

Axonal, bladder and bowel impairment: evidence based clinical review of gaps in guidelines for spinal stenosis

Deficiencia de axones, vejiga e intestino: Revisión basada en evidencia de vacíos en guías de estenosis espinal

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ABSTRACT

The axonal damage of sacral roots, the bladder dysfunction and constipation that slowly progress in severe cases of spinal stenosis, are not assessed in literature of high scientific evidence. The decision-making process to choose interventions lacks of guidance to confirm the presence of these three conditions, their natural evolution, impact on quality of life and functionality, and its management. The symptom of pain and the wait for an advanced loss of motor function seem to be the criteria that determine the follow up in spinal stenosis, although the guidelines and systematic reviews show a limited effect of exercise or medication. The usefulness of electrodiagnostic studies is compared with that of MRI to diagnose spinal stenosis, limiting their true diagnosis power. This article suggests an alternate use of these two diagnostic tests, using the Bayes Theorem, the Fagan nomogram and the pre test and post test likelihood ratios to confirm the presence of axonal destruction by paraspinal electromyography and the tibial nerve H reflex, as a complement to a positive MRI for lumbar stenosis. With the same method, the bladder ultrasound and urodynamics are evaluated to confirm bladder dysfunction. A case of spinal stenosis exemplify the guidelines follow up, the functional decline and the proposal to use tools of scientific evidence to broaden the evidence in decision making for best judgment on spinal stenosis

Keywords: Spinal stenosis, low back pain, cauda equine, polyradiculopathy, bladder, constipation, paraspinal muscles, electromyography, H reflex, bladder ultrasound, urodynamics, diagnosis, likelihood ratio, fagan nomogram, Bayes Theorem, Pretest probability, Posttest probability

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RESUMEN

La destrucción de los axones de raíces sacras, la disfunción de vejiga y la constipación que lentamente progresan en casos graves de estenosis espinal, no se evalúan en literatura de alta evidencia científica. Las decisiones de intervención carecen de orientaciones para confirmar la presencia de estas tres condiciones, su evolución natural, el impacto en la calidad de vida y la funcionalidad, o su manejo. El síntoma de dolor y la espera de una pérdida avanzada de función motora parecen ser los criterios que determinan el seguimiento en estenosis espinal aunque las guías de manejo y revisiones sistemáticas muestran un efecto limitado del ejercicio o los medicamentos. La utilidad de los estudios de electrodiagnóstico se ha comparado con la de la resonancia magnética para diagnosticar la estenosis lumbar, limitando su verdadero poder diagnóstico. Este artículo propone un uso alternativo de estos dos métodos, utilizando el Teorema de Bayes, el Nomograma de Fagan y los cocientes de probabilidad pre test y post test para confirmar la presencia de destrucción axonal mediante la electromiografía de músculos paraespinales y el reflejo H del nervio tibial, como complemento de una resonancia magnética positiva para estenosis lumbar. Con el mismo método se evalúan la ecografía de vejiga y la urodinamia para confirmar la disfunción vesical. Se presenta un caso de estenosis espinal para ilustrar el seguimiento de guías, el declive funcional y la propuesta para usar herramientas de evidencia científica que amplíen los elementos de juicio en la toma de decisiones de intervención en estenosis espinal.

Palabras clave: Estenosis espinal, dolor lumbar, lumbalgia, cauda equina, poliradiculopatía, vejiga, constipación, músculos paraspinales, electromiografía, Reflejo H, ecografía de vejiga, urodinamia, diagnóstico, cociente de probabilidad, Nomograma de Fagan, Teorema de Bayes, probabilidad pre-test, probabilidad postest.

INTRODUCCIÓN

For patients with spinal stenosis, there are no definite agreements on deciding what should be the best treatments. On the clinical settings, there seem to be an acceptance on offering a conservative initial approach, although there is no clear criteria on which clinical changes might be screened on follow up to decide a change in the course of the medical decisions.

It could be frustrating when patients report no improvement on their symptoms or even a worse presentation, no matter all efforts to follow the available scarce evidence.

This article is the result of a search for the best available evidence during a 20 months fo-

llow up of a patient with a torpid clinical painful state with deterioration of his lumbosacral related symptoms and visceral functions that are not described in the highest evidence-based literature. The objective was to highlight what patients report on their sacral function from the best available scientific evidence and to report how difficult is to answer whether their bladder or bowel symptoms had an origin in the process of aging, the prostatic hypertrophy or medications. What improved his condition was confronted with the results of the search.

METHODOLOGY

A PICO search (Patient, Intervention, Comparison, Outcome) was conducted to answer the questions brought by the clinical course of a patient with back pain, radiation and sen-

sory symptoms to lower extremities. The diagnosis, screening, prognosis and treatment was considered to answer every patient's follow up appointment. An OVID search was conducted on Medline (1996 to May 2014) and EMBASE (1980-May 2014). Manual search was used when the retrieval yielded few articles and was updated to October 1st, 2015. In many instances a comparison was omitted due to lack of results.

Numerous related *Selected Terms* from OVID Display Indexes were included for each component of the PICO search. The results were initially filtered as per systematic reviews, meta analysis, tw and guidelines. When no results were obtained, ongoing filters were used as randomized controlled trials, mp, observational studies, mp, cohort studies, diagnostic studies or screening tests. Opinion papers were used when critical questions were discussed. When the search did not retrieve any articles, the type of study was omitted to obtain exploded results and series of cases were included if it was the only source of information. When a level of evidence or grade of recommendation was required, the criteria and grading from the original paper was reported, as it was originally defined by the authors of each paper.

CASE ORIENTED EVIDENCE AND RESULTS

A 74 year old man was referred by a surgeon to a pain clinic in October 2012. He used to play golf and to walk one hour three times a week. He referred a 10 year low back pain. Since one year the pain was triggered by a walk of 100 yard (91m), followed with painful cramping and numbness in lateral aspect of his thighs and left leg that was relieved after 2 minutes of rest. On average, the pain was 5/10 in severity. He had an intermittent sense of weakness in the lower extremities and numbness in the forearms. He denied bladder or bowel symptoms, night pain or saddle anesthesia.

He reported hypertension, dyslipidemia, stopped smoking 40 years ago, and adherent to irbesartan, hydrochlorothiazide and simvastatin. He received a total knee replacement in 2011.

His gait was normal, the strength 5/5 in all the myotomes, the patellar and Achilles reflexes were normal and symmetrical. The straight leg test and sensory to light touch were normal. The range of motion was complete and painless in all four extremities and trunk. Tibial pulses and skin were normal and eutermic.

The Probability of presenting spinal stenosis can be obtained by the Likelihood Ratio and the Bayes Theorem^{1,2}. The positive and negative Likelihood ratios are used to determine the Posttest probability when the diagnostic test is positive or negative respectively. (Table 1).

$\text{Pretest odds} = (\text{Pretest probability} / (1 - \text{Pretest probability}))$ $\text{Posttest odds} = \text{Pretest odds} * \text{Likelihood ratio}$ $\text{Posttest probability} = \text{Posttest odds} / (\text{Posttest odds} + 1)$ $\text{LR+} = \text{sensitivity}/(1-\text{specificity})$ $\text{LR-} = (1-\text{sensitivity})/\text{specificity}$
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Table 1. Steps to calculate the Posttest probability. LR: Likelihood ratio.

The Fagan's Nomogram is an easier alternative to calculate the posttest probability^{3,4} (figure 1) by drawing a straight line from the pre-test value to cross it through the LR+ when the result is positive or the LR- when the result is negative.

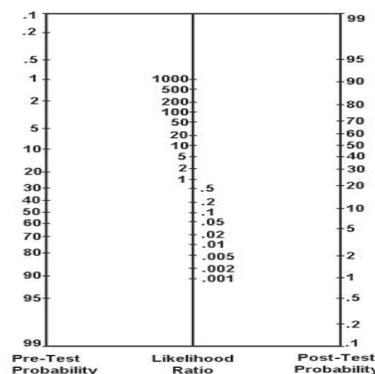


Figure 1. Fagan's Nomogram as found elsewhere.

In adults with back pain and numbness in the lower extremities, lumbar stenosis is present in 47% of cases (Pretest probability)⁵. A reported LR+ of 3,7 for a positive clinical findings⁶, this

patient has a probability of 76% of having spinal stenosis. The question “back or leg dominant pain” is not useful to confirm the spinal stenosis, because the retest reliability is low for patient responses (0.36 (0.10–0.62)) or pain diagram (0.09 (-0.24 to 0.43))⁷. The MRI is recommended to confirm spinal stenosis (grade recommendation B).(8) Its LR+ of 6,9 and its LR- of 0,1 are useful in this patient to confirm or rule out spinal stenosis⁸⁻¹¹.

In elderly, the prevalence of obstructive arterial disease is 10 % (pretest probability). The symptom of claudication (LR+3,3)¹²⁻¹⁴ would bring a posttest probability of 26,7 %. Normal pulses, non-smoker and absence of skin changes (LR-0,38)¹⁵ brings a posttest probability of 4% of arterial claudication.

In November 2012 the patient referred exacerbated left calf pain after physical activity forcing him to take a cart in golf practices. On examination there was hyperalgesia and allodynia in the Lateral aspect of the left leg. The ESR was 8, hemoglobin 160 g/l, WBC (x10E9/L): 6.6, neutrophils 3.43, lymphocytes 2.24, monocytes: 0.59, eosinophils 0.26, basophils 0,07. HbA1C: 0.055, Total Cholesterol/HDL-C ratio 3.6 and non-HDL-Cholesterol 3.52. The x Rays in May 2012 showed reversal lordosis in C4-7, mild anterolisthesis C3-4, C4-5, facet osteoarthritis and neural foraminal stenosis from C4-5 to C6-7. There was a grade I anterolisthesis L4-5. The MRI in Nov 2012 showed bulging in all discs from L1-2 to L5-S1, severe facets hypertrophy in L3-4 and L4-5, severe stenosis with an AP diameter of 5 mm in L3-4 and L4-5 and severe nerve root foraminal stenosis in left L5-S1. A cervical CT scan in Dec 2004 confirmed the previous findings of plain radiographs. Celecoxib 400mg and increasing dose of Gabapentin to 900mg were prescribed, with subsequent improvement one month later, enabling him to walk further, restricting the pain to the lower back and occasional radiation to the buttocks. He was trained in exercises for core strengthening. In December 2012, extension-flexion dynamic lumbar spine radiographs reported stable listhesis in L4-5, so the surgeon postpone a surgical intervention if the pain was

controlled and no neurological involvement was present.

The blood test results ruled out Infection, diabetes or uncontrolled hypercholesterolemia^{16,17}.

The reversal lordosis in cervical X rays would bring the concern of possible changes in the cervical spine¹⁸. However, symptomatic claudication and imaging confirmed severe lumbar and left L5-S1 foraminal stenosis although the neurological exam was normal.

Exercise seems to partially improve pain for the short term, but not long term, when compared with NSAIDs or no treatment. Unweighted treadmill walking or stationary cycling could also be offered. There is a very low quality evidence of improvement of leg pain and walking distance with gabapentin¹⁹ up to 4 months of treatment^{19,20}.

In January 2013 he received bilateral medial branch blocks to the L3-4, L4-5 and L5-S1 without significant relief of pain.

In February 2013 the deep tendon reflexes were absent in the lower extremities. He visited the spine surgeon, who found a mechanical back dominant low back and leg pain that the patient rated as 4/10 at rest and 8/10 with activity, with unremarkable strength and sensory examination to light touch and pinprick in the lower extremities. The L4-5 spondylolisthesis increased to grade 2 on plain film flexion and extension views. Considering that the medication partially resolved the leg pain and it was such a widespread lumbar spine disease that would likely require multilevel fusion, it was discussed with the patient and a conservative treatment was indicated at that point.

The Medial branch block did not relieve the pain, so no further procedures for zygapophyseal joints were proposed^{21,22}. The loss of reflexes is not mentioned as criteria for surgical intervention^{8,11}. The magnitude of surgery was outweighed against the potential benefit. A shared decision-making is recommended to decide with the patients whether to face the natural course

of LSS or the risks of procedure-related adverse events^{23,24}.

Few days after, an electromyography showed 2+ positive sharp waves and fibrillations in left and 1+ in right paraspinal muscles, with fasciculations in the left tibialis anterior and gastrocnemius. The bilateral tibial nerves, left peroneal and sural showed normal distal latencies and velocities. In the following five months the Gabapentin was increased to 1200mg and Acetaminophen to 3g a day, with a resulting pain of 5/10, dull in the back and numb in the left thigh and leg.

There is no evidence based literature about axonal, demyelination, nerve damage, nerve injury, radiculopathy or Seddon or Sunderland classification^{25, 26, 27, 28} to decide whether an early versus delayed surgery would modify the natural evolution of LSS.

When sciatica is diagnosed with combined clinical and imaginologic criteria, early surgery (mean 2.2 weeks; 1.9-2.5, 95% CI) seems to provide better short (but not long term) outcomes of back or leg pain, than conservative treatment; no differences are found at 2 years, although 44% of patients with conservative treatment end up in surgery^{29,30}. Early surgery provides acceptable healthcare costs, less absenteeism and better quality of adjusted life years. Nevertheless, there are no articles selecting patients according to demyelinating, axonal nerve damage or normal electrodiagnostic studies³⁰, which could mean high risk of selection bias.

The electromyographic signs of denervation are better recorded 3 to 4 weeks after the nerve injury²⁶. Confounding factors, such as prior neuropathy or muscular trauma²⁸ and operator dependent reliability³² can be overcome by standardized methods³³. However, no clear accepted electrodiagnostic guidelines have been published for LSS. Paraspinal EMG could reach sensitivities of 72 to 97% and specificities of 87.5 to 100% under reproducible criteria and can confirm acute denervation in poliradiculopathy (Level III evidence). Electromyographic paraspinal mapping is suggested to confirm the diagnosis of degenerative LSS (Level II Evidence and

Grade B recommendation)^{8,34}. In absence of active denervating signs –Positive sharp waves or fibrillations–, a chronic nerve damage needs to be ruled out –Polyphasic or Giant Motor Unit Action Potentials³⁵.

Fibrillations in any muscle (LR+ of 3,82) leads to no more value than MRI to confirm LSS³⁶, unless costs are considered. However its truly value is the specificity³⁷: a combined paraspinal and limb EMG showed a bilateral L4,S1 root axonal damage. A positive MRI for LSS yields a post test probability of 85%, which in turn might be the pretest probability for electrodiagnostic studies to confirm nerve damage: this, subsequently means a post test probability of 95% of L4, S1 axonal damage. The fasciculations would suggest a chronic damage.

In June 2013, the patient preferred to skip an opioid treatment. In August 2013 the Gabapentin and Tylenol gave a partial relief of pain to a score of 6/10 with radiation only to his buttocks. Pregabalin 50mg tab BID was started. He reported an increase to 3 voidings every night and feeling of incomplete emptying. In September 2013, the H Reflex was absent in both sides, indicating a neural abnormality anywhere from the tibial nerves to the S1 roots.

The H reflex reaches a LR+ of 4,39, which yields a 96% post test probability of S1 root damage if obtained from the previously positive MRI³⁶.

In October, an Ultrasound Post-void residual was 82ml. He rejected trigger point injections to the right gluteus medius and quadratus lumborum. He accepted Tramadol/Acetaminophen, 1 tablet every morning for a lumbar pain of 8-9/10 radiated to thighs on standing, sitting and walking with painful pins and needles in both legs. It allowed him to walk longer distances till December when it had no longer beneficial effect. Constipation and reluctance to try laxatives made him stop it.

The muscarinic effects and impact of opiates over dysfunctional neuropathic bladder and bowel in LSS are unknown³⁸. Its impact on pain and quality of life in LSS needs to be defined.

The US post void residual cutoff of 50 ml equals a LR+ 1,24.⁽³⁹⁾ Significant bladder impairment is reported in 26% of patients with LSS⁽⁴⁰⁾ (pre-test probability), so the risk of such impairment under this low sensitive and low specific method was 30% (posttest probability) in this patient. Wall thickness (LR+ 16,6/LR- 0,18) was not measured.

In January 16, 2014 an epidural injection reduced the back pain to 5/10 and neuropathic pain became as non-painful numbness.

He reported a slowly progressive inability to empty the bladder with intermittent strained micturition. An urodynamic study in January 22 showed late urge at 310 ml with strong urge at 317ml -interpreted as decreased sensation-, a residual of 41ml with a peak flow of 18 ml/s, strong inhibited voluntary contractions and high pressure -59 cm H₂O -. No obstruction was found. He completed the American Urology Association Symptoms questionnaire⁴⁰, with a Score of 26 (severe bladder symptoms). A physical examination revealed perineal hypoesthesia to dull and sharp pinprick with an inconsistent response of Bulbocavernous reflex. A Transrectal Ultrasound -Nov 2013- showed a prostate gland within normal volumes. The Prostate Specific Antigen -PSA-, September 2013, was normal -1,73 ug/L-. A cervical MRI was ordered and patient referred to the spinal surgeon.

The abnormal sensory urge in urodynamics suggested a S2 - S4 impairment. Unexplained elevated pressure of the detrusor^{41,42} was suggestive of upper motor neuron syndrome. A residual within normal limits contrasted against several bladder symptoms. A cauda equina syndrome is suspected with a sudden bladder retention, so there are no clear criteria to urge its assessment or treatment when the bladder dysfunction is insidious. It lacks of validated methods to confirm or grade its severity^{43,44,45,46}.

Moreover, there are non-well defined criteria or guidelines to decide when a patient with LSS has mild, moderate or severe neurological damage to decide for surgery⁴⁷.

Epidural injections every 2 months controlled the pain to an intensity of 2-4/10 allowing

him to walk more than 100 yards. A MRI cervical spine in April 2014 showed multiple osteoarthritic changes from C2 to C7, reversal cervical lordosis with an inverted vertex at C4-5-6 and a flat spinal cord with and high signal intensity at that level. The patient was off Tramadol since one month, although still with constipation, partially controlled with prunes and same bladder symptoms.

The need of a repeated Epidural injection was consistent with Level II Evidence in the short term (2 weeks to six months) to relieve the pain⁸. In contrast against the absence of opiates, the persistent bladder and bowel symptoms suggested a true neurological origin. The signs of upper neuron motor resulting from the cervical cord damage¹⁸, were masked by the stenosis at the lumbar level. The high pressure found in urodynamics was the only study that rose the warning about it. Surgery seems to offer the better outcomes in LSS^{8,23,48}.

In June 2014 a posterior L3-4-5 decompression and bilateral foraminotomies, plus a L2-S1 spinal fusion was performed under intra operative monitoring with no complications. The postoperative pain was controlled with acetaminophen and physical therapy. On a quarterly follow-up from July 2014 the patient reported a gradual significant relief of the back pain that he rated as 3/10 in February 2015 when a Trigger point in the right Quadratus Lumborum was found. Since November 2014 he denied any leg pain and stop the analgesics by December 2014. He returned to practice indoors and outdoors golf in January and June 2015 respectively without pain. Overall, the bladder and bowel symptoms improved.

DISCUSSION

The presence of sacral nerve root damage with insidious rather than abruptly bowel or bladder symptoms in LSS is not well described in the literature, so physicians would sub estimate the severity of a sacral root damage^{8,49}. Even more, the diagnosis of cauda equina syndrome and spinal stenosis are considered two different diagnoses⁵⁰. Spinal stenosis related to OA rarely end up in acute cauda equina with emergent uri-

nary retention. Electrodiagnostic tests⁵¹ or urodynamics⁴¹ are not yet addressed as complementary studies to define severity of nerve damage in already diagnosed LSS by MRI. There is no information available on how a sacral damage should be confirmed and how its prevention modifies the quality of life.

Not yet completely well known mechanisms of central sensitization^{52, 53, 54} or centralization could play a failure of either late surgical or non-surgical management^{55,56} This could explain confusing results and bias related to intention to treat analysis on outcomes about surgery⁵⁷ that usually is decided as a last option of treatment rather than neurological, bladder or bowel dysfunction.

Neither myelin or axonal damages (electrodiagnostic-proven) nor sacral involvement (either electrodiagnostic or urodynamics) have been studied or considered to decide for surgery. In high evidence literature, the critical outcomes such as axonal damage, bladder or bowel were not included in their search terms^{48;49;58;59}. At most, the criteria “leg predominant symptoms” for decompression is the most generally accepted^{60,60} despite the conflicting mask effect by analgesics. The question “leg or back dominant pain” is unreliable and depends on which questions are asked, inasmuch that 32% of patients provide a completely opposite response on a two weeks-difference test-retest, (Grade Recommendation Insufficient as clinical test) but “leg dominant pain” is used to decide surgery (Grade Recommendation B8).

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