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Predictors for long-term curve progression after Boston brace treatment of idiopathic scoliosis.

Brief running title: Predictors in bracing of idiopathic scoliosis

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ABSTRACT

BACKGROUND: Identifying factors that predict successful bracing in patients with idiopathic scoliosis may help planning treatment.

AIM: To assess predictors for long-term curve progression and health-related quality of life after Boston brace treatment.

DESIGN: Observational retrospective cohort study with analysis of brace treated patients followed from start until at least 10 years after treatment.

SETTING: Patients recruited from the country's entire population consecutively treated at the National Hospital.

POPULATION: 365 patients (339 girls/26 boys) with idiopathic scoliosis. Mean (SD) chronological age/bone age at start bracing was 13.2 (1.9)/12.6 (1.9) years. The primary major curve measured 33.2 (7.4)°, and the major levels were thoracic (n=248), thoracolumbar (n=78) and lumbar (n=39). Mean bracing time was 2.8 (1.5) years. Long-term follow-up was in average 23.3 (4.1) years after weaning with a mean major curve of 33.0 (13.1)°.

OUTCOME MEASURES: Successful treatment was defined as a stable primary curve with progression $\leq 5^\circ$, and secondary the SRS-22 questionnaire assessed quality of life.

METHODS: We applied linear or logistic regression with backward elimination. Internal validation was assessed by bootstrapping. 12 variables were included in the prediction models: age, bone age, scoliosis in close family, major curve size, level, shape, flexibility and in-brace redressement, compliance, curve magnitude after 1 year, treatment time and quality of life (SRS-22). The study was funded by an institutional grant. No authors had any conflicts of interest.

RESULTS: 290 patients (79%) had rated good compliance using the brace >20 hours daily. Treatment failure was observed in 65 patients (18%), and 27 of them were operated. The best baseline predictors were age and brace redressement. During treatment compliance, major curve after 1 year, and treatment time were the best predictors, while thoracic major

curve, curve size at start bracing and scoliosis in close family also contributed to the final model. The model's ability to predict quality of life was low.

CONCLUSIONS: The best predictors for a long-term success were good redressement and compliance, unchanged or reduced major curve after one year and short treatment time.

CLINICAL REHABILITATION IMPACT: Predictors at baseline and during early treatment can help identifying patients who benefit from bracing.

Key words: Idiopathic scoliosis; Brace; Conservative treatment; Orthosis; Predictors; Curve progression; Long-term.

Introduction

The effectiveness of brace treatment in idiopathic scoliosis has been debated for years because it is a challenge for the adolescent child to wear the brace, and since it has not been supported by credible research evidence, it has been questioned if bracing changes the natural development of the curve.¹ In 2013 a randomized controlled trial (RCT) indicated that bracing is effective and that good compliance improves outcome.² The importance of compliance is supported by the results of long-term cohort studies.^{3, 4} In a Cochrane systematic review including 7 studies with 662 participants Negrini et al. concluded that bracing prevents curve progression, but the strength of evidence was low due to a high rate of failure to complete the RCTs.⁵ There is no formal evidence of the effectiveness of surgical versus non-surgical treatment for adolescent idiopathic scoliosis (AIS) with curves $>45^\circ$.⁶ Recently, high-quality evidence has started to emerge, particularly in the area of efficacy of bracing, and in 2018 the 2016 SOSORT guidelines for orthopaedic and rehabilitation treatment of idiopathic scoliosis during growth were published.⁷ Curve deformity progression $>5^\circ$ was defined as failure of treatment by Peterson & Nachemson in 1995⁸ and is recommended as a clinically significant change by the SOSORT/SRS guidelines on the standardization of methods of non-operative research reporting.⁹ Poor compliance, young age, lower Risser sign and lower initial curve correction are reported to predict curve progression $>5^\circ$.¹⁰ Also genotypes, the combination of double curve pattern with a thoracic curve $>35^\circ$ and initial Cobb angle reduction velocity following bracing are reported to be

associated with curve progression.¹¹⁻¹³

The aim of the present cohort study was to assess demographic and clinical factors for long-term prediction of success defined as curve stability with progression $\leq 5^\circ$ and no operation in patients with juvenile and adolescent scoliosis. In addition, we evaluated the association between demographic, clinical and radiological factors and health related quality of life.

Materials and methods

Patients

365 (339 females/26 males) Boston brace treated patients with juvenile (n=79) or adolescent (n=286) idiopathic scoliosis and with their last radiological control at least 10 years after weaning were selected for the present study. The patients were recruited from the country's entire population and from an invited cohort of 496 patients consecutively treated at the National Hospital during the years 1976-1988. Mean (SD) chronological age and bone age at start bracing was 13.2 (1.9) and 12.6 (1.9) years, respectively. They were examined at start bracing and at ordinary follow-ups the first 24 months after brace weaning before the long-term examination with an average post brace observation time of 23.3 (4.1) years. 338 (93%) of the selected patients answered the nationally validated version¹⁴ of the standardized Scoliosis Research Society 22 form (SRS-22) which is widely used for the evaluation of health-related quality of life (HRQL).

The Ethical Committee for medical research in Health Region South East and the Institutional Review Board approved the study (REK 2010-3677). Written informed consent was obtained from the participating patients.

Bracing

The indication for start bracing was a major scoliotic curve $\geq 20^\circ$ with an observed progression $> 5^\circ$ after 4 months and skeletal immaturity evaluated by bone age or Risser sign

<3. The primary major curve was thoracic (n=248), thoracolumbar (n=78) and lumbar (n=39) with average values of 33.9 (7.0), 31.5 (8.0) and 31.2 (7.2) degrees, respectively.

Prior to bracing standing radiographs were taken in the frontal and lateral projections, and major curve flexibility was measured by comparing curve values in the standing position with lateral flexion to the convex side standing or sitting, or with the spine unloaded lying in the prone position (if the patient was uncomfortable or unsteady with lateral flexion, straightening of the curve deformity could be best lying prone during exposure). The percentage difference between the measured magnitudes of the major curve in the 2 positions represented the curve flexibility. After brace fit the magnitude of the in-brace major curve on standing x-rays was compared with the curve on standing films without the brace, and the percentage difference represented the measured redressement value. The in-brace images finalized the brace customization period. Thereafter the brace was approved and the patient discharged.

A team comprising a spine surgeon (JEL), an experienced orthotist, and a nurse were responsible for brace fit and for informing the young patient and parents about brace wear. They were instructed to wear the brace day and night except when taking a bath or during exercise. Accordingly, they were recommended a brace wearing time of 23 hours daily. Weinstein et al.² reported that the efficacy decreases when brace wearing time is less than 17 hours daily. Patients were followed with outpatient visits including clinical and radiological examination at 4 months intervals throughout the brace treatment period. At follow-ups the brace was removed the evening before the radiological examination. A standardized form was used to obtain clinical and radiological data at baseline and follow-ups. Patients did not have regular physiotherapy, but were advised to participate in sports and ordinary physical activity at school. Ordinary brace treatment was continued until skeletal maturity (bone age 14 years in girls and 16 years in boys), corresponding to Risser grade 4 or 5.^{2, 15} Unplanned early weaning occurred in 32 patients. In addition, 57 patients had planned early weaning.¹⁶ All were young patients and had at least 2-3 years of predicted brace treatment before reaching puberty. Weaning was recommended if imaging demonstrated a stable reduction of the major curve to $\leq 25^\circ$ at repeated measurements. Fourteen (25%) patients had to resume bracing after a mean of 2 years and one was operated. According to protocol standardized weaning was performed by 2 hours less

bracing time every week during a period of 2-3 months, and the curve was controlled after 4 months. After brace weaning all patients had follow-ups at 6, 12, and 24 months. The majority of patients had one or more additional follow-up examinations before the long-term follow-up.

Compliance

Wearing of the brace was conscientiously and consistently assessed by one orthopaedic spine surgeon (JEL) and scored on a standardized form at all examinations during the brace treatment period. Scoring was based upon questioning the patient and the parents, and wearing of the brace <20 hours daily was noted as irregular or bad. Compliance was dichotomised and patients were classified as compliant if the brace was used >20 hours daily until weaning.

Radiology

A standardized form was used to obtain clinical and radiological data. Skeletal maturity evaluated by Risser sign¹⁷ and left hand bone age (Greulich and Pyle)¹⁸ was assessed by 2 experienced radiologists. Curve measurements were performed by a senior orthopaedic scoliosis surgeon (JEL) and controlled by an experienced radiologist; both used the Cobb method¹⁹ manually and digital measurements were used at long-term follow-up. All relative measurements were compared to the curvature at start of bracing treatment. The intra-observer error for the Cobb angle was about 3° in a study using manual and digital measurements.²⁰ In the present study, the measurement error was within these limits as evaluated by the reproducibility of radiographic readings with repeated measurements of all radiographs from 10 patients at regular intervals. In general the >5° definition of a significant curve progression from start bracing accounts for a measurement error of ±5° which is in agreement with the SOSORT/SRS guidance (recommendation # 8) in the review article by Negrini et al.⁹ Radiologically derived concepts, like curve flexibility and redressement are outlined in the bracing paragraph.

Surgery

Surgery was recommended in immature patients with curve progression to $>45^\circ$ at follow-up during bracing or at weaning, and $>50^\circ$ during later follow-ups. Information about surgery was obtained from the long-term questionnaire and crosschecked in the medical journals.

Questionnaires

At long-term follow-up a standardized questionnaire was filled in. It comprised validated measures of pain, disability, quality of life, work, comorbidity, surgery, and questions about demographics, among them the SRS-22 disease specific quality of life form used in the present study analysis. The SRS-22 was not available at baseline. It covers four domains (function/activity, pain, self-perceived image, and mental health) each with five questions, and one additional domain (satisfaction with treatment) with two questions. Each question of the four domains has five verbal response alternatives ranging from 1 (worst) to 5 (best) with a sum score ranging from 5 to 25 for each domain. For the additional domain the sum score ranges from 2 (worst) to 10 (best). Results are expressed as the total sum of all the domains with an overall score range of 22 - 110.

Statistical analysis

Stata/SE 15.0 (College Station, TX, USA) was used for statistical analysis. A total of 12 predictor variables were selected. At start bracing: age and bone age; scoliosis in close family; major curve magnitude, level, shape, flexibility and in-brace redressement. During bracing: compliance; major curve magnitude after 1 year and treatment time. At follow-up: quality of life (SRS-22). Continuous variables were described with mean and standard deviation (SD) or median and interquartile range (IQR) expressed as 25th and 75th percentile depending on an assumed normal or skewed data distribution. The difference between study participants with successful treatment or failure of treatment was assessed by independent samples t-test or non-parametric Mann-Whitney test. Categorical variables were described as number of observations and percentage. The difference between study participants with success or failure was assessed by the Pearson chi-square test.

Predictors for curve progression were selected through logistic regression with backward elimination. A p-value >0.2 was used as the criterion for elimination of the independent variable.²¹ The McFadden's R^2 model fit statistic, C statistic and calibration slope (where 1.00 is ideal) assessed the performance (explanatory power and discrimination capability) of the model. We applied two models to evaluate predictors for curve progression. The first included only variables assessed at baseline, and the second included additionally variables recorded during treatment. To correct measures of predictor performance for optimism (over-fitting), we conducted internal validation by bootstrapping 100 samples. We repeated the model development in each bootstrap sample and applied the model to the same bootstrap sample to quantify apparent performance. Finally we applied the model to the original dataset to test model performance (calibration slope and C statistic) and optimism (difference in test performance and apparent performance). Overall optimism across all models (for example, derive shrinkage coefficient = average calibration slope from each of the bootstrap samples) was estimated.²² The original β regression coefficients from the logistic regression model were multiplied by the uniform shrinkage factor in the final model to account for over-fitting. The intercept was then re-estimated on the basis of the shrunken β coefficients to maintain overall calibration and to produce a final model as described by Sultan et al.²³

For SRS-22, linear lasso regression with 10-fold cross-validation for continuous outcome was conducted using the user-developed command lassoregress for Stata.²⁴ With increasing constraints on the sums of the absolute values of the coefficients in lasso regression, the solutions were shrunken versions of estimated coefficients, with some potential decreasing to the zero value, and thereby eliminated from the model.²⁵

Finally we performed an additional post hoc sensitivity analysis defining treatment failure alternatively as curve progression to ≥ 50 degrees and/or operation, applying the same statistical methods.

Results

Patients

Table 1 describes the basic characteristics for study participants with failure of treatment or successful treatment. The success rate was 82% (300 of 365 patients). Failure due to curve progression in spite of brace treatment occurred in 65 patients (18%), 52 (80%) of them had a thoracic major curve and 27 (7% of total) were operated. Percentage thoracic scoliosis was higher than in those defined with success. At baseline age, bone age and percentage brace redressement were higher in the success group. During treatment compliance and percentage curve reduction after 1 year was better, treatment time was shorter and at long-term quality of life was better among the patients with successful treatment (Table 1). Because (chronological) age and bone age were highly correlated ($r=0.88$), only age was used in the regression models to avoid collinearity issues. Treatment time was associated with age ($r=-0.7$), but was not a proxy predictor for age and maturity at brace start. Curve progression was in average 6.9 (95% CI 4.1 to 9.3)[°] larger in those with poor compliance (N=75) compared to those with good compliance (N=290) when adjusted for several other predictors.

Predictors of success (curve progression $\leq 5^\circ$)

Age and initial percentage redressement at start bracing were the only variables at baseline predicting success (Table 2). The model fit was 11% (McFadden's $R^2=0.11$) and the ability of discrimination after internal validation was moderate (optimism adjusted C-statistic 0.68). Two illustrative examples with relative high or low probability of successful outcome are presented (Table 2 - Box 1). The estimated odds ratios (ORs) of age and percentage brace redressement express the effect of one year at start or 1% brace redressement. For example, 10% brace redressement increase corresponds to an OR of $1.04^{10}=1.48$.

Six variables were retained in the final model using variables at start bracing and from during treatment. The model fit was 35% (McFadden's $R^2=0.35$) with a high ability of discrimination after internal validation (optimism adjusted C-statistic 0.86). The best predictors of success were good compliance, reduction of major curve after 1 year and short treatment time, while also single thoracic major curve, scoliosis in close family and the size of the major curve at start bracing contributed to the model. The final prediction model with the original β coefficients multiplied by the optimism adjusted calibration slope to account

for over-fitting is presented in Table 3, including two illustrative examples with relatively high or low probability for a successful outcome (Table 3 - Box 2). The estimated ORs of major curve at start bracing, percentage 1 year major curve reduction and treatment time express the effect of one unit increase. For example, an increase of 12 months treatment time corresponds to an OR of $0.94^{12}=0.48$.

Predictors of quality of life (SRS-22)

The mean SRS-22 values of patients with successful versus failure of treatment were 88.1 (12.6) versus 82.5 (13.8), respectively ($p<0.002$). None of the baseline predictor variables at start bracing had significant influence on healthrelated quality of life at long-term follow-up (results not shown). In the final model including additional parameters registered after onset of treatment (Table 4), the explained variance was low (5-6%). The best predictors were treatment time and success in terms of curve progression while also compliance and curve flexibility contributed to the model. Two illustrative examples with relatively high or low predicted life quality are given (Table 4 - Box 3).

Sensitivity analysis (curve progression to ≥ 50)

With treatment failure defined as curve progression to ≥ 50 degrees and/or operation we observed a reduction of failures from 65 (18%) to 39 (11%). The major curve's magnitude was higher at start bracing in the failure group (mean 39.9 (8.7)) versus those with success (mean 32.3 (6.7)). The size of the major curve was the only significant predictor in the model when variables at start of treatment were included. In the final model age at start bracing was the only predictor of curve progression to ≥ 50 .

Discussion

In the present long-term follow-up study after Boston brace treatment of idiopathic scoliosis in 365 patients, we applied logistic regression to assess predictors of success defined as curve progression $\leq 5^\circ$. We analysed both predictors at start bracing and from during

treatment. We also analysed predictors of health-related life quality (SRS-22). Despite the relatively large population included, our results should be interpreted with caution. Our analyses are limited to the study of associations, and the predictors identified should not be interpreted as causative factors for success.

The best long-term predictors for minimal curve progression after Boston brace treatment were good compliance, reduced major curve after one year and short treatment time. In addition, scoliosis in family, single thoracic major curve and the size of the major curve at start bracing contributed to the final model. Ideally, a model with a high degree of discrimination or accuracy at the beginning of treatment is most useful in clinical practice. In the current study the models improved considerably by using predictors collected during treatment.

Previous studies

A few methods have been proposed to predict a braced patient's risk of curve progression, but according to Chalmers et al.²⁶ most of them have poor or unclear accuracy and do not easily integrate into a clinic's existing workflow. From 14 clinical measurements in only 62 patients they predicted success or failure of brace treatment for adolescents with idiopathic scoliosis. They found that rotation of the curve (scoliometer value) and percentage in-brace correction were the two most useful predictor variables (<http://www.ece.ualberta.ca/~dchalmer/SimpleBracePredictor.html>). Similarly, Ajemba et al.²⁷ presented a regression model with reported high accuracy. Lonstein & Carlson²⁸ found that the best predictors at the initial examination were: magnitude of the curve, the Risser sign and the patient's chronological age. In a four-factor regression equation model Peterson & Nachemson⁸ found skeletal immaturity (Risser sign of 0 or 1), an apical curve level cephalad to the twelfth thoracic vertebra, plumb line imbalance less than 10 mm and younger age to be significantly associated with progression of the scoliotic major curve. They reported that a logistic regression model allowed correct classification of 81% of all curves as progressive or not progressive.

Including most of the predictors described above, we predicted curve progression and successful outcome at least 10 years after brace weaning in 365 patients with juvenile

(diagnosed at 7-9 years) and adolescent (10 years and older) idiopathic scoliosis. Since the definition of subgroups reflects the age at discovery of the scoliotic curve, brace treatment often starts at a later stage in the juvenile subgroup, but usually earlier than in patients with AIS. In the current study juvenile and adolescent idiopathic scoliosis had similar characteristics with respect to curve development (except for age and treatment time as expected) and quality of life scores, corresponding to previously reported results.^{4, 29}

Our prediction model using variables at start bracing and from during the treatment (Table 3) had comparable accuracy to the previous published models²³⁻²⁶ with a C-statistic of 0.85 (or 85%) which is a standard measure of the predictive accuracy of a logistic regression model. Depending on the scores of the predictor variables identified, successful outcome defined as curve progression $\leq 5^\circ$ and no operation could be predicted. Using 5° or a value at least $1-2^\circ$ larger than the measurement error as the success/failure cutting point may seem artificial relative to clinical and patient significance (e.g. quality of life), but is frequently used as a relevant and objective parameter.

Bone age

Bone age ad modum Greulich & Pyle¹⁸ has in our hospital for many years been and still is regarded as the “gold standard” parameter of biological maturation with most consistent and reliable assessments without missing values. Risser stage and age at menarche were also recorded maturation parameters in the present study, but chronological age (highly correlated to bone age) was the best maturity predictor in the prediction models. Risser is not as accurate as bone age for assessment of skeletal maturity, and we have bone age values noted for all 365 patients at all visits in the present study from onset of bracing to cessation of growth. Risser and exact time of menarche were subsidiary in use and have missing values. A simplified skeletal maturity scoring system by Sanders et al.¹⁵ has been shown to be reliable and more strongly correlated with the behavior of idiopathic scoliosis than the Greulich & Pyle bone age and Risser sign.¹⁷ A retrospective application of this method to hand films at onset of bracing could have added credibility to our study, but unfortunately these films are no longer available.

Compliance

As reported in previous articles^{2, 3, 30, 31} the juvenile and adolescent patients of the current study with poor compliance had increased curve progression, suggesting that compliance is a key predictor. Adherence to the intervention was modified by growth, discomfort and skin reactions (allergic or wear and tear), which was registered carefully more than 30 years ago when lack of objective measurements, e.g. monitoring of pressure or temperature by sensors mounted in the brace,³² were not available. This is a weakness of the present study. Compliance was dichotomized into good and poor using a cut-off at 20 hours per day based on patient/parent reports. Our registration most likely overestimates the number of good compliers. The poor compliers had somewhat lower age at start bracing, lower percentage brace redressement and 1 year major curve reduction, and shorter treatment time compared to the good compliers. Lou et al.³³ found that the Boston style brace was used in average in 57% of the prescribed time and that curve progression could be predicted in 41-54% of the cases based on brace tightness and wear time.

Pre-brace curve and treatment time

A number of previous studies have identified that the size of the primary pre-brace curve is a risk factor for curve progression,³⁴⁻³⁸ and the initial correction rate is reported to be associated with curve progression.^{9, 10} Upadhyay et al.³⁷ found brace redressement of the curve to be associated with reduced risk of progression. In keeping with this, we found that the major curve at start bracing and the curve size at 1 year of bracing were good predictors.

Treatment time was associated with age, but age and treatment time do not describe the same phenomenon, and treatment time was a better predictor than age in the models where variables during treatment were included. Short treatment time was partly related to older age at start bracing. With increasing age it is reasonable to assume that the major curve has reached the magnitude indicative of treatment with a moderate progression intensity. The patient has a corresponding relatively elevated biological maturity with less residual growth potential and less curve progression, and an expected shorter remaining treatment time. Short treatment time also occurred in younger selected patients with early planned weaning without relapse of major curve. They had none-progressive, stable minor

curves less than 25° after 1-2 years of treatment, most likely due to a milder form of scoliosis.

Health-related quality of life

Long treatment time and curve progression >5° predicted lower quality of life scores (Table 4). Even with a significant difference in mean SRS-22 values between the treatment groups of success versus failure, the explained variance and predictive ability for the single patient was low, and results should not be overinterpreted. Our results suggest that factors not examined in this study are important for health related quality of life in middle aged patients with idiopathic scoliosis.³⁹

Sensitivity analysis

The additional post hoc analysis defining treatment failure alternatively as curve progression to ≥50 degrees and/or operation with application of the same statistical methods, showed a change of significant predictors. Hence, the used models are able to discriminate between different outcome definitions, demonstrating that the choice of these definitions is critical with respect to the result of the analysis.

Limitations

Observations were not blinded. The population studied was restricted to patients willing to participate at long-term follow-up, which hampers the generalisability of the findings. People had various reasons for non-participation, most did not give any reason. Under-reporting by missing data may bias results. In the present study all the applied variables at start of treatment were fully numbered, except for the variable “Scoliosis in close family” with 93/365 (25%) missing values. We assumed that those with missing values had not scoliosis in their close family. Hence, the influence of genetics as a predictor may have been underestimated in our model.

Conclusions

The best predictors for a successful long-term curve development using only measures at start bracing were older age and good brace redressement, but model fit and ability of discrimination were low. Including measures assessed during bracing improved the model fit and ability of discrimination with good compliance and increased percentage curve reduction after one year as the most important predictors for treatment success.

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Notes

Conflicts of Interest.- All authors declare nothing to disclose.

Authors' contributions.- All authors made substantial contributions to the current work. Harald Steen participated in the conception, design and coordination, acquisition of data, analysis and interpretation of data and drafted the manuscript. Are H. Pripp performed the statistical analysis and helped to draft the manuscript. Johan E. Lange participated in the conception, design and coordination and acquisition of data. Jens I. Brox participated in the conception, design and coordination, acquisition of data, analysis and interpretation of data and helped to draft the manuscript. All authors read and approved the final manuscript.

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Table 1. Basic characteristics of study participants with failure or successful treatment

Variable	Failure of treatment (n=65; 27 operated)	Successful treatment (n=300)	p-value
Mean (SD) age (years) at start bracing	12.3 (2.4)	13.3 (1.8)	<0.001
Mean (SD) bone age (years) at start bracing	11.5 (2.1)	12.8 (1.8)	<0.001
Mean (SD) follow-up (years)	23.2 (4.4)	23.4 (4.0)	0.75
Scoliosis in close family (%)	11 (16.9)	47 (15.7)	0.80
Thoracic major curve (%)	52 (80.0)	196 (65.3)	0.022
Single major curve (%)	27 (41.5)	120 (40.0)	0.82
Mean (SD) major curve (°) at start bracing	34.1 (8.3)	33.0 (7.1)	0.25
Mean (SD) percentage major curve flexibility	29.3 (13.9)	31.0 (13.9)	0.37
Mean (SD) percentage brace redressement	44.8 (20.3)	53.2 (16.1)	<0.001
Mean (SD) percentage 1 year major curve reduction	7.7 (19.6)	23.3 (16.7)	<0.001
Poor compliance (brace wear <20 hrs daily)	36 (55.4)	39 (13.0)	<0.001
Median (IQR) treatment time (months)	33.5 (21.3 – 51.8)	27.9 (22.3 – 38.5)	0.048
Mean (SD) SRS-22 quality of life	82.5 (13.8)	88.1 (12.6)	0.002

SD standard deviation, *IQR* interquartile range.

Failure of treatment: More than 5° progression of primary major curve and/or operation.

Successful treatment: 5° or less progression of primary major curve and no operation.

Table 2. Logistic regression model for probability of successful treatment at long-term follow-up using predictor variables at start bracing

Predictor variables	Regression model with backward elimination		Internally validated regression model with shrunken coefficients	
	OR (95% CI), p-value	β coef	OR (95% CI)	β coef
Age at start (years)	1.41 (1.22 – 1.63), p<0.001	0.35	1.35 (1.19 – 1.52)	0.31
Percentage brace redressement	1.04 (1.02 – 1.06), p<0.001	0.04	1.03 (1.02 – 1.05)	0.034
(Constant)	-	-4.87	.	-3.98
Model fit and performance (with 95% CI)				
	Apparent	Optimism	Optimism corrected	
McFadden's R^2	0.11	-	-	
C-statistic	0.72 (0.65 – 0.79)	0.04	0.68 (0.61 – 0.75)	
Calibration slope	1.00 (0.65 – 1.35)	0.14	0.86 (0.51 – 1.21)	

The following predictor variables: Scoliosis in close family, thoracic scoliosis, single major curve, major curve start bracing and percentage major curve flexibility were excluded from the model after backward elimination.

OR odds ratio, CI confidence interval, β coef regression coefficients.

Apparent: Model performance estimated directly from original dataset.

Optimism: Difference between model performance in bootstrap data and test performance in original dataset.

Optimism corrected: The optimism subtracted from the apparent model performance, i.e. model performance after internal validation.

McFadden's R^2 : Pseudo R-Squared measure of model fit. A value of 0 represents no model fit and 1 represents perfect model fit (only estimated for the logistic model fitted in the original dataset, i.e. apparent model performance).

C-statistic: A measure of the model's discrimination between study participant with failure of treatment or successful treatment. A value of 0.50 represents no discrimination and 1.0 represents perfect discrimination.

C-slope: Calibration slope - regression slope of linear predictor, used in the model validation and 'shrinkage' of regression coefficients.

Box 1: Prediction model from internally validated model in Table 2

Linear predictor (LP) from a logistic regression model to predict successful treatment after completed bracing is $-3.98 + 0.31\text{age at start} + 0.034\text{percentage brace redressement}$. The value -3.98 is the intercept, and the other numbers are the estimated regression coefficients. The regression coefficients represent the log odds ratio for a change of 1 unit in the corresponding predictor variable. The predicted probability of successful treatment = $1/(1+e^{-LP})$.

Example 1: A 13 year old participant with 80 % brace redressement has a predicted probability of successful treatment = $1/(1+e^{-LP}) = 1/(1+e^{-(-3.98 + 0.31 \cdot 13 + 0.034 \cdot 80)}) = 0.94 = 94 \%$.

Example 2: A 9 year old participant with 30% brace redressement has a predicted probability of successful treatment = $1/(1+e^{-LP}) = 1/(1+e^{-(-3.98 + 0.31 \cdot 9 + 0.034 \cdot 30)}) = 0.46 = 46 \%$.

Table 3. Logistic regression model for probability of successful treatment at long-term follow-up using predictor variables at start bracing and from during the treatment

Predictor variables	Regression model with backward elimination		Internally validated regression model with shrunken coefficients	
	OR (95% CI), p-value	β coef	OR (95% CI)	β coef
Scoliosis in close family	0.37 (0.15 – 0.93), p=0.035	-0.99	0.43 (0.20 – 0.94)	-0.84
Single major curve	0.42 (0.20 – 0.86), p=0.019	-0.87	0.48 (0.26 – 0.88)	-0.74
Major curve at start bracing	0.96 (0.82 – 1.00, p=0.080	-0.039	0.97 (0.93 – 1.00)	-0.033
Percentage 1 year major curve reduction	1.07 (1.05 – 1.10), p<0.001	0.075	1.07 (1.04 – 1.09)	0.064
Poor compliance	0.077 (0.036 – 0.17), p<0.001	-2.56	0.11 (0.06 – 0.22)	-2.18
Treatment time (months)	0.94 (0.93 – 0.96), p<0.001	-0.060	0.95 (0.93 – 0.97)	-0.051
(Constant)	-	5.20	-	4.58
Model fit and performance (with 95% CI)				
	Apparent	Optimism	Optimism adjusted	
McFadden's R^2	0.350	-	-	
C-statistic	0.88 (0.83 – 0.93)	0.03	0.85 (0.80 – 0.90)	
C-Slope	1.00 (0.76 – 1.24)	0.15	0.85 (0.61 – 1.09)	

The following predictor variables: Age at start, thoracic scoliosis, percentage major curve flexibility and percentage brace redressement were excluded from the model after backward elimination.

OR odds ratio, CI confidence interval, β coef regression coefficients.

Apparent: Model performance estimated directly from original dataset.

Optimism: Difference between model performance in bootstrap data and test performance in original dataset.

Optimism corrected: The optimism subtracted from the apparent model performance, i.e. model performance after internal validation.

McFadden's R^2 : Pseudo R-Squared measure of model fit. A value of 0 represents no model fit and 1 represents perfect model fit (only estimated for the logistic model fitted in the original dataset, i.e. apparent model performance).

C-statistic: A measure of the model's discrimination between study participant with failure of treatment or successful treatment. A value of 0.50 represents no discrimination and 1.0 represents perfect discrimination.

C- slope: Calibration slope - regression slope of linear predictor, used in the model validation and 'shrinkage' of regression coefficients.

Box 2: Prediction model from internally validated model in Table 3

Linear predictor (LP) from a logistic regression model to predict successful treatment after completed bracing is $4.58 - 0.84\text{scoliosis in close family} - 0.74\text{single major curve} - 0.033\text{major curve at start bracing} + 0.064\text{percentage 1 year major curve reduction} - 2.18\text{poor compliance} - 0.051\text{treatment time}$. The value 4.58 is the intercept, and the other numbers are the estimated regression coefficients. All categorical variables are coded as binary (0 or 1 for absence or presence of a risk factor). The regression coefficients represent the log odds ratio for a change of 1 unit in the corresponding predictor variable. The predicted probability of successful treatment = $1/(1+e^{-LP})$.

Example 1: A participant with no scoliosis in close family, no single major curve, 30° major curve at start bracing, 40 % reduction in major curve after 1 year, good compliance and 20 months treatment time has a predicted probability of successful treatment = $1/(1+e^{-LP}) = 1/(1+e^{-(4.58 - 0.84 \cdot 0 - 0.74 \cdot 0 - 0.033 \cdot 30 + 0.064 \cdot 40 - 2.18 \cdot 0 - 0.051 \cdot 20)}) = 0.994 = 99\%$.

Example 2: A participant with scoliosis in close family, single major curve, 40° major curve at start bracing, 0 % reduction in major curve after 1 year, poor compliance and 40 months treatment time has a predicted probability of successful treatment = $1/(1+e^{-LP}) = 1/(1+e^{-(4.58 - 0.84 \cdot 1 - 0.74 \cdot 1 - 0.033 \cdot 40 + 0.064 \cdot 0 - 2.18 \cdot 1 - 0.051 \cdot 40)}) = 0.073 = 7\%$.

Table 4. Linear regression models for predicted life quality (SRS-22) at long-term follow-up

	Regression model with backward elimination	Lasso regression
Predictor variables	β coef (95% CI), p-value	β coef
Percentage major curve flexibility	-0.092 (-0.19 – 0.0051), p=0.063	-0.023
Poor compliance	-3.48 (-7.22 – 0.25), p=0.068	-2.71
Treatment time (months)	0.13 (0.047 – 0.21), p=0.002	0.067
Successful treatment	5.45 (1.50 – 9.40), p=0.007	3.0
(Constant)	82.0	83.7
Model fit		
	Backward multivariable regression	Lasso regression
Adj R ²	0.069	0.053

The following predictor variables: Age at start, scoliosis in close family, thoracic scoliosis, single major curve, major curve at start bracing, percentage brace redressement and percentage 1 year major curve reduction were excluded from the model after backward elimination and in the lasso regression model.

Coef regression coefficient, *CI* confidence interval.

Adj R²: R-squared adjusted, i.e. the coefficient of determination adjusted for number of predictor variables that measure proportion of variance explained by the model.

Box 3: Prediction from lasso regression in Table 4

Linear predictor (LP) from a linear regression model to estimate health related life quality SRS-22 at long-term follow-up. $LP = 83.7 - 0.023 \text{percentage major curve flexibility} - 2.71 \text{poor compliance} + 0.067 \text{treatment time} + 3.0 \text{successful treatment}$. The value 83.7 is the intercept, and the other numbers are the estimated regression coefficients for the predictor variables. All categorical variables are coded as binary (0 or 1 for absence or presence of a risk factor). The regression coefficients represent the change of 1 unit in the corresponding outcome value.

Example 1: A participant with 40 % major curve flexibility, poor compliance, 20 months treatment time and failure of treatment has a predicted SRS-22 life quality outcome = $LP = 83.7 - 0.023 \cdot 40 - 2.71 \cdot 1 + 0.067 \cdot 20 + 3.0 \cdot 0 = 81.4$.

Example 2: A participant with 30 % major curve flexibility, good compliance, 60 months treatment time and successful treatment has a predicted SRS-22 life quality outcome = $LP = 83.7 - 0.023 \cdot 30 - 2.71 \cdot 0 + 0.067 \cdot 60 + 3.0 \cdot 1 = 90.0$.