Neurosurgical forum

Letters to the editor

Lumbar interbody fusion

TO THE EDITOR: The undersigned authors have questioned the reported data in the study submitted by Marchi et al.³ (Marchi L, Oliveira L, Coutinho E, et al: Results and complications after 2-level axial lumbar interbody fusion with a minimum 2-year follow-up. Clinical article. *J Neurosurg Spine* 17:187–192, September 2012), as we were involved in the adjuvant evaluation of Dr. Pimenta's initial patient series. Given the excellent results that Dr. Pimenta and coauthors presented at several meetings in 2008, with 100% fusion rates in the first 10 patients, it is not mathematically possible to achieve the results reported in this new article, even if treatment fails in every other patient (Pimenta L, Pesantez C, Oliveira L, et al., presentations to the AANS/CNS Annual Meeting and the Spine Arthroplasty Society, 2008).⁴

Because of these concerns, we revisited the data collected independently on what we believe to be the first 19 of the 27 patients reported by Marchi et al. The study data presented in this letter were collected in July of 2008 as an outside, independent review of the clinical and radiographic data submitted by Dr. Pimenta on his prospective, nonrandomized study of 19 patients treated with a 2-level presacral axial lumbar interbody fusion (AxiaLIF) implant supplemented with posterior fixation, intended for regulatory submission.

Methods. The clinical data, plain radiographs, and multiplanar CT scans were submitted to each author in a blinded and independent fashion. Following our individual review, each case was then reviewed collectively over a 2-day period. There was consensus of our findings in all but one case, which was considered a minor difference in findings.

Results. At the 6-month follow-up, 4 of 19 subjects demonstrated radiolucencies. Included among these were the patients in Cases 4 and 17, who are considered study outliers. The patient in Case 4, an 85-year-old woman had dislodged her S-1 pedicle screws following multiple documented falls. Significant radiolucencies were noted around the axial rod and the pedicle screws during revision surgery at 14 months. The patient in Case 17 had extensive osteolysis within the L-3 and L-4 vertebral bodies with perforation of the superior endplate of L-4. This was thought to be the result of infection or other pathological process. A sedimentation rate and white cell count were reported as normal. It was unknown to the reviewers if bone morphogenetic protein was used. At 6 months, the patients in Cases 15 and 16 exhibited minor radiolucencies of 1 mm or less at the tip of the axial rod at L-4. The patient in Case 15 had fusion at both levels. The patient in Case 16, a 287-lb man with a body mass index of 37.2 had a nonunion at L4–5 with a solid fusion at L5–S1.

At 12 months, 4 of 14 patients (Cases 10, 11, 14, and 16) had radiolucencies (29%) around the axial rod. These radiolucencies were less than or equal to 1 mm in diameter and were observed along the L-4 portion of the rod. The patient in Case 11 underwent removal of pedicle screws to address complaints of pain after the 6-month follow-up. This may have contributed to the radiolucency noted at 12 months given that no radiolucency was observed at 6 months' follow-up for this patient. In Cases 10, 11, and 14, fusion was, in fact, achieved at both levels at 12 months. In Case 16, fusion was achieved at L5–S1 but not at L4–L5. At 12 months, 19 (100%) of the patients had fusion at one level and 16 (84%) at both levels (Table 1).

Pedicle screws were placed at L-4 and S-1 bilaterally in 15 patients and at L-4, L-5, and S-1 bilaterally in 3 patients. One patient had dynamic fixation at L4–5 which failed prior to a revision done with a 2-level axial rod and facet screws at L5–S1. We did not find any dislodgment, breakage, or significant separation of the 2 components of the axial rod. On review of multiple CT scans there was a well-demarcated formation of dense bone surrounding the radiolucent region in the vicinity of the axial rod in Cases 10, 11, and 14, indicative of new bone formation.

Discussion of Marchi et al. It is difficult to comprehend the 22% fusion results reported by Marchi et al. in their 29 patients, when 16 of the first 19 of those patients had radiographically confirmed 2-level fusions at 12 months and the remaining 3 patients had radiographically confirmed fusions at 1 level (Table 1). It is also difficult to correlate the 50% improvement in visual analog scale scores and 40% improvement in the Oswestry Disability Index scores at 24 months in these 27 patients with the 22% fusion rate as reported by Marchi et al. Others have found significant improvement in pain scores and functional outcomes in conjunction with high rates of fusion using the presacral approach.^{2,5–7} It should be pointed out that some of the devices used in the study by Marchi et al. were early-generation implants that have not been marketed in the United States. However, the subsequent 2-level axial rod that is marketed in the United States has recommended surgical techniques for use from the manufacturer that include rigid posterior segmental fixation and interbody bone grafting with osteoinductive and osteoconductive material and preferably autograft bone. The authors reported that the grafting material used was only calcium phosphate and some bone marrow aspirate. On our review we noted less than optimal graft material seen on most of the postoperative CT scans, and only 3 patients had segmental posterior fixation.

Additional observations identified that the patients with radiolucencies did not have segmental fixation at every level. A biomechanical study by Erkan et al. confirmed the need for segmental posterior fixation at L-4, L-5, and S-1 to provide uniform stability across each motion seg-

TABLE 1: Fusion status of 19 patients treated with 2-level AxiaLIF rod and supplemental posterior fixation

Classification	Follow-Up			Overall Fusion Status
	6 Mos	12 Mos	24 Mos	
no. of patients	19	15	2	19
total no. of patients w/ at least 1-level fusion	18 (95%)	15 (100%)	2 (100%)	19 (100%)
total no. of patients w/ fusion at both levels	15 (79%)	13 (87%)	2 (100%)	16 (84%)
1. fused: bridging bone advanced	14 (both levels); 2 (1 level)	12 (both levels); 2 (1 level)	1 (both levels); 1 (1 level)	15 (both levels); 3 (1 level)
2. fused: bridging bone	1 (both levels); 1 (1 level)	2 (1 level)	1 (1 level)	2 (1 level)
3. developing bone	1 (both levels); 1 (1 level)			
4. no early evidence of bone remodeling	1 (1 level)			1 (1 level)
5. no radiographic progress	1 (1 level)	2 (1 level)		2 (1 level)

ment and decrease the load transfer to the fixation points of the implant.¹ In other words, greater points of fixation along the lumbar spine allow for greater distribution of the loads across the implant, resulting in lower loads distributed at each point of fixation. By skipping fixation at L-5, greater stresses and micromotion are transferred to the L-4 vertebra, possibly resulting in radiolucent areas around the axial rod at L-4. Lack of pedicle fixation at L-5 in all but 3 patients may have resulted in the loss of disc space height achieved at surgery, rod subsidence, and loss of lordosis, thus transferring greater stress to the fixation points which were at the terminal ends of the fusion construct.

A clinical review of 52 patients treated with AxiaLIF 2-level implants and supplemental posterior fixation with an average 29 months' follow-up showed that 99 of 104 interspaces were fused. There was no implant subsidence, deep infection, neurological deficit, or rectal perforation.⁷

In summary, we believe that additional review of the authors' clinical and radiographic data pertaining to these 27 patients would be helpful in clarifying the conflicting clinical outcomes between such low fusion rates reported in the recent article and the 100% fusion rates and outcomes previously presented by the authors for the same patient set.

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Disclosure

Dr. Nasca reports serving as a consultant for and being on the Scientific Advisory Board of Trans1.

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RESPONSE: We thank Dr. Nasca and colleagues for giving their own analysis on a subset of patients from our cohort.

As cited above, short-term and partial results were presented by our group in international societies meeting during 2008. In such abstracts only 10 cases were analyzed. Before writing the article published in the *Journal of Neurosurgery: Spine* in 2012, other abstracts were presented during international meetings in 2009 (L Pimenta, E Coutinho, L Oliveira: Is radiolucency a signal of pseudarthrosis? Radiological evaluation after axiaLIF 2 levels. Presentation to EuroSpine, 2009; L Pimenta, J Lhamby, E Coutinho, et al: Is radiolucency a signal of pseudarthrosis? Presentation to IMAST, 2009) and 2012.⁵ At those opportunities we presented results based on 20 and 27 patients, respectively, in which 80% and 78% of the spine levels presented radiolucent lines around the axial rod.

Results presented after 2008 differ substantially in 3 important factors: first, experience based on 20 or 27

cases; second, complete 2-year follow-up; third and most important, different fusion criteria.

The FDA suggests in its IDE (Investigational Device Exemption) guidance:⁶ “The tolerance for presence of radiolucent lines may be dependent on the type of spinal system. If the sponsor chooses to incorporate radiolucency data as a fusion criterion, then specific information should be provided in order to better assure that adequate radiological assessments are being made to measure the accurate presence or absence of radiolucencies. Even if the sponsor does not choose to incorporate the radiolucency data as a fusion criterion, these data should be collected as confirmatory information.” Radiological data were collected from the beginning, and radiolucency was incorporated later as a fusion criterion, at the time that this occurrence had gained importance in the eyes of researchers. Since then, radiolucency has been considered by this group as a sign of failed fusion in this system.

Surgical technique was performed in a standard fashion, following the same steps and using the same instruments described before by the same author.⁴ Both interbody grafting and posterior supplementation were performed percutaneously. As described in the original paper, calcium phosphate bone graft with some bone marrow aspirate collected during the procedure was used as bone substitute to fill the interbody space. As a minimally invasive technique, neither autograft harvested from a distant site nor posterior/lateral mass was used in the cases. Indeed, that may cause insufficient stability to the construction and lead to the results shown in our series.

In a few cases we observed failure of the hardware, some with failure of the posterior supplementation (screw/bar) and others with some degree of detachment (disunion) of the 2 axial rods at the point at which they interlock (L5–S1 disc space).

Together with other imaging, biomechanical, and clinical studies,^{1–3} our original article integrates a limited literature about the 2-level procedure. Additionally, it reports a single-center experience—a fact that limits broad conclusions. Further reports will integrate and clarify the utilization of this new indication for this spinal system.

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Disclosure

Dr. Pimenta reports being a consultant for and owning stock in NuVasive, Inc.

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Cervical decompression

TO THE EDITOR: Traynelis et al.⁵ generously share the experience of their hospital in nonusage of neurophysiological intraoperative monitoring (IOM) for cervical spine surgeries (Traynelis VC, Abode-Iyamah KO, Leick KM, et al: Cervical decompression and reconstruction without intraoperative neurophysiological monitoring. Clinical article. *J Neurosurg Spine* 16:107–113, February 2012). They present 7 years of retrospective data, for a total of 720 unmonitored cervical spine surgeries, of which only 3 patients (0.4%) had documented new postoperative neurological deficits. Furthermore, none of these patients had persistent deficits on follow-up during as much as 1 year after the fact. The authors conclude that IOM was unnecessary for these surgeries and the total cost savings to the hospital was \$1,024,754 (calculated from 2011 CMS [Centers for Medicare & Medicaid Services] reimbursement rates for multimodal IOM).

While Traynelis and his coauthors provide an excellent summary of the issues surrounding IOM, the study itself is methodologically flawed. The authors state that they used consecutive surgeries over a 6.5-year time period (December 29, 2000–May 25, 2007), but it is unclear why this time frame was chosen, and no calculations are provided to determine how they arrived at the final sample size. With high-grade deformities and focal neoplasms excluded, none of the remaining cases had concurrent IOM. Either IOM usage was an additional exclusion criterion, or there was some selection bias at the time of surgery that systematically resulted in nonusage of IOM.

Assuming that the discovery of these data was merely a happy accident and not the result of institutional or research-related selection biases, the outcomes reported in this study are at variance with the best-documented study in the current literature. In a series of 4097 cervical spine surgeries,² 12 patients (0.3%) awoke with postoperative tetraparesis (global Medical Research Council scale strength rated 2/5 or less). At a maximum follow-up of 3 years, only 25% had completely recovered and 2 had died. According to the editorial by Amin and Mummaneni¹ in the same issue of *Journal of Neurosurgery: Spine*, the University of Iowa Hospital and Clinics are fortunate that

they did not experience these outcomes, but not all medical centers may be either so lucky or gifted with such skilled surgeons.

Although Traynelis et al. indicate that their hypothesis was that “decompressive and reconstructive spine surgery can be safely performed without IOM,” they make no attempt to prove it statistically or otherwise. For a study to reach statistical significance ($p < 0.05$) and power of 0.9 for the hypothesis that nonusage of IOM would cause one persistent neurological deficit in 720 trials (0.13%) would require 1182 subjects in a nonbiased sample.

The secondary (economic) argument of the study is likewise problematic. The literature supports the belief that persistent motor deficits are relatively rare events.⁴ But these events have devastating consequences. If just one patient has a persistent C5–8 level tetraplegia at age 50 (the mean age of the study patients), his lifetime direct health care costs alone would be \$1,250,701.83 (from 2009 Spinal Cord Injury Data, medically inflated to 2011 dollars).³ When lost wages and benefits as well as damage to quality of life are included, this amount can grow considerably larger. So, if the University of Iowa’s surgeons had not been so talented, allowing for just one poor outcome in the sample, the article’s entire premise would have shifted to how IOM could be hypothetically cost saving.

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Disclosure

Dr. Ney is an employee of Surgical Neuromonitoring and Surgical Neuromonitoring Associates and serves as Medical Director of both entities. The company was unaware of his authorship, and the letter was written independently of his duties. Dr. van der Goes was participating in a postdoctoral fellowship sponsored by Pfizer, Inc. at the time this letter was written.

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RESPONSE: We appreciate the interest of Drs. Ney and van der Goes in our retrospective review examining the immediate postoperative outcome in a group of surgi-

cally treated patients with subaxial degenerative cervical spine disease. The study time frame was the result of a number of variables including the initiation of the electronic medical record, the availability of a researcher to identify the cases, and the departure of the senior author from the University of Iowa. Our intent was to examine the outcomes of these patients to determine if performing surgery for degenerative cervical spine disease without monitoring was safe.

A more detailed review of the work on perioperative morbidity reported by Cramer et al., cited by Drs. Ney and van der Goes as it refers to our recent publication, brings to light a number of issues.¹ In this retrospective study 4097 patients were treated with cervical spinal surgery and 12 patients were noted to have significant “postoperative” neurological deficits. One patient had surgery at the craniovertebral junction and another for an intramedullary tumor; these pathologies would not have been included in our study. In 6 patients the cause of the deficit was an epidural hematoma and, in another, graft dislodgment. Neither epidural hematoma nor graft dislodgment would have occurred during the actual procedure but in the hours or days following the surgery, and therefore these problems would not have been detected by IOM. Another patient was presumed to be worse due to direct operative trauma, which also could not have been prevented by monitoring. Finally, 2 patients were judged to be worse due to “inadequate decompression.” This category is very problematic in that inadequate decompression should have resulted in no neurological improvement as opposed to a worsened state, and unfortunately the manuscript does not offer any further data concerning these cases. It is noteworthy that the authors state in the discussion, “Despite many reports attesting to its efficacy in reducing neurologic injury, in only 1 of 7 patients in which IOM was performed was impending neurologic compromise detected.” Our patients did not suffer significant neurological problems either acutely or in the postoperative period, which we attribute to the focus on preoperative planning and assessment, meticulous operative technique, and close postoperative clinical monitoring.

No attempt was made to determine sample size or perform a statistical analysis, as noted by Drs. Ney and van der Goes, because of all of the problems associated with retrospective reviews that dominate this body of literature. The key factor needed to determine sample size relates to the incidence of significant spinal cord injury following routine cervical spine surgery for symptomatic subaxial degenerative disease: this value is unknown but is admittedly very small. While the utility of IOM in patients undergoing surgery for symptoms referable to degenerative spine disease has not been defined in a scientifically rigorous manner, the costs of such monitoring are easy to accurately calculate, and it is clear that the utilization of this technology represents a significant expense.

Intraoperative monitoring certainly has a valuable role in treating high-grade focal deformity and intramedullary lesions and was used as a surgical adjunct in such patients over the time period of this study; this should not be construed as creating a bias in the study population. Although such monitoring is very useful for certain conditions and procedures, it is not universally necessary or

effective, just as penicillin is not an appropriate treatment for all infections.

This study is the first of three we plan to complete. The second will be to monitor surgical procedures for degenerative cervical spine disease in a blinded protocol to determine the false-positive rate of monitoring in this patient population (which to our knowledge has never been done). This work will hopefully provide the data necessary to calculate an appropriate sample size to proceed with a multicenter study in which patients are randomized to monitoring or not while undergoing surgery for symptomatic degenerative cervical spine disease.

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Disclosure

Dr. Traynelis serves as a consultant for and holds patents with Medtronic. He receives fellowship support from Globus and NREF.

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Acute motor-sensory axonal neuropathy and *Helicobacter pylori* infections

TO THE EDITOR: We read with great interest the article by Miscusi et al.¹¹ (Miscusi M, Currà A, Della Rocca C, et al: Acute motor-sensory axonal neuropathy after cervical spine surgery. Case report. *J Neurosurg Spine* 17:82–85, July 2012). The authors reported a case with acute motor-sensory axonal neuropathy (AMSAN), an axonal variant of Guillain-Barré syndrome (GBS) that occurred immediately after cervical spinal surgery, suggesting an association between AMSAN and acute colitis caused by *Helicobacter pylori*. However, we have some concerns about the diagnosis for this case.

First, the sentence in the first paragraph of the paper “AMSAN has been associated specifically with *Helicobacter pylori* infections” is misleading. The prevalence of *H. pylori* infections in developing countries may reach 70% or more and 40% or less in developed countries.² However, most people infected with *H. pylori* do not show any clinical sign or symptom and do not develop AMSAN. Moreover, the reference the authors cited⁵ provided very weak evidence to support their view, because only 2 patients with AMSAN were included in the study. The sample size is too small to draw a reliable conclusion; therefore, large-scale studies are still needed to verify the association between *H. pylori* infections and AMSAN development. Of note is a correlation between

H. pylori infections and acute inflammatory demyelinating polyradiculoneuropathy (AIDP), the most common subtype of GBS.⁸ According to the report by Kountouras and colleagues, infection with *H. pylori* has been found in 92% of AIDP patients, which is more frequent than in healthy controls.⁸ Elevated anti-*H. pylori* immunoglobulin antibodies were associated with the severity of clinical symptoms and involved in the proximal parts of peripheral nerves in AIDP.⁸ Nevertheless, without further studies, this correlation cannot be directly applied to diagnose AMSAN.

Second, the diagnosis of AMSAN seems inappropriate, since critical illness polyneuropathy (CIP) and critical illness myopathy (CIM), the most common acquired neuromuscular diseases³ in intensive care units, cannot be ruled out in this case. The risk factors for development of CIP/CIM include sepsis, systemic inflammatory response syndrome, multiple organ dysfunction syndrome, hyperglycemia, hypoalbuminemia, and use of corticosteroids.⁹ Critical illness polyneuropathy shares some clinical features with AMSAN, both mainly presenting as flaccid weakness (distal more than proximal), attenuated or absent tendon reflexes, and distal sensory loss.^{9,13} Moreover, patients with CIP may also suffer from ventilatory dysfunction due to phrenic nerve involvement. In this case, a high fever and an elevated sedimentation rate suggest an underlying infection or even sepsis. We thus would like to know of the blood test results that may help to identify infections. In this regard, CIP should be highly suspected, since the incidence of CIP reached 76% in the patients with sepsis.¹² Based on electrophysiological tests, it has been recognized that CIM often coexists with CIP.^{6,10} In the patients with CIM, electromyography may reveal abnormal spontaneous activity, including fibrillation potentials and positive sharp waves.⁴ Evidence of intense denervation activity alone is not enough to exclude CIM. Rather, direct muscle stimulation is often recommended when it is difficult to distinguish CIM from CIP or their combination by routine electrophysiological tests. Furthermore, to help differentiate among AMSAN, CIP, and CIM, nerve and muscle biopsies should be taken into consideration.¹⁹ Taken together, an accurate diagnosis of GBS should rely on careful analysis of disease history, clinical manifestations, laboratory testing, electrophysiological investigations, and nerve and muscle biopsies, especially for the patients with sepsis.

Third, nephrotic syndrome seems misdiagnosed. The proteinuria did not reach the diagnosis criterion of nephrotic syndrome,⁷ which is typically defined as greater than 3–3.5 g protein in a 24-hour urine collection. Renal biopsy should be used to confirm or exclude the diagnosis of nephrotic syndrome, to establish the pathological subtype, to assess disease severity, and to evaluate the prognosis.⁷ Given the manifestations of high fever, elevated sedimentation rate, peripheral nerve involvement, and renal dysfunction, other disorders, for example, connective tissue diseases, cannot be completely excluded either.

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The authors report no conflict of interest.

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RESPONSE: We thank the authors for their interest in our paper and for their contribution to the discussion.

First, we did not argue that AMSAN is only or mainly associated with *H. pylori* infections; rather, we proposed a possible association between these 2 diseases that has already been reported in the literature.¹ Such an association might be not conclusive, but we aimed to contribute to this clinical discussion in a case report. We agree that *H. pylori* infections are associated more frequently with AIDP than other variants of GBS. Acute motor-sensory axonal neuropathy represents the most common form of GBS, but it is worth noting that in the early phase of GBS the distinction between AIDP and axonal variants may be impossible in some patients.² Nevertheless, in our case, electrophysiological evidence pointed to a diagnosis of axonal GBS.

It seems unlikely that the patient's symptoms could

have been related to CIP or CIM because such a diagnosis was not supported by clinical and electromyography data.

Before surgical treatment the patient was in good health, and no symptoms related to general diseases were evident. Type 2 diabetes was in the normal range and was being treated with oral metformin. Surgical time was less than 2.5 hours and neurological symptoms occurred 18 hours after surgery. The patient was never admitted to the intensive care unit, and he did not manifest clear signs of sepsis or multiple organ dysfunction syndrome. The patient's white blood cell count ranged from 7500 to 9500 mm³, his reactive C protein ranged from 2.02 to 2.55, his temperature remained always lower than 37.5°C, and seriated blood cultures were all negative. Furthermore, CSF testing proved positive for protein content and a high anti-GM1 antibodies titer.

Serial electrodiagnosis performed after treatment and before transfer to a rehabilitation facility showed progressive improvement of compound muscle action potential amplitudes without development of excessive temporal dispersion.

We did not perform a muscle biopsy because we observed a quick and very good response to immunoglobulins; for the same reason, we decided to perform no other invasive procedure, including kidney biopsy, which would have not changed our therapeutic conduct.

To consider the renal involvement and consequent systemic serosal fluid collections, although a protein loss of 2.8 g/24 hours only approaches the value typically found in nephrotic syndrome, we thought it would be better to treat the dangerous condition before it reached its full-blown phase. On the other hand, the strict adoption of the criterion for nephrotic syndrome leads to further excluding a multiorgan failure needed for suspecting a critical illness.

In conclusion, although in some cases the differential electrodiagnosis of AMSAN and CIP/CIM may be difficult or impossible, a number of clinical clues in our patient pointed toward a diagnosis of axonal GBS. Even in rare conditions (due to genetic susceptibility, different antecedent infections or triggering factors, and electrophysiological criteria used), the axonal variants may represent variable percentages (from 1% to 15%) in different series of patients with acute inflammatory polyneuropathies.²

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