



## Effectiveness and safety of posterior titanium instrumentation in children with adolescent idiopathic scoliosis: a prospective study

Adölesan idiopatik skolyozlu çocuklarda titanyum posteriyor enstrümantasyonun etkinliği ve güvenliliği: Prospektif çalışma

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**Objectives:** This study aims to determine the effectiveness and the relative safety of posterior spinal fusion with titanium instrumentation in children with adolescent idiopathic scoliosis (AIS).

**Patients and methods:** A prospective cohort (case-only) study was conducted to determine this effectiveness and safety. There were 24 patients (21 girls, 3 boys; mean age 14.1±1.8 years; range 11 to 17 years) who underwent surgery between January 2002 and December 2003 in our clinic, with a minimum of two years follow-up. Upper thoracic, thoracic, and thoracolumbar coronal curves as well as kyphosis from T5-T12 were measured as main outcome variables and repeated measure ANOVA was used to assess the data.

**Results:** The main thoracic curve (coronal plane) correction achieved at the first erect period (the first 4 weeks postoperative) (mean 12.21±9.78 degrees), this correction was maintained at 24 months follow-up (mean 15.71±7.15 degrees) and both were significantly lower than the preoperative values (mean 57.0±12.75 degrees), (p<0.001). Sagittal plane (kyphosis angle between T5-T12) curve was not worsened by posterior titanium instrumentation and it was 19.50±10.53 degrees preoperatively, 16.45±6.68 degrees at the first erect period and 17.73±8.40 degrees at the 24 months follow-up (p=0.74). There were no evidence of pseudoarthrosis, no loss of correction and no infections.

**Conclusion:** Posterior titanium instrumentation in the treatment of AIS is effective due to its ability to achieve and maintain curve correction. Further, this instrumentation does not worsen hypokyphosis and is safe since there were no adverse events.

**Key words:** Adolescent; fusion; posterior instrumentation; scoliosis; titanium.

**Amaç:** Bu çalışmada adölesan idiyopatik skolyozlu (AIS) çocuklarda titanyum enstrümantasyonuyla gerçekleştirilen posteriyor spinal füzyonun etkinliği ve güvenliğinin tespit edilmesi amaçlandı.

**Hastalar ve yöntemler:** Bu etkinlik ve güvenliliğin belirlenmesi için prospektif bir özdeş grup (sadece olgu) çalışması yapıldı. Çalışmada Ocak 2002 ve Aralık 2003 tarihleri arasında kliniğimizde ameliyat edilmiş 24 hasta (21 kız, 3 erkek; ort. yaş 14.1±1.8 yıl; dağılım 11-17 yıl) yer aldı ve en az iki yıllık bir takip uygulandı. Ana sonuç değişkenleri olarak üst torasik, torasik ve torakolomber koronal eğrilikler ve T5-T12 arasındaki kifoz ölçüldü ve tekrar ölçümlü ANOVA kullanılarak veriler değerlendirildi.

**Bulgular:** Ana torasik eğrilikte (koronal planda) ilk doğrulma periyodunda (ameliyat sonrası ilk 4 hafta) düzelme olduğu (ortalama 12.21±9.78 derece), 24 aylık takip sonunda bu düzelmenin korunduğu (ortalama 15.71±7.15 derece) ve her iki ölçümünde ameliyat öncesi derecelerden (ortalama 57.0±12.75 derece) istatistiksel olarak anlamlı şekilde daha düşük olduğu, gözlemlendi (p<0.001). Sagittal planda (T5-T12 arası kifoz açısı) eğriliğin posteriyor titanyum enstrümantasyon ile kötüleşmediği ve ameliyat öncesinde 19.50±10.53 derece, ilk doğrulma periyodunda 16.45±6.68 derece ve 24 aylık takip sonunda 17.73±8.40 derece olduğu gözlemlendi (p=0.74). Psödoartrozise ilişkin herhangi bir kanıt mevcut değildi ve düzeltme kaybı ya da enfeksiyon meydana gelmedi.

**Sonuç:** Titanyum enstrümantasyon, AIS tedavisinde posteriyor eğriliğin düzeltilmesini sağlamak ve bu düzelmeyi korumakta etkin olarak saptanmıştır. Ayrıca bu enstrümantasyon hipokifozisi kötüleştirmemektedir ve herhangi bir advers olay görülmemiş olması ışığında güvenlidir.

**Anahtar sözcükler:** Adölesan; füzyon; posterior enstrümantasyon; skolyoz; titanyum.

Adolescent idiopathic scoliosis (AIS) is a three-dimensional deformity of the spine which results in a lateral curvature, axial plane rotation and frequently, loss of kyphosis in the sagittal plane. In severe, progressive cases, patients with AIS require surgical correction, and instrumentation and fusion has been the technique of choice for this condition for the last 40 years. The major aim of AIS surgery is to achieve a balanced correction and solid fusion with improved truncal alignment while preventing back pain and subsequent systemic problems.<sup>[1-8]</sup> Since the introduction of the Harrington distraction rod, different instrumentation systems with varying results and follow-up have been reported,<sup>[9]</sup> but little is known about implant biomaterials and their contribution to deformity correction.

Stainless steel and titanium alloys are two major options for spinal implants and each has its own biomechanical features. The limitations of titanium instrumentation include decreased strength and stiffness compared to stainless steel, notch sensitivity,<sup>[10]</sup> reduced fatigue failure<sup>[11,12]</sup> and screw pull-out due to metal memory.<sup>[13]</sup> On the other hand, titanium has several advantages such as greater biocompatibility, producing smaller artifacts on computed tomography (CT) and magnetic resonance imaging (MRI)<sup>[14]</sup> and lower incidence of corrosion. Gurappa<sup>[15]</sup> reported that stainless steel had greater corrosion levels than titanium. Based on a literature review, there is a single study by Mueller and Gluch<sup>[16]</sup> reporting on 50 patients with AIS treated by posterior titanium instrumentation. In this retrospective study, they concluded that posterior titanium instrumentation was safe and effective.

To our knowledge, there are no prospective studies regarding posterior titanium instrumentation in AIS. The aim of this current study was to assess the effectiveness and safety of titanium instrumentation in AIS using a prospective repeated measure design.

## PATIENTS AND METHODS

After obtaining institutional review board approval, we conducted a prospective cohort (case only) study to assess the effectiveness and safety of titanium instrumentation in patients with AIS.

### Study population

This study sample comprised 24 patients (21 girls and 3 boys; mean age 14.1±1.8 years, range 11 to 17 years) with AIS who had posterior spinal fusion (PSF) with titanium instrumentation between January 2002 and December 2003. The minimum follow-up was two years. The inclusion criteria for participation in the study were: (i) clinical and radiographic diagnoses of AIS and (ii) preoperative Cobb angle 50-90 degrees. The

exclusion criteria were (i) previous surgery for scoliosis and (ii) onset of scoliosis before the age of 10 years.

### Sample size and power estimation

To determine the sample size needed in this study in order to have sufficient statistical power, the following parameters were used: (i) type 1 error =0.05, (ii) power (1-β) =90%, (iii) mean difference in Cobb angle =10 degrees, standard deviation (SD) =12.21 and (iv) repeated measures design. With these assumptions and parameters, we estimated the sample size to be 24 patients.

### Surgical technique

All patients were treated with posterior spinal fusion and instrumentation by a single surgeon (SAS) in a standardized fashion. The details of this surgical procedure are described elsewhere.<sup>[16]</sup> The Monarch™ Titanium Spine System (DePuy Spine, Inc. Raynham, MA, USA) with 5.5 or 6.35 mm rods were employed in this study.

### Outcome variables

We measured upper thoracic, thoracic and thoracolumbar coronal curves as well as kyphosis from T5-T12 as main outcome variables. Radiographic measurements were obtained from a standing posterior-anterior (PA) 36 inch X-ray and lateral standing X-ray at the preoperative visit, first erect (FE) visit (4 weeks) and postoperative 6, 12 and 24 month periods. The main curve was measured by using Cobb method.<sup>[5,17]</sup> These outcome variables were ascertained in continuous scale and measured as degrees.

### Other related variables

Proximal junctional kyphosis (PJK) and distal junctional kyphosis (DJK) were recorded at preoperative, FE and PO 24 month periods. The level of pain was measured subjectively by patients' self-report of pain perception on a scale ranging from 0-10. Four levels of pain were characterized by: (i) no pain =0, (ii) mild pain =1-3, (iii) moderate= 4-6, and (iv) severe= 7-10.

### Intraoperative variables

These variables included: (i) estimated blood loss (cc) and (ii) duration of surgery (minutes from incision to last suture).

### Statistical analysis

The data were examined for normality, skewness and outlier using Shapiro-Wilk test for normality as well as box plot and histogram. The categorical variables (sex, rod size, loss of correction, and level of pain) were summarized using frequency and percentage, while

the continuous variables were summarized using the mean and SD.

To test the study-specific hypothesis of no mean difference between the preoperative and the postoperative outcome measures (thoracic curve, thoracolumbar curve, upper thoracic curve and kyphosis T5-T12) as well as the possible complications of surgery (proximal and distal junctional kyphosis), we utilized repeated measure analysis of variance (ANOVA). To determine where in the ANOVA model a significant change of cohort occurs, we performed a pair wise comparison using Bonferroni method. All tests were two-tailed, with  $<0.05$  as the significance level. The Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 17.0 and STATA version 10.0 (StataCorp, College Station, TX, USA) were used to perform the analyses.

## RESULTS

There were 24 patients with AIS. The mean estimated blood loss was  $1.322\pm 730.3$  cc. The mean surgery time was  $360\pm 108.1$  minutes. The mean hospital stay was

$4.4\pm 0.86$  days. The average weight during surgery was  $62.2\pm 19.3$  kg.

Twenty-two (91.7%) of the patients maintained correction, with  $<10^\circ$  loss during the two-year follow-up period. Twenty-two patients (91.7%) had a rod size of 5.5 mm and two (8.3%) patients had 6.35 mm. None of the patients had severe pain scores on FE and postoperative two-year follow-up visits.

Coronal and sagittal curve corrections are presented in table I. There was a statistically significant difference in main thoracic curve Cobb angle between Preoperative (mean= $57.0^\circ\pm 12.75^\circ$ ), and FE measurements (mean= $12.21^\circ\pm 9.78^\circ$ ),  $p<0.001$ . Correction was obtained in the upper thoracic curve with a statistically significant change between the preoperative (mean= $25.88^\circ\pm 11.21^\circ$ ) and FE measurements (mean= $9.38^\circ\pm 6.52^\circ$ ),  $p<0.001$ . Similarly, there was a significant difference between preoperative (mean= $38.96^\circ\pm 15.24^\circ$ ) and FE thoracolumbar curve measurements (mean= $12.54^\circ\pm 8.18^\circ$ )  $p<0.001$ . There was no loss of thoracic kyphosis between the

TABLE I

The outcome measures and complications of spine fusion with titanium in maintaining correction in patients with adolescent idiopathic scoliosis

Covariate	Mean $\pm$ SD	F(df)	p
Thoracic curve (main curve)		220.36(2)	<0.001
Preoperative	57 $\pm$ 12.75		
Immediate postoperative	12.21 $\pm$ 9.78		
Two year follow-up	15.71 $\pm$ 7.15		
Upper thoracic curve		32.69(2)	<0.001
Preoperative	25.88 $\pm$ 11.21		
Immediate postoperative	9.38 $\pm$ 6.52		
Two year follow-up	13.92 $\pm$ 7.51		
Thoraco-lumbar curve		119.51(2)	<0.001
Preoperative	38.96 $\pm$ 15.24		
Immediate postoperative	12.54 $\pm$ 8.18		
Two year follow-up	12.17 $\pm$ 9.61		
Kyphosis T5-T12		0.31(2)	0.74
Preoperative	19.50 $\pm$ 10.53		
Immediate postoperative	16.45 $\pm$ 6.68		
Two year follow-up	17.73 $\pm$ 8.40		
Proximal junctional kyphosis		4.17(2)	0.02
Preoperative	2.52 $\pm$ 3.78		
Immediate postoperative	4.27 $\pm$ 4.64		
Two year follow-up	6.67 $\pm$ 7.55		
Distal junctional kyphosis		5.06(2)	0.01
Preoperative	-8.20 $\pm$ 10.54		
Immediate postoperative	-2.10 $\pm$ 10.46		
Two year follow-up	-2.75 $\pm$ 11.77		

SD: Standard deviation; sample size n=24; F: Ratio of variance; df: Degree of freedom. The significance level ( $\alpha$ ) is  $<0.05$ .

preoperative, FE and two-year follow-up, ( $p=0.74$ ). In addition, there was no evidence of pseudoarthrosis, no loss of correction and no infection. We observed a significant difference in PJK between Preoperative (mean= $2.52\pm 3.78^\circ$ ) and two-year follow-up period (mean= $6.67\pm 7.55$ ) ( $p=0.02$ ). Distal junctional kyphosis improved and had a statistically significant mean difference between Preoperative (mean= $-8.2\pm 10.54^\circ$ ) and postoperative two years of follow-up (mean= $-2.75\pm 11.77$ ),  $p=0.01$  (Table I). Both PJK and DJK were  $<10^\circ$  in all patients at two-year follow-up.

## DISCUSSION

There is no consensus about the superiority of stainless steel or titanium instrumentation in AIS and the choice remains largely surgeon-dependent. Titanium spinal instrumentation is appealing due to its compatibility with MRI and CT imaging,<sup>[14]</sup> less corrosion,<sup>[17]</sup> reduced allergenicity<sup>[18]</sup> and fibrogenicity.<sup>[19]</sup> There is even some evidence about titanium inhibition of polymorphonucleocytes<sup>[20]</sup> and bacterial glycocalyx which may bestow resistance to infection. We conducted a prospective study to provide clinical data on the effectiveness and safety of titanium spinal instrumentation.

This study provides several findings of clinical relevance in orthopedic surgical practice. First, spine fusion with titanium instrumentation achieves and maintains thoracic, thoracolumbar curves (coronal plane) correction at two-year follow-up. Second, thoracic kyphosis (measured from T5-T12) is not worsened by titanium spinal instrumentation in AIS.

Whereas, to our knowledge there are no other prospective studies providing similar or contrasting evidence that have assessed the outcome of titanium instrumentation in AIS, our finding supports previous studies using other forms of instrumentation to achieve and maintain correction in AIS.<sup>[21]</sup> We have illustrated that titanium instrumentation maintains kyphosis. Our finding is remarkable and refutes previous findings that claim that spinal fusion with titanium instrumentation for AIS leads to unsatisfactory correction, loss of kyphosis or proximal screw pullout and tends to revert to its original shape.<sup>[13]</sup>

Proximal junctional kyphosis has been reported in AIS following posterior spinal fusion (PSF).<sup>[22]</sup> Lee et al.<sup>[23]</sup> observed PJK  $>10^\circ$  in 46% of the patients at a two-year follow-up after hook and rod instrumentation (who had  $>5^\circ$  preoperative one-level junctional kyphosis). Rhee et al.<sup>[24]</sup> reported PJK  $>10^\circ$  in 35% of the AIS patients following PSF. In a recent study Glattes et al.<sup>[22]</sup> observed PJK in 26% of the patients in a 7.3 year follow-up and noted that the average proximal junctional

angle increased  $15.2^\circ$  in the first two-year follow-up. In our study population, we had a mean of  $2.5^\circ$  PJK in the Preoperative and  $6.7^\circ$  at two-year follow-up. None of the patients in our study had a PJK  $>10^\circ$  in two years follow-up. Based on our results, PSF with titanium instrumentation did not worsen PJK.

Distal junctional kyphosis was defined as the angle  $>10^\circ$  between the superior endplate of the lowest instrumented vertebra and the inferior endplate of the adjacent distal vertebra.<sup>[25]</sup> Lowe et al.<sup>[25]</sup> reported DJK with an incidence of 14.7% following PSF in AIS. Richards et al.<sup>[26]</sup> noted DJK in 30% of patients with AIS following PSF with Cotrel-Dubousset instrumentation. There were no patients with DJK  $>10^\circ$  at the end of two-years follow-up and DJK improved from a mean of 8.2 to mean of 2.75 in our study.

Mueller and Gluch<sup>[16]</sup> reported the safety and efficacy of titanium in a retrospective study with long term follow-up (range 8 to 12 years). They reported a 57% correction rate for thoracic curves in the postoperative period while 78.9% correction was achieved in our study. They had a 50.3% correction in their last follow-up (range 8-12 years), while our final correction rate was 73.7% (2 years). According to this study two out of 50 patients had pseudoarthrosis and seven had revision surgeries. Data related to PJK or DJK were missing in their study<sup>[16]</sup> in contrast to ours. In addition, we did not have any infection (acute/late), implant failure, loss of correction, pseudoarthrosis or revision surgery.

Despite the strength of this repeated measure prospective design, which eliminates between-subject variability in terms of the prognostic factors, there are some limitations. First, there are possibilities of potential selection, measurement and misclassification biases. However, this is unlikely since we performed validity checks on data sources prior to the data editing/cleaning for this study. Second, it is possible as in most studies that our results may be influenced by unmeasured confounding variables.

In conclusion, posterior titanium instrumentation in AIS achieved a satisfactory correction. In addition, there were no major complications like infection, pseudoarthrosis, or increase in PJK and DJK.

## Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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