Residual Limb Pain: More Than a Single Entity?

To the Editor:

We read with interest the paper of Karanikolas *et al.*[1] demonstrating the importance of effective perioperative analgesia in the prevention of phantom limb pain. Their finding that appropriate pain relief, regardless of the method of delivery, reduces the prevalence of phantom limb pain at 6 months is an important contribution to the postamputation pain literature. We also noted there was no significant difference between the treatment and control groups with respect to the prevalence of residual limb pain at 1 and 6 months. Although this lack of treatment effect certainly could be a result of small sample size, it also may be secondary to lack of differentiation of the subtypes of residual limb pain.

Previous reports of persistent postamputation pain[2–4] have differentiated between pain arising from a phantom and that from the residual limb; however, subclassifications of residual limb pain are not performed typically (or at least reported). In the Durham Veterans Administration Medical Clinic postamputation pain clinic, we recently recognized the existence of at least three distinct residual limb pain subtypes: somatic pain, complex regional pain syndrome-like pain, and neuroma/neuralgia pain. Although these are well-recognized pain diagnoses in their own right, they usually are not used in the specific clinical setting of persistent postamputation pain. We believe that recognition of these distinct subtypes may help to better identify effective prevention strategies and/or treatments. These subtypes have different proposed etiologies and are unlikely to respond to similar treatments.

For these reasons, we believe that the historic failure to recognize distinct subtypes of residual limb pain has led us to paint with too wide a brush, and in the article by Karanikolas *et al.*, this could have hidden a positive treatment effect in one or another residual limb pain subtype.

To address what we see as a deficiency in the current state of the art regarding postamputation pain taxonomy, we have developed a diagnostic algorithm that is capable of differentiating the subtypes of residual limb pain described above. We are validating this algorithm in our amputation pain clinic and encourage others in the field to consider further differentiating residual limb pain into its component subtypes.

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In Reply:

We would like to thank Drs. Lindsay, Pyati, Buchheit, and Shaw for their interest in our study[1] and for raising the important issue of residual limb pain. As they correctly point out, our study had a small sample size and did not differentiate between subtypes of residual limb pain. However, based on data from previous studies by Bach *et al.*[2] and Nikolajsen *et al.*,[3] our clinical trial was designed to study phantom limb pain (phantom limb pain intensity at 6 months was our primary endpoint), whereas residual limb pain was only one of several secondary outcomes.

At the 6-month follow-up, our study did not show any difference between treatment and control groups with regard to residual limb pain, and in fact only one or two patients in each group (including the control group) had any residual limb pain. Therefore, we believe that even if we had looked at subclassifications of residual limb pain, we would not be able to show any significant differences because of small sample size and the need to use Bonferroni correction, to avoid spurious "significant" findings due to multiple comparisons.

Of course, we agree that residual limb pain after amputation is an important issue that deserves more study. A clinical trial designed to evaluate subtypes of residual limb pain would be very interesting and could provide answers to some important questions. However, such a study probably would need a bigger sample size and perhaps a simpler study design so that multiple comparisons and the need for Bonferroni correction would not be an issue, as was the case in our study.

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