Author’s response to reviews

Title: Correlation of lateral stenosis in MRI with symptoms, walking capacity and EMG findings in patients with surgically confirmed lateral lumbar spinal canal stenosis

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Author’s response to reviews: see over
Dear editor Prof Alberto Tagliafico

cc: Mr Reynaldo R. Aldea Jr.

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Title: Correlation of lateral stenosis in MRI with symptoms, walking capacity and EMG findings in patients with surgically confirmed lateral lumbar spinal canal stenosis

Authors: Pekka Kuittinen and colleagues

We are grateful for the encouraging comments and constructive criticism of the Editor and the Reviewers concerning our research article. We have read the comments and have revised our manuscript accordingly. Our detailed response to the comments is enclosed on the following pages. We hope that the resulting revised manuscript adequately addresses all the points noted by the reviewers, and that it is now ready for publication in the BMC Musculoskeletal Disorders.

Yours sincerely,

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Reviewers’ comments with responses

Referee: 1

General comments: The relationships between various clinical, radiological, anatomical and statistical concepts of ‘lumbar spinal stenosis’ are increasingly confused. So an article that takes a multifactorial look at the problem is of substantial value. This is especially true for lateral stenosis, since radiological measures of the lateral regions have made research on ‘stenosis’ of that area difficult.

Thank you for comment.

This article is quite clearly written.

Thank you.

The word ‘stenosis’ is used in confusing and incorrectly interchangeable ways throughout the article. For example, “Lateral lumbar spinal canal stenosis (LLSCS) is a related condition...” meaning related to the NASS definition of clinical stenosis which requires anatomical findings AND clinical consequences. However a few sentences further on, “The purpose of the current study was to evaluate the clinical significance of LLSCS found by MRI...” In this context LLSCS is only an imaging concept. Therefore, in each instance throughout the article define whether the word, ‘stenosis’ is clinical stenosis (the NASS guideline definition) or anatomical stenosis (some deviation from normal measurements of spinal architecture, regardless of symptoms) It would be nice if the authors actually defined the ‘deviation’ that allows them to use the word ‘stenosis’ for radiological findings).

Thank you for this annotation.

We have now defined LLSCS in the first paragraph of the introduction.
12 authors is an unusual number for a study such as this. The academic contributions of each should be documented.

Thank you for this annotation.

Guarantors of integrity for the entire study, OA, HK; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of the final version of the submitted manuscript, all authors; literature research, PK, PS, VL, TA; clinical studies, TA, SS, TS, SM; statistical analysis, PK, VL, PS; and manuscript editing, all authors.

This Authors’ contributions are also in the end of the manuscript.

Abstract:

Abstract Methods: This is an uncontrolled study. State that in the first line of the ‘methods’ section of the introduction.

Thank you for precise comment.

We have now added this important information to the abstract methods section.

The inclusion criteria of, ‘LSS severe enough to indicate operative treatment’ is not a valid criteria (unless surgery was offered prior to review of MRI, which is not likely). The literature suggests that a surgeon’s impression of the need for surgery is biased by imaging findings. So, state this more carefully. Perhaps you really mean, “LSS diagnosed by a treating surgeon who reviewed clinical and imaging findings. Potential subjects who were not offered surgery were not included.” Also, did the study include everyone whom a surgeon thought was surgical? Or only those who accepted (or eventually got) an operation?

The number of qualifying subjects eventually was 14. Not a big number when one considers the millions of operations performed for spinal stenosis. However it’s reasonable in relationship to any prior literature that addresses imaging vs. clinical stenosis, and no one that I know of has looked in detail at lateral recess on MRI vs. EMG.
Thank you for this annotation.

We have now reworded the inclusion/exclusion criteria.

Abstract results: “LLSCS was confirmed in all patients during surgery.” The authors should not present a surgeon’s opinion of his or her operative findings as any evidence of pathology or disease. I am unaware of any research whatsoever that validates the surgical ‘findings’ (whether an opinion, some pathological aspect such as edema, or some actual measurement) as diagnostic of clinical stenosis. I don’t think anyone has even codified these or looked at inter-rater reliability. Furthermore, it would be uncommon for a surgeon to operate and actually admit that his or her findings were not related to the reason for surgery.

Thank you, we have removed this sentence of the abstract results.

Abstract conclusions: A substantial prior literature on positive imaging for radiological stenosis in asymptomatic older people means that an uncontrolled study cannot claim that “lateral stenosis seen by MRI is a clinically significant finding.” We don’t know from this study the sensitivity or specificity of this finding in comparison to people who do not hurt at all. A more correct statement would be, ‘Among persons previously selected for surgery, lateral stenosis seen on MRI correlates with EMG, and thus may be a clinically significant finding.’

Define the abbreviation ‘LLSCS’ in the abstract.

Thank you for this annotation.

We have now reworded abstract conclusions and defined LLSCS to the first paragraph of the introduction.
Main paper: The above comments require changes in the main paper, as well. I will not belabor them.

Introduction: Concise and well written
Thank you.

Methods:
Reword the inclusion criteria. Address the problem of defining stenosis and severity. Currently it is based on circuitous logic. Imaging is used as an informal inclusion criteria (the surgeon who decided surgery was needed likely saw the images) and yet it is used as an outcome measure.

Provide more detail about how the cumulative MRI measures were viewed as ‘normal’ or ‘abnormal’. What was the norm to which the MRI’s were compared?
What statistical deviation resulted in an ‘abnormal’ finding? The problem of 4 measures x 10 roots per patient requires statistical correction if some normative cutoff (e.g. p<.05 for ONE measure) is used to define abnormal. How is this addressed or not addressed? If statistical norms were not used and justified with a Bonferonni or other correction for multiple measures, explicitly state this as a problem and discuss the ramifications.

Thank you for comment.

Image analysis was performed as previously described in detail. Repeatability of assessments varied from moderate to substantial (Sipola et al. Acta Radiol. 2011 Nov 1;52(9):1024-31).

In visual analysis, the grading system classified the lumbar nerve root canals into three grades: 0 = normal, 1 = narrowing without root compression and 2 = nerve root compression. In quantitative analysis, the minimal width of the subarticular (entrance) zone (lateral recess) and the cross-sectional (mm²) area of the foraminal zone (mid zone area) were measured. At the foraminal zone, no space below the line parallel to the lower end plate was included in area measurements as previously described in detail (Sipola et al. Acta Radiol. 2011 Nov 1;52(9):1024-31).

In statistical analyses, MRI and EMG where analyzed root by root altogether 140 roots. We used X² test to examine relationship between EMG (normal/abnormal) and visual evaluation of the entrance and mid zones of the lateral lumbar nerve root canal (normal/narrowed/compressed), where severity of the mid
zone stenosis in MRI correlated with abnormal EMG findings \((p = 0.015)\). According our statistician, if applying Bonferroni correction in this case p-value would be 0.0167 \((0.05/3)\) which is more than 0.015.

T-tests or non-parametric tests were used to compare means of ODI, VAS, NRS leg pain, NRS low back pain, BDI and walking distance results of EMG normal/abnormal groups. Patients with abnormal EMG had higher scores in the VAS \((41.9 \pm 25.7 \text{ vs } 31.5 \pm 18.1; \ p = 0.018)\), NRS leg pain \((7.5 \pm 1.5 \text{ vs } 6.3 \pm 2.1; \ p = 0.000)\) and BDI \((9.8 \pm 3.8 \text{ vs } 8.0 \pm 3.9; \ p = 0.014)\). According our statistician there is no need for Bonferroni correction if there are only two groups in EMG (normal/abnormal).

Was the EMG examination masked?

Thank you for comment.

Lumbar paraspinal and lower limb needle EMG were recorded pre-operatively by a neurophysiologist who was blinded to the radiological data and clinical assessment.

It sounds like the Paraspinal Mapping codified EMG protocol (e.g. reference 4) was used. However the authors do not state this explicitly. If they did use paraspinal mapping they should state this, report findings based on paraspinal mapping scores, and define abnormal based on published statistical norms for paraspinal mapping. If they did not use paraspinal mapping or some other validated, codified technique with established norms, then the authors need to describe this as a methodology weakness. It’s important because asymptomatic older people do have needle EMG fibrillations. Thus the amount of fibrillation has to fall outside of some range of normal. As Elaine Date has shown, simply assuming that any fibrillation is abnormal leads to huge problems with false positives.

We did not use paraspinal mapping technique (reference 4). Our EMG data was scaled in the following way:

0= none or no reproducible spontaneous activity, 1= rare or occasional (two or more) trains of fibrillation potentials, 2= frequent spontaneous potentials recordable at more than one depth, 3=abundant spontaneous activity nearly filling the screen

Categories 1-3 were considered abnormal.

We have now added this information to methods section.
As far as we can tell, S1 does not innervate the paraspinal muscles. Reword wherever this assumption is written, e.g. “bilateral paraspinal roots (L2-S1)” might be reworded as ‘Bilateral paraspinal MUSCLES innervated by the L2-L5 posterior primary rami’ if you used paraspinal mapping or a similar technique.

Provide more detail about how the EMG cumulatively was judged to be abnormal. Was an EMG abnormal if ‘any’ fibrillation was found in the limbs or paraspinals? Or paraspinals only? Or limb muscles only? Or F wave (not found useful in previous studies) or H-wave? Or some combination?

And what defined involvement of a specific root? Paraspinal muscle localization?

The classic ‘two muscles from two nerves but the same root, plus the paraspinals’? etc.

Thank you for this annotation.

Nerve root level specific (L2 – S1) EMG was abnormal if abnormal spontaneous activity associated with axonal damage (fibrillation and positive sharp waves) was found in the limbs or paraspinals. Specific nerve root involvement was defined by that nerve root innervated paraspinal muscles (nerves L2 – L5) or lower limb muscles (vastus lateralis, tibialis anterior, extensor hallucis longus and gastrocnemius) (nerves L3 – S1). We have now added this to methods section.

Please clarify, ‘the analysis was done online.’ I’m left wondering who physically did the test, who interpreted the findings of fibrillations etc. and who aggregated the findings to create an impression. Then I wonder what part of that was done from a distance, e.g. ‘on line’.

EMG was performed by experienced clinical neurophysiologists (AP or SM) who also interpreted the findings.

Online, means just that examination was performed with EMG equipment. We removed this confusing sentence.
Results:

Unless the authors have a valid standard for confirming stenosis at surgery, strike the first sentence.

Thank you, we removed this sentence of the results.

Explain the offer of surgery to 2 or 3 people with minimal pain and minimal disability. I suspect it relates to a surgeon’s bias after reviewing an MRI, but there could be other explanations.

Thank you for exact comment.

One patient had ODI scores under 20 points but this patient had NRS leg pain 9. Two patients had overall VAS under 20 points but these patients still had ODI scores over 40 points or NRS leg pain over 6 points.

The F- and H-wave results are presented, however the needle EMG data is not. A paragraph and probably a table are needed to present the data in a way that helps us understand how to distill the myriad individual tests into the ‘normal’ vs. ‘abnormal’ data that is used for analysis.

Thank you for comment.

Nerve root level specific (L2 – S1) EMG was abnormal if abnormal spontaneous activity associated with axonal damage (fibrillation and positive sharp waves) was found in the limbs or paraspinals. Specific nerve root involvement was defined by that nerve root innervated paraspinal muscles (nerves L2 – L5) or lower limb muscles (vastus lateralis, tibialis anterior, extensor hallucis longus and gastrocnemius) (nerves L3 – S1). We have now added EMG data to results section.

Discussion:

Discuss methodology flaws, as noted above.

Correct this sentence: “[the] Incidence of lumbar spinal stenosis is increasing probably due to the better quality and availability of radiological imaging facilities”
and also due to the aging population” I understand that the authors mean that lumbar stenosis is detected more frequently these days. However the incidence (actual presence of disease) is not influenced by the availability of radiological imaging. Also I have no idea how the quality of imaging would increase either the incidence of disease or the detection of previously undetected disease. Certainly ageing does affect incidence. Please rewrite more carefully.

Thank you for this annotation.

We have now reworded this more precisely.
Remove this statement: “MR images are thus needed to establish the level and severity of a stenosis.” It is contradicted two sentences later, “The degree of the severity of the disease cannot be judged based only on MR images either.” The author’s own data, consistent with the rest of the controlled trials in the literature, shows that MRI is not a good measure of severity of the syndrome. If you do need to say something about the utility of MRI, first caution that it is not diagnostic, then state that MRI may be useful in surgical planning and elimination of unusual etiologies of the stenosis syndrome.

Thank you for this annotation.

We have now removed this sentence.

Again, although small, and full of many assumptions and confusions, this study data provides an important first insight into the anatomy and physiology of the clinical syndrome of spinal stenosis as presenting in lateral spaces. With careful thought to definitions and wording, and some additional information, I believe it can be a useful contribution to the literature.
Referee 2

Major compulsory revisions

1. The authors evaluated the significance of lateral lumbar spinal stenosis (LLSCS) and enrolled 14 out of 88 patients with lumbar spinal stenosis. It is not explicitly specified if these 14 patients only had LLSCS or also, at least some of them, a narrowing of the central canal.

Thank you for this annotation.

All the 14 patients had only LLSCS which was confirmed with the preoperative MRI, none of the patients had central canal stenosis. We have specified this more precisely now.

2. Had some patients a LLSCS on more than one level? A table showing the results would be helpful for the reader

Thank you for comment.

Our radiological findings are presented in the results section. Some patients had more than one level LLSCS radiological stenosis findings but surgical decompression had done only for one level for all patients.

3. The authors do not report at which time the patients were enrolled in the study? If he last patient have undergone surgery at least 6 months ago the authors could (should) report on the postoperative course of the patients. How many of the patients improved after surgery, was the proportion of patients with improvement after surgery different in the groups with normal and abnormal EMG-findings?

Thank you for pointing out this aspect.

This study aim was to investigate the severity of LLSCS by MRI and its associations with preoperative clinical symptoms and EMG findings in patients with surgically confirmed LLSCS. In one of our submitted manuscripts we have studied post-operative outcomes.
4. Authors used the term “clinical significance” of an LLSCS identified by MRI to describe the purpose of the study. It is for me not clear what this term really indicates. What the authors can evaluate or demonstrate is the association between MRI findings and EMG findings. Does “clinical significance” indicate that the identified lesions, conditional on the EMG findings, are causal for the symptoms of patients? Authors should explain the meaning of “clinical significance” in the context of this study.

Thank you for this annotation.

We have now reworded this introduction section more precisely.

Minor essential revisions

Fourth paragraph in the results section; F-responses were normal in 13 patients, abnormal in 14 patients and in 1 patient was missing ... This must be mix-up between patients and roots, I assume

Thank you.

We have now reworded this more precisely.