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Effect of Sagittal Plane Deformity of the Lumbar Spine on Epidural Fibrosis Formation After Laminectomy

An Experimental Study in the Rat

Cengiz Cabukoğlu, MD,* Osman Güven, MD,† Yakup Yildirim, MD,‡ Hasan Kara, MD,* and Saime Sezgin Ramadan, MD§

Study Design. An animal model of postlaminectomy lumbar column sagittal plane deformity was designed in rats.

Objectives. To analyze the effect of lumbar column deformity (lordosis and kyphosis) on postlaminectomy epidural fibrosis formation.

Summary of Background Data. Incidence of peridural fibrosis formation after lumbar spinal surgery is considerably high. Instability and sagittal plane deformity of the lumbar spine has been implicated (not proven) as the factors for the development of epidural fibrosis. The effect of traction (kyphosis) or relaxation (lordosis) of the lumbar spine on epidural fibrosis formation is not known.

Methods. L4 laminectomies were performed in 30 rats. Three equal groups were formed. In the control group (group I), only laminectomy was performed. In other groups after laminectomy, lumbar lordosis (group II) and kyphosis (group III) was maintained with steel implants. The scar formation was evaluated both histologically and histomorphometrically on the 12th postoperative week.

Results. Kyphosis developed in group I. The mean amount of peridural scar tissue was significantly more evident in groups I and III than the lordosis group. The extent of adherence to the dura mater and the nerve roots was most apparent in group III.

Conclusions. Kyphosis and consequent traction of the lumbar spine is one of the causes for increased epidural fibrosis formation after laminectomy. On the contrary, establishment of lordosis and relaxation of the lumbar spine decreased the scar tissue formation in rats.

Key words: laminectomy, kyphosis, lordosis, epidural fibrosis. **Spine 2004;29:2242–2247**

Postoperative epidural fibrosis is a common occurrence after lumbar spinal surgery and is one of the most challenging problems to the surgeon. Although it is defined as a normal postsurgical biologic response,[1,2] epidural fibrosis is 1 of the major contributing factor in suboptimal patient outcome.[3–5]

Key and Ford were the first who defined the formation of epidural fibrosis after lumbar laminectomy and theorized the annulus fibrosis as the source of the scar tissue.[6] LaRocca and McNab have shown that epidural fibrosis originates from the paravertebral musculature and described it as "laminectomy membrane."[7]

Numerous materials and methods have been investigated to prevent epidural fibrosis formation after spinal surgery[3,8–13]; however, the concerns about the etiology take much less attention. A variety of causes for the development of extradural fibrosis have been suggested, including retained surgical swab debris,[14] compression of epidural veins,[15] surgical manipulation, bleeding,[16]and defective fibrinolysis.[17] Although instability and sagittal plane deformity of the lumbar spine has been implicated as the cause of epidural fibrosis,[17–20] the relation was not thoroughly investigated in the literature.

In the current study, the effect of lumbar instability and sagittal plane position of the lumbar spine (ie, kyphosis or lordosis) on the constitution of epidural fibrosis was investigated in rats.

Materials and Methods

Animals. Thirty female Sprague-Dawley rats, aged 7 months, weighing an average of 280 g, were used in the experiment.

Operative Procedure. Before the operative procedure, lateral radiographs of the lumbar spine were taken after the animals were anesthetized with a mixture of 35 mg/kg ketamine and 5 mg/kg xylazine hydrochloride administered intraperitoneally, Each animal underwent bilateral L4 laminectomy.

The lumbar area of the rat was shaved with a standard animal clipper. The operative field was then prepared in a sterile manner using povidone–iodine solution. The operative site was then draped in a standard fashion. A midline longitudinal incision was made down to the spinous process.

The paraspinous muscles were stripped away from the lamina and spinous process. The muscles were retracted bilaterally with retractors. The L4 lamina was identified by counting up from the sacrum. Complete bilateral L4 laminectomy was performed, including excision of the spinous process of L4 and ligamentum flavum, supraspinous and interspinous ligaments of L3–L4 and L4–L5. The underlying dura was exposed but not opened. Hemostasis was obtained with a bipolar electrocautery.

Groups. The rats were divided into 3 equal groups. In group I (control group), only L4 laminectomy was performed. In group

From the *Department of Orthopaedic Surgery, Pendik Şifa Hospital, Istanbul, Turkey; †Department of Orthopaedics, Marmara University School of Medicine, Istanbul, Turkey; ‡Department of Orthopaedic Surgery, Acıbadem Hospital, Istanbul, Turkey; and §Department of Pathology, Marmara University School of Medicine, Istanbul, Turkey.
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Address correspondence and reprint requests to Yakup Yildirim, MD, Acibadem Hastanesi Bagdat Caddesi Plk. Bagdat Cad. 347/7-8 Erenkoy 81070 Istanbul, Turkey; E-mail: yakup_69@hotmail.com or cengizcab@hotmail.com

Figure 1. Formation of lumbar lordosis with tightened steel wire.

II (lordosis group), after L4 laminectomy, a steel wire was passed through the spinous processes of the L3 and L5, and it was tightened to compress the spinous processes up to decrease the distance approximately to 0.5 cm in between. This procedure shortened the posterior spinal column leading to lordosis of the involved region of the lumbar spine (Figure 1). In group III (kyphosis group), after laminectomy, a specially designed standard stainless steel implant was inserted between the spinous processes of L3 and L5 for distraction. This procedure lengthened the posterior spinal column leading to kyphosis of the involved region of the lumbar spine (Figure 2).

The wounds were closed in an anatomic fashion using interrupted 3–0 Vicryl sutures to close the fascia and subcutaneous layers and by running 3–0 Dexon sutures in the subcuticular layer. The early postoperative lateral radiographs of the lumbar spine were obtained while the animals were still under anesthesia.

Radiologic Evaluation. Measurement of the radiographic lateral lumbar angles was obtained from the superior end plate of L3 and the inferior end plate of L5 using Cobb's method.[21] Kyphotic angles were assigned positive values (Figure 3), and lordotic angles were assigned negative values (Figure 4).

Figure 2. Establishment of lumbar kyphosis with a specially designed implant.

Figure 3. Measurement of the kyphosis angle from the radiograph.

Histologic Examination. The animals were killed 12 weeks after the surgery with a concentrated solution of pentobarbital, and lateral radiographs of the lumbar spine were obtained immediately. The lumbar spine with paravertebral muscles were excised *en bloc* for histologic and histomorphometric studies after removal of the hardware.

All fixation and dehydration procedures were performed at room temperature. The lumbar spine with intrinsic musculature was placed in buffered formaldehyde for 3 days. It was later placed in hydrochloric acid for 3 days for decalcification. The L4 level was sewn and the entire laminectomy site removed without damage. This block was isolated for further decalcification for 4 days. Eight axial sections with a thickness of 4 m were prepared for each laminectomy site and stained with hematoxylin and eosin (H&E) and Masson's trichrome. All sections were examined by a light microscope (Olympus BX-50). Histologic analysis consisted of subjective evaluation of the extent of fibrous tissue, the relation of the scar tissue with the dura mater, nerve roots, and the regeneration of bone at the laminectomy site.

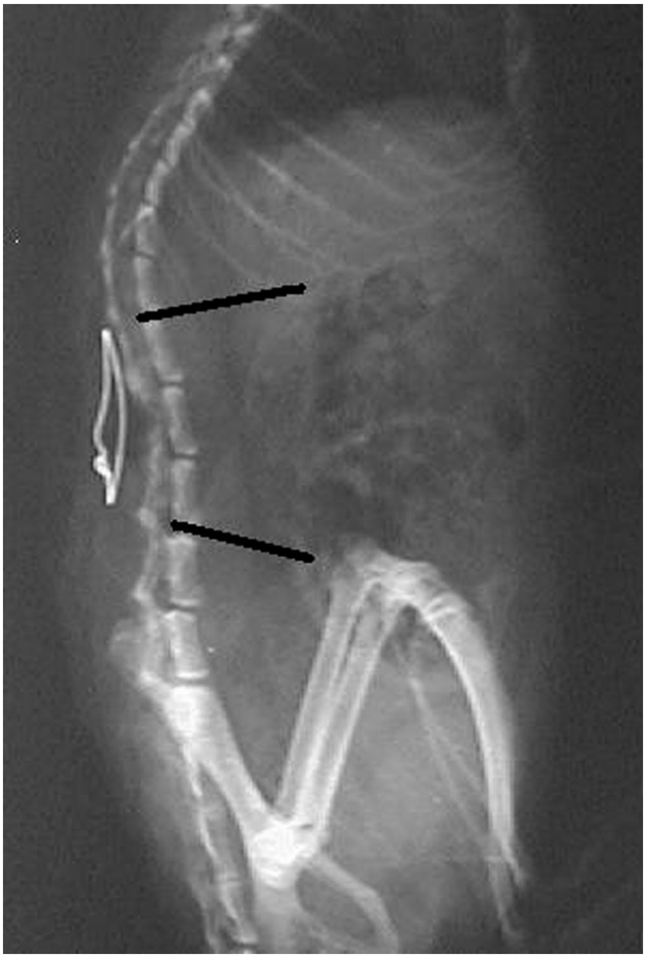

Figure 4. Measurement of the lordosis angle from the radiograph.

Histomorphometry. Histomorphometric measurements were done using a personal computer (Intel Pentium MMX 223 MHz, Matrox Meteor vision card). A Zeiss Vision KS400 version 3.0 analysis program was used for the entire histomorphometric evaluation. The macros necessary for the evaluation were prepared from standard 3 × 2-mm templates. The template was placed so that the 3-mm inferior edge was passing tangent to the inner site of the dura mater ventrally. The line that was crossing perpendicular to the midline of the dura mater was also passing through the midline of the template's 3-mm edge (Figure 5). The ratio of fibrosis was calculated from 3 × 2-mm areas. The mean of the 8 axial fields was considered

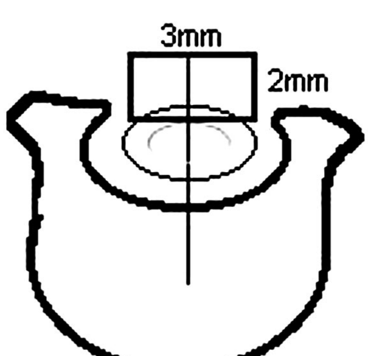

Figure 5. The ratio of fibrosis was calculated from a 3 × 2-mm area.

Table 1. The Average Lateral Lumbar Angles

	Group I	Group II	Group III	*P*
Preoperative	−1.9°	−1.7°	−1.8°	*NS*
Early postoperative	−1.9°	−11.4°	19°	<0.0001
Late postoperative	12.8°	−10.8°	19.2°	<0.001

NS = not significant.

the fibrosis ratio result for each rat and was expressed in percentage numbers.

Preoperative, early postoperative, and late postoperative radiologic lumbar lateral angle values were compared with each other in groups and also between each surgical group by using the paired *t* test.

Comparison of fibrous tissue percentage among the laminectomy, laminectomy lordosis, and laminectomy kyphosis groups was analyzed by analysis of variance. If a significant difference ($P < 0.05$) was found, the groups were compared by Tukey-Kramer multiple comparison test.

■ Results

Two rats from group II and 1 rat from group III were excluded from the study as a result of radiologically defined implant loosening and insufficiency. Also, 1 rat from group I was not included, because some of the prepared histologic specimens were not passing through the laminectomy site.

Radiographic Evaluation

The average preoperative lateral lumbar angle was -1.9^0 in group I, -1.7^0 in group II, and -1.8^0 in group III. The difference was not statistically significant (Table 1).

The average early postoperative lateral lumbar angle was -1.9^0 in group I, -11.4^0 in group II, and $+19^0$ in group III. The difference was statistically significant between the groups ($P < 0.0001$).

The average late postoperative lumbar angle was $+12.8^0$ in group I, -10.8^0 in group II, and $+19.2^0$ in group III. The late postoperative values were statistically significant between the groups ($P < 0.01$).

Comparison of the average early postoperative and late postoperative values for group I were statistically significant ($P < 0.001$); however, statistical significance was not defined for groups II and III.

Histology

In group I, a fibrous tissue layer that had developed at the laminectomy site was identified in all of the specimens. The collagen fibers in this tissue were predominantly parallel to the dura mater, but in some sections, the fibers lay in other directions, especially into the paravertebral musculature (Figure 6). In some specimens, the nerve roots were wrapped by fibrous tissue. In some parts, the laminectomy site had been partially closed by new bone formation, which did not affect the presence of fibrous tissue dorsal to the dura mater.

In group II, although formation of epidural fibrous tissue is obvious, it is more demarcated than group I. The amount of the fibrous tissue was denser in 2 of the spec-

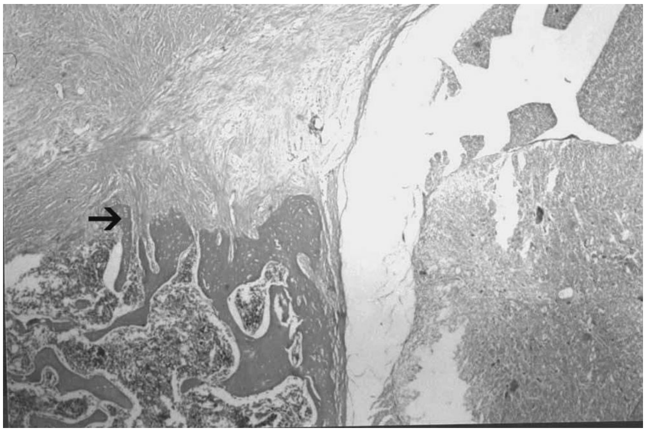

Figure 6. Extension of fibrosis into the paravertebral muscles (Masson's trichrome; magnification, ×20).

imens. No case of nerve entrapment by fibrosis was observed. In 1 specimen, massive infiltration of lenfoplasmocyte was detected. Bone regeneration to some extent was seen in all cases (Figure 7).

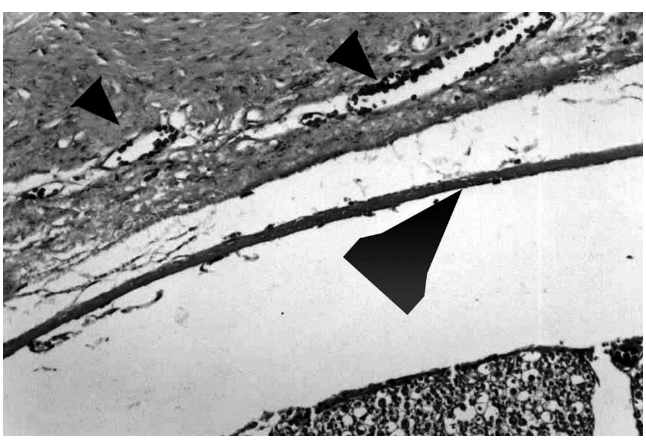

Figure 7. New bone formation is apparent within the fibrosis (small arrowheads) over the dura mater (big arrowhead) (Masson's trichrome; magnification, ×40).

Table 2. The Amount of Epidural Fibrosis Formation

	Group I	Group II	Group III
Minimum	51.15	40.00	71.20
Maximum	83.15	63.40	85.44
Mean	69.92	50.95	77.14
Standard deviation	9.33	7.73	5.13

The values are in percentage numbers. Comparison of group I and III (not significant), whereas group II is significantly different from both of them ($P <$ 0.001).

In group III, a very dense fibrous tissue layer had developed in all of the specimens (Figure 8). Massive scar tissue was sited on the laminectomy defect and adherent to dura mater. The extent of adherence was extensive. The fibrosis was progressing into the paravertebral muscles and the nerve roots. Nerve root entrapment by fibrosis was prominent in all of the specimens. Lenfoplasmocyte infiltration was apparent in 1 specimen. New bone formation was detected to some degree.

Histomorphometric Evaluation

Considering all the slides together, the mean percentage of scar tissue was 69.9% in group I, 50.9% in group II, and 77.1% in group III (Table 2).

There was no statistically significant difference between group I and III; however, group II is significantly different from both of them regarding percentage of fibrous tissue formation ($P <0.001$).

Discussion

Traction of the nerve roots and dura mater resulting from the encircling epidural fibrosis is well documented[16,22–24]; on the contrary, the consequence of traction of the lumbar spine on formation of epidural fibrosis is yet to be defined.

Many factors, including instability of the lumbar spine and dependent sagittal plane deformity, has been implicated in the etiology of the perineural fibrosis.[17–20]

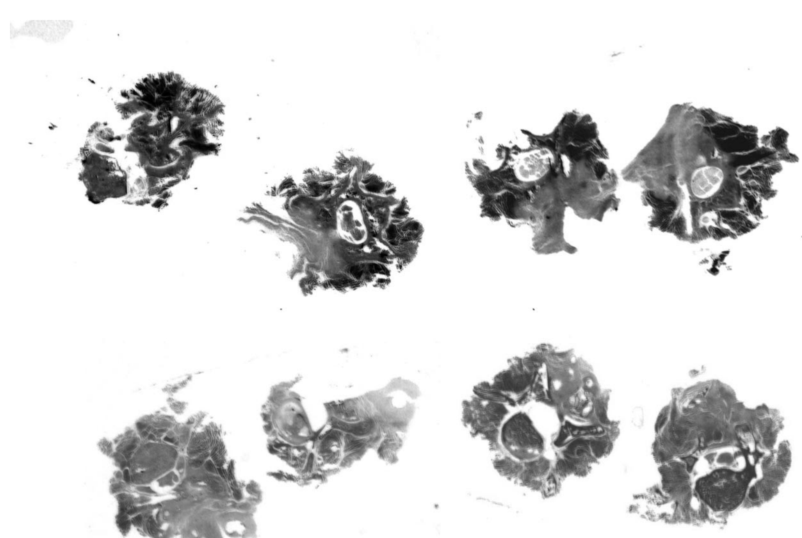

Figure 8. Macroscopic cross-sectional appearance of extensive fibrosis formation in kyphosis (group III) (Masson's trichrome).

However, an examination of the literature reveals that instability and deformity of the lumbar spine is more often presumed than proven for the formation of epidural fibrosis.

In the current study, epidural fibrosis formation was investigated in laminectomy, laminectomy lordosis, and laminectomy kyphosis groups on a rat model. Laminectomy was preferred as the surgical model because it is one of the most common lumbar spinal procedures. Peridural scar formation, instability, and failed back syndromes with kyphosis are the main problems with this procedure.[25–27]

Epidural fibrosis formation was more evident both histologically and histomorphometrically in group I and group III in which kyphosis developed. The amount of scar tissue was significantly less in the lordosis group. In the kyphosis group, heavy scar formation, including thick dural adhesions associated with nerve root entrapment in all of the cases, have indicated the severity of the epidural fibrosis formation. The extent and density of the fibrous tissue formation was less in the lordosis group. The formed scar tissue was more organized and the intensity was decreased so that no nerve root was compressed by the fibrous tissue. New bone formation at the laminectomy site was present in all of the groups. Although adult humans do not regenerate bone except over small defects,[28] regeneration of bone across the laminectomy defect is common for small animals.[29,30]

Increased scar tissue formation in lumbar kyphosis may be directly related to mechanical stretching of the nerves and the surrounding tissues that stimulates fibrosis formation or indirectly related to compression of the epidural circulation, which leads to increased pressure and secondary development of epidural fibrosis.[31] Similar findings were reported for peripheral nerves in which traction and ischemia were defined as the causes of thickening of the fibrous elements of the nerves.[32] Contradictory to kyphosis, decreased epidural fibrosis formation in the lordosis group (group II) is presumably related to the prevention of cord tethering by shortening the posterior column. This finding is in accordance with the clinical study of Güven *et al.*[33] in which restoration of the physiological lordosis and concomitant relaxation of the cord resulted in good functional outcome in patients with epidural fibrosis.

Development of lumbar kyphosis in group I is an expected but interesting progression. Unlike the human lumbar spine, the lumbar region of the rats have minimal lordosis. The quadrupedal stance of the rat loads the posterior elements and paraspinal musculature of the lumbar spine more than the upright human as a result of bending moment.[34] Laminectomy and sectioning of the posterior elements weakened the load-bearing posterior part of the lumbar spine, which led to progressive kyphosis in rats.

In this study, although the subjective histologic findings were defined, we mainly relied on objective histomorphometric parameters. The histomorphometric fibrosis percentage was measured as the average of 8 slices because the amount of fibrosis cannot be evaluated accurately using only 1 section per animal.[16]

Evaluation of postlaminectomy fibrosis in rats was present in other studies and found to be reproducible.[10,11] However, the results observed in animal models should be applied with caution to humans. The main difference is that the rat is a continuously growing mammal with a readily healing process, which may be an explanation for new bone formation over the laminectomy site. Despite the limitations in the use of animal models, the difficulties of studying postlaminectomy scar formation in the human requires the use of such models before clinical trials.[10]

In conclusion, kyphosis was found as a factor for increased formation of epidural fibrosis. Contradictory to kyphosis, establishment of lordosis with the accompanying relaxation and stabilization of the lumbar spine decreased peridural scar tissue formation in the rat model. In clinical settings, although rat data are different from human data, when extensive or multilevel laminectomy should be performed, special attention must be paid to instability and the dependent loss of lumbar lordosis. Prevention of spinal instability and maintenance of physiological lordosis are important factors in the prevention of epidural fibrosis. By providing these conditions, better long-term results with low recurrent pain and revision surgery may be possible after spinal surgery.

■ Key Points

- Establishment of lumbar lordosis decreased epidural fibrosis formation.
- On the contrary, kyphosis increased this process.

References

1. DiFazio FA, Nichols JB, Pope MH, et al. The use of expanded polytetrafluoroethylene as an interpositional membrane after lumbar laminectomy. *Spine* 1995;20:986–91.
2. Greenwood JJR, McGuire TH, Kimbell F. Study of causes of failure in herniated intervertebral disc operation: analysis of 67 reoperated cases. *J Neurosurg* 1952;9:15–20.
3. Jacobs RR, McClain O, Neff J. Control of postlaminectomy scar formation. An experimental and clinical study. *Spine* 1980;5:223–9.
4. Keller JT, Dunsker SB, McWhorter JM, et al. The fate of autogenous grafts to the spinal dura. *J Neurosurg* 1978;49:412–8.
5. Yong-Hing K, Reilly J, Korompany V, et al. Prevention of nerve root adhesions after laminectomy. *Spine* 1980;5:59–64.
6. Key JA, Ford LT. Experimental intervertebral-disc lesions. *J Bone Joint Surg [Am]* 1948;30:621–30.
7. LaRocca H, Macnab I. The laminectomy membrane. *J Bone Joint Surg [Br]* 1974;56:545–50.
8. Abitbol JJ, Lincoln TL, Lind BI, et al. Preventing postlaminectomy adhesion: a new experimental model. *Spine* 1994;19:1809–14.
9. Barbera J, Gonzalez J, Esquerdo J, et al. Prophylaxis of the laminectomy membrane: an experimental study in dogs. *J Neurosurg* 1978;49:419–24.
10. He Y, Revel M, Loty B. A quantitative model of post-laminectomy scar formation. Effects of a nonsteroidal anti-inflammatory drug. *Spine* 1995;20: 557–63; discussion 79–80.
11. Hinton JL, Warejcka DJ, Mei Y, et al. Inhibition of epidural scar formation after lumbar laminectomy in the rat. *Spine* 1995;20:564–70; discussion 79–80.
12. Langenskiold A, Kiviluoto O. Prevention of epidural scar formation after operations on the lumbar spine by means of free fat transplants; a preliminary report. *Clin Orthop* 1976;115:92–5.

13. Quist JJ, Dhert WJA, Meij BP, et al. The prevention of peridural adhesions. A comparative long-term histomorphometric study using a biodegradable barrier and a fat graft. *J Bone Joint Surg [Br]* 1998;80:520–6.
14. Hoyland JA, Freemont AJ, Denton J. Retained surgical swab debris in post-laminectomy arachnoiditis and peridural fibrosis. *J Bone Joint Surg [Br]* 1988;70:659–62.
15. Jayson MIV. The role of vascular damage and fibrosis in the pathogenesis of nerve root damage. *Clin Orthop* 1992;279:40–8.
16. Fritsch EW, Heisel J, Rupp S. The failed back surgery syndrome. Reasons, intraoperative findings, and long-term results: a report of 182 operative treatments. *Spine* 1996;21:626–33.
17. Cooper RG, Mitchell WS, Illington KJ, et al. The role of epidural fibrosis and defective fibrinolysis in the persistence of postlaminectomy back pain. *Spine* 1991;16:1044–8.
18. Barr JS. Low-back and sciatic pain. *J Bone Joint Surg [Am]* 1951;33:633–49.
19. Benini A. Lumbar discectomy without or with spinal fusion? Revival of an old dilemma. *Z Orthop* 1989;127:276–85.
20. Walker N, Schreiber A. Diagnose und therapie des engen lumbalen spinalkanals. *Orthopade* 1985;14:122–32.
21. Cobb JR. Outline for the study of scoliosis. *AAOS Instr Course Lect* 1948; 5:261.
22. Benoist M, Ficat C, Baraf P, et al. Post-operative lumbar epiduro-arachnoiditis: diagnosis and therapeutic aspects. *Spine* 1980;5:432–6.
23. Burton CV, Kirkaldy-Willis WH, Yong-Hing K, et al. Causes of failure of surgery on the lumbar spine. *Clin Orthop* 1981;157:191–9.
24. Gabriel EM, Friedman AH. The failed back surgery syndrome. In: Wilkins RH, Rengachary SS, eds. *Neurosurgery*. New York: McGraw-Hill; 1996: 3863–70.
25. Kostuik JP, Errico TJ, Gleason TF. Techniques of internal fixation for degenerative conditions of lumbar spine. *Clin Orthop* 1986;203:219–31.
26. Lehmer SM, Keppler L, Biscup RS, et al. Posterior transvertebral osteotomy for adult thoracolumbar kyphosis. *Spine* 1994;19:2060–7.
27. Yucesoy K, Ozer K. Inverse laminoplasty for the treatment of lumbar spinal stenosis. *Spine* 2002;27:E316–20.
28. Lawson KJ, Malycky JL, Berry JL, et al. Lamina repair and replacement to control laminectomy membrane formation in dogs. *Spine* 1991;16(suppl 6):222–6.
29. Boot DA, Hughes SPF. The prevention of adhesions after laminectomy. Adverse results of Zenoderm implantations into laminectomy sites in rabbits. *Clin Orthop* 1987;215:296–302.
30. Robertson JT, Meric AL, Dohan CF Jr, et al. The reduction of postlaminectomy peridural fibrosis in rabbits by a carbohydrate polymer. *J Neurosurg* 1993;79:89–95.
31. Hoyland JA, Freemont AJ, Jayson MIV. Intervertebral foramen venous obstruction. A cause of periradicular fibrosis? *Spine* 1989;14:558–68.
32. Sakurai M, Miyasaka Y. Neural fibrosis and the effect of neurolysis. *J Bone Joint Surg [Br]* 1986;68:483–8.
33. Guven O, Bezer M, Gokkus K, et al. Transpedicular decancellation osteotomy in the treatment of peridural fibrosis. *Arch Orthop Trauma Surg* 2001; 121:517–20.
34. Fields MJ, Hoshijima K, Alexander HP, et al. A biomechanical, radiologic and clinical comparison of outcome after multilevel cervical laminectomy or laminoplasty in the rabbit. *Spine* 2000;25:2925–31.