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Multilevel Spinal Growth Modulation With an Anterolateral Flexible Tether in an Immature Bovine Model

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Study Design. A bovine model was used to evaluate the effects of a multilevel anterolateral flexible tether in a growing spine.

Objective. To evaluate the radiographic changes in a growing spine with a multilevel anterolateral tether.

Summary of Background Data. Spinal growth modulation has long been considered as a conceptually attractive and elegant possible alternative to arthrodesis in the treatment of idiopathic scoliosis. Although some experimental studies have described spinal growth modulation, few have described a purely mechanical tether. Clinical studies of spinal epiphysiodesis have described inconsistent curve stabilization and/or correction.

Methods. A total of 33 one-month-old male calves underwent a single thoracotomy and placement of vertebral screws at T6–T9. In 11 animals, one screw per level was connected by a 3/16 in. stainless steel cable (single tether). In 11 animals, two screws per level were connected by two cables (double tether). In the remaining 11 animals, single screws in each level were left unconnected (control). After 6 months, the spines were harvested and underwent radiographic analysis.

Results. In the control group, there was little change in the coronal and sagittal measurements during the survival period. In the single tether group, there was variable instrumentation fixation and inconsistent creation of coronal deformity, which ranged from 0° to 31°. The double-tether group had more consistent creation of deformity, ranging from 23° to 57°.

Conclusions. Given adequate bony fixation, a flexible lateral spinal tether can affect growth modulation. This technique of growth modulation may serve as a future fusionless method of correction in a growing patient with scoliosis.

Key words: experimental scoliosis, idiopathic scoliosis, lateral tether, growth modulation, scoliosis correction. **Spine 2005;30:2608–2613**

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In the modern treatment of adolescent idiopathic scoliosis, there are only two options: bracing or arthrodesis. Both options have limitations. Bracing is noninvasive; however, outcome evaluations have posed serious doubts about whether spinal orthoses change the natural history of adolescent idiopathic scoliosis. In the best of scenarios, bracing merely prevents progression.[1,2] Arthrodesis (with instrumentation) decreases spinal deformity but does so at the expense of spinal flexibility. Ideally, an option that maintained spinal mobility yet provided a means of correction would be developed to take advantage of the best features of these two current forms of treatment. This hybrid third option could be a type of "internal brace." Conceptually, this internal brace, in the form of a mechanical spinal tether, would inhibit growth on the convex side of the curve while allowing the concave side continued growth and subsequent curve correction. After completion of growth or adequate curve correction, removal of the tether would yield a flexible spine with reduced deformity.

This concept of growth modulation to correct deformity is not new to orthopedics. In the early 1940s, Blount's work in epiphyseal stapling used the Heuter Volkmann law to the surgeon's advantage to correct angular deformity in long bones.[3] Since that time, various investigators have used the same principle to attempt correction of spinal deformity or the creation of experimental scoliosis with variable results.[4–9] The goal of the current study was to determine if a flexible anterolateral spinal tether could cause coronal and sagittal plane deformity in an immature bovine model. A stainless steel cable connected between anterior vertebral body screws was used to study growth modulation (deformity creation) in a rapidly growing animal model.

Methods

Surgical Protocol. The animal subjects committee of the participating institution approved the study protocol. Four-week-old male calves were obtained and housed at a large animal facility. In preparation for anesthesia, calves were sedated with midazolam (0.3 mg/kg IV) and a maintenance infusion of Lactated ringers solution was established at a rate of 10 mL/kg per hour for the first hour, then 5 mL/kg per hour thereafter. Induction with intravenous propofol (2 mg/kg) was followed by intubation with a 7.5 to 10.0 mm inner diameter, cuffed endotracheal tube. Anesthesia was maintained with 1% to 3% volatilized isoflurane until the end of the procedure. The calf's right chest was prepared with an iodine-based scrub and the surgical site appropriately draped.

A right-sided thoracotomy between the seventh and eighth ribs was used to visualize the spine. The lung was retracted and the pleura was incised. The segmental vessels over each vertebra T6 through T9 were isolated and cauterized and spinal instrumentation was placed. In 11 calves, a single 6.25-mm stainless steel vertebral screw 30 mm in length (Isola, DePuy Spine, Raynham, MA) was placed laterally in each vertebra with bicortical fixation. A single nontensioned 3/16 in. stainless steel cable that was secured by setscrews connected to all four levels (single-tether group [ST]). In a second group of 11 calves, a vertebral staple and two 6.5-mm titanium cancellous vertebral screws 45 mm in length (Frontier, DePuy Spine) were placed laterally in each vertebra with bicortical fixation. Two nontensioned 3/16 in. stainless steel cables were placed connecting the anterior and posterior screws in all four levels and secured with setscrews (double-tether group [DT]). In a third group of 11 animals, screws were placed in each vertebra but left without the intervening cable (sham control group). During implantation, neither the discs nor growth plates were disturbed in any of the groups. After instrumentation, routine closure of the thoracotomy was performed over a chest tube. Per veterinarian recommendation to reduce herd aggression, all calves underwent castration under the same anesthesia as the surgery.

Postoperative regimen included intramuscular (IM) injections of 3.0 mg buprenorphine for analgesia and 500 mg cefazolin delivered every 12 hours for 3 days after surgery. After 6 months, all calves were killed. The thoracic spine with the screws was harvested *en bloc* to include motion segments T5 through T10.

Radiographic Analysis. Dorsoventral and lateral plain radiographs were taken of each thoracic spine in the frontal and sagittal planes, both immediately following surgery and following harvest. Vertebral body heights were measured of the surgical levels from control group radiographs both immediately following surgery and following harvest. The degree of coronal and sagittal deformity and vertebral wedging were measured for each of the instrumented thoracic segments using standard Cobb angle technique. The Statistical Package for the Social Sciences software (SPSS, Inc., Chicago, IL) was used to conduct multivariate analyses of variance to detect differences between groups with significance set at $\alpha = 0.01$.

Results

Surgical Data

At the time of surgery, the average animal weight was 46 ± 5 kg. There was no animal morbidity attributed to the surgical procedure. At the time of harvest, the average animal weight was 164 ± 23 kg, reflecting a 263% average increase in weight. There was no difference in preoperative weight, postharvest weight, or weight increase between groups ($P = 0.407$).

Radiographic Analysis

Over 6 months, vertebral body heights grew 8 ± 2 mm per level, resulting in a 27% length increase over the four surgical levels. The radiographic parameters measured from immediate postoperative and the 6-month postsurvival radiographs are summarized in Tables 1 and 2.

Table 1. Radiographic Parameters for Experimental Groups

	Control (°)	Single Tether (°)	Double Tether (°)	Significance (*P*)
Initial coronal	1 ± 1	1 ± 2	1 ± 3	0.124
Initial sagittal	4 ± 2	2 ± 3	2 ± 1	0.168
Final coronal	5 ± 4	11 ± 10	37 ± 8	<0.001*
Final sagittal	−1 ± 4*	7 ± 6	19 ± 7	<0.001†
Coronal change	5 ± 5	10 ± 9	38 ± 9	<0.001*
Sagittal change	−5 ± 4	5 ± 5	17 ± 8	<0.001†

Values are mean ± SD.
*Significant difference between control and double tether and between single and double tether groups.
†Significant difference between all groups.

There was no significant difference in T6 through T9 coronal or sagittal deformity immediately after surgery between groups. There was a significant difference between groups in the amount of sagittal and coronal deformity created during the 6-month survival period. In the control group, the change in the T6 through T9 coronal Cobb angle averaged 5°± 5° with a range from −3° to 13° (a positive coronal value denotes a left thoracic curve, concave on the side of the tethering implants) (Figure 1). This was not significantly different from the ST group, which had an average change in the overall coronal Cobb angle of 10°± 9° (range, 0°–31°) ($P = 0.257$) (Figure 2). The DT group had an average change in coronal Cobb of 38°± 9° (range, 23°–57°), which was significantly different from both the control and ST groups ($P < 0.001$ for both comparisons) (Figure 3).

In both tethered groups, there was increased kyphosis across the tether levels. Ten of the 11 control specimens had increased lordosis following the survival period (T6–T9 sagittal change: −5°± 4°; range, −12° to 2°). This change was significantly different from the increasing kyphosis in the ST group, which averaged 5°± 5° (range, −3° to 16°) with a significance of $P = 0.002$. The increasing kyphosis in the DT group averaged 17°± 8° (range, 6°–34°) and differed from both the control and ST groups ($P < 0.001$ for both groups).

Patterns of vertebral wedging differed between groups (Table 2). In the control group, vertebral wedging aver-

Table 2. Coronal Vertebral Wedging for Experimental Groups

	T6	T7	T8	T9
Control (°)	3 ± 2	1 ± 2	1 ± 3	0 ± 1
Single tether (°)	1 ± 3	4 ± 5	5 ± 5	2 ± 3
% backed out	45	36	18	64
% plowed	82	64	9	82
% levered	100	73	36	100
Double tether (°)	2 ± 4	12 ± 4	14 ± 6	8 ± 6
% backed out	0	0	0	0
% plowed	100	27	0	64
% levered	100	36	0	82
Significance (*P*)	0.420	<0.001*	<0.001*	<0.001*

*Significant difference between control and double tether and between single and double tether groups.

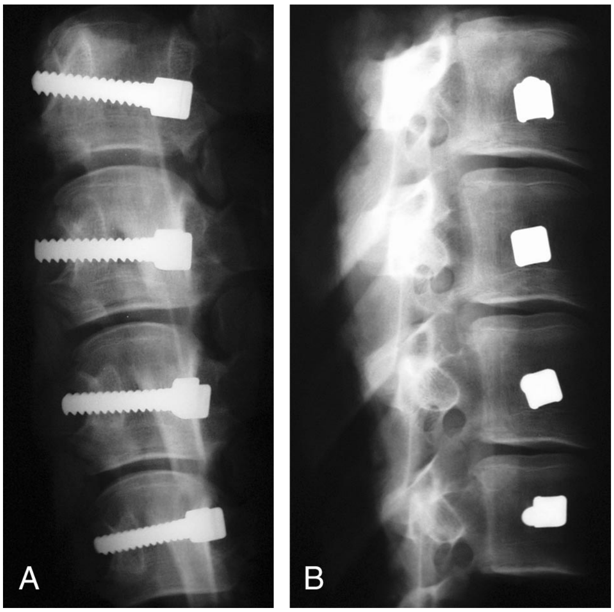

Figure 1. Dorsoventral (**A**) and lateral (**B**) radiographs of a control group spine following harvest with 2° coronal change and 6° increased lordosis from immediate postoperative radiographs.

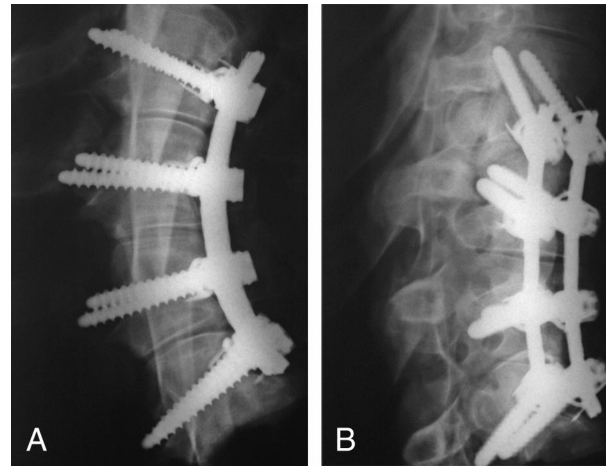

Figure 3. Dorsoventral (**A**) and lateral (**B**) radiographs of the most deformed spine in the double tether group with 57° created scoliosis and 34° increased kyphosis from immediate postoperative radiographs.

aged 1°± 2° and ranged from −2° to 7°. In both tethered groups, the least amount of wedging occurred in the most proximal vertebra, T6, which did not differ between groups (P = 0.420). At this level, there was substantial loss of fixation. In the ST group, 45% of the T6 screws backed out of the vertebral body while 82% plowed distally and 100% levered in the bone (Figure 4). Likewise, in the DT group, 100% of the specimens plowed distally and levered in the bone; however, none of the T6 screws in the DT group backed out of the bone. In both the tethered groups, most of the deformity was created in the middle two vertebrae, T7 and T8. In the ST group, there was more back out, plowing and levering of screws in these central levels than in the DT group, explaining the significantly increased vertebral wedging in the DT group (P < 0.001). In both tethered groups, the T8 level had the most vertebral wedging, which averaged 14°± 6° in the DT group and 5°± 5° in the ST group. In the ST group, 18% of screws backed out of, 9% plowed through, and 36% levered in the vertebral bone; by comparison, there was no loss of fixation in the T8 level of any of the DT specimens. In the most distal level, T9,

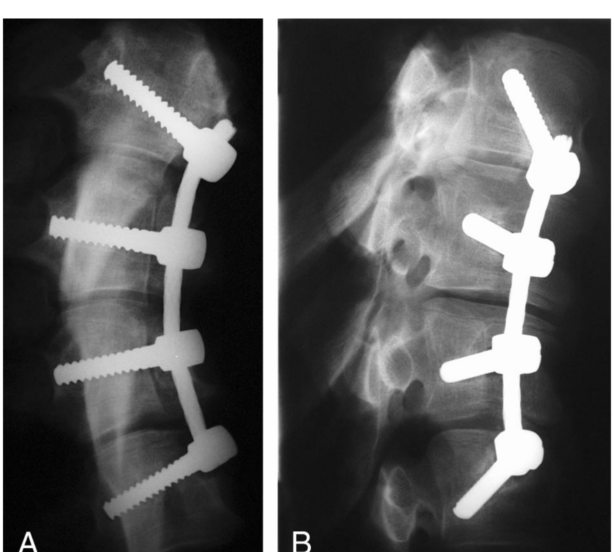

Figure 2. Dorsoventral (**A**) and lateral (**B**) radiographs of the most deformed spine in the single tether group with 31° created scoliosis and 16° increased kyphosis from immediate postoperative radiographs.

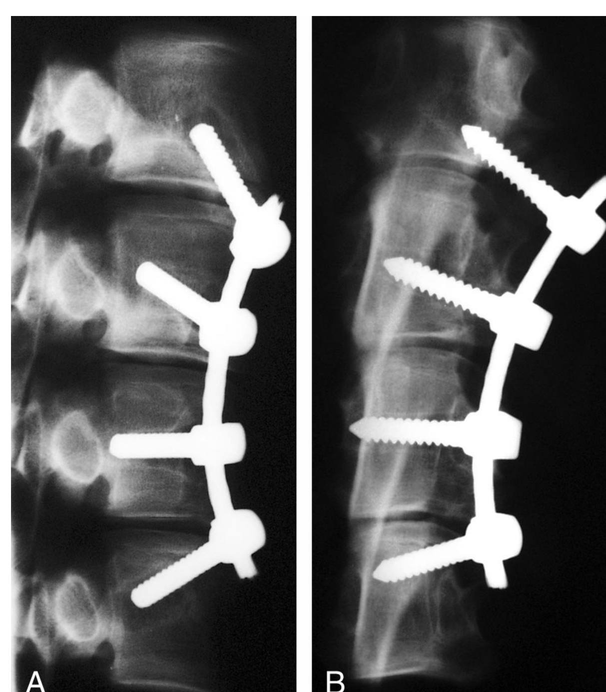

Figure 4. Dorsoventral radiographs of spines in the single tether groups with loss of fixation as screws levered in and plowed through the bone as seen in the most proximal and distal levels of (**A**) and screw pullout as seen in the most proximal vertebral level in (**B**).

there was a similar degree of levering and plowing between the two tether groups; however, no screws in the DT group backed out of the bone. This superior fixation explains the increased T9 vertebral wedging in the DT group (8°± 6° *vs.* 2°± 3° [ST] *vs.* 0°± 1° [control], $P < 0.001$).

Discussion

The goal of this study was to determine if a flexible mechanical tether placed on the anterolateral aspect of the spine in a bovine model could cause growth modulation and subsequent deformity. Two different tethering constructs were placed in immature bovine spines and compared with sham-operated controls after a 6-month survival period. The ST construct caused variable vertebral wedging with overall coronal deformity ranging from 0° to 31°. The DT construct caused consistent vertebral wedging with overall scoliosis ranging from 23° to 57°. Both tethering constructs caused increased kyphosis over the instrumented segments, although the more effective DT construct caused more kyphosis compared with the ST group. From these findings, the authors conclude that an anterolateral mechanical tether can cause spinal growth modulation, given adequate bony fixation.

Spinal growth modulation as a potential treatment for scoliosis is based on mechanical theories about the development of scoliosis. As early as 1865, Sir William Adams described the development of scoliosis in the following equation: "rotation plus lordosis equals lateral flexion."[10] Somerville and others have suggested that a relative anterior spinal overgrowth results in relative thoracic lordosis, which eventually leads to coronal plane curvature (scoliosis) and apical rotation.[11–14] The theory of anterior overgrowth is given further support by the occurrence of the crankshaft phenomenon in young patients with posterior fusions (anterior growth continuing).[15] This process mimics the posterior tether and continued anterior growth that is the driving force behind scoliosis development in the anterior overgrowth theory. If scoliosis is truly related to anterior overgrowth, then limiting anterior growth with a tether may reverse or limit this process.

Spinal growth modulation has been studied experimentally since the mid 1940s. In some studies, the placement of vertebral staples has affected spinal deformity. Nachlas and Borden created spinal deformity in dogs by placing staples into the vertebral bodies and then corrected the deformity by stapling the opposite side.[5,6] Newton *et al* placed an anterolateral flexible cable tether over a single motion segment in a bovine spine and found a significant creation of scoliosis as well as a modest increased kyphosis in the tethered segments compared with internal controls.[7] Braun *et al*[4] used a left-sided rigid posterior construct from T5 to L1 in combination with convex rib resection and concave rib tethering in an immature goat spine to yield an average of 18° of scoliosis and 4° of lordosis created over 15 weeks of growth. The authors noted additional radiographic features of scoliosis in this experimental model including vertebral rotation, apical displacement, and vertebral wedging.[4] The present study also had creation of coronal and sagittal deformity, although the length and placement of the mechanical tether differed from these previous studies.

Sevastik *et al* used rib elongation in mature rabbits and two mature pigs to produce a three-dimensional scoliotic deformity.[16–18] He also corrected scoliotic deformities, produced by intercostal nerve resection, in rabbits using rib elongation on the convex side of the curve.[19] There is a single case of a 7-year-old girl that had shortening of three ribs on the concavity of a scoliotic curve and 27 months postoperatively has a 54% reduction in the magnitude of her curve.[20]

The use of growth tethering in clinical practice has yielded inconsistent results. In 1954, Smith *et al* described the stapling of vertebral bodies in three patients with congenital scoliosis.[8] The procedure was able to halt progression of the curve over the treated levels; however, there was no curve correction and compensatory curves developed above and below the treated levels.[8] Roaf *et al* described the use of spinal hemiepiphysiodesis in 188 patients with paralytic, congenital, and idiopathic scoliosis.[21] This "hemifusion" was attempted to arrest growth on the convex side of the curve, allowing the concave side to grow and reduce deformity. With greater than 2 years of follow-up, the authors reported a uniform cessation of curve progression; 23% of cases had deformity reduction of 20° or more, while 37% of cases improved 10° to 19° and the remaining 40% had no significant change in curvature.[21,22] More recently, Nitinol staples have been applied clinically by Betz *et al* with early results suggesting at least stabilization of progressive scoliosis. Long-term results of this method of limiting growth are pending.[23]

The current study contained two flexible tether constructs. The ST construct was considerably less effective than the DT construct for many reasons. At the time of the index procedure, the 30-mm screws in the ST construct were long enough and achieved far cortex fixation; however, by the time of harvest, the vertebral bodies had grown in diameter and the far cortex fixation was lost. The ST screws were also cortical screws that were not fully threaded; therefore, the screw fixation in cancellous bone and the fixation of the near cortex were suboptimal. With inadequate near cortex fixation and loss of far cortex fixation, the ST construct, as with many other experimental tethers, was not able to hold onto the rapidly growing spinal bone. The DT construct not only doubled the instrumentation but also had the advantage of a much longer screw to maintain the far cortex, a cancellous screw to hold the vertebral cancellous bone and a vertebral staple and fully threaded screw to secure fixation of the near cortex. Just as the ST construct was too little fixation, the DT construct may be too much fixation; however, the two constructs help "frame" the fixation needs in this tether model and direct construct development for future studies.

The use of an immature bovine model had both benefits and limitations. The size of the 1-month-old calf spine was similar to the adolescent human spine, facilitating the use of similar instrumentation.[24,25] In the first 6 months of life, these calves undergo an enormous amount of growth as reflected by the 263% increase in calf weight and 27% increase in vertebral body height during the duration of the current study. This rapid growth in vertebral height generates a large amount of growth potential to harness with the tether and create deformity. This rapid growth held disadvantages as well. Much faster than that seen in adolescents, the rapid growth of the calf spine required a very strong mechanical tether construct as described above. Because the vertebral body grew in diameter by 10 to 15 mm over the 6-month survival period, the length of vertebral screw necessary for the maintenance of far cortex fixation necessitated a screw tip that protruded 10 to 15 mm beyond the far cortex. Despite being dangerously close to vital structures such as the aorta, there were no detectable sequelae during or after the survival period from these protruding screw tips that withdrew into the bone as it grew around them. Using an animal model with growth rates more comparable to the adolescent spine could solve these limitations.

A further extension of the present study would be an investigation of the effect of tether location on scoliosis and, more particularly, sagittal deformity. The increase in kyphosis averaged 17° in the DT group and reflected the relative anterior placement of the tether. In the ST group, the average increase in kyphosis was 5°; this smaller increase in kyphosis likely reflects the loss of fixation but also may be a result of the ST construct placement. In both constructs, the initial screw in each vertebra was placed as posterior in the vertebral body as possible; in the DT construct, the use of a vertebral staple and additional anterior screw in each vertebra moved the center of the tether anteriorly, giving it more kyphogenic force than the more posterior ST construct.[21] This phenomenon of increasing kyphosis has been seen clinically in skeletally immature patients with anterior instrumented fusions; as posterior growth continues in the face of arrested anterior growth, a "sagittal crankshaft" may develop.[26] As thoracic hypokyphosis is often associated with thoracic idiopathic scoliosis, this increased kyphosis generated by the tethering force may be beneficial and restore normal thoracic kyphosis in these patients. Further study of the exact effect of tether placement on coronal and sagittal deformity is required.

■ Conclusion

The growing scoliosis spine presents challenging treatment issues with the timing of fusion being a delicate balance between preserving trunk height and limiting deformity. The concept of spinal growth modulation as a mode of scoliosis correction attempts to harness the power of the growing spine to reduce deformity while preserving spinal motion. Previous studies of mechanical spinal tethering have yielded variable results. In the present study, an anterolateral flexible tether with adequate bony fixation produced modulated spinal growth. It is postulated that such a tethering concept may be a future means of controlling or even correcting progressive idiopathic scoliosis. Further studies to assess disc physiology and spinal mobility following longer-term spinal tethering will be necessary to ascertain the viability of spinal tethering as a future "fusionless" option for treatment of adolescent idiopathic scoliosis.

■ Key Points

- The placement of a flexible anterolateral tether in a growing bovine spine can produce both coronal and sagittal deformity, given adequate bony fixation.
- Spinal growth modulation by the temporary placement of a mechanical tether may ultimately provide a form of scoliosis correction that preserves intervertebral discs and spinal flexibility.

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