Interpreting the MINT randomized clinical trials evaluating radiofrequency denervation for lumbar facet and sacroiliac joint pain

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LETTERS

Interpreting the MINT randomized clinical trials evaluating radiofrequency denervation for lumbar facet and sacroiliac joint pain: a reply to Provenzano *et al*

In July 2017, we published the results of three randomized clinical trials (RCTs) evaluating the effect of radiofrequency denervation on pain intensity among patients with chronic low back pain (the Minimal Interventional Treatment (MINT) RCTs) in the Journal of the American Medical Association (JAMA).[1] JAMA selected three letters to the editor, which the editors had decided were representative for all the replies received by JAMA. As authors of the original study, we were given the opportunity to respond to this selection. The fact that JAMA selected only three letters to the editor might have prompted the publication of critical letters/articles in other journals interpreting the MINT study. One of these articles by Provenzano *et al* in Regional Anesthesia and Pain Medicine.[2] This is an example of an article for which we had not yet been given the opportunity to reply. Provenzano *et al* highlight three frequently reported points of discussion related to the MINT study: (1) patient selection, (2) study design and data interpretation and (3) radiofrequency denervation technique.

This first criticism is related to the fact that we did not use controlled diagnostic facet blocks. The use of single versus double blocks and the threshold for diagnosis are a matter of controversy. The MINT study was a study in which patient selection and interventions were performed as occurs in Dutch daily practice. A single diagnostic block is recommended in the guideline 'evidence based interventional pain medicine according to clinical diagnoses' edited by van Zundert *et al*. This guideline was originally developed in the Netherlands and Belgium after being translated in English in collaboration with US key opinion leaders and endorsed by the World Institute of Pain (WIP). This guideline is also advised as a theoretical base in the preparation of the WIP Fellow of International Pain Practice examination.[3] We agree with Provenzano *et al* that performing a single block could result in lower specificity and higher false-positive rates.[4] However, a reference standard diagnostic block is not available. More than two diagnostic blocks decreases false-positive rates, but increases false-negative rates. Although a cut-off higher than 50% (eg, 80%) is also described in the literature, a 50% cut-off is most frequently used in studies and clinical practice. This informed our decision to use this cut-off for patient selection in the MINT study.

Second, the radiofrequency denervation technique is criticized on multiple aspects:

1. A perpendicular approach was used rather than the recommended parallel placement with a caudal-to-cranial cannula trajectory.
2. A single lesion was created by applying current for 90 s duration. Limiting the heating period to 90 s significantly increases lesion size variability, resulting in a smaller than maximal mean surface area.

This criticism mentioned in point 1 and 2 seem to be based on expert opinion. Different anatomical approaches, sizes of needles, duration and temperature of lesion are described in scientific literature, and we are not aware of a head-to-head study that shows superiority of any of these techniques. We strongly support the development of new studies which can give direction in the future.

3. No attempt was made to optimize sensory stimulation to guide needle placement.

Although not described in detail, we used a sensory 50 Hz stimulation current to optimize needle placement in the radiofrequency procedures for facet joint and sacroiliac (SI) joint pain. Obtaining stimulation at ≤0.5 V was used to confirm optimal needle placement. In the facet joint RCT, we also used motor stimulation at 2 Hz to confirm correct needle placement via contraction of the musculus multifidis. Again, we are aware of different expert opinions. We performed these procedures as described in the guidelines evidence based interventional pain medicine according to clinical diagnosis.[3] Also for this criticism, we advocate the development of new studies to improve knowledge in this area.

Third, in the article by Provenzano *et al*, it is briefly mentioned that questions have been raised regarding the appropriate use and interpretation of minimal clinically important differences and group averages. Although no specifications about this comment have been provided, Provenzano *et al* refer to the study of Ostelo *et al* when raising questions regarding the appropriate use and interpretation of minimal clinically important differences and group averages.[5] We have used the study of Ostelo *et al* to define the minimal clinically important differences for participants with chronic low back pain for pain and functioning. We understand the critical note about this choice, since Ostelo *et al* describe minimal clinical important change and in the design of the MINT study we used these values of change to define difference. Change and difference are two different dimensions. However, in light of the aim of the study, it is not the change but the difference that is important. In the facet joint pain RCT, we did not find any statistically significant nor clinically relevant differences between the intervention and the control group at the primary endpoint on 3 months. Only in the sacroiliac joint RCT and the combination RCT, we found statistically significant differences which did not fulfill this predefined minimal clinical important difference. We did not adjust for multiple comparisons, which could have resulted in some statistically significant findings by chance. Moreover, the studies are not blinded, and if treatment effects for subjective outcomes may be overestimated, it is likely that this is an advantage for the intervention group. Despite the lack of blinding, we did not find clinical important differences between the control and intervention group. The effects in the control group were unexpectedly high and although long follow-up data should be interpreted carefully they remained high until 1 year after treatment. This raised the question if this is the natural course of low back pain, but this hypothesis has not been tested.

The findings of the MINT study do not support radiofrequency denervation as an add-on to a standardized exercise programme within 3 months after the intervention. But there is still a possibility that radiofrequency denervation could be beneficial in a subset of participants. Our recommendation is that radiofrequency denervation for chronic low back pain should preferably be performed in a research setting. Future research should focus on patient selection, treatment techniques and outcome parameters. Similar to Provenzano *et al*, we also advocate for better education programme for physicians. Besides new studies, guideline development like evidence based interventional pain medicine according to clinical diagnosis are necessary.

In conclusion, the article by Provenzano *et al* also does not offer any new insights, rather the criticism given is similar to that described in the JAMA, and our response would have been similar to our reply to the letters to JAMA. We feel that prospective, randomized, controlled trials can only be refuted or confirmed by other prospective, randomized, controlled trials. There is a

need to gain more knowledge about optimal patient selection, diagnostic procedure and treatment techniques through high-quality research; to improve care for patients with chronic low back pain.

Radiofrequency denervation is no longer being reimbursed in the Netherlands, and exercise therapy only for a limited number of sessions for those who can afford private health insurance. This trend of a decreasing number of evidence-based reimbursed treatment options for patients with chronic low back pain is shown worldwide. We encourage the evaluation of different treatments and procedures for treating patients with chronic low back pain in randomized controlled trials as rigorous and large as ours.

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