N. Tolboom
E. A. Cats
P. J. M. Helders
J. E. H. Pruijs
R. H. H. Engelbert

Osteogenesis imperfecta in childhood: effects of spondylodesis on functional ability, ambulation and perceived competence

Received: 4 December 2002
Revised: 14 March 2003
Accepted: 25 April 2003
Published online: 8 November 2003
© Springer-Verlag 2003

N. Tolboom · E. A. Cats
Utrecht University Medical School,
Utrecht, The Netherlands

P. J. M. Helders · R. H. H. Engelbert (✉)
Department of Pediatric Physical Therapy,
Wilhelmina Children's Hospital,
Room KB 02.056.0,
University Medical Center,
P.O. Box 85090, 3508 AB Utrecht,
The Netherlands
Tel.: +31-30-2504030,
Fax: +31-30-2505333,
e-mail: R.Engelbert@wkz.azu.nl

J. E. H. Pruijs
Department of Pediatric Orthopedics,
Wilhelmina Children's Hospital,
University Medical Center Utrecht,
The Netherlands

Abstract We studied the effects of spondylodesis on spinal curvature, functional outcome, level of ambulation and perceived competence in 11 children with osteogenesis imperfecta (OI). Mean age at surgical intervention was 13.1 years (SD 2.5 years) and follow-up amounted to 3.4 years (SD 2.3 years). Spinal curvature was measured according to Cobb. The level of ambulation was scored according to the modified criteria of Bleck. Functional abilities and the amount of parental assistance were scored using the Dutch version of the Pediatric Evaluation of Disability Inventory (PEDI). Perceived competence was measured using the Harter Self-Perception Profile for Children. The amount of fatigue, spinal pain and presence of subjective dyspnea were scored with a visual analog scale. The median progression per year before spondylodesis was 6.1° (interquartile range 2.9°–12.9°) and after the spondylodesis it was 5.0° (interquartile range 1.6°–11.0°).

No significant progression or regression in the level of ambulation was found. Perceived competence improved slightly. In the total score of the perceived competence, a borderline significant increase was found (*P*-value 0.068). We concluded that spinal fusion in children with OI does not materially influence functional ability and level of ambulation. Self-perceived competence seemed to improve after surgery. The amount of pain, fatigue and subjective dyspnea seemed to diminish after spinal surgery. Progression of scoliosis proceeded, as did development of spinal curvature at the junction of the spondylodesis. Therefore, oral or intravenous bisphosphonates before and after spinal surgery should be considered.

Keywords Osteogenesis imperfecta · Scoliosis · Spondylodesis · Children · Functional ability · Perceived competence

Introduction

Osteogenesis imperfecta (OI) is an hereditary skeletal disease characterized by bone fragility caused by quantitative and qualitative defects in the synthesis of collagen I [5]. Major clinical characteristics beside fragility of bone are scoliosis, osteopenia, variable degrees of short stature and progressive skeletal deformities. Additional clinical manifestations, such as blue sclerae, dentinogenesis im-

perfecta, joint laxity and maturity onset deafness are described. OI probably affects 1 in 5000 to 10,000 individuals, without a racial or ethnic preference [21]. OI is subdivided into four types (I, II, III and IV) based on clinical, radiographic and genetic characteristics, according to Sil-
lence et al. (Table 1) [20].

Medical intervention consists of symptomatic pain relief and surgical correction for deformities of long bones and spine. However, recent experience with bisphosphonates suggests that anti-resorptive therapy of bone may re-

Table 1 Current classification of osteogenesis imperfecta (OI) according to Silience et al. [20]

Type OI	Clinical features	Inheritance	Main biochemical defects
I	Normal stature, little or no bone deformity, blue sclerae, hearing loss in about 50%, dentinogenesis imperfecta rare	Autosomal dominant	Decreased production of type I procollagen
II	Lethal in the perinatal period, minimal calvarian mineralization, beaded ribs, compressed femurs, marked long bone deformity	Autosomal dominant (new mutation)	Substitutions of glycyl residues in the triple helical domain of $\alpha 1$ or $\alpha 2$ chain
III	Progressively deforming bones, usually with moderate deformity at birth, sclerae variable in hue, often lighten with age, dentinogenesis imperfecta common, hearing loss common, stature very short	Some autosomal dominant	As for type II
IV	Normal sclerae, mild to moderate bone deformity and variable short stature, dentinogenesis imperfecta common, hearing loss in some patients	Autosomal dominant	As for type II

duce fracture frequency, increase bone density, promote remodeling of previously crushed and fractured vertebrae, reduce chronic pain and improve mobility in both children and infants [14].

The incidence of spinal deformities in OI depends on the classification system used, and has been reported to be between 11 and 92% [1]. Patients with the severest types of OI have a higher incidence of scoliosis. Benson et al. stated that scoliosis was rare before the age of 6 years; after this age a rapid progression of scoliotic deformity was observed [2]. The scoliosis usually progresses until severe kyphoscoliosis is present in adulthood [15].

Severe scoliosis and concomitant chest deformity will interfere with self-care. Mobility and vital functions may also decrease. Therefore, it is important to correct the scoliosis or at least to arrest the progression of scoliosis. Surgery of the spine in OI is difficult due to the bone fragility. Therefore, Benson and Newman recommended spinal fusion at a young age with or without instrumentation [1]. Janus et al. described an overall improved sitting balance and an increased functional ability in 7 of 20 patients after halo gravity traction (HGT) and posterior spondylodesis with instrumentation, and stated that although partial loss of correction seems inevitable, operative stabilization is possible [18].

Disease-related profiles regarding functional outcome, ambulation and perceived competence in children with OI have been established. However, the effects of spondylodesis on these outcome parameters are poorly documented [10, 12, 13].

Therefore, the purpose of this study was to evaluate the effects of spondylodesis on spinal curvature, functional outcome, level of ambulation and perceived competence in children with OI.

Materials and methods

From 1993 to 2001, 11 patients with OI underwent a spondylodesis at the Wilhelmina Children's Hospital (University Medical Center Utrecht) (Table 2). Seven children underwent a posterior spondy-

lodesis (Luque), one child underwent an anterior spondylodesis and three a posterior spondylodesis with Cotrel-Dubousset instrumentation. All, but one of the patients underwent long fusion from T2 to L5, as is performed in neuromuscular scoliosis. Only one case (type IV), with a modified Bleck score of 9, was treated as an idiopathic curve and only the thoracic spine was fused. Bone grafting was performed by adding homologous bone bank bone.

Spinal radiography was performed on a regular basis (at least once a year). The amount of spinal curvature was measured according to Cobb. Because of the well-known interobserver variation when measuring Cobb angles, two independent observers (N.T. and E.A.C.) measured the Cobb angles on 21 postero-anterior spinal radiographs, after an intense training in measuring of spinal curvatures (J.E.H.P) with two instruments: a 360° goniometer and a spinal rotation meter (SRM). The interobserver difference, using the coefficient of repeatability according to Bland and Altman [3], was found to be less when using the SRM than the 360° goniometer. We found that 95% of the differences between the two measurements were less than 5.6° and 8.8° respectively. The intraobserver difference was equal when using the two measurements: 95% of the differences between the two measurements were less than 5.0°. This is in line with previous studies of the interobserver error and accuracy [19]. Therefore, the amount of spinal curvature in this study was measured with the SRM.

Functional ability

The level of ambulation was scored according to the modified criteria of Bleck [4]. We classified the level of ambulation from 1 to 9 [12]:

1. Non-walker older than 2 years of age
2. Therapy walker with the use of crutches or canes
3. Therapy walker without the use of crutches or canes
4. Household walker with the use of crutches or canes
5. Household walker without the use of crutches or canes
6. Neighborhood walker with the use of crutches or canes
7. Neighborhood walker without the use of crutches or canes
8. Community walker with the use of crutches or canes
9. Community walker without the use of crutches or canes

Functional abilities and the amount of parental assistance were scored using the Dutch version of the Pediatric Evaluation of Disability Inventory (PEDI) [16]. The PEDI consists of two major dimensions (functional skills and caregiver assistance) in the content domains of self-care, mobility and social function. The performance of functional tasks and activities is measured by the functional skills scale, which samples a set of behaviors that are believed to be important for daily functioning. The amount of assistance required to accomplish daily tasks is measured by the care-

Table 2 Patient characteristics and details regarding spinal surgery ($n=11$) ($P50$ 50th percentile, $P25$ 25th percentile, $P75$ 75th percentile)

OI Type		
I	1	9%
III	6	55%
IV	4	36%
Gender (males)	5/11	45%
Dentinogenesis imperfecta (positive)	8/11	73%
Scoliosis: convexity		
Thoracolumbar right	4	37%
Thoracolumbar left	2	18%
Lumbar right	2	18%
Lumbar left	3	27%
Age at surgical intervention (years): mean ($\pm$ SD); range	13.1 ($\pm$ 2.5)	10.5–17.9
Age at last examination (years): mean ($\pm$ SD); range	16.5 ($\pm$ 3.9)	12.1–24.2
Follow-up (years): mean ($\pm$ SD); range	3.4 ($\pm$ 2.3)	1.1–9.5
Cobb angle measurements: median ^a (IQR) ^b ; Range		
Cobb angle before surgery	55.0° (45.0°–62.0°)	40.0°–120.0°
Cobb angle after surgery	39.0° (27.0°–45.0°)	5.0°–46.0°
Correction angle	20.0° (8.0°–35.0°)	–1.0°–75.0°
Angle at follow-up (at last radiograph)	46.0° (34.0°–53.0°)	23.0°–75.0°
Progression of Cobb angle before surgery per year	6.1° (2.9°–12.9°)	2.4°–40.0°
Progression of Cobb angle after surgery per year	5.0° (1.6°–11.0°)	0.0°–21.6°

^a Median = 50th percentile^b IQR = interquartile range (25th to 75th percentile)

giver assistance scales. Reference values are provided for children aged between 0.5 and 7.5 years. Results of children older than 7.5 years are calculated as a scaled score. In healthy children over 7.5 years of age, the normal score is 100%. Custers et al. [7] concluded that the discriminative validity of the Dutch PEDI between children with and without disability is excellent. The functional content and feasibility of the Dutch PEDI for rehabilitation outcome measurement appears to be reliable [8].

In our study, a significant correlation between the modified Bleck score and PEDI scaled score regarding mobility was found (Pearson correlation coefficient 0.8; P -value 0.002).

Perceived competence

Perceived competence was measured using the Harter Self-Perception Profile for Children (SPPC), which has been cross-culturally validated for Dutch children [9].

The Harter SPPC contains six subscales for children between 8 and 12 years of age: scholastic competence, social acceptance, athletic performance, physical appearance, behavioral conduct and global self-worth. For children aged between 12 and 16, this instrument is extended with two subscales: romance and friendship.

Data regarding the amount of spinal curvature, level of ambulation, functional abilities, the amount of parental assistance and perceived competence were obtained during regular visits to our hospital before and after surgery. The questionnaires were filled in preoperatively by the children in the presence of the last author, who had previous experience of using these questionnaires in studies on OI children [13]. At follow-up, the same questionnaire was filled in by the children in the presence of the first two authors, who first received extensive training in its use.

We also scored the amount of fatigue, spinal pain and presence of subjective dyspnea at last examination, on a 10-cm visual analog scale on which they had to indicate the current levels of fatigue, spinal pain and dyspnea. A score of 0 indicated no complaints, and a score of 10 indicated very severe complaints.

We also asked the children whether these factors were changed after spinal surgery.

All children and their parents gave consent to participation in this study. Since this study was a part of regular patient care, the Medical Ethical Review Committee found no review was indicated.

Statistical analysis

The acquired data were processed and analyzed with the use of the Statistical Package for the Social Sciences (SPSS). Data were not normally distributed, therefore data were analyzed non-parametrically with the Wilcoxon Rank Test.

Results

Patient characteristics are presented in Table 2. Mean age at surgical intervention was 13.1 years (SD 2.5 years) and mean time from spondylodesis until latest follow-up was to 3.4 years (SD 2.3 years). Median Cobb angle of the scoliosis at surgical intervention was 55.0° (interquartile range 45.0°–62.0°), and after spondylodesis the spinal curvature decreased to a median of 39.0° (interquartile range 27.0°–45.0°). This indicates a median correction of 20.0° (interquartile range 8.0°–35.0°). At radiographic follow-up, the median angle was 46.0° (interquartile range 34.0°–53.0°). The median progression per year before spondylodesis was 6.1° (interquartile range 2.9°–12.9°), and after the spondylodesis 5.0° (interquartile range 1.6°–11.0°). There was no significant difference between the progression before and after the spondylodesis (P -value 0.77).

Data regarding functional ability and level of ambulation are presented in Table 3. No significant progression or regression in the level of ambulation, and no regression in functional ability regarding mobility, was found. The

Table 3 Functional ability (using the Pediatric Evaluation of Disability Inventory, PEDI [16]) and level of ambulation (according to the modified criteria of Bleck [4]) in children with OI who un-

derwent a spondylodesis. Data are presented as median (50th percentile) and interquartile range (P25–P75)

	Before surgery		After surgery		<i>P</i> -value
	P50	P25–P75	P50	P25–P75	
Level of ambulation (Bleck)	2.0	1.0–4.0	2.0	1.0–6.0	0.14
PEDI (scaled score)					
Self-care	93.0	83.3–100.0	100.0	100.0–100.0	0.066
Mobility	60.0	54.8–67.6	59.1	54.8–70.1	0.92
Social skills	100.0	98.2–100.0	100.0	100.0–100.0	0.18
Self-care Caregiver assistance	79.5	71.2–100.0	100.0	76.6–100.0	0.08
Mobility Caregiver assistance.	65.00	55.1–86.4	78.3	66.7–100.0	0.12
Social skills Caregiver assistance.	100.0	100.0–100.0	100.0	100.0–100.0	1.00

Table 4 Perceived competence in children with OI who underwent a spinal spondylodesis, measured with a validated Dutch version of the Harter Self-Perception Profile for Children (SPPC). Data are

presented as median (50th percentile: P50) and interquartile range (25th to 75th percentile: P25–P75)

	Before spondylodesis		After spondylodesis		<i>P</i> -value
	P50	P25–P75	P50	P25–P75	
Scholastic competence	2.7	2.6–3.4	3.4	3.0–3.4	0.017
Social acceptance	3.3	2.5–3.7	3.4	2.8–3.4	0.092
Athletic competence	2.7	2.1–2.8	2.2	2.0–3.0	0.87
Physical appearance	3.2	2.5–3.4	2.7	2.6–3.2	1.00
Behavioral conduct	3.0	2.7–3.5	3.2	3.0–3.4	0.40
General self-worth	3.2	2.9–4.0	3.8	2.8–4.0	0.69
Total SPPC (first 6 items/6) ^a	3.1	2.6–3.2	3.1	2.6–3.4	0.12
Total SPPC (all 8 items/8) ^a	3.1	2.4–3.2	3.3	2.7–3.5	0.068

^a The profile consists of six subscales for children between 8 and 12 years of age, with a further two – romance and friendship – for children aged between 12 and 16

score of the PEDI domains ‘self-care’ and ‘caregiver assistance self-care’ showed a borderline significant improvement (*P*-values 0.066 and 0.08 respectively).

Perceived competence (Table 4) improved slightly. In the total score, a borderline significant increase was found (*P*-value 0.068). Among the individual scores, only scholastic competence showed a significant increase (*P*-value 0.017).

Assessments after spinal surgery found no spinal pain (median 0.3, interquartile range 0–2.0), little fatigue (median 0.5, interquartile range 0–2.9) and no subjective dyspnea (median 0, interquartile range 0–0.2). Children reported that before spinal surgery, spinal pain, fatigue and dyspnea were frequently present, with median (interquartile range) values of 7.5 (2.7–9.0), 5.7 (0.5–8.0) and 1.0 (0–5.5), respectively.

After spinal fusion, 3 of the 11 patients developed a new curvature, proximal of the spondylodesis, in the cervical region, necessitating additional surgical intervention. One patient developed a complication after surgery (bacterial infection of the Luque material).

Discussion

The present study demonstrated a non-significant, but clinically important increase in self-care with a decrease in caregiver assistance regarding self-care after spinal surgery. No change in ambulatory status was found, but there was a borderline significant increase in perceived competence. A decrease in spinal pain, fatigue and dyspnea was reported.

This study has intrinsic limitations. Although our hospital is a national referral center for treatment of children with OI (*n*=200), only a small sample of children with the most severe types of OI received surgical intervention for their scoliosis. Statistical analysis could, therefore, be biased. This may be the reason that in the domains of functional ability and perceived competence, borderline significant increases were found. Although data reported in past literature are descriptive or reported, and not measured objectively with generic instruments, our results are in line with those of previous studies. After spinal surgery, no negative influence on functional ability or ambulatory

status was reported [6, 18]. Whether our findings were caused by spinal fusion or by aging cannot be answered. We know from cross-sectional and follow-up studies that children, especially those with the most severe types, reach plateau phases in their functional ability [10, 12]. Remarkably, after spinal surgery, self-care increased borderline significantly, with a decrease in amount of caregiver assistance to normal values. We hypothesize that hand function may be improved after spinal stabilization due to restoration of spinal alignment.

We have previously investigated the influence of aging on prognosis for walking, and found that children who reached puberty lose the ability to walk primarily due to gain of body-weight [11]. Therefore, it is surprising that all children who were operated on during puberty did not lose their ambulatory status. It is also remarkable that, although spinal stiffening was performed, children feel themselves as competent as before surgery. Data are comparable with data of OI children who did not receive spinal fusion [13]. Data regarding spinal pain, fatigue and dyspnea should be interpreted with caution, since data were recorded retrospectively, and therefore subjective feelings may be overinterpreted. Therefore, statistical analysis is not indicated.

Widmann et al. found that thoracic scoliosis of more than 60° has severe adverse effects on pulmonary function in adults with osteogenesis imperfecta [22]. Therefore, data regarding fatigue and dyspnea should be carefully assessed in childhood as well, and when indicated measurements of pulmonary function should be made.

The mean progression per year of the spinal curvature after spondylodesis was relatively high compared to presur-

gical measurements (5.0°, range: 1.6°–11.0° vs 6.1°, range: 2.9°–12.9°). This does not imply that the operation is not capable of preventing progression, and longer follow-up is indicated to observe whether stabilization occurs. On the other hand, the basic problem in OI, a qualitative and quantitative collagen defect resulting in bone fragility, is not influenced by spinal surgery. We know that the number of wedge-shaped vertebrae increases, due to vertebral collapse, which influences progression of development of scoliosis [17]. This retrospective study was performed on patients not treated with oral or intravenous bisphosphonates. Since a beneficial effect of bisphosphonates in OI patients is reported in the literature, resulting in an increase in bone mineral density, we have now changed our treatment protocol. Therefore, in our opinion, treatment with oral or intravenous bisphosphonates before and after spinal surgery should be considered.

Conclusion

We concluded that spinal fusion in children with OI does not materially influence functional ability and level of ambulation. Self-perceived competence seem to improve after surgery. The amount of pain, fatigue and subjective dyspnea seem to diminish after spinal surgery. Progression of scoliosis proceeded as well as development of spinal curvature at the junction of the spondylodesis. Therefore oral or intravenous bisphosphonates before and after spinal surgery should be considered.

References

1. Benson DR, Newman DC (1981) The spine and surgical treatment in osteogenesis imperfecta. *Clin Orthop* 159: 147–153
2. Benson DR, Donaldson DH, Millar EA (1978) The spine in osteogenesis imperfecta. *J Bone Joint Surg Am* 60: 925–929
3. Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 8:307–310
4. Bleck EE (1981) Nonoperative treatment of osteogenesis imperfecta: orthotic and mobility management. *Clin Orthop* 159:111–122
5. Byers PH, Steiner RD (1992) Osteogenesis imperfecta. *Annu Rev Med* 43: 269–282
6. Cristofaro RL, Hoek KJ, Bonnet CA, Brown JC (1979) Operative treatment of spine deformity in osteogenesis imperfecta. *Clin Orthop* 139:40–48
7. Custers JW, van der Net J, Hoijsink H, Wassenberg-Severijnen JE, Vermeer A, Helders PJ (2002) Discriminative validity of the Dutch Pediatric Evaluation of Disability Inventory. *Arch Phys Med Rehabil* 83:1437–1441
8. Custers JW, Wassenberg-Severijnen JE, van der Net J, Vermeer A, Hart HT, Helders PJ (2002) Dutch adaptation and content validity of the 'Pediatric Evaluation of Disability Inventory (PEDI)'. *Disabil Rehabil* 24:250–258
9. Dongen-Melman van JEWM, Koot HM, Verhulst FC (1993) Cross-cultural validation of Harter's Self-perception Profile for Children in a Dutch sample. *Ed Physiol Measurement* 53:739–753
10. Engelbert RHH, Graaf van der Y, Empelen van R, Beemer FA, Helders PJM (1997) Osteogenesis imperfecta in childhood: impairment and disability. *Pediatrics* 99:E3
11. Engelbert RHH, Gerver W, Uiterwaal CSPM, Custers JWM, Gulmans VAM, Puijs JE, Helders PJM (1999) Osteogenesis imperfecta in childhood; impairment and disability – a four years follow-up study. Presented at the Seventh OI conference, Montréal, Canada. *Arch Phys Med Rehabil* (in press)
12. Engelbert RHH, Uiterwaal CSPM, Gulmans VAM, Puijs JE, Helders PJM. (2000) Osteogenesis imperfecta in childhood; prognosis for walking. *J Pediatr* 137:397–402

13. Engelbert RHH, Gulmans VAM, Uiterwaal CSPM, Helders PJM (2001) Osteogenesis imperfecta, in childhood – aspects of quality of life in relation impairment and disability. *Arch Phys Rehabil Med* 82:943–948
14. Glorieux FH (2001) The use of bisphosphonates in children with osteogenesis imperfecta. *J Pediatr Endocrinol Metab* 6:1491–1495
15. Hanscom DA, Winter RB, Lutter L, Lonstein JE, Bloom BA, Bradford DS (1992) Osteogenesis imperfecta: radiographic classification, natural history and treatment of spinal deformities. *J Bone Joint Surg Am* 74:598–616
16. Hayley SM, Coster WJ, Ludlow LH, Haltiwanger JT, Andrellos PJ (1992) *Pediatric Evaluation of Disability Inventory (PEDI)*. New England Medical Center, Boston
17. Ishikawa S, Niigata-Shi S, Kumar J, Takahashi HE, Homma M (1996) Vertebral body shape as a predictor of spinal deformity in osteogenesis imperfecta. *J Bone Joint Surg Am* 78:212–219
18. Janus GJM, Finidori G, Engelbert RHH, Pouliquen M, Pruijs JEH (2000) Operative treatment of severe scoliosis in osteogenesis imperfecta: results of 20 patients after halo traction and posterior spondylodesis with instrumentation. *Eur Spine J* 9:486–491
19. Pruijs JEH, Hageman MA, Keessen W, Van der Meer R, Van Wieringen JC (1995) Spinal rotation meter: development and comparison of a new device. *Acta Orthop Belg* 61:107–112
20. Sillence DO, Senn A, Danks DM (1979) Genetic heterogeneity in osteogenesis imperfecta. *J Med Genet* 16:101–116
21. Vetter U, Pontz B, Zauner E, et al (1992) Osteogenesis imperfecta. A clinical study of the first ten years of life. *Calcif Tissue Int* 50:36–41
22. Widmann RF, Bitan FD, Laplaza FJ, Burke SW, DiMaio MF, Schneider R (1999) Spinal deformity, pulmonary compromise, and quality of life in osteogenesis imperfecta. *Spine* 24:1673–1678