

Letters to the Editor

e Osteopontin Induces the Extension of Epidural Fibrosis into the Spinal Canal

TO THE EDITOR:

We read with great interest the recent article by Paulo Pereira and colleagues (1).

In the study, 24 patients with typical symptoms of persistent or recurrent low back and/or leg pain after lumbar spine surgery were reported to have osteopontin (OPN) and an absence of beta3-tubulin. Thus, the study proved an epidural scar does not contain nociceptive fibers that could explain the source of pain associated with epidural fibrosis.

As the authors stated, the limitation of the study was an unavailable control group. In the present letter,

related research on rats was undertaken for breaking this limitation.

We have been focusing on epidural fibrosis (EF). Some interventions were tried out, and a certain level of success was achieved (2-4). Being similar with the authors' experience, OPN came into our view since 2011 (5). And to investigate the association between OPN and EF, the following research, which could be a supplement for Paulo Pereira and colleagues, was designed.

As shown in Fig. 1, 15 healthy adult female Wistar

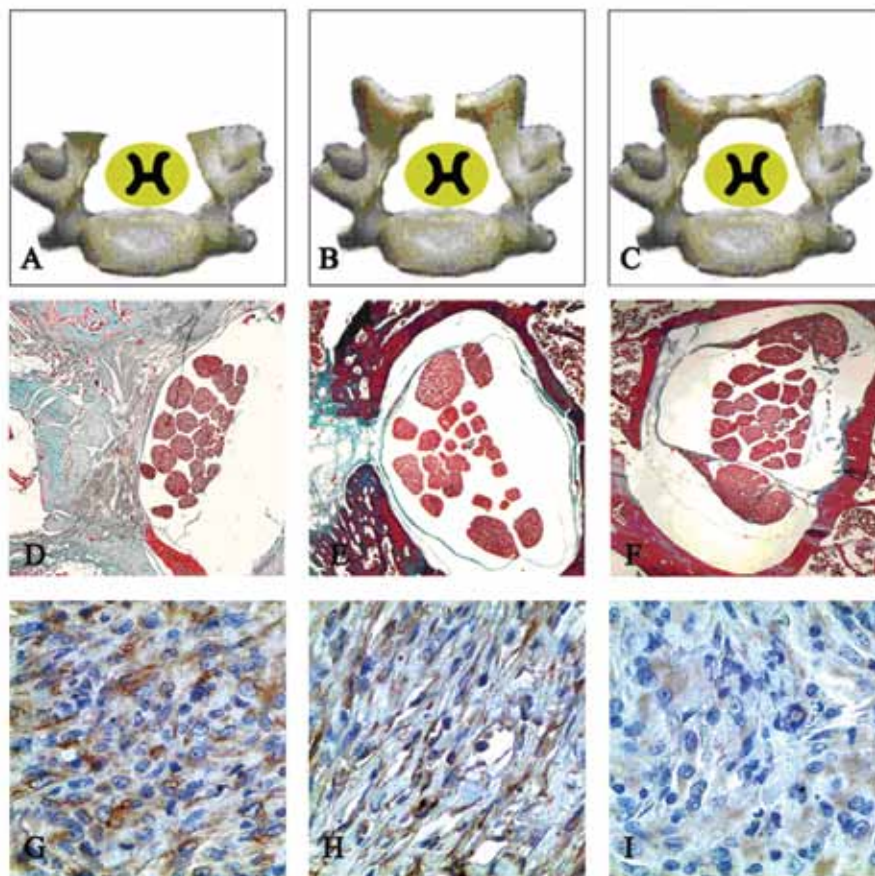


Fig. 1. A-C: Modeling of laminectomy rats in 3 groups. D-F: Masson's trichrome staining of L1 on post-operative 6 week. G-I: osteopontin immunohistochemistry evaluation of epidural scar tissue (D-F, G-I original magnification 40 \times and 100 \times , respectively).

Table 1. Rydell classification.

Group	Grade			
	0	1	2	3
1	0	0	0	5
2	5	0	0	0
3	5	0	0	0

rats (mean weight 220g) were randomly divided into 3 groups (5 rats per group). Group 1: total L1 laminectomy; Group 2: perforation at the L1 level with a micro-drill; Group 3: removal of the spinous process with a rongeur. Six weeks post laminectomy, Rydell classification, Masson's trichrome and OPN immunohistochemistry were performed.

As shown in Table 1, Rydell classification showed no significant difference between group 2 and group 3. Still, during the operation we found the hiatus was filled with scar tissue, and some light scar tissue extended into the spinal canal (Fig. 1 E). As shown in Fig. 1 (G, H and I), first of all, a similar result that the OPN was detectable in epidural scar tissue was gained. At the same time, for the condition of groups 2 and 3, the expressional levels of OPN was significantly lower than group 1. The expressional level in group 3 was significantly lower than group 2.

Combined with both Paulo Pereira and colleagues' research and the previous report (4), we hypothesized that OPN, as the major player in the formation of EF, also promotes the extension of epidural fibrotic tissue into the spinal canal. How OPN links adhesion between epidural scars and dorsal root ganglions (DRG) is unclear. Thus, this may explain some if not all of the possible mechanisms that make EF related to persistent or recurrent low back and/or leg pain after lumbar spine surgery. We think we have answered the question Paulo Pereira and colleagues raised in the end of their discussion. OPN could be a good target for preventing and/or treating EF. Undoubtedly, further research will be carried out in the future.

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Conflict of Interests

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In Response

We deeply appreciate the interest in our article (1) and the comments related to it. We would also like to highlight the extensive and important research carried out by the authors of this letter on epidural fibrosis and on designing strategies to prevent it [2-4].

In the experiment reported in this letter to the editor, the authors found that the epidural scar tissue was firmly adherent to the dura mater on rats that underwent laminectomy, whereas no adherence between the epidural scar tissue and the dura mater was present on animals whose lamina was left intact or perforated with a micro-drill. Moreover, the authors pointed out that the expression of osteopontin (OPN) in the epidural scar tissue was significantly decreased on specimens with intact laminae in comparison to the laminectomy ones and reached an intermediate level on specimens with a perforated lamina.

While we find these results highly relevant, we would be very pleased to have the opportunity to analyze them in a structured article, since a full explanation of the methods and discussion of the results are beyond

the scope of a short report, such as a letter to the editor. In particular, detailed descriptions of the histological sections and the exact location where the epidural scar tissue was collected on rats with intact laminae would certainly be relevant information for the reader.

Our article [1] documented, for the first time, the expression of OPN in human postoperative epidural scar tissue. Animal experiments, such as the one described by the authors of the present letter, offer an irreplaceable opportunity to control for confounding factors and to test strategies drawn to counteract the tethering effect of epidural fibrosis on the neural structures. Hopefully, further research will greatly enhance the scientific knowledge on this matter.

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Cost-Benefit of Vertebral Augmentation: How to Assess the Benefit

LETTER TO THE EDITOR:

We read the article "Vertebral augmentation versus conservative therapy for emergently admitted vertebral compression deformities: An economic analysis" (Pain Physician 2013; 16:441-445) (1) with great interest. The authors compared 39 inpatients who had undergone vertebral augmentation (VA) with 209 medically treated patients. The authors found that daily cost was the same between the VA and medically managed groups. The results showed a tendency of lower 30-days readmission rate in VA group without statistical significance. The authors drew the conclusion that VA could be a cost-effective treatment for inpatients with painful osteoporotic vertebral fractures (OVFs). However, as an average hospital stay was longer in the VA group than that in the medically treated group, total cost was significantly higher in the VA group in this research.

To further assess the cost-benefit of VA, we repeated their research methods in our inpatients with OVFs admitted last year (Jan 1, 2013 to Sep 31, 2013). The results are shown in Tables 1 and 2.

In this series, we performed a questionnaire about satisfaction with treatment outcome. Three questions were included:

1. Are you satisfied with the outcome?
2. Did you know that vertebral augmentation costs about thirty thousands yuan per patient, while the medical management costs about four thousands yuan per patient?
3. Now you know the cost of both treatments. If you could choose again, which one is your choice, vertebral augmentation or medical management? (Table 3)

In our series, there was no statistical difference in demographic data between both groups. Case mix index, length of stay, readmission rate and home discharge were similar in both groups. VA showed a significantly higher total cost and daily cost ($P < 0.001$). This was caused mainly by the high cost of surgical instruments and low charge for labor under our medical care system. A set of instruments for a single level VA demands about 21,000 CNY (\$3,360 USD), while doctors' daily visit was free and daily room fee is up to 120 CNY (\$20 USD).

The results also showed a higher satisfaction rate in the VA group (84.1% vs 55.6%). The results indicated that 93.2% of patients (41/44) undergoing VA considered the cost was worthy, while about one-third of patients (6/18) originally receiving medical treatment would prefer to spend more money for the possibility of better outcomes.

Although the cost of VA was much higher under our medical care system, we still considered that VA should be a first-line treatment for patients with painful OVFs, especially severely disabled patients. VA has a good result of pain relief, which has been proven by

Table . Demographic Data.

	VA	Medical Management
Number of Patients	44	18
Average Age	77.8	76.4
Men/Women	7/37	7/11
Case Mix Index*	1.1	1.5

*Case Mix Index: comorbidities per patient

Table 2. Comparison of VA and medically managed patients.

	VA	Medical Management	P-Value
Length of stay (days)	3.6	2.8	P=0.19
Total Cost (CNY/USD)*	30,455/4872.8	4,307/689.1	P<0.001
Cost/Day (CNY/USD)*	10,305/1648.8	1,337/213.9	P<0.001
Readmission Rate (>60 days follow-up)	0	6%(1/18)	P=0.29
Home Discharge	91%	83%	P=0.40

*CNY: Chinese Yuan. USD: United States Dollar.

Table 3. Analysis of satisfaction with outcome.

	VA	Medical Management	P-Value
Q1(Yes/No)	37/7	10/8	P<0.05
Q2(Yes/No)	44/0	11/7	P<0.01
Q3 (Same choice/Changed choice)	41/3	12/6	P<0.01

many studies. More importantly, patients undergoing VA have a better quality of life (2-4). A meta-analysis published in 2013 showed strong evidence that cement augmentation had better outcomes than nonoperative or sham treatments (5). More specifically, functional outcome and health-related quality of life was significantly in favor of vertebroplasty (5). These high-level studies suggest that vertebroplasty might be a cost-effective treatment all over the world, even under different cost structures in different areas.

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In Response

Thank you for providing us the opportunity to respond to the letter by Dr. Zhang discussing further ways to evaluate the cost-benefit of vertebral augmentation within the hospital inpatient population. Proving the cost-benefit of vertebral augmentation (VA) in this particular group of patients can be challenging as the majority of the costs are incurred during their hospitalization and the majority of the benefits are likely accumulated over the longer term through lower readmission rates, higher rates of home discharge, and a higher functional quality of life. As was the case in our study, multiple factors can complicate this analysis including delayed identification of inpatients who may benefit from VA, multiple medical comorbidities, and discharge planning issues delaying care. We applaud the continued efforts by Dr. Zhang and others who continue to study this issue. If VA is in fact cost-effective and beneficial to inpatients with vertebral compression fractures, it should be considered a first-line treatment, rather than a salvage therapy when medical treatment has failed.

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