial direction (Figure 2). A representative case is shown in Figure 3.

In the 17 patients who had the main curve in the thoracic spine, the maximum movement of the aorta in the main thoracic curve was 8.9 ± 3.5 mm (range, 3.9–14.9). Level of the maximum movement was T4 in 1 case, T5 in 1, T6 in 1, T7 in 2, T9 in 1, T10 in 3, T11 in 1, T12 in 1, L1 in 3, L2 in 2, L3 in 0, and L4 in 1. Level of the maximum movement was periapical (±1 vertebra of the apex) in 8 cases. The maximum movement of the aorta correlated with the preoperative AVT (Pearson correlation coefficient, −0.55; P = 0.02), preoperative sagittal alignment (−0.52, P = 0.03), and change of the sagittal alignment (0.57, P = 0.02) (Figure 4).

Sensitivity analysis (Tables 2–4) revealed that long pedicle screw (40 mm) with moderate direction error

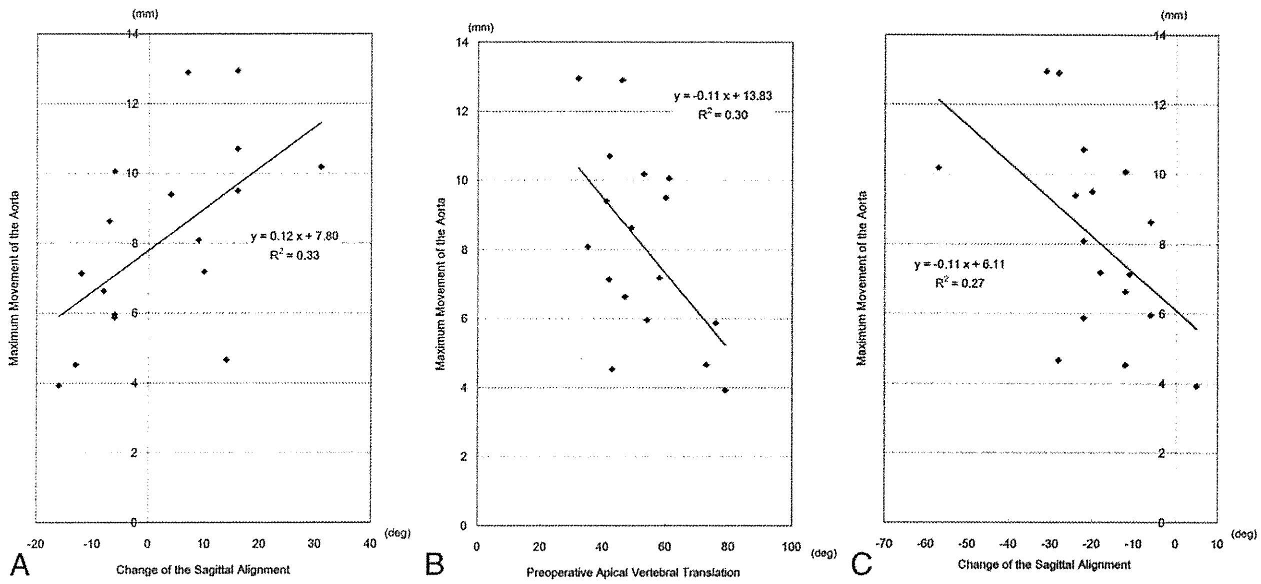

Figure 4. **A,** Relationship between change of the sagittal alignment (T5–T12) and the maximum aorta movement in the main thoracic curve of 17 patients. Positive change denotes more kyphotic change. Pearson correlative coefficient was 0.571 ($P = 0.017$); *i.e.,* more correction of the main curve meant greater aorta movement. **B,** Relationship between the postoperative apical vertebral translation and the maximum aorta movement. Pearson correlative coefficient was −0.550 ($P = 0.022$); *i.e.,* lower apical vertebral translation after surgery meant greater aorta movement. **C,** Relationship between the preoperative sagittal alignment (T5–T12) and the maximum aorta movement in the main thoracic curve of 17 patients. Positive change denotes more kyphotic change. Pearson correlative coefficient was −0.521 ($P = 0.032$); *i.e.,* more correction of the main curve meant larger aorta movement.

imposed risk on the aorta, but a large direction error (30°) by itself put the aorta at a high risk in any spine level regardless of the length of the pedicle screw.

There were only 5 warning pedicles in 96 examined lumbar spine and all were first lumbar spine. Therefore, further analysis was limited only in the thoracic spine. The distribution of the warning pedicles revealed 3 groups. The middle thoracic level (T7–T9) had a low ratio of warning pedicles before surgery, and the ratio increased statistically significantly after deformity correction. The upper thoracic level (T4–T6) as well as the lower thoracic level (T10–T12) had a moderate ratio of warning pedicles before surgery, and did not change considerably after deformity correction.

Discussion

The present study revealed that the aorta moved more than 10 mm in 17 of the examined 240 spines (5.8%), with a shift to the anterior and medial positions after posterior surgery. From our previous study,[8] the aorta may be at risk at left concave pedicle at T4, T5, and T10–T12 before surgery, and there was a relative safety of the aorta for pedicle screw placement at the apical level. The present study showed that the dangerous pedicle ratio increased at the midthoracic level after surgery. At the apical level, the aorta often resides far lateral of the vertebral body which is far from the axis of the trunk. Surgeons assume from the preoperative imaging that the

Table 2. Warning Pedicles—Direction Error Within 10°

		Preoperative			Postoperative			
Screw Length	Level	Warning (+)*	Warning (−)†	Ratio	Warning (+)*	Warning (−)†	Ratio	Difference
25 mm	T4–T6	2	46	4.2%	0	48	0.0%	−4.2%
25 mm	T7–T9	0	66	0.0%	0	66	0.0%	0
25 mm	T10–T12	0	65	0.0%	0	65	0.0%	0
30 mm	T4–T6	5	43	10.4%	2	46	4.2%	−6.2%
30 mm	T7–T9	0	66	0.0%	1	65	1.5%	+1.5%
30 mm	T10–T12	0	65	0.0%	1	64	1.5%	+1.5%
35 mm	T4–T6	7	41	14.6%	5	43	10.4%	−4.2%
35 mm	T7–T9	0	66	0.0%	1	65	1.5%	+1.5%
35 mm	T10–T12	4	61	6.2%	6	59	9.2%	+3.0%
40 mm	T4–T6	7	41	14.6%	5	43	10.4%	−4.2%
40 mm	T7–T9	0	66	0.0%	1	65	1.5%	+1.5%
40 mm	T10–T12	8	57	12.3%	11	54	16.9%	+4.6%

*Number of the warning pedicles.
†Number of the nonwarning pedicles.

Table 3. Warning Pedicles—Direction Error Within 20°

		Preoperative			Postoperative			
Screw Length	Level	Warning (+)*	Warning (−)†	Ratio	Warning (+)*	Warning (−)†	Ratio	Difference
25 mm	T4–T6	7	41	14.6%	5	43	10.4%	−4.2%
25 mm	T7–T9	1	65	1.5%	0	66	0.0%	−1.5%
25 mm	T10–T12	1	64	1.5%	1	64	1.5%	0
30 mm	T4–T6	11	37	22.9%	12	36	25.0%	+2.1%
30 mm	T7–T9	2	64	3.0%	1	65	1.5%	−1.5%
30 mm	T10–T12	1	64	1.5%	5	60	7.7%	+6.2%
35 mm	T4–T6	13	35	27.1%	16	32	33.3%	+6.2%
35 mm	T7–T9	4	62	6.1%	2	64	3.0%	−3.1%
35 mm	T10–T12	10	55	15.4%	14	51	21.5%	+6.1%
40 mm	T4–T6	13	35	27.1%	18	30	37.5%	+10.4%
40 mm	T7–T9	4	62	6.1%	2	64	3.0%	−3.1%
40 mm	T10–T12	19	46	29.2%	21	44	32.3%	+3.1%

*Number of the warning pedicles.
†Number of the nonwarning pedicles.

aorta stays out of the spine and become less careful of this organ during screw placement. In fact, after correction of the scoliosis in some cases, the vertebrae return to a more physiologic position, which is the center of the body: this movement of the spine results in the medialization of the aorta relative to the spine and the risk of the aorta by a pedicle screw increased by correction of the deformity at the middle thoracic spine. Accordingly, all left pedicles have substantial risk of indenting the aorta indentation if a pedicle screw breaches outside the pedicle.

Few authors have reported change of the aorta position after deformity surgery. The first analysis was reported by Bullmann *et al.*[9] They analyzed the aorta movement in their experience of anterior surgery and found that the aorta migrates from a more posterolateral to a more anteromedial position in relation to the thoracic vertebrae. However, patients were scanned in supine position for preoperative CT and in a lateral decubitous position for postoperative magnetic resonance imaging. As the aorta location depends on the patient position at examination especially in the midthoracic level as clearly shown by the study of Huitema *et al*,[10] the aorta movement in Bullman's report may come from a difference in the patient's position in the 2 examinations.

Recently, Wang *et al*[11] analyzed the change of the position of the aorta after anterior or posterior instrumentation of type I Lenke curve and concluded that the aorta moved more in anterior surgery than in posterior surgery. They measured by 2 methods: one was from the aorta to the closest point of the cortex of the vertebral body and the other was from the posterior wall of the aorta to the anterior edge of the left rib head, neither of which was associated with the pedicle screw impingement. They measured 2 angles which were not suitable to describe the aorta position as for pedicle screw placement. Accordingly, parameters they adopted could not clarify the aorta movement relative to the spine, as do our results.

The present analysis indicated that the aorta position has a relationship with the curve characteristics of spinal deformity. The aorta movement highly correlated with the deformity characteristics: change of the sagittal alignment, preoperative AVT and sagittal alignment. Therefore, the

Table 4. Warning Pedicles—Direction Error Within 30°

		Preoperative			Postoperative			
Screw Length	Level	Warning (+)*	Warning (−)†	Ratio	Warning (+)*	Warning (−)†	Ratio	Difference
25 mm	T4–T6	15	33	31.3%	15	33	31.3%	0
25 mm	T7–T9	3	63	4.5%	15	51	22.7%	+18.2%‡
25 mm	T10–T12	6	59	9.2%	8	57	12.3%	+3.1%
30 mm	T4–T6	19	29	39.6%	23	25	47.9%	+8.3%
30 mm	T7–T9	9	57	13.6%	22	44	33.3%	+19.7%§
30 mm	T10–T12	14	51	21.5%	18	47	27.7%	+6.2%
35 mm	T4–T6	21	27	43.8%	27	21	56.3%	+12.5%
35 mm	T7–T9	11	55	16.7%	23	43	34.8%	+18.1%§
35 mm	T10–T12	24	41	36.9%	30	35	46.2%	+9.3%
40 mm	T4–T6	21	27	43.8%	29	19	60.4%	+16.6%
40 mm	T7–T9	11	55	16.7%	23	43	34.8%	+18.1%§
40 mm	T10–T12	33	32	50.8%	38	27	58.5%	+7.7%

*Number of the warning pedicles.
†Number of the nonwarning pedicles.
‡$P < 0.01$ (Fisher exact test).
§$P < 0.05$.

degree of the aorta movement may be estimated from preoperative deformity and the degree of correction.

We did not measure and analyze the rotation of the spine as most CT did not include the pelvis because of the retrospective nature of this study. Accordingly, we could not estimate the effect of derotation.

In summary, the aorta moved anteromedially relative to the spine after the posterior correction and the risk of the aorta by a pedicle screw increased by correction of the deformity at the middle thoracic spine. Surgeons are recommended to anticipate the aorta movement in the surgical planning.

Key Points

- We evaluated the aorta positions before and after scoliosis surgery by multiplanar reconstruction of computed tomography.
- The aorta had a tendency to migrate to the anteromedial direction after corrective surgery of the scoliosis.
- The risk of the aorta by a pedicle screw increases by correction of the deformity at the middle thoracic spine.

References

1. Kakkos SK, Shepard AD. Delayed presentation of aortic injury by pedicle screws: report of two cases and review of the literature. *J Vasc Surg* 2008; 47:1074–82.
2. Minor ME, Morrissey NJ, Peress R, et al. Endovascular treatment of an iatrogenic thoracic aortic injury after spinal instrumentation: case report. *J Vasc Surg* 2004;39:893–6.
3. Wegener B, Birkenmaier C, Fottner A, et al. Delayed perforation of the aorta by a thoracic pedicle screw. *Eur Spine J* 2008;17(suppl 2):S351–4.
4. Cheung KM, Luk KD. Prediction of correction of scoliosis with use of the fulcrum bending radiograph. *J Bone Joint Surg Am* 1997;79:1144–50.
5. Vora V, Crawford A, Babekhir N, et al. A pedicle screw construct gives an enhanced posterior correction of adolescent idiopathic scoliosis when compared with other constructs: myth or reality. *Spine* 2007;32:1869–74.
6. Luk KD, Cheung KM, Lu DS, et al. Assessment of scoliosis correction in relation to flexibility using the fulcrum bending correction index. *Spine* 1998; 23:2303–7.
7. Takeshita K, Maruyama T, Chikuda H, et al. Diameter, length, and direction of pedicle screws for scoliotic spine- analysis by multiplanar reconstruction of computed tomography. *Spine* 2009 59 34:798–803.
8. Takeshita K, Maruyama T, Chikuda H, et al. New parameters to represent the position of the aorta relative to the spine for pedicle screw placement. Paper presented at: The Scoliosis Research Society Annual Meeting; 2008; Salt Lake City, UT.
9. Bullmann V, Fallenberg EM, Meier N, et al. The position of the aorta relative to the spine before and after anterior instrumentation in right thoracic scoliosis. *Spine* 2006;31:1706–13.
10. Huitema GC, Cornips EM, Castelijns MH, et al. The position of the aorta relative to the spine: is it mobile or not? *Spine* 2007 20;32:1259–64.
11. Wang W, Zhu Z, Zhu F, et al. The changes of relative position of the thoracic aorta after anterior or posterior instrumentation of type I Lenke curve in adolescent idiopathic thoracic scoliosis. *Eur Spine J* 2008;17:1019–26.

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ORIGINAL ARTICLE

New parameters to represent the position of the aorta relative to the spine for pedicle screw placement

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Abstract Parameters of the position of the aorta in previous reports were determined for anterior surgery. This study evaluated the relative position of the aorta to the spine by new parameters, which could enhance the safety of pedicle screw placement. Three parameters were defined in a new Cartesian coordinate system. We selected an entry point of a left pedicle screw as the origin. The transverse plane was determined to include both the bases of the superior facet and to be parallel to the upper endplate of the vertebral body. A line connecting the entry points of both sides was defined as the *X*-axis. The angle formed by the *Y*-axis and a line connecting the origin and the center of the aorta was defined as the left pedicle–aorta angle. The length of a line connecting the origin and the aorta edge was defined as the left pedicle–aorta distance. Distance from the edge of the aorta to the *X*-axis was defined as the pedicular line–aorta distance. These parameters were measured preoperatively in 293 vertebral bodies of 24 patients with a right thoracic curve. We simulated the placement of the pedicle screw with variable length and with some direction error. We defined a warning pedicle as that when the aorta enters the expected area of the screw. Sensitivity analysis was performed to find the warning pedicle ratio in 12 scenarios. The left pedicle–aorta angle averaged 29.7° at the thoracic spine and −16.3° at the lumbar spine; the left pedicle–aorta distance averaged 23.7 and 55.2 mm; the pedicular line–aorta distance averaged 18.3 and 51.0 mm, respectively. The ratio of warning pedicles was consistently high at T4–5 and T10–12. When a left pedicle screw perforates an anterior/lateral wall of the vertebral body, the aorta may be at risk. These new parameters enable surgeons to intuitively understand the position of the aorta in surgical planning or in placement of a pedicle screw.

Keywords Scoliosis · Pedicle screw · Aorta · Computed tomography

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Introduction

Several authors have reported serious injuries of the aorta due to inappropriate placement of screws or plates in anterior surgery [8, 9]. Sucato et al. [10] reported that 12% (13/106) of vertebral screws in right thoracic scoliosis created some contour defect in the aorta on the contralateral side of the vertebral body, although patients had no sequela. They subsequently analyzed the position of the aorta in patients with scoliosis compared to those with non-scoliotic spine and found that the aorta often resides on the lateral side of the vertebral body and concluded that a potential risk of the aorta by a vertebral screw increases in the scoliotic spine. Maruyama et al. [7] studied the spatial relations between the spine and the aorta in adolescent idiopathic scoliosis and concluded that the aorta can be located in the direction of the screw passage in 33 of 40 vertebrae (83%) between T6 and T9. These studies, however, paid less attention to the relationship between the aorta and a pedicle screw. Accordingly, parameters describing the position of the aorta in these reports were not intuitive and surgeons have had difficulty utilizing these values in posterior surgery. The purpose of the present study was to evaluate the relative position of the aorta to the spine by new parameters, which can enhance the safety of pedicle screw placement.

Materials and methods

Thirty-seven patients with scoliosis underwent posterior instrumentation and fusion at the University Hospital from 2005 to 2007. Patients with congenital scoliosis were excluded. A total of 24 patients with a right thoracic curve were included in this study. Scoliosis was idiopathic in 17 patients, Chiari-syrinx in 2, Marfan syndrome in 2, multiple epiphyseal dysplasia in 1, Noonan syndrome in 1, and tuberous sclerosis in 1. Age at surgery was 10–29 (mean 17.1) years; 19 patients were women and 5 were men. Lenke's classification of scoliosis [4] was type 1 in eight patients, type 2 in five, type 3 in two, type 4 in four, type 5 in one, and type 6 in four. Preoperative Cobb angle averaged 66.4° (50°–103°). The apex vertebra ranged from T5 to T10 (median T10). All patients were treated by posterior correction and fusion by pedicle screw instrumentation. One patient with a curve of 103° had undergone anterior release before posterior spinal fusion. Computed tomography was taken before surgery and pedicle screws were placed with guidance of the CT-based navigation system. Postoperative Cobb angle averaged 20.3° (11°–39°).

A computer tomography was taken from the upper thoracic to the lower lumbar spine with a width of 1.25 mm for navigation. All DICOM data were transferred to a personal computer and analyzed by DICOM software (ExaView LITE: ©Ziosoft, Tokyo, Japan). We defined three parameters in a new Cartesian coordinate system and those parameters from T4 to L4 were measured in 293 vertebral bodies of 24 patients. We selected the middle of the base of the left superior facet as the origin of this coordinate system (Fig. 1), because the most probable threat to the aorta by a pedicle screw is on the left side at the thoracic spine. The transverse plane was determined to include both the bases of the superior facet and to be parallel to the upper endplate of the vertebral body. A line connecting the middle points of both bases of the superior facets is defined as the pedicular line (PL) (*X*-axis). The *Y*-axis perpendicular to the *X*-axis is drawn ventrally from the origin. The angle formed by the *Y*-axis and a line connecting the origin and the center of the aorta is defined as the left pedicle–aorta angle length of a line connecting the origin and the edge of the aorta as the left pedicle–aorta distance, and distance from the edge of the aorta to the *X*-axis as the pedicular line–aorta distance. Moreover, we break down the left pedicle–aorta distance into the *X*- and *Y*-unit. The *X*-unit is the rectangular component of the left pedicle–aorta distance to the *X*-axis and the *Y*-unit is that to the *Y*-axis.

We simulated placement of the pedicle screw with a direction different from the ideal trajectory. Sensitivity analysis was performed by changing the direction error and the length of the screw independently. The direction error started from 10° up to 30° with 10° increments (three scenarios). The length of the screw started from 25 to 40 mm with increments of 5 mm (four scenarios). We set up a total of 12 scenarios (three by four). We defined a warning pedicle as that when the aorta enters the expected area of the screw. The ratio of warning pedicles was calculated from T4 to L4 in the 12 scenarios (Fig. 2). From the repeatability test from our previous study, interclass correlation coefficients were 0.922–0.957 in the intraobserver measurement and 0.896–0.929 (0.864–0.961) in the interobserver measurement [12].

To determine the relationship of the location of the aorta and the characteristics of scoliosis, the Cobb angle of the main thoracic curve, apical vertebral translations of the main thoracic curve, and the angle at T5–T12 in the sagittal plane were measured, and correlations between these

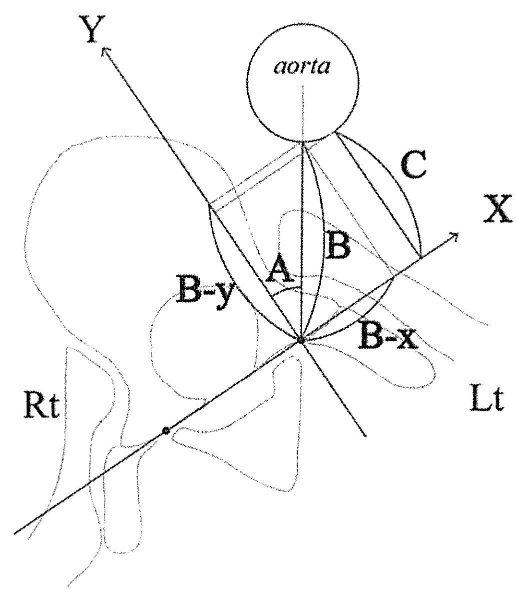

Fig. 1 Measurement of new parameters. The origin is set at the middle of the base of the left superior facet. A line joining the middle points of both bases of the superior facets is defined as the *X*-axis (*the pedicular line*). The *Y*-axis, perpendicular to the *X*-axis, is drawn ventrally from the origin. *A* The left pedicle–aorta angle. *B* The left pedicle–aorta distance. *B-x* the *X*-unit of the left pedicle–aorta distance. *B-y* the *Y*-unit of the left pedicle–aorta distance. *C* the pedicular line–aorta distance

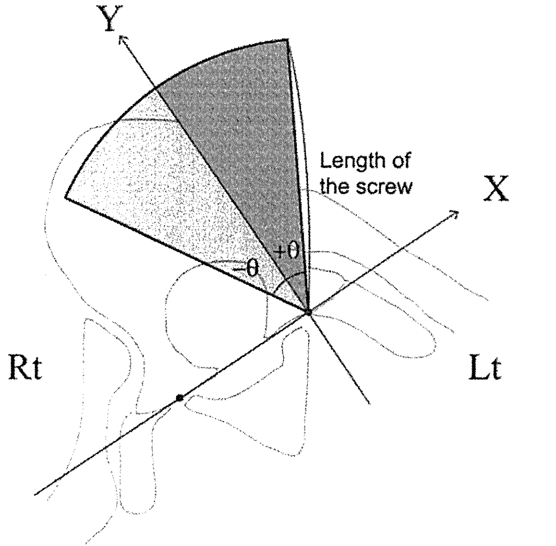

Fig. 2 The expected area of the pedicle screw. We simulated the pedicle screw placement with some direction error (±θ) and the variable length (length of the screw) with sensitivity analysis. We defined a warning pedicle as that when the aorta enters this zone

parameters and the X-and Y-unit of the left pedicle–aorta line at the apex were calculated.

Results

The relative position of the aorta to the spine changed dramatically at the thoracic spine (Table 1; Fig. 3). The left pedicle-aorta angle spanned from −46° to 78° (average 29.7°) at the thoracic spine and from −38° to 13° (average −16.3°) at the lumbar spine; the left pedicle–

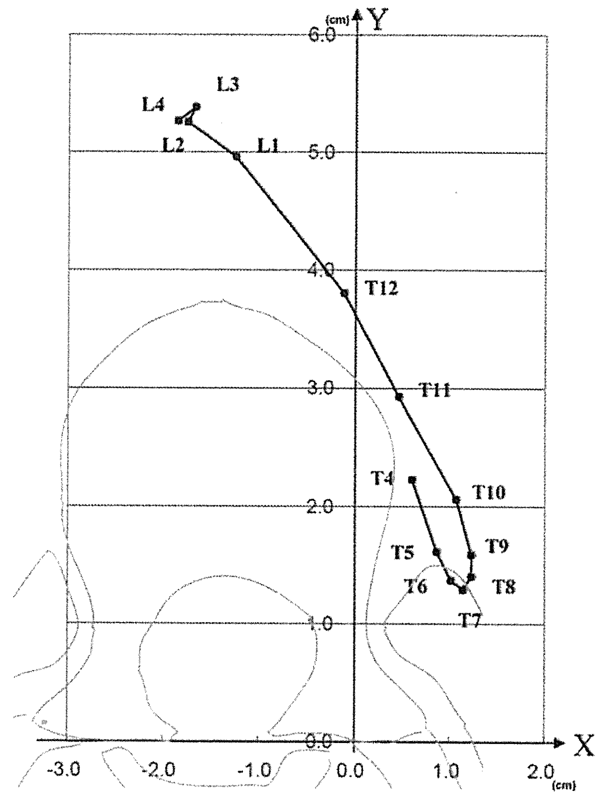

Fig. 3 The average course of the aorta relative to the spine. The origin is set at the middle of the base of the left superior facet. A line joining the middle points of both bases of the superior facets is defined as X-axis. The aorta begins to be seen from T4. It descends laterally and posteriorly and turns back at T7. At T12, the aorta is in front of the left pedicle and moves to the right side at the lumbar level. Attention should be paid to the spine drawn in the figure, because the size of the spine changed considerably at the level of the spine

Table 1 Distribution of the left pedicle-aorta angle, the left pedicle-aorta distance, and the pedicular line-aorta distance

	Left pedicle–aorta angle (°)	Left pedicle–aorta distance (mm)	The pedicular line–aorta distance (mm)
T4	20.1 ± 22.7	24.5 ± 6.2	20.9 ± 9.7
T5	32.1 ± 20.3	19.4 ± 4.4	14.1 ± 8.5
T6	39.5 ± 17.3	17.8 ± 3.5	10.9 ± 7.2
T7	43.8 ± 13.6	17.6 ± 3.6	10.1 ± 6.3
T8	42.8 ± 11.9	19.0 ± 4.2	11.4 ± 6.5
T9	40.0 ± 12.8	20.6 ± 4.9	13.6 ± 7.2
T10	30.2 ± 15.1	24.0 ± 6.4	19.2 ± 8.6
T11	13.0 ± 19.9	31.5 ± 8.1	29.1 ± 11.0
T12	0.3 ± 15.6	39.3 ± 8.3	36.9 ± 8.4
L1	-12.9 ± 13.3	52.4 ± 7.1	48.3 ± 7.0
L2	-17.7 ± 10.3	56.2 ± 6.2	51.2 ± 5.2
L3	-16.9 ± 6.8	56.7 ± 5.4	52.9 ± 4.2
L4	-19.4 ± 5.0	56.0 ± 5.0	52.4 ± 7.4

aorta distance ranged from 11 to 52 mm with an average of 23.7 mm and from 36 to 72 mm with an average of 55.2 mm, respectively; the pedicular line–aorta distance ranged from −4 to 59 mm (average 18.3 mm) and from 33 to 75 mm (average 51.0 mm), respectively. From the cephalad to the caudal direction, the aorta was seen at the antero-lateral position of the vertebral body of T4 or T5. The aorta moved to the left side laterally and posteriorly as it descended, changing its course at T7 and moving medially and anteriorly. It located in front of the vertebral body at the left T12 pedicle. At the lumbar spine, the aorta moved to the right side.

The ratio of warning pedicles increased as the direction error or the screw length increased (Fig. 4). When the direction error was within 30° and the screw length was 40 mm, the ratio was highest at T4 with 69%, followed by T11 (67%), T5 (54%), T10 (46%) and T12 (39%), and this trend was consistent in any scenario.

No parameter of the main thoracic curve correlated with the *X*-unit of the left pedicle–aorta distance at the apex.

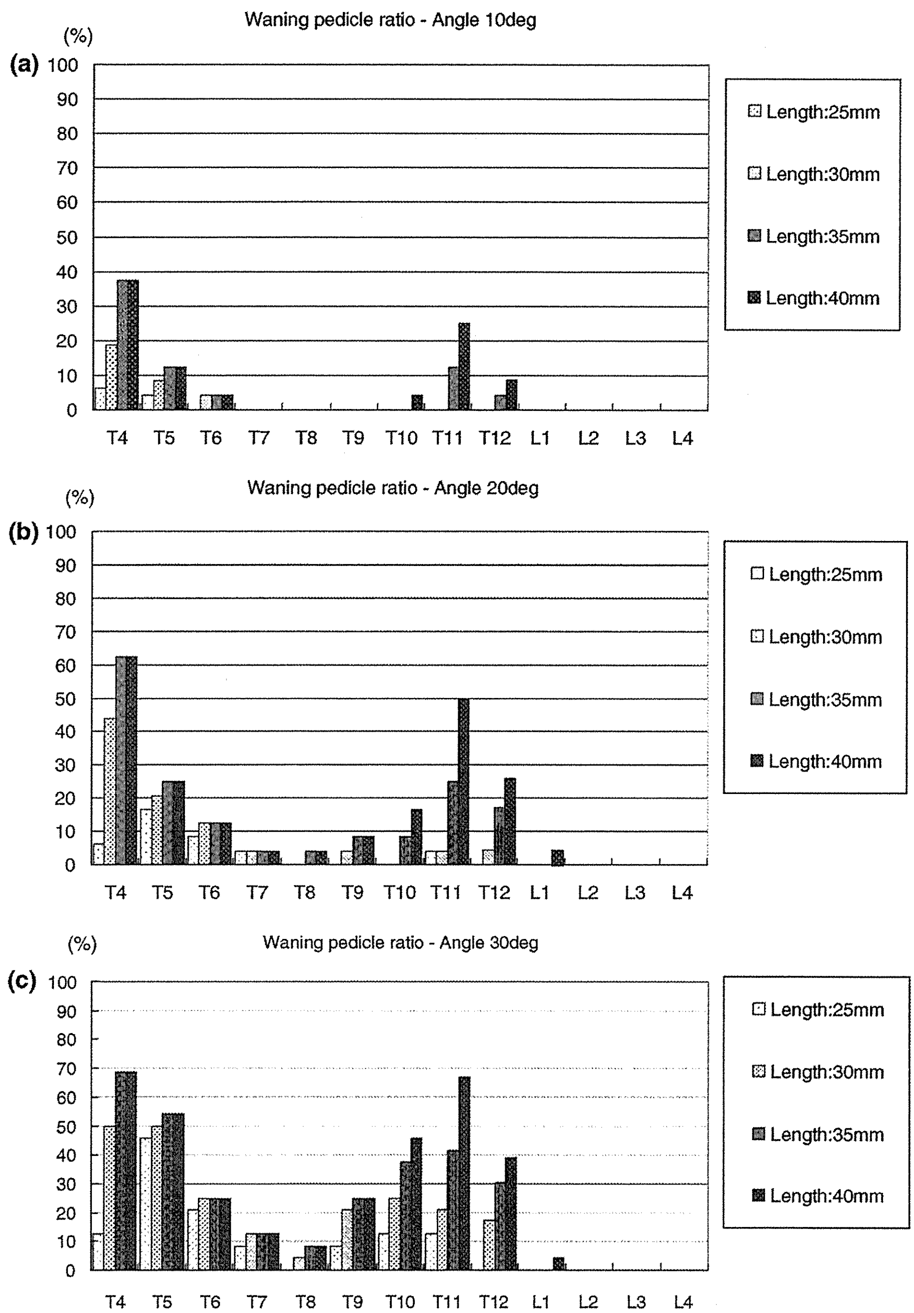

Fig. 4 Distribution of warning pedicle ratios from T4 to L4 in 12 scenario. In any scenario, there was a high percentage of warning pedicles at the thoracic spine except at T7 and T8. **a** The warning pedicle ratio when the direction error is within 10° and the screw length changes from 25 to 40 mm. **b** The warning pedicle ratio when the direction error is within 20° and the screw length changes from 25 to 40 mm. **c** The warning pedicle ratio when the direction error is within 20° and the screw length changes from 25 to 40 mm

Sagittal angle at T5–T12 in the sagittal plane significantly correlated with the *Y*-unit ("anterior–posterior" direction for the spine) of the left pedicle–aorta distance at the apex (−0.44; $p = 0.03$).

Discussion

Liljenqvist et al. [5] measured the distance from the aorta to the vertebral body, and reported that the closest distance averaged 6–7 mm between T4 and T9 and <5 mm between T10 and L4. Sucato and Duchene [11] analyzed the position of the aorta in patients with idiopathic scoliosis in magnetic resonance scans and found that the thoracic aorta in idiopathic scoliosis is positioned more posteriorly and laterally compared with straight spines. From their analysis, the aorta begins to be seen as the aortic arch in front of the T4 vertebral body and changes its position posteriorly and laterally as it descends. The aorta turns back anteriorly and medially at the apical region and passes in front of the T12 through the hiatus of the diaphragm. The present study supports their analyses.

Vaccaro et al. [13] analyzed a non-scoliotic thoracic spine and found that the aorta and the esophagus are at greatest risk of injury when a pedicle screw penetrates an anterior cortex of the vertebral body. Liljenqvist et al. [6] analyzed 22 patients with idiopathic scoliosis by computed tomography postoperatively. They found that 3 of 120 pedicle screws penetrated the anterior vertebral cortex and 1 of these three screws was replaced because of its direct proximity to the thoracic aorta.

When a pedicle screw is placed by a free-hand technique [3] or with a fluoroscope, the direction of placement largely depends on several landmarks of the explored surface of the spine: facet joints, transverse processes and laminae. Our new parameters defined by both sides of superior facet are easy to comprehend in posterior surgery. Additionally, we could compare the relative risk of pedicle screw placement between spine levels in various settings by the sensitivity analysis.

The present study elucidated that the aorta usually stays on the anterior or left-lateral side of the vertebral body at T4, T5 and at T10–T12, and a small breach of a pedicle screw outside the vertebral body at these levels may result in indentation of the aorta. Faro et al. [1] studied the influence of indentation of the aorta by a screw in their bovine model and found that the major impingement of vertebral screws on the aorta caused acute and chronic histopathologic and biomechanical changes in the vessel wall. Though sequelae of moderate to mild indentation of the aorta have not yet been known, screws will stay inside the body for over tens of years in this young population. It is recommended that any screw either in anterior or in posterior surgery be placed away from the aorta.

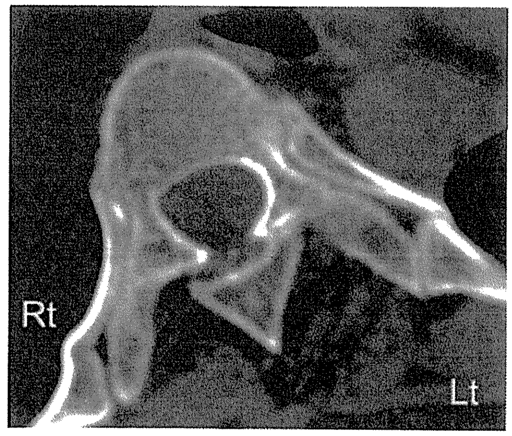

Fig. 5 A case with a typical position of the aorta around the apex level. Though a distance to the left base of the superior facet (an insertion point of a pedicle screw) is closer than other levels, the aorta often resides in the most lateral position from the spine and allows wider maldirection of the pedicle screw

The present study shows that the aorta at the middle thoracic spine is often located away from the spine and resides in front of a left rib (Fig. 5), which leads to a low percentage of dangerous pedicles at T7 and T8. However, in turn, the spinal cord deviates to the left concave pedicles at the apical area at the right thoracic spine [5]. Moreover, the aorta may not stay in the same position. Huitema et al. [2] examined 50 patients by computed tomography or magnetic resonance scans before surgery, and reported that the aorta moves more anteromedially in a prone position than in a supine position especially at levels T5–T10. Their study indicates that the aorta is fairly mobile at the mid-thoracic level when a subject changes his position. Though the present study showed a relative safety of the aorta at T6–T9, the aorta might reside closer to the spine when a subject is at another position. Admittedly, segmental pedicle screw instrumentation is a most powerful construct for correction and maintenance in spinal deformity. Surgeons, however, must be vigilant about the positions of the aorta and the spinal cord in placement of pedicle screws, especially on the left side, and screw breach may necessitate reoperation for replacement.

In summary, new parameters enable surgeons to intuitively understand the position of the aorta in their preoperative planning or during placement of a pedicle screw. When a left pedicle screw perforates an anterior/lateral wall of the vertebral body, the aorta may be at risk, especially at T4, T5 and T10–T12.

References

1. Faro FD, Farnsworth CL, Shapiro GS et al (2005) Thoracic vertebral screw impingement on the aorta in an in vivo bovine model. Spine 30(21):2406–2413
2. Huitema GC, Cornips EM, Castelijns MH et al (2007) The position of the aorta relative to the spine: is it mobile or not? Spine 32(12):1259–1264
3. Kim YJ, Lenke LG, Bridwell KH et al (2004) Free-hand pedicle screw placement in the thoracic spine: is it safe? Spine 29:333–342
4. Lenke LG, Betz RR, Harms J et al (2001) Adolescent idiopathic scoliosis: a new classification to determine extent of spinal arthrodesis. J Bone Joint Surg Am 83(8):1169–1181
5. Liljenqvist UR, Allkemper T, Hackenberg L et al (2002) Analysis of vertebral morphology in idiopathic scoliosis with use of magnetic resonance imaging and multiplanar reconstruction. J Bone Joint Surg Am 84(3):359–368
6. Liljenqvist UR, Halm HF, Link TM (1997) Pedicle screw instrumentation of the thoracic spine in idiopathic scoliosis. Spine 22(19):2239–2245
7. Maruyama T, Takeshita K, Nakamura K et al (2004) Spatial relations between the vertebral body and the thoracic aorta in adolescent idiopathic scoliosis. Spine 29:2067–2069
8. Matsuzaki H, Tokuhashi Y, Wakabayashi K et al (1993) Penetration of a screw into the thoracic aorta in anterior spinal instrumentation. A case report. Spine 18:2327–2331
9. Ohnishi T, Neo M, Matsushita M et al (2001) Delayed aortic rupture caused by an implanted anterior spinal device. J Neurosurg 95(2 Suppl):253–256
10. Sucato DJ, Kassab F, Dempsey M (2004) Analysis of screw placement relative to the aorta and spinal canal following anterior instrumentation for thoracic idiopathic scoliosis. Spine 29(5): 554–559
11. Sucato DJ, Duchene C (2003) The position of the aorta relative to the spine: a comparison of patients with and without idiopathic scoliosis. J Bone Joint Surg Am 85(8):1461–1469
12. Takeshita K, Maruyama T, Chikuda H et al (2009) Diameter, length, and direction of pedicle screws for scoliotic spine: analysis by multiplanar reconstruction of computed tomography. Spine 34:798–803
13. Vaccaro AR, Rizzolo SJ, Balderston RA et al (1995) Placement of pedicle screws in the thoracic spine. Part II. An anatomical and radiographic assessment. J Bone Joint Surg Am 77(8):1200–1206

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ORIGINAL ARTICLE

High prevalence of vertebral artery tortuosity of Loeys-Dietz syndrome in comparison with Marfan syndrome

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Abstract
Purpose. Loeys-Dietz syndrome (LDS) is a connective tissue disease caused by mutations in the genes encoding the transforming growth factor-β receptor (TGFBR). LDS is associated with aneurysms or dissections of the aorta similar to Marfan syndrome (MFS) as well as arterial tortuosity and aneurysms in the peripheral arteries. The purpose of this study was to evaluate the arterial diseases of LDS to differentiate it from MFS.
Materials and methods. A total of 10 LDS patients with an identified mutation in TGFBR (6 male, 4 female; mean age 36.3 years) and 20 MFS patients with an identified mutation in fibrilin-1 who were age- and sex-matched to the LDS subjects (12 male, 8 female; mean age 37.1 years) were reviewed. The prevalence of vertebral arterial tortuosity (VAT) and peripheral aneurysm (PAN) was studied using computed tomography angiography.
Results. In all, 9 of the 10 LDS patients had VAT, and five PANs were observed in 3 patients. In contrast, 8 (40%) of the MFS patients had VAT, and 1 patient had a PAN. LDS had a higher prevalence of VAT ($P = 0.017$) by Fisher's exact test.
Conclusion. The VAT was highly prevalent among LDS patients. Thus, the presence of VAT has the potential to differentiate LDS from MFS.

Key words Loeys-Dietz syndrome · Vertebral artery tortuosity · Peripheral aneurysm · Transforming growth factor-β receptor

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Introduction

Aortic dissection typically occurs in older patients with a peak incidence during the sixth decade, but 7.2% of cases occur in young subjects.[1] Aortic dissection in this subgroup is related to connective tissue diseases, such as Marfan syndrome (MFS), vascular Ehlers-Danlos syndrome, and Loeys-Dietz syndrome (LDS). LDS is a newly described phenotype caused by mutations in the genes encoding transforming growth factor-β receptor (TGFBR).[2–4] Clinical features of LDS include vascular disease, craniosynostosis, cleft palate/bifid uvula, hypertelorism, congenital heart defects, and mental retardation. Patients with LDS, similar to those with MFS, have an aneurysm or dissection of the ascending aorta and dilatation of the aortic root. In contrast to MFS, generalized arterial tortuosity and aneurysms of arteries have been noted in patients with LDS.[4] Aortic rupture and dissection can occur in LDS patients with aortic root diameters not considered at risk in MFS.[5]

The exact prevalence of LDS is unknown, and its characteristics are not familiar to radiologists. However, given the fact that LDS has recently been discovered, many cases might not have been diagnosed yet. Because vascular pathology is more aggressive in LDS than in MFS, it is important to recognize the characteristics of this disorder and to diagnose it correctly.

The purpose of this study was to review radiological findings of the arterial diseases of LDS and to differentiate them from those found in MFS. Particular attention was given to computed tomography angiography (CTA), which is used quite frequently in the clinical setting.

Materials and methods

The study was approved by our institutional review board. Written informed consent to use the patients' clinical and imaging data was not required because it was a retrospective study.

A total of 10 LDS patients with an identified mutation in TGFBR (6 men, 4 women; mean age 36.3 years, range 20–54 years) were retrospectively reviewed. Causes of hospitalization were aortic root dilatation in four patients and aortic dissection in six. Among these 10 LDS patients, 9 (90%) were in a postoperative state (1 with aortic repair, 3 with valve replacement, 5 with both).

A group of 20 MFS patients with an identified mutation in fibrilin-1 (12 men, 8 women; mean age 37.1 years, range 20–56 years) were also reviewed. MFS patients who were age- and sex-matched to the LDS patients were selected randomly from our database. Causes of hospitalization were aortic root dilatation in 11 patients, aortic dissection in 8 patients, and mitral valve regurgitation in 1 patient. In all 17 MFS patients (85%) were in a postoperative state (3 with aortic repair, 7 with valve replacement, 7 with both).

All patients had had clinical examinations including a physical examination and laboratory data by a cardiovascular team. Initial and follow-up CTA was performed in a clinical setting as described below. All patients had undergone genetic analysis according to the method reported by Akutsu et al.[6]

CT protocol

The CT angiography was performed using a multislice CT scanner (16 or 64 slices) with an iodine contrast material injection of 1 ml/kg with an iodine content of 350 mg I/ml or 370 mg I/ml. Injection time varied from 30 to 40 s with a variable injection rate. A saline chaser of 25 ml with the same injection rate as the contrast material was applied with a dual-syringe power injector. The scan started when the density in the region of interest (ROI) positioned at the ascending artery increased 100 HU from a baseline value using an intermittent monitoring scan. The CT scan covered from the neck to the pubis. A field of view (FOV) of 320 or 400 mm was adopted according to the patient's body size. For three-dimensional (3D) reconstruction, a 1 or 2 mm slice thickness data set without slice gap was used. The data set was sent to a commercially available workstation and a CT image server.

Imaging analysis

All CT images were reviewed on a Picture Archiving and Communication System (PACS) viewer with an adjustable optimal widow setting and stack-view system. Reconstructed images, such as 3D volume rendering or multiplanar reconstruction, were also used if needed.

The prevalence of arterial diseases was studied in both LDS and MFS subjects. Peripheral aneurysm and peripheral idiopathic dissection in the abdominal aortic branches were evaluated. Tortuosity in the vertebral artery and the common carotid artery was also evaluated.

The presence of aneurysm and dissection was analyzed visually. The tortuosity was graded on a 3-point scale (Fig. 1): 0, the artery runs straight or with a mild curve; 1, the artery turns with multiple curves or a severe curve of 10 mm distance from the upper to the lower portion of a curve; and 2, the artery has a pigtail-like or corkscrew-like curve. After summing up each score for the right and left arteries, the score for patients varied from 0 to 4.

Statistical analysis

For the statistical analysis, JMP software (version 7.0; SAS Institute, Cary, NC, USA) was used. Continuous

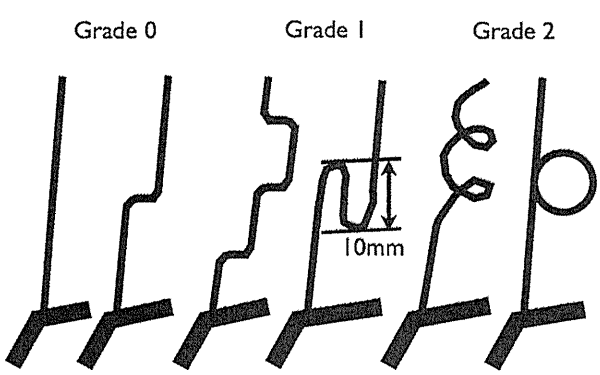

Fig. 1. Grading vertebral artery tortuosity. For grade 0, the artery runs straight or with a mild curve. For grade 1, the artery turns with multiple curves or has a severe curve, with 10 mm distance from the upper to the lower portion of a curve. For grade 2, the artery has a pigtail-like, or corkscrew-like, curve

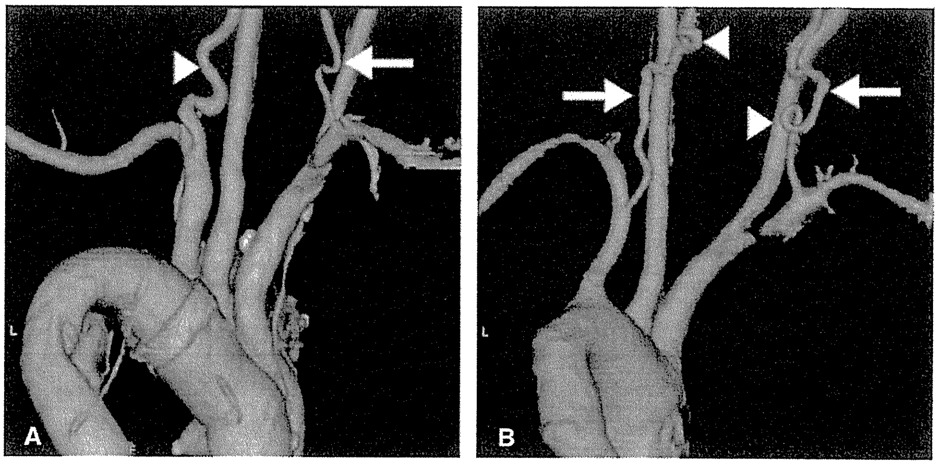

Fig. 2. **a** Computed tomography angiography (CTA) image, posterior view, of a 37-year-old patient with Loeys-Dietz syndrome (LDS). The patient is in a postoperative stage after aortic dissection. The right vertebral artery (*arrow*) is graded 0, and the left vertebral artery (*arrowhead*) as 1 because of its multiple curves. **b** CTA image from posterior view of a 19-year-old LDS patient. The patient underwent CT examination for preoperative evaluation of annuloaortic ectasia. Both vertebral arteries (*arrows*) are graded 2 owing to the pigtail-like curves (*arrowheads*). The right subclavian artery shows pseudostenosis owing to the artifact of contrast material in the vein

Table 1. Patient characteristics of Loeys-Dietz syndrome and Marfan syndrome

Characteristic	LDS	MFS	Difference
Gene mutation	TGFBR	FBN1	
No. of patients	10	20	
Age (years), mean ± SD	36.3 ± 12.6	37.1 ± 11.2	NS
Sex (M:F)	6:4	12:8	NS
Vascular disease:[a] (AAE/AD/other)	4/6/0	11/8/1	NS
Postoperative state	9 (90%)	17 (85%)	NS

AAE, annuloaortic ectasia; AD, aortic dissection; TGFBR, transforming growth factor-β receptor; FBN1, fibrilin-1; LDS, Loeys-Dietz syndrome; MFS, Marfan syndrome; NS, not significant using a significance level of $P < 0.05$

[a]Vascular disease that caused the patients' hospitalization

data were expressed as the mean ± SD. A two-tailed Student's *t*-test was used to compare continuous variables. The χ^2 test or Fisher's exact test was used for discrete variables. $P < 0.05$ was considered statistically significant.

Results

Patients' characteristics and vascular pathologies are summarized in Tables 1 and 2.

Arterial tortuosity

In all, nine (90%) of the LDS patients had vertebral arterial tortuosity (Fig. 2): two on the right side, three on the left, and four on both sides. Among the MFS patients,

Table 2. Vascular pathologies in Loeys-Dietz syndrome and Marfan syndrome

Characteristic	LDS	MFS	*P*
No. of patients	10	20	
Vertebral artery tortuosity			
Prevalence (no.)	9 (90%)	8 (40%)	0.017
Score[a]			
0	1	12	
1	3	4	
2	3	2	
3	1	2	
4	2	0	
Carotid artery tortuosity (no.)	0	0	NS
Peripheral aneurysm			
Abdominal branch	3 (30.0%)	1 (5.0%)	NS
Iliac artery	3 (33.3%)	3 (20.0%)	NS
Abdominal aortic aneurysm	1 (14.3%)	1 (8.3%)	NS

NS, not significant using a significance level of $P < 0.05$

[a]Score was calculated by the summation of both grades of vertebral arteries shown in Fig. 1

eight (40%) had vertebral artery tortuosity: two on the right side, two on the left, and four on both sides. The tortuosity scores are also noted in Table 2. The common carotid artery showed no tortuosity in any patients.

The LDS patients had a high prevalence of vertebral artery tortuosity ($P = 0.017$). The mean tortuosity score was 2.0 [95% confidence interval (CI) 1.26–2.73] for LDS patients and 0.7 (95% CI 0.18–1.22) for MFS patients.

Aortic and peripheral artery disease

A total of five peripheral aneurysms were observed in three LDS patients (30%). Three aneurysms presented in the hepatic artery, one in the superior mesenteric artery, and one in the pancreatic arcade. Three patients (33.3%) had common iliac artery aneurysms, and one (10%) had a common femoral artery aneurysm. Because one patient had iliac artery involvement secondary to aortic dissection, we excluded him from the analysis of iliac aneurysms. Among the seven patients without abdominal aortic dissection, an abdominal aortic aneurysm was observed in one patient (14.3%). No aneurysms were observed in the thoracic aorta and its branches. Because four patients had undergone thoracic aortic replacement, three of which were due to dissection, they were excluded from the analysis of the prevalence of aortic aneurysms.

Among the MFS patients, one (5%) had a hepatic artery aneurysm, and three (20%) had common iliac aneurysms. Among the 12 patients without abdominal aortic replacement, 1 (8.3%) had an abdominal aortic aneurysm. Because two patients had involvement of the celiac trunk and five of the iliac artery secondary to aortic dissection, such territories were excluded for evaluation of the prevalence of peripheral aneurysms. Because seven patients had thoracic aortic replacement and eight had abdominal aortic replacement, they were excluded from the analysis of the prevalence of aortic aneurysms.

The prevalence of peripheral aneurysms was not significantly different between LDS and MFS ($P = 0.057$).

Discussion

Our results showed that the high prevalence of vertebral artery tortuosity in LDS helps to differentiate LDS from MFS. Patients with LDS have aneurysms or dissection of the ascending aorta, similar to those observed in patients with MFS. In contrast to MFS, however, generalized arterial tortuosity and aneurysms of other arteries have been noted in patients with LDS.[4] On the other hand, there are some reports[7,8] that arterial tortuosity had not been found in their LDS groups although they had not been systematically evaluated in all patients. The exact prevalence of arterial tortuosity, especially in the vertebral artery, has not yet been reported. Our results showed that the vertebral arteries were highly affected in LDS patients.

Assessing the vertebral artery to help differentiate LDS from MFS is a superior method for a few reasons. First, the lower portion of the vertebral artery is easy to evaluate with thoracic or thoracoabdominal CTA. Second, the vertebral artery is rarely affected by aortic dissection, in contrast to the subclavian artery or carotid artery. Third, the vertebral artery is easy to evaluate because it runs straight, especially in young subjects. According to our unpublished data, among 10 subjects without either LDS or MFS (five men, five women; mean age 26.7 years), tortuosity was not observed in the vertebral artery. Arteries other than the vertebral artery (e.g., abdominal visceral arteries, iliac arteries) are difficult to evaluate because they sometimes display tortuosity even in normal populations. For these reasons, we recommend that the vertebral artery be evaluated.

An autosomal dominant genetic disorder, MFS has symptoms that include those of cardiovascular diseases (ascending aortic aneurysms, aortic dissections, mitral valve abnormalities), skeletal manifestations (pectus deformities, scoliosis, dolichostenomelia, arachnodactyly, joint laxity, highly arched palate), and ocular complications (ectopia lentis, retinal detachment, myopia). Diagnostic criteria for MFS, currently known as the Ghent criteria, emphasize the aortic aneurysms and dissections, a constellation of skeletal findings, ectopia lentis, dural ectasia, and the family history.[9] LDS has many similarities to MFS with regard to cardiovascular disorders or skeletal manifestations; therefore, if LDS patients did not show some characteristic manifestation, differentiation from MFS would be difficult without genetic analysis. Vertebral artery tortuosity may be the factor that can differentiate these disorders and so would be helpful in the clinical setting when genetic analysis is not immediately available.

Cardiovascular disease is more aggressive and widespread in LDS than MFS. Aortic rupture and dissection can occur in patients with aortic root diameters not considered at risk in MFS (<4.5 cm).[5] Recognition of LDS is important, especially for the management of these patients. The two major causes of death in LDS patients were reported to be aortic dissection and rupture in the thoracic (67%) and abdominal (22%) regions.[10] The third cause of mortality was intracranial hemorrhaging due to rupture of cranial arterial aneurysms (7%) because in LDS aneurysms are not confined to the aortic root, as with MFS, but occur throughout the entire arterial tree.

Our results indicated that peripheral aneurysms in LDS patients were present in the hepatic and mesenteric iliac arteries. These results were consistent with the fact that LDS has a high prevalence of peripheral aneurysms. The difference in the prevalence of peripheral aneurysms was not significant ($P = 0.057$), but it might be because the sample number was too small. It is important to know the prevalence of peripheral aneurysms for diagnosis and management.

Limitations

The number of patients in our sample was small, which was due to the requirement of genetic analysis to confirm the diagnosis of LDS and MFS in this study. Genetic analysis is not widely available in clinical settings. Also, bias may be present because our institution is a cardiovascular center. Hence, the patients referred to our hospital might have a higher prevalence of cardiovascular diseases than patients in other hospitals or institutions. Although the use of CT images for the initial diagnosis is preferred, because many of the LDS and MFS patients were referred to our hospital after the first operation we used the images obtained in the pre- or postoperative state. The mutation of TGFBR was classified as TGFBR-1 and TGFBR-2. Because both of these types have an aggressive vascular pathology, we did not mention the TGFBR types in this study. Further examination of a larger sample is needed to understand the relation between the gene type and the phenotype.

Conclusion

Vertebral artery tortuosity and peripheral aneurysms had a high prevalence among LDS patients. Identifying tortuosity in the vertebral artery has a potential to differentiate LDS from MFS. In the diagnosis of patients suspected of connective tissue disease, we should pay attention to peripheral artery diseases as well as aortic pathologies.

References

1. Januzzi JL, Isselbacher EM, Fattori R, Cooper JV, Smith DE, Fang J, et al. Characterizing the young patient with aortic dissection: results from the International Registry of Aortic Dissection (IRAD). J Am Coll Cardiol 2004;43:665–9.
2. Mizuguchi T, Collod-Beroud G, Akiyama T, Abifadel M, Harada N, Morisaki T, et al. Heterozygous TGFBR2 mutations in Marfan syndrome. Nat Genet 2004;36:855–60.
3. Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, et al. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. Nat Genet 2005;37:275–81.
4. Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, et al. Aneurysm syndromes caused by mutations in the TGF-beta receptor. N Engl J Med 2006;355:788–98.
5. Williams JA, Loeys BL, Nwakanma LU, Dietz HC, Spevak PJ, Patel ND, et al. Early surgical experience with Loeys-Dietz: a new syndrome of aggressive thoracic aortic aneurysm disease. Ann Thorac Surg 2007;83:S757–63; discussion S85–90.
6. Akutsu K, Morisaki H, Takeshita S, Sakamoto S, Tamori Y, Yoshimuta T, et al. Phenotypic heterogeneity of Marfan-like connective tissue disorders associated with mutations in the transforming growth factor-beta receptor genes. Circ J 2007;71:1305–9.
7. Alberts JJ, van den Berg MP, Bergman JE, du Marchie Sarvaas GJ, Post JG, van Unen H, et al. The many faces of aggressive aortic pathology: Loeys-Dietz syndrome. Neth Heart J 2008;16:299–304.
8. Singh KK, Rommel K, Mishra A, Karck M, Haverich A, Schmidtke J, et al. TGFBR1 and TGFBR2 mutations in patients with features of Marfan syndrome and Loeys-Dietz syndrome. Hum Mutat 2006;27:770–7.
9. De Paepe A, Devereux RB, Dietz HC, Hennekam RC, Pyeritz RE. Revised diagnostic criteria for the Marfan syndrome. Am J Med Genet 1996;62:417–26.
10. Johnson PT, Chen JK, Loeys BL, Dietz HC, Fishman EK. Loeys-Dietz syndrome: MDCT angiography findings. AJR Am J Roentgenol 2007;189:W29–35.

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ORIGINAL ARTICLE
Molecular Cardiology

Genetic Analysis of Young Adult Patients With Aortic Disease Not Fulfilling the Diagnostic Criteria for Marfan Syndrome

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Background: Although the existence of the young patients with aortic disease not fulfilling the diagnostic criteria for Marfan syndrome (MFS) has been known, the etiology of their disease has not yet been elucidated. The purpose of the present study was to elucidate the genetic and clinical features of the young patients with aortic disease not having MFS.

Methods and Results: Eighty young adult patients with aortic disease were examined. They were divided into a definite MFS (n=51) and a non-definite MFS group (n=29) according to the Ghent nosology. Clinical and genetic characteristics were compared between the 2 groups. Among 29 non-definite MFS probands, 1 (3%) *FBN1*, 2 (7%) *TGFBR1*, and 3 (10%) *TGFBR2* mutations were found, and 4 *ACTA2* mutations were found in the 23 probands examined without *FBN1*, *TGFBR1*, or *TGFBR2* mutations. In total, more than 10 out of 29 (34%) probands in the non-definite MFS group were associated with genetic mutations. Skeletal involvement was less frequent in the non-definite than in the definite MFS group (7% vs 82%, P<0.01).

Conclusions: In the probands with aortic diseases in young who cannot be diagnosed with MFS, mutations other than *FBN1* mutations accounted for at least one-third of all causes of aortic disease. (*Circ J* 2010; **74:** 990–997)

Key Words: *ACTA2*; Aortic disease; Marfan syndrome; *TGFBR1*; *TGFBR2*

Aortic dissection or annulo-aortic ectasia (AAE) often develops in young patients with Marfan syndrome (MFS), which is caused by mutations in the *FBN1*.[1] Recently, progress in genetic analysis has revealed genetic disorders other than *FBN1* mutations, such as mutations of *TGFBR1* or *TGFBR2*, *ACTA2*, *MYH11*, and *SLC2A10*, which also cause aortic disease in young patients.[2–7] It is often believed that the cause of aortic disease in young patients is MFS. However, these patients cannot always be diagnosed as MFS.

Although the existence of the young patients with aortic disease not fulfilling the diagnostic criteria for MFS has been known, the details of their disease have not yet been elucidated. The purpose of the present study was to elucidate the genetic and clinical features of young patients with aortic disease not fulfilling the diagnostic criteria for MFS.

Methods

Patients who were suspected of connective tissue disorders and who consented to undergo genetic analysis (n=129) were initially enrolled for the present study to investigate the characteristics of young patients with aortic disease, such as, aortic dissection, AAE and other forms of aortic aneurysm. Then, patients with the following characteristics were excluded: age <15 years (n=5), patients with relatives diagnosed with MFS (n=21), patients who did not have aortic disease (n=11), patients whose aortic dissection developed at age ≥50 years or whose aneurysms were found at age ≥50 years (n=9), and patients with aortitis that was regarded as having other etiologies (n=3). In total, 80 young adult patients (probands) with aortic disease who were suspected of connective tissue disorders were included in the present study.

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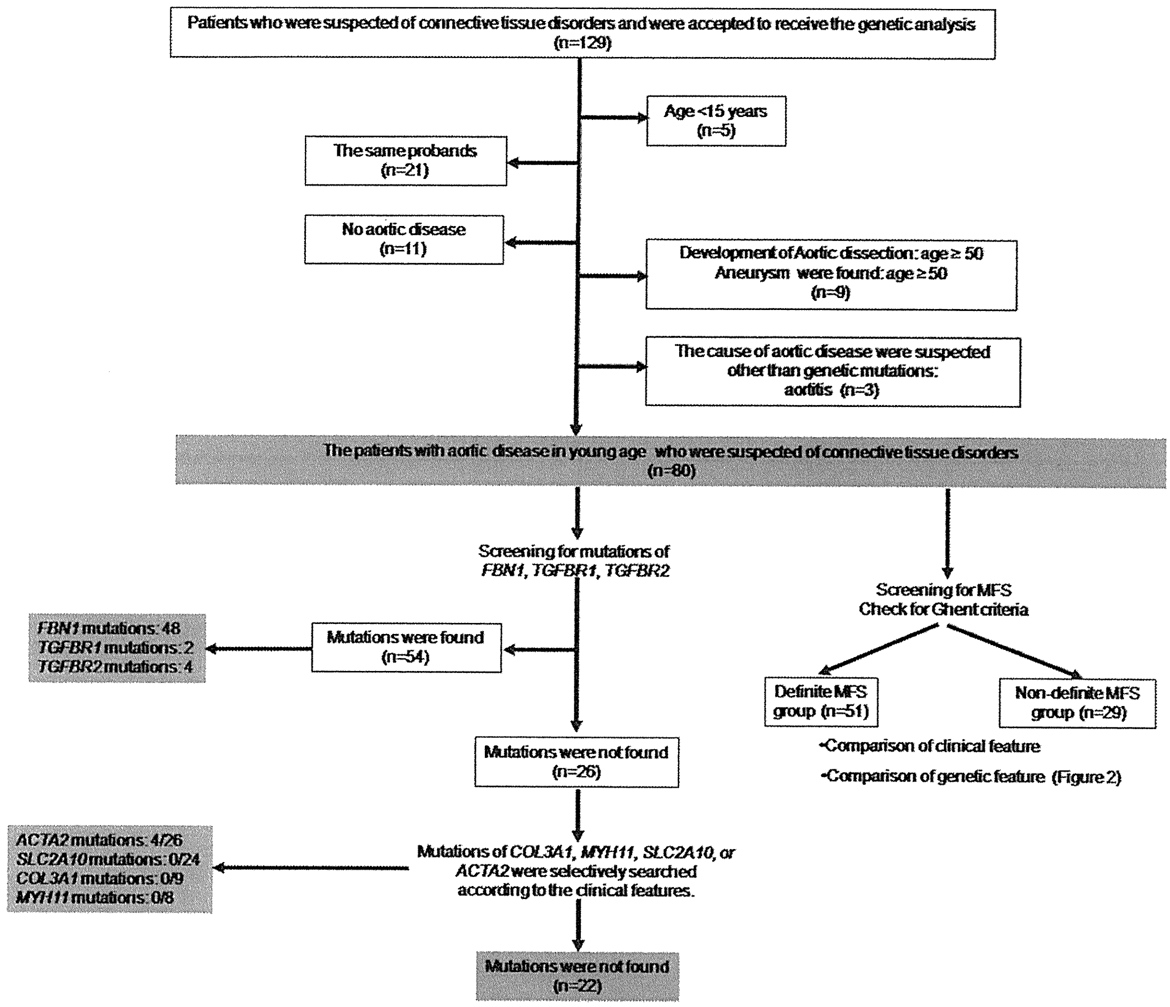

Figure 1. Genetic mutations of *FBN1*, *TGFBR1*, or *TGFBR2* were investigated for all 80 patients suspected of having connective tissue disorders. If no mutations could be found in these genes, *COL3A1*, *MYH11*, *SLC2A10* and *ACTA2* mutations were selectively examined according to the clinical findings. MFS, Marfan syndrome.

Genetic Features

The probands of all 80 probands were investigated for *FBN1*, *TGFBR1*, or *TGFBR2* mutations. If we could find no mutations in these genes, *COL3A1*, *MYH11*, *SLC2A10* and *ACTA2* mutations were selectively examined according to the clinical findings of each patient. A flow diagram of the investigations is shown in Figure 1.

FBN1, *TGFBR1*, *TGFBR2*, *ACTA2*, and *SLC2A10* mutations were examined using genomic DNA, which was isolated from the peripheral blood leukocytes of patients and amplified using polymerase chain reaction as described previously.[5] Genetic variants were screened with a denaturing high performance liquid chromatography method and the detected variations were further confirmed using direct sequencing as described previously.[1,2,5,8] *COL3A1* and *MYH11* mutations were examined using mRNA, which was obtained from surgical tissue specimens. Therefore, we could not determine the existence of *COL3A1* and *MYH11* mutations if the surgical specimen could not be obtained.

Clinical Features Related to the Ghent Nosology

In order to determine whether the patients fulfilled the diagnostic criteria of MFS using the Ghent nosology, all patients received careful assessments, including physical examination, computed tomography scanning or magnetic resonance imaging, echocardiography, and slit-lamp examination for ocular lesion, which covered all criteria listed in the Ghent nosology.[8] We defined the patients who fulfilled the Ghent nosology as the "definite MFS group", and the rest as "non-definite MFS group". According to the results of these examinations, all 80 probands were divided into definite MFS group (n=51) and non-definite MFS group (n=29).

Comparison of Probands in the Definite MFS Group and the Non-Definite MFS Group

First, clinical features were compared between the definite and non-definite MFS groups with respect to: (1) age, gender, height; (2) family history of aortic dissection or sudden death at age <50 years, or family history of suspected MFS; (3)

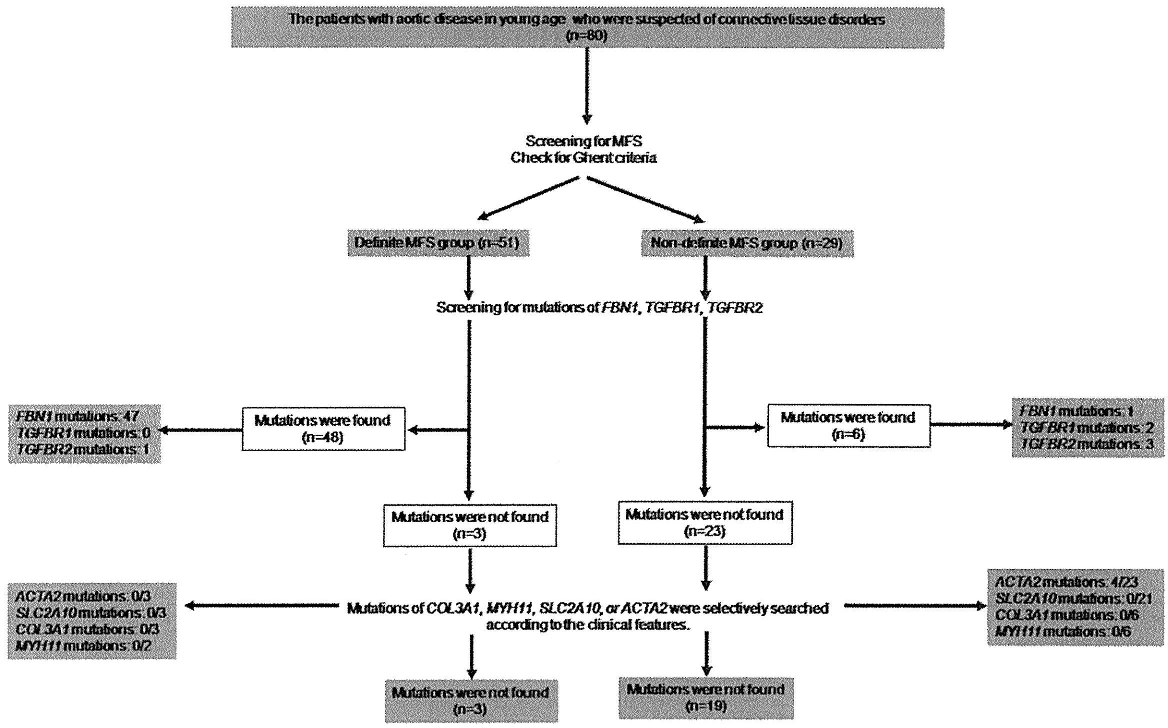

Figure 2. Genetic mutations of *FBN1*, *TGFBR1*, or *TGFBR2* were investigated for each of the 51 probands with definite MFS and 29 probands with non-definite MFS. If no mutations could be found in those genes, *COL3A1*, *MYH11*, *SLC2A10*, and *ACTA2* mutations were selectively examined according to the clinical findings. MFS, Marfan syndrome.

Ghent nosology. Ghent nosology included: involvement of skeletal system such as arm-span-to-height ratio, thumb and wrist signs, and joint hypermobility; involvements of the cardiovascular system, such as AAE, aortic dissection or mitral valve prolapse; ectopia lentis; dural ectasia; involvement of the pulmonary system, such as pneumothorax and apical blebs in the apex; and involvement of skin system, such as atrophic striae and recurrent hernia. Second, the genetic features were compared between the 2 groups (**Figure 2**).

Specific Clinical Features in the Non-Definite MFS Group

We divided the non-definite MFS group into 2 groups, the patients with some mutations in *FBN1*, *TGFBR1* or *TGFBR2*, *ACTA2*, *MYH11*, *SLC2A10*, or *COL3A1* (Mutation (+) group) and the patients without these mutations (Mutation (–) group). Then, we investigated specific clinical features in each group, which were the characteristics of connective tissue disorders other than MFS, such as Loeys-Dietz syndrome (LDS), Ehlers-Danlos syndrome type IV, arterial tortuosity syndrome (ATS), and thoracic aortic aneurysm and/or aortic dissection (TAAD). The following specific features of each disease were examined: hyperterolism; bifid uvula; aortic branch aneurysms; squint (which were often seen in LDS); easy bruising; thin and visible veins, (which were often seen in Ehelers-Danlos syndrome type IV); arterial tortuosity (which were often seen in LDS or ATS); livedo reticularis; iris flocculi (which were often seen in patients with *ACTA2* mutation); and patent ductus arteriosus (LDS and patients with *MYH11* mutations).[4,6,9–12] In addition to comparing the phenotypes of patients with non-definite MFS with the definite MFS group, we examined how the patients in non-definite MFS group fulfilled each feature of Ghent criteria.

Ethical Considerations

The present study was conducted according to the articles of the Declaration of Helsinki regarding the participation of human subjects in clinical studies and was approved by the Ethics Committee of the National Cardiovascular Center (Suita, Japan). All patients gave written informed consent to participate in the present study.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD). The Student t-test was used to analyze significant differences in factors between the 2 groups. Differences in percentages between the 2 groups were evaluated using Fisher's exact test. SPSS (11.0) software (SPSS Inc, Chicago, IL, USA) was used for all statistical analyses. A P value<0.05 was considered statistically significant.

Results

Genetic Features of Patients

For all 80 probands, mutations of *FBN1*, *TGFBR1*, and *TGFBR2* were investigated. Mutations of *FBN1*, *TGFBR1*, and *TGFBR2* were found in 48 (60%), 2 (3%), and 4 (5%) of the probands, respectively. At the next step, *COL3A1*, *MYH11*, *SLC2A10*, and *ACTA2* mutations were selectively examined according to the clinical features among the 26 probands who did not have any mutations in *FBN1*, *TGFBR1*,