NHS England

Evidence review: Vertebral Body Tethering for Treatment of Idiopathic Scoliosis

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First published: June 2018

Updated: Not applicable

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Contents

1. Introduction

'Scoliosis' refers to a curvature of the spine that can occur in any age group. In the paediatric population, progressive scoliosis can lead to comorbidities. In a younger child (below the age that growth of the skeleton has stopped or slowed down) a scoliosis can progress significantly due to the amount of growth remaining. This can result in a visible deformity, pain, psychological morbidity and, if severe, cardiorespiratory problems.

The prevalence of idiopathic scoliosis is estimated at 2% to 3% of children between 10 and 16 years of age, using a definition of over 10^0 spine curvature. Larger curves present at a lower frequency and it is estimated that 40 degree curves make up 0.1% of the total population of patients with idiopathic scoliosis.

In the growing spine, current intervention consists of monitoring, bracing or surgery (instrumented fusion). Currently, scoliosis surgery consists of fusion of the spine with instrumentation. There is evidence of long term complications following surgery with a higher prevalence of back pain compared to the general population. These complications may lead to further surgery in later life.

Fusion of the spine is inappropriate in a young child as it will stunt spinal growth. As such growth modulation techniques, such as vertebral body tethering, have been developed for use in children who are still growing in order to modify the growth of individual spine bones in an effort to correct the curvature with time.

Vertebral body tethering (VBT) uses screws as anchors onto the front of the spine bones on the outside of a curve with a flexible tensioned cord or tether that runs through the screws that squeezes the bones to slow down growth on that one side.

The advantage of this surgery is to maintain a flexible spine into adulthood and to allow early intervention that can limit surgery to a shorter section of the spine. It may avoid the complications reported for current growing rod techniques and for instrumented spinal fusion. There are potential significant advantages for this group of patients. The purpose of this literature review is to examine the published literature for evidence of the clinical effectiveness of this technique.

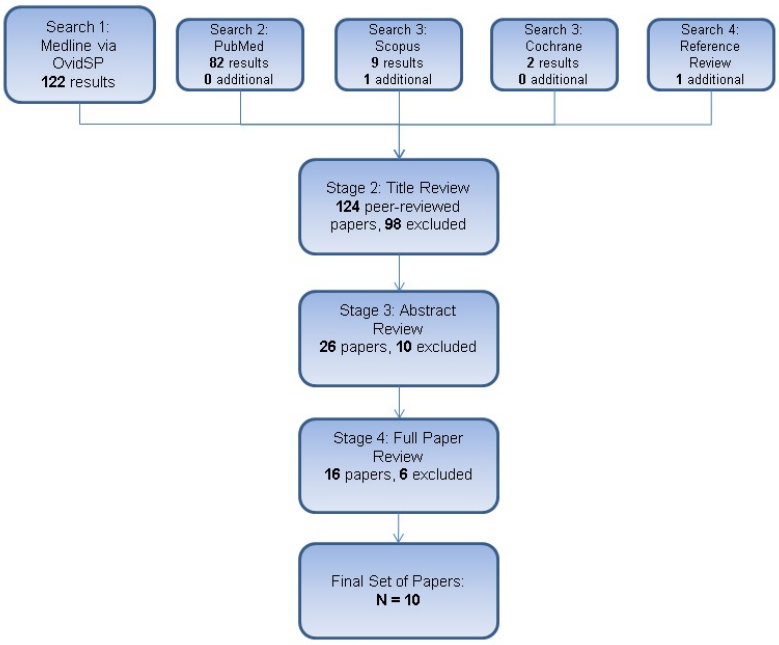
2. Summary of results

- There is an emerging body of case-report evidence to the effect that Vertebral Body Tethering is a surgical technique which can be effective in significantly correcting scoliotic curves, of the order of a 50% improvement on first erect.
- The potential for overcorrection is reported in the literature, with some patients requiring repeat surgery to loosen the tether.
- The evidence is limited in that there are no experimental trials reported in the literature, and only a small number of case reports currently published. It is not possible at present, given the lack of experimental studies, to confirm that this treatment is relatively effective, safe and acceptable when compared to standard care.

3. Methodology

A search of electronic databases was conducted in April 2018. A staged search was designed, with stage 1 consisting of multiple searches of electronic databases intended to produce an initial set of peer-reviewed journal articles. Stage 2 would see the title of each paper being assessed for relevance, with any result being excluded that clearly met the exclusion criteria, or failed to meet the inclusion criteria (See table 1). Included results would then progress to abstract review (Stage 3) and then a review of the full paper (Stage 4). Data extraction would then be conducted using the final set of papers and a critical appraisal and narrative review conducted. Figure 1 depicts the search design and stages, as well as the results of each stage.

Figure 1: Stages Search Design and Results



Stage 1 – Database Searches

An initial search was performed using the Medline via OvidSP system, searching for peer-reviewed academic papers with no constraints on date of publication or language. The logical statement used for this search was designed to be inclusive, ensuring a wide set of potentially relevant papers:

(Scoliosis OR adolescent idiopathic scoliosis) AND (vertebral body tethering OR tethering OR tether).

Titles, keywords and abstracts were searched, and related terms (as defined by the OvidSP system) were included in the search. This initial search produced a set of 122 potentially relevant results.

Additional searches were then performed using the PubMED and SCOPUS databases, using the same logical search term construction. The results from these searches were then cross-referenced with the results from search 1, and duplicates identified. This resulted in one additional result that was added into the complete set of results.

The Cochrane database of systematic reviews was searched using the strings ‘Vertebral+body+tethering’ and ‘anterior+vertebral+body+growth+modulation’, and no additional results were found.

Finally, a reference review was conducted using the output of Search 1 (Medline via OvidSP) as this contained references used in the included papers. This process found 1

further paper which appeared relevant, and this was added into the set of titles for review in Stage 2.

Therefore, the final set of unique papers found via all searches numbered 124.

Stage 2 – Title Review

The title of each paper was then reviewed against the population, comparator, intervention and outcomes under investigation and the exclusion and inclusion criteria were applied. 98 papers were excluded at this stage as not relevant. 26 papers progressed to Stage 3.

Stage 3 – Abstract Review

A review of the abstract was conducted for the remaining 26 papers, and 10 were excluded. Although animal studies were included in the criteria for this search, 8 abstracts were excluded because they were solely concerned with the creation of deformity, not treatment, in an animal model. 1 further paper was excluded because it was a comment piece, and another as it was a cadaver study. 16 papers thus progressed to Stage 4.

Stage 4 – Full Paper Review

For the final 16 papers, full text versions were downloaded. At this stage of review another 6 papers were excluded, 3 because the full texts of the papers were unavailable on any system, and 3 as the growth modulation intervention was, on close reading, not the intervention under study.

During the course of title and abstract reviews, it was identified that ‘anterior vertebral body growth modulation’ was a term used by some researchers that was synonymous with ‘vertebral body tethering’. An additional search for ‘vertebral body growth modulation’ was then performed on all systems to ensure no relevant results had been omitted that used this nomenclature. No additional relevant results were found.

This resulted in a final set of 10 papers for review, as detailed in table 2.

Overview of Final Set of Papers for Review

Of the final 10 papers, 2 papers were biomechanical simulations which contained simulations of the intervention under review and simulated outcomes including Cobb Angle (Aubin, Clin, & Rawlinson, 2018), (Braun, Akyuz, Udall, Ogilvie, Brodke, & Bachus, 2006). 1 paper was an animal study of the intervention which included a study of correction, as well as creation, of deformity (Moal, et al., 2013). 1 paper was a photo study, included only because of 1 example of post-operative complications following VBT surgery (Alsharief, El-Hawary, & Schmit, 2018). 6 were case reports from a total of 4 different treatment centres,

detailing results of treatment from a combined cohort of 40 patients. (Crawford & Lenke, 2010) (Skaggs, Myung, Brasher, & Skaggs, 2013) (Boudissa, Eid, Bourgeois, Griffet, & Courvoisier, 2017) (Ames, Samdani, & Betz, 2016) (Samdani, et al., Anterior vertebral body tethering for idiopathic scoliosis: Two-year results, 2014) (Samdani, et al., Anterior vertebral body tethering for immature adolescent idiopathic scoliosis: one-year results on the first 32 patients, 2015).

After finalisation of the set of papers relevant to the research question, and meeting the criteria as set in the search strategy (table 1), each full-text paper was read, appraised and data extracted relating to the outcomes under consideration. Table 3 contains summarises these elements for each paper.

4. Results

Overview of Study Designs and Strength of Evidence

Of the ten papers included in this review, only six contain direct evidence relating to the treatment of adolescent idiopathic scoliosis with vertebral body tethering. One paper (3) is an animal study, in which evidence is presented that demonstrates the principle of using a flexible tether to create, and then correct, scoliotic curves in vertebrates. One paper (7) is a photo study, included only as it contains one example of a complication following surgery. Two further papers (9 and 10) are *in silico* biomechanical simulations of the intervention, and provide corroborating evidence in support of the underlying biomechanical principle that this intervention uses.

No experimental studies were found, limiting the evidence base on this intervention to two case studies relating to a single patient, one retrospective review of the results from treatment of 6 patients, and three papers retrospectively reviewing the notes relating to treatment of the same 32 patients. Consequently, the literature reports a total of 40 instances of treatment using Vertebral Body Tethering. No paper has an evidence grading higher than IV, the lowest grade of evidence (National Institute for Health and Care Excellence) . Note that in the papers 4, 5 and 8, which constitute the bulk of the case-report evidence in this review, the authors declared the evidence level to be IV. The animal study and biomechanical simulations only evidence the underlying biomechanical principle. The photo study is included only as it contains evidence of one instance of postoperative complications.

Number of Patients and Follow-up.

The literature reviewed represents evidence that the intervention, Vertebral Body Tethering (VBT), has been used in the treatment of approximately 40 young people diagnosed with Adolescent Idiopathic Scoliosis. Paper 1 (Crawford & Lenke, 2010) reports a single case with 2 years of follow-up. Paper 2 (Skaggs, Myung, Brasher, & Skaggs, 2013) reports a single case with 31 months of follow-up in total. Paper 4 (Samdani *et* al, 2015) reports 32 instances of treatment, with 1 year of follow-up. The same authors report the outcomes from 11 patients at 2-years follow up (Paper 5, Samdani *et al*, 2014) and subsequently from 25 patients at skeletal maturity - Paper 6, (Ames, Samdani, & Betz, 2016). It is expected that these three papers represent the same cohort of patients. Finally, outcomes of 6 patients with 2 years of follow-up are reported by Boudissa *et al* in paper 8 (Boudissa, Eid, Bourgeois, Griffet, & Courvoisier, 2017).

Outcomes: Cobb Angle Preoperatively, at First Erect, and at 1 to 2 years

Table 3 displays the outcomes of the case reports in terms of Cobb Angle at first erect, and at subsequent follow-up. A significant immediate correction is reported by all authors, with Paper 4 (Samdani *et al,* 2015) reporting a pre-operative mean Cobb Angle of 42.8 degrees across 32 patients, and a mean Cobb Angle on first erect of 21 degrees, with a range of 8.9 to 47. This order of mean initial correction (approximately 50%) is seen throughout the case reports included in this review. Progressive correction is evidenced in Papers 4, 5 and 6 and Paper 8, with the longest-scale review - Paper 6, (Ames, Samdani, & Betz, 2016) – evidencing a mean Cobb Angle of 14 degrees (+/- 11, range 10 to 31) amongst 25 patients at skeletal maturity. Progressive correction is not reported in papers 1 and 2 (two patients in total).

In the controlled animal study - paper 3 (Moal, et al., 2013) - the intervention group had a Cobb Angle of 27.9 degrees (+/- 12) at 20 weeks compared to 52.7 degrees (+/- 10) in the control group.

The biomechanical simulation studies (Papers 8 and 9) reported simulated significant correction in the coronal and sagittal planes, with improvement of Cobb Angle at a simulated 2 years post-intervention from 21 to 14 degrees (+/- 8) with 100N loading and to 9 degrees (+/- 11) with 200N loading.

Other Outcomes

No papers were identified that reported the other outcomes of interest for this review. These outcomes were SRS 22 / EQ-5D scores, pulmonary function tests, Gait analysis and range of motion (thoracic and lumbar) and sitting height / T1-S1 and T1-T12 length. Consequently, no evidence was found of the effect of the intervention regarding such outcomes.

Complications and further surgery

The potential for over-correction using this intervention is consistently noted by the authors of the papers here reviewed. At skeletal maturity, Ames, Samdami *et al* reported 5 patients from the cohort of 25 requiring repeat surgery to loosen the tether in order to treat or prevent overcorrection (Ames, Samdani, & Betz, 2016), Paper 6. Boudissa *et al* report no complications from their 6 patients (paper 8). Skaggs, Myung *et al* report that their patient experienced unintended spinal fusion by 31 months of follow up.

Further complications reported by Ames *et al* at skeletal maturity are transient thigh pain or numbness (5 patients) and 1 patient with unresolved intercostal neuralgia. 1 instance of inter-operative complications is reported, with 1 patient experiencing persistent atelectasis which required bronchoscopy (Samdani *et al*, 2015).

The photo study included in this review - Paper 7, (Alsharief, El-Hawary, & Schmit, 2018) includes a radiographic image detailing an instance of a large pleural effusion/haemothorax post VBT surgery.

5. Discussion

Although the biomechanical principles behind VBT are reasonably well-established from animal models, the literature at present contains only limited evidence that Vertebral Body Tethering is a safe, acceptable and effective treatment of Idiopathic Scoliosis. This evidence is limited in that it consists entirely of clinical case reports, with no experimental or controlled studies in humans, and thus no systematic reviews or randomised controlled trials. Furthermore, no evidence was found for key outcomes, including patient experience (SRS 22 / EQ-5D), pulmonary function tests, gait analysis and range of motion (thoracic and lumbar) and sitting height / T1-S1 and T1-T12 length. Complications are reported in the literature, with the potential for overcorrection clear. There were six instances reported where further surgery was required. As this is a relatively new technique, long-term follow-up studies are lacking, with only a total of 25 instances of this treatment followed-up to skeletal maturity.

The clinical opinion expressed in the reviewed studies is that this is a promising technique and further studies are required to demonstrate effectiveness. It is clear from the literature that this treatment has the potential to correct scoliotic curves; however, the lack of comparison in the studies here reviewed means that, at present, the literature does not contain strong evidence that this technique is more effective than standard care. The evidence for the reduction in Cobb Angle at first erect has been graded as Evidence Grade C, as no experimental studies are seen in the literature, and the only directly applicable studies thus have a low score on the Grade of Evidence rating.

Further research, including experimental studies, is therefore needed to confirm the safety, patient acceptability & effectiveness of this technique. Further studies should include long-term follow up (beyond skeletal maturity) and outcomes relating to

pulmonary function, gait analysis, range of motion and patient experience.

6. Conclusion

These results are important as there are no previous evidence reviews relating to this surgical intervention in the literature. The biomechanical principle utilised by this technique is established in digital and animal models, and there is case-report evidence in the literature that this technique can be effective in reducing scoliotic curves. This review, however, has found no evidence for other important outcomes, such as patient experience (SRS 22 / EQ-5D), pulmonary function tests, gait analysis, range of motion (thoracic and lumbar) and sitting height / T1-S1 and T1-T12 length. Complications and the requirement for further surgical intervention are reported in the literature, and this review thus suggests that further research is needed regarding this intervention.

7. Evidence Summary Table

Use of Vertebral Body Tethering to Treat Adolescent Idiopathic Scoliosis									
Study reference	**Study Design**	**Population characteristics**	**Intervention**	**Outcome measure type**	**Outcome measures**	**Results**	**Quality of Evidence Score (NICE / GRADE)**	**Applicability**	**Critical Appraisal Summary**
Crawford & Lenke, 2010	Case Report	1 case	Vertebral Body Tethering, T6 to T12, screws, 4.5-mm-diameter polypropylene tether	Primary	Coronal Cobb Angle	preop = 40, immediate postop = 25, 48 months = 6	IV / 3	Direct	single case study, no comparator, no analysis of gait and/or range of motion
Skaggs, Myung *et al,* 2013	Case Report	1 case	hydroxyapatite(HA)-coated pedicle screws with a flexible polymer cord from T3 to T11	Primary	Cobb Angle	preop = 41, immediate postop = 26, 26 months = 26	IV / 3	Direct	single case study, no comparator, no comparator, no analysis of gait and/or range of motion
Moal *et al,* 2013	Animal Study	n/a	Anterior Corrective Tether	Primary	Cobb Angle (in a porcine model)	Int group: 27.9 ± 12.0 , Comparator group: 52.7 ± 10.0	IV / 6	Indirect	animal study
Samdani *et al,* 2015	Case Report, n = 32	32 cases reported	Anterior Vertebral Body Tethering, mean 7.7 levels (range 7 to 11)	Primary	Cobb Angle	Pre-op (range) 42.8 ± 8.0 (31 to 66) 1st erect (range) 21.0 ± 8.5 (8.9 to 47) 6 months (range) 21.2 ± 7.4 (9 to 40) 12 months 17.9 ± 11.4	IV / 3	Direct	no comparator, no analysis of gait and/or range of motion

Samdani *et al,* 2014	Case Report, n = 11	11 cases reported	Anterior Vertebral Body Tethering, mean 7.8 levels (range 7 to 9)	Primary	Cobb Angle	Preop 44.2 ± 9.0 1st erect 20.3 ± 11.0 24 months 13.5 ± 11.6	IV / 3	Direct	no comparator, no analysis of gait and/or range of motion
Use of Vertebral Body Tethering to Treat Adolescent Idiopathic Scoliosis									
Ames, Samdani *et al,* 2016	Case Report, n = 11	11 cases reported	Anterior Vertebral Body Tethering, mean 7.8 levels (range 7 to 9)	Primary	Cobb Angle	Preop 41 ± 7 (30-66) 1st erect 20 ± 8 (8-42) 12 months 17 ± 9 (1-35) Skeletal maturity 14 ± 11 (10 to 31)	IV / 3	Direct	no comparator, no analysis of gait and/or range of motion
Alsharief, el-Hawary & Schmit, 2018	Photo Study	n/a	n/a	n/a	n/a	n/a	IV / 0	Indirect	Reports 1 instance of post-surgical complications, no other evidence
Boudissa, Eid *et al,* 2017	Case Report, n = 6	6 Cases Reported	Vertebral Body Tethering, up to 7 levels, using staples and two superimposed polyethylene terephthalate (PET) bands.	Primary	Cobb Angle	Mean thoracic curve: preop 45, 7 days 38.3, 1 year 38.3 Mean lumbar curve: preop 33.3, 7 days 23.3, 1 year 25	IV / 3	Direct	no comparator, no analysis of gait and/or range of motion
Aubin, Clin *et al*, 2018	Biomechanical simulation	n/a	biomechanical simulation of Vertebral Body Tethering	Primary	Simulated Cobb Angle	From 21 ± 8 (Constrained Cobb T6-T10) to 14 ± 10 at 100N loading and 9 ± 11 at 200N	IV / 6	Indirect	biomechanical simulation, only evidences biomechanical principle of intervention

Cobetto, Parent, Aubin, 2018	Biomechanical simulation	n/a	biomechanical simulation of Vertebral Body Tethering	Primary	Simulated Cobb Angle	The results suggest that AVBGM can be adjusted to provide 'significant correction' in the coronal and sagittal planes. In the transverse plane, although the axial rotation progression was controlled, it was not significantly corrected.	IV / 6	Indirect	biomechanical simulation, only evidences biomechanical principle of intervention

9. Literature Search Terms

(Scoliosis OR adolescent idiopathic scoliosis) AND (vertebral body tethering OR tethering OR tether).

Additionally, each database was searched for the term 'anterior+vertebral+body+growth+modulation.'

The Cochrane database of systematic reviews was searched using the strings 'Vertebral+body+tethering' and 'anterior+vertebral+body+growth+modulation', and no additional results were found.

10. Search Strategy

Search strategy *Indicate all terms used in the search*	
P – Patients / Population Which patients or populations of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?	Patients with idiopathic scoliosis who have skeletal growth potential

I – Intervention Which intervention, treatment or approach should be used?	Vertebral body tethering
C – Comparison What is/are the main alternative/s to compare with the intervention being considered?	Treatment of patients with idiopathic scoliosis who have skeletal growth potential without vertebral body tethering
O – Outcomes What is really important for the patient? Which outcomes should be considered? Examples include intermediate or short-term outcomes; mortality; morbidity and quality of life; treatment complications; adverse effects; rates of relapse; late morbidity and re-admission; return to work, physical and social functioning, resource use.	*Critical to decision-making:* - SRS 22 / EQ-5D - Pulmonary function tests - Cobb angle (coronal and sagittal) of all curves, coronal balance, sagittal balance, scoliometer measurements - Gait analysis and range of motion (thoracic and lumbar) - Sitting height / T1-S1 and T1-T12 length - Complications and further surgery *Important to decision-making:*
Assumptions / limits applied to search *Inclusion and exclusion criteria e.g. study design, date limits, patients, intervention, language, setting, country etc.* ***Inclusion criteria*** *English language peer reviewed publications after 2006*	

Studies in both animals and humans ***Exclusion criteria*** *Abstracts.* *Conference papers.* *Letters and commentaries*

11. Evidence selection

- Total number of publications reviewed: 124
- Total number of publications considered relevant: 10
- Total number of publications selected for inclusion in this briefing: 10

12. References

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Ames, R., Samdani, A., & Betz, R. (2016). Anterior Scoliosis Correction in Immature Patients with Idiopathic Scoliosis. *Operative Techniques in Orthopaedics*.

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