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**Rigid Thoracolumbar Orthosis Does Not Improve Outcomes of Acute Adolescent Spondylolysis
as Compared with Placebo. Bony Union Predicts Improved Health-Related Quality of Life
Outcomes at 2-year Follow-Up**

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25 **Introduction**

26

27 Spondylolysis is the most common cause of low back pain in young athletes.¹ It can be treated with
28 restriction of sports, physical therapy, brace, and cast treatment.²⁻¹² Various kinds of braces have been
29 used for treatment of adolescent spondylolysis with good results.²⁻¹² A small proportion of adolescents
30 with acute spondylolysis do not achieve bony union of the stress fracture, regardless the treatment. In
31 retrospective studies, low back pain has alleviated in most of these patients and they are able to
32 continue in their previous activity level¹³, but they are also in the risk of developing spondylolisthesis.
33 However, there are no previous prospective studies evaluating the HRQoL outcomes of conservative
34 treatment in acute pediatric spondylolysis, and thus it remains unclear whether these outcomes equal in
35 patients achieving or not achieving bony union of the spondylolysis.

36 In this study, we aimed to investigate union rates of spondylolysis and the HRQoL
37 outcomes after treatment of acute adolescent spondylolysis with a rigid thoracolumbar orthosis (Boston
38 brace) or a placebo (elastic lumbar support) with a two-year follow-up time. We aimed to figure out if
39 treatment type, achieving bony union of the spondylolysis or development of spondylolisthesis affects
40 patients HRQoL during the two-year follow-up time. We also wanted to investigate incidence of
41 development of spondylolisthesis during two-year follow-up time, and factors predicting this. We
42 hypothesized that thoracolumbar orthosis would increase the bony union rate and thus decrease the risk
43 for development of spondylolisthesis, and that non-union would predict inferior HRQoL and back pain
44 during two-year follow-up time.

45

46 **Materials and methods**

47

48 **Trial Design**

49 This study was designed as a randomized, nonblinded clinical trial comparing the outcomes of acute
50 adolescent spondylolysis treated with a Boston brace or a placebo (elastic lumbar support). Sample size
51 was calculated with the use of study power of 80% and type-I error (α) of 0.05. The bony union rate of
52 spondylolysis with a Boston brace was assumed to be 90%^{6,10} and with a placebo 56% based on our
53 clinical experience (superiority trial). This led to sample size of 26 patients per group and to allow
54 dropouts, a total of 60 patients were included.

55 Study was started in June 2016 and the first 14 patients were randomized regarding the brace type
56 (randomized cohort). Randomization was performed after informing the families about the study and
57 after receiving an informed consent. Randomization was continued until September 2018. During this
58 period significant number of patients (4/18, 22%) refused from the study due to randomization. To
59 secure the recruitment process, the study was modified into a prospective patient preference study
60 (patient preference cohort, 46 patients) (Figure 1, Flowchart).

61

62 **Patients**

63 Sixty consecutive adolescents with acute uni- or bilateral spondylolysis were included to this study
64 between June 2016 and January 2022. All patients were examined in the paediatric orthopedic
65 outpatient clinic due to low back pain. Inclusion criteria were:

- 66 • Uni- or bilateral spondylolysis (fracture line) with bone edema in the magnetic resonance
67 imaging (MRI, T2 sagittal and axial) as a sign of active lesion.
- 68 • No bony sclerosis in the computed tomography (CT).
- 69 • Age between 8 and 18 years in the beginning of the treatment.

70 Exclusion criteria included lack of bone edema in lumbar MRI images; spondylolisthesis in a standing
71 lateral radiograph of the lumbar spine; lesions with bony sclerosis in the CT as a sign of healing

72 process already has begun; a systemic skeletal illness (e.g. osteogenesis imperfecta or Marfan's
73 syndrome) or lack of interest.

74

75 **Interventions and follow-up protocol**

76 Patients were treated with a custom-made, rigid thoracolumbar orthosis (individual Boston brace;
77 Respecta, Finland) or a placebo (Porostrap, Donjoy). Boston brace is a rigid thoracolumbar underarm
78 orthosis, which immobilizes the lumbar spine¹⁴ whereas placebo (Porostrap) is an elastic, nonrigid
79 textile which does not immobilize or support the lumbar spine. Treatment time for all patients was four
80 months and patients were advised to wear the brace or the placebo 23 hours a day. All patients were
81 advised to cease all sports for 4 months and only walking and cycling were allowed during the
82 immobilization period. Patients received guidance on isometric abdominal and spinal muscle exercises
83 from a physiotherapist in the beginning of the treatment. Patients were followed up at the end of the 4
84 months treatment, at 12 months, and at 24 months after the first appointment.

85

86 **Radiographic and HRQoL measures**

87 Before treatment began all patients underwent a standing lateral radiograph of the lumbar spine, a
88 lumbar spine MRI and a CT targeted on posterior elements of the fractured lumbar vertebra (Figure 2).
89 From the lumbar radiographs spondylolisthesis was excluded whereas from the MRI and CT the
90 acuteness of the spondylolysis was secured, and spondylolysis was staged based on classifications
91 presented by Hollenberg et al.¹⁵ for MR images and Fujii et al.⁴ for CT. In the Hollenberg et al.¹⁵ MRI
92 classification grade 1 is a stress reaction without a fracture line, grade 2 is an incomplete visible
93 fracture, grade 3 is a visible complete fracture and grade 4 is a pseudoarthrosis. In the Fujii et al.⁴ CT
94 classification fractures are divided to early, progressive and terminal. Early lesions are narrow fissures
95 (hairline fracture), terminal lesions are wide with sclerosis (pseudoarthrosis), and progressive lesions

96 are between these two. At the four months follow-up visit bony union was evaluated with a CT targeted
97 on the posterior elements of the spondylolysis (Figure 3). Bony union was defined as bony bridging
98 over the stress fracture, but trabeculation did not need to be complete. If spondylolysis was bilateral
99 both sides needed to show signs of bony union for the patient to be categorized as healed. At 12 months
100 and 24 months follow-up visits the development of spondylolisthesis was evaluated from a standing
101 lateral lumbar spine radiograph (Figure 4). All radiographic images were evaluated for this study by an
102 independent musculoskeletal radiologist blinded to the treatment chosen.

103 HRQoL was measured with a Scoliosis Research Society-24 (SRS-24) outcome
104 questionnaire that patients filled in each visit (0 months, 4 months, 12 months, 24 months). This
105 questionnaire is originally developed for evaluating HRQoL of patients with adolescent idiopathic
106 scoliosis but is accepted for evaluating HRQoL of patients with other back conditions as well.^{10,16-17}

107

108 **Outcome parameters**

109 The primary outcome parameter of this study was the HRQoL at 24 months follow-up visit and
110 whether treatment type, bony union of the spondylolysis or development of spondylolisthesis affected
111 this. Secondary outcome parameters were the bony union rates of spondylolysis with a Boston brace
112 and a placebo, probability for development of spondylolisthesis during follow-up time and factors
113 predicting development of spondylolisthesis.

114

115 **Statistical analysis**

116 Counts (n) and percentages were used to describe categorical data and Fischer's exact tests to examine
117 the significance of the associations between brace type. Age, treatment time and Body Mass Index
118 (BMI) were normally distributed, and hence reported with mean and standard deviation (SD). Analysis
119 of variance (ANOVA) was used to compare brace types. Duration of symptoms before treatment and

120 follow-up time exhibited skewed distributions. Median and lower (Q1) and upper quartiles (Q3) were
121 reported, and Wilcoxon rank sum tests were performed to assess brace type differences.

122 Associations between the HRQoL all domains of the SRS-24 and brace type, uni- vs bilaterality and
123 bony union were analyzed using a hierarchical linear mixed model with repeated measures including
124 one within-factor variable (time), between-factor variable (brace type, laterality or bony union) and the
125 interaction between time and brace type, laterality or bony union. We used unstructured covariance for
126 time and performed Kenward–Roger correction for degrees of freedom.

127 The proportion of spondylolisthesis was reported with 95% confidence interval. Spondylolisthesis rates
128 were calculated using log-binomial models. Due to small number of patients developing
129 spondylolisthesis, only univariate analysis was performed for the analysis of the association between
130 spondylolisthesis and brace type and other characteristics. Association between spondylolisthesis and
131 stage or level of spondylolysis was carried out using Fischer’s exact test since spondylolisthesis
132 patients were not scattered in all categories of the factor. Associations between the HRQoL all domains
133 of the SRS-24 and spondylolysis were analyzed using a hierarchical linear mixed model with repeated
134 measures including one within-factor variable (time), between-factor variable (brace type or bony
135 union).

136 All tests were performed as two-sided tests with a significance level set at 0.05. Analyses were
137 performed using SAS (Version 9.4) for Windows.

138

139 **Ethical committee approval**

140 Ethical committee approval was applied from a Local Ethics Committee for Human Sciences
141 (Registration number ETMK 149 /1801/2015). All procedures were followed according to the Helsinki
142 declaration of the World Medical Association. A written informed consent from the patient and if
143 needed from his guardians was required. Study was registered to Clinicaltrials.gov (NCT03675152).

144

145 **Results**

146

147 A total of 60 patients were included to this study. One patient was lost to follow-up before first control
148 at 4 months due to lack of interest and two patients were excluded from all the analysis as they did not
149 fulfill the inclusion criteria (no bone edema in the MRI). Therefore, a total of 57 patients were included
150 to the analysis (Table 1). All patients were active in sports. Patients reported various sports, with soccer
151 (18/57), ice hockey (8/57) and gymnastics (5/57) being the most common sports. Of these fifty-seven
152 patients 30/57 (53%) were treated with a Boston brace and 27/57 (47%) with a placebo. Duration of
153 symptoms prior to the initiation of active treatment was a median of 75 (interquartile range 59, 111) days
154 in the Boston brace group and a median of 65 days (interquartile range 35, 122) in the Placebo group
155 ($p=0.232$). The four-month results have been published in a previous article.¹¹

156 The overall bony union rate of spondylolysis in patients treated with a Boston brace was
157 20/30 (67%) and in patients treated with a placebo was 17/27 (63%) ($p=0.789$). When bony union rates
158 of different stages of spondylolysis in the CT were viewed separately, no statistically significant
159 difference was found in the union rates of these stages between treatment groups ($p> 0.05$ in all
160 analysis). The bony union rate did not differ between uni- and bilateral lesions (RR 1.373, 95%CI
161 0.443-4.250, $p=0.583$). One patient in the placebo treatment group, who had bilateral spondylolysis in
162 both L3 and L4 vertebra, did not achieve bony union of these and needed surgical management
163 (revision of stress fracture, bone grafting, and screw fixation of the fracture site bilaterally at two
164 levels) due to ongoing symptoms just before 12 months follow-up visit. No other patient required
165 operative intervention. Two patients reappeared with pain symptoms after successful treatment of
166 spondylolysis with a placebo. Both of these patients were noted to have a recurrent spondylolysis in the

167 same place as originally. ~~and were successfully treated with a Boston brace with no further low back~~
168 ~~pain.~~

169 Five patients (5/57, 9% (95% CI 3.8, 18.9)) developed spondylolisthesis during two-year
170 follow-up time. In terms of proportion of patients who did not achieve bony union of the spondylolysis
171 25% (95% CI 11.2, 46.9, 5/20) developed spondylolisthesis. All spondylolisthesis remained low-grade
172 (Meyerding grade I¹⁸) through follow-up time (mean slip 4.2 mm, range 1.8-7.4 mm) and none of the
173 patients needed operative intervention for spondylolisthesis. Two of the patients who developed
174 spondylolisthesis (2/5) were originally treated with a Boston brace and 3 of the patients (3/5) with a
175 placebo (p=0.506). In univariate analysis non-union predicted development of spondylolisthesis
176 (p=0.005).

177 There were no statistically significant differences in the HRQoL in any domain of the
178 SRS-24 at 1- or 2-year follow-up between treatment groups (p>0.05 for all domains, Table 2). When
179 HRQoL was compared between patients who achieved bony union of spondylolysis and who did not, it
180 could be noted that patients who did not achieve bony union of the spondylolysis had lower total SRS
181 score (p=0.005) and lower satisfaction domain score (p<0.001) at the 24 month follow-up visit (Table
182 3), whereas pain, self-image, function, activity, posttreatment self-image and posttreatment function
183 domain scores did not differ significantly. The change from baseline to 2-year follow-up in total SRS
184 score (-0.55 (95% CI -0.68, -0.42)) and in satisfaction domain score (-0.47 (95% CI -0.66, -0.27)) was
185 greater in patients who achieved bony union of the stress fracture compared to patients who developed
186 non-union of the spondylolysis (p<0.001 for both comparisons). The laterality (uni- vs. bilateral
187 lesions) did not affect the SRS-24 outcomes at 1-year or 2-year follow-up. Patients with
188 spondylolisthesis had on average 0.61 (95% CI 0.27, 0.94) lower satisfaction domain (p<0.001)
189 compared to patients without spondylolisthesis.

190

191

192 **Discussion**

193 To our knowledge, this study represents the first prospective, comparative study of HRQoL of acute
194 pediatric spondylolysis patients with a two-year follow-up time. Treatment with a brace did not affect
195 the bony union rate nor the HRQoL when compared to a placebo treatment (an elastic lumbar support)
196 during two-year follow-up time. Additionally, we showed that adolescents who did not achieve bony
197 union of the spondylolysis had lower HRQoL during two-year follow-up time and therefore, the goal of
198 acute adolescent spondylolysis treatment should be achieving bony union of the stress fracture.
199 Therefore, even though earlier studies²⁻¹² have shown good results of rigid thoracolumbar orthosis
200 treatment for adolescent spondylolysis, based on this study conservative treatment using activity
201 restriction for four months is as effective as brace treatment.

202 There is lack of studies examining the risk of developing spondylolisthesis after
203 unsuccessful treatment of adolescent spondylolysis but in a population-based study of the natural
204 history of spondylolysis and spondylolisthesis¹⁹, 55% of patients who had asymptomatic spondylolysis
205 at the age of six developed spondylolisthesis until adulthood. All these patients remained asymptomatic
206 and all the slips remained low grade. In our study the risk of developing spondylolisthesis during two-
207 year follow-up time was 9% in whole cohort and 25% in patients with non-union of spondylolysis. All
208 spondylolisthesis remained low-grade (Meyerding I) and could be treated conservatively. Seitsalo et
209 al.²⁰ followed up 272 children with spondylolisthesis for a mean of 15 years. The percentage amount of
210 primary slip at initial evaluation and growth spurt (girls 9-12 years; boys 11-14 years) were predictive
211 for spondylolisthesis progression. Most of our patients were older and had already gone through growth
212 spurt. Therefore, it is possible that a higher-grade of spondylolisthesis is more likely to develop and
213 proceed if spondylolysis appears before the growth spurt.

214

215 **Strengths and limitations**

216 There are limitations to this study. Ideally this study would have continued as a randomized clinical
217 trial till its end, but due to difficulties in patient enrollment the study was modified to patient preference
218 cohort after two years of enrollment. Similar problem was in the BRAIST trial²¹ concerning adolescent
219 idiopathic scoliosis treatment with a brace. Blinding was not an option as both treatment options were
220 introduced to the adolescents and their families before informed consent. However, comparing a rigid
221 thoracolumbar orthosis with a placebo can be seen as a strength of this study as well as the fact that the
222 radiologist was blinded to the treatment type. There was no monitoring device inside the brace or the
223 placebo and therefore, the actual use of treatment option remains uncertain even if patients were
224 routinely asked for brace compliance. Overall patients were dedicated to executing the planned
225 treatment protocol. Without the sensor, we have no measured data on how many hours the patients
226 actually used the rigid brace or the placebo. It remains also unclear, whether a non-removable cast would
227 be a more effective and whether earlier treatment following an acute fracture would enhance union. All
228 patients were allowed to return to their previous level of activity after the four months sport restriction.
229 Our study protocol did not include a specific question on how many of patients were able to do this.
230 However, in our study only two patients had a refracture, which in both cases was treated successfully
231 conservatively.

232 Treatment time of four months was based on the previous study by Sakai et al.⁸, where
233 they noted that the average time for achieving bony union of the adolescent spondylolysis was 3.6
234 months for progressive lesions in the CT and the treatment time can therefore be considered as
235 sufficient. High signal intensity on MR images was our inclusion criteria as this has been a predictor of
236 bony healing.⁸ The follow-up time of two years can be seen satisfactory for evaluating the HRQoL
237 after treatment and the risk of developing spondylolisthesis.

238 Cohort size of 57 patients is considered as sufficient, but a larger cohort would bring
239 stronger evidence and could have shown more differences in the HRQoL of patients who developed
240 spondylolisthesis when compared to patients who did not and to show associations between
241 characteristics and development of spondylolisthesis. Strengths of this study also include a prospective,
242 standardized clinical and radiographic follow-up including advanced imaging before and after
243 immobilization period to evaluate bony union and the use of a standardized and validated SRS-24
244 questionnaire to evaluate the HRQoL. The changes in the SRS domains between the non-union and
245 union groups exceeded the minimally clinically important differences.²²

246

247 **Clinical implications**

248 Immobilization using rigid thoracolumbar orthosis is not indicated for paediatric acute
249 spondylolisthesis simplifying conservative treatment in adolescent athletes. Patients achieving union of
250 these isthmic stress fractures obtained better HRQoL outcomes than those not achieving union during
251 2-year follow-up. Adolescent athletes developing activity related low back pain should undergo early
252 lumbar MR images to allow early identification and adequate conservative treatment of acute
253 spondylolysis. Two-thirds of these athletes with acute lesions demonstrated bony union using four
254 months activity restriction with only walking, cycling, and isometric trunk muscle activation allowed.
255 One-fourth of patients with non-union develop spondylolisthesis which remained low-grade (less than
256 25% forward slip) in these adolescents.

257

258 **Conclusion**

259 Based on this study a rigid brace is not needed for treatment of acute paediatric spondylolysis, as bony
260 union nor HRQoL with a placebo and a 4-month sport restriction did not differ during 2-year follow-
261 up. The goal of treatment of an acute, adolescent spondylolysis should be bony union as non-union

262 significantly affects HRQoL during two-year follow-up time. Patients receiving bony union of the
263 stress fracture showed a significantly better improvement in SRS-24 outcomes as compared with those
264 not achieving union. There is a 25% risk of developing a low-grade spondylolisthesis if the bony union
265 of the spondylolysis is not achieved.

266

267