

Author's response to reviews

Title: Acupuncture for dyspnea in advanced cancer: a randomized, placebo-controlled trial (ISRCTN89462491)

Authors:

Andrew J Vickers (vickersa@mskcc.org)
Marc B Feinstein (feinstem@mskcc.org)
Gary E Deng (dengg@mskcc.org)
Barrie R Cassileth (cassileth@mskcc.org)

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Response to reviewers

Doreen Oneschuk

No significant concerns were raised by this reviewer.

Eduardo Bruera

Comment: Only [some] patients had continuous dyspnea. How was dyspnea expected to improve in patients who only developed increased dyspnea upon movement?. It is not clear why the patients chose to include jointly patients with continuous and episodic dyspnea. They should point this a major potential limitation of the study, and attempt to analyze the sub-group with continuous dyspnea separately. Otherwise this may well be a false negative study.

Response: We concur with the reviewer's comment that the patient population included both patients with continuous symptoms and those whose symptoms were apparent only on activity. We therefore report our analyses separately for the immediate effects of treatment (of relevance only to patients with continuous symptoms) and for the daily diary of breathlessness completed in the week after treatment (of interest primarily to patients with episodic symptoms). We also present an analysis of the immediate effects of treatment excluding patients with low baseline scores (i.e. those with episodic dyspnea). The results of the three analyses are similar. We have now clarified our approach as follows:

We give results separately for dyspnea measured immediately after acupuncture, and for dyspnea assessed by daily diary. Some patients reporting dyspnea scores immediately after acupuncture treatment had negligible pre-treatment dyspnea. Hence we also provide a sub-group analysis of the immediate post-treatment scores, excluding patients scoring a mean of 2 or below. For all analyses, patients receiving true acupuncture reported slightly higher post-treatment scores, approximately equivalent to 10% of baseline.

Comment: The choice of "response" has not been well explained. The authors should better discuss this important point because they argue that their results suggest that there was no effect based on this definition. They should provide literature support if possible for their choice of clinical improvement.

Response: We have added the following to the discussion:

Based on our clinical judgment of how much improvement we should expect from acupuncture to make worthwhile the time and trouble associated with treatment, we pre-specified a 20% difference between groups as clinically meaningful. It is against this criterion that we draw our conclusion of "no effect". Yet we can exclude even smaller levels of benefit, such as 10%. We find it unlikely that any patient or clinician

would deem acupuncture to be worthwhile for a benefit of one third of a point on a 0 – 10 scale.

Comment: Should future studies address dyspnea that occurs with movement? Should multiple dose trials be conducted? If so, what type of design would the authors recommend?

Response: We do not recommend further research on the basis of our findings.

Comment: The large number of refusals for this study is concerning due to the innocuous nature of the intervention. Why did the authors find such a large number of refusals to participate? This is important for other potential researchers in the area.

Response: We have clarified this in the discussion section, which now reads:

Patients with advanced cancer admitted to MSKCC generally have severe medical problems. Accordingly, they often feel overwhelmed, and a clinical trial, regardless of its perceived benefits and risks, is perceived as an additional burden. Patients commonly noted in response to the invitation to participate that “I just can’t face dealing with this right now”.