

Peer Review File

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Reviewers 1

Comment 1: *Apart from knowing the Rivers MPS diagnostic criteria, they don't learn with an expert to perform the technique? There is no supervision to know if the technique is performing in the same way and correctly by all caregivers?*

Response: We appreciate your thoughtful feedback. We have added the relevant text to the Methods and Results sections as follows (page 10, lines 147–151; page 16, lines 255–257):

“For the ischemic compression and sham compression groups, direct instruction on the technique was given by the clinicians to family caregivers for approximately 5 minutes on day 0 (T0, the day before the start of the intervention). Patients were assessed by clinicians to ensure that they had been treated as indicated and properly on day 14 (T1, 14 days after the start of the intervention).”

“On T1, all patients who were followed up were confirmed by clinicians to have received appropriate interventions when indicated.”

Comment 2: *In my opinion, is important to introduce as an exclusion criteria the change of medication in the patient, it's mentioned below but I believe it is essential specify it as exclusion criteria.*

Response: We have added the relevant text to the Study participants section as follows: (page 8, lines 120-121):

“(d) patients wanting to use superficial massage or new medication in the near future.”

Comment 3: I consider a limitation section necessary, since I understand that this treatment, when performed at home, is not supervised by the researchers.

Response: We have added relevant text to the limitations section as follows: (page 22, lines 362-364):

“(1) the procedure was not consistent because the interventions were administered by family caregivers and non-supervised by clinicians”

Comment 4: It is necessary in all tables and figures to place a footnote which includes the explanation of the table or figure.

Response: This was a complete mistake. We apologize for the mistake in attaching the figure legends and footnotes. We have taken care of this issue.

Reviewers 2

Comment 1: Line 89: I don't get the idea of how mindfulness and lung cancer patients relate to your objectives. If your population are affected of myofascial pain, you shouldn't focus on one pathology. Maybe you could enhance this with other pathologies.

Response: We appreciate the thoughtful feedback. We have removed this sentence.

Comment 2: In general, introduction is quite short. I would recommend the authors to deep on the origin of myofascial pain, the effects on other outcomes (e.g. quality of life) and how these changes may affect their caregivers.

Response: We have added the following sentence to the Introduction section as follows: (Page 5, lines 56-58; Page 5, lines 63-66; Page 6, lines 79-80; Page 6, lines 85-86)

“According to the US Centers for Disease Control and Prevention, three main conditions that cause daily life disability include heart disease, arthritis, and back pain (2). Of patients with cancer, 11.9–45% complained of back pain and experienced MPS (3-5).”

[2] Center for Disease Control and Prevention. Disability and Health. Atlanta GA, CDC, 2011. Available at: <https://www.cdc.gov/ncbddd/disabilityandhealth/healthyliving.html>. Accessed July 1, 2021.

“In addition, the decreased activity is expected to be related to psychological stress (7). Psychological stress has been reported to be associated with low back pain in mice One report found that more than half of patients with cancer have MPS with psychological stress (8).”

[7] La Porta C, Tappe-Theodor A. Differential impact of psychological and psychophysical stress on low back pain in mice. *Pain* 2020;161(7):1442–58.

“Family caregivers of patients with cancer feel guilty that they are not doing enough for their patients (19).”

[19] Hileman JW, Lackey NR, Hassanein RS. Identifying the needs of home caregivers of patients with cancer. *Oncol Nurs Forum* 1992;19(5):771–7.

“One of the factors affecting the low QOL of family caregivers is the degree of patient distress (22).”

[22] Kim Y, Given the BA. Quality of life of family caregivers of cancer survivors: across the trajectory of the illness *Cancer* 2008;112:2556–68.

Comment 3: *The objective isn't clear enough. I would rather separate it into two objectives: 1) to check the efficacy of ischemic compression, and 2) to check the self-esteem of caregivers after their application.*

Response: We have separated the two objectives in the Objective section as follows (page 7, lines 94–96):

“The objective of this study was to verify the following: the effects of ischemic compression performed by family caregivers for MPS (a) in patients and (b) the care burden of the family.”

Comment 4: *Line 117: please explain the Rivers' MPS diagnostic criteria. Thereby, there are not inclusion or exclusion criteria regarding the pathology of the patients, and this could bias your sample. Criteria are not specific enough for your sample to be homogeneous! Were there any specific criteria (inclusion or exclusion) related to any pathology? (e.g. cancer, reumathoid pathologies...)*

Response: We have added the relevant text to the Study participants section as follows: (page 8, lines 111–116; page 8, lines 118–119):

“MPS is diagnosed according to the following criteria: (a) a tender spot found on palpation with or without referral of pain; (b) recognition of pain symptoms by the patient on palpation of a tender spot; and at least three of the following: (c) muscle stiffness or spasm; (d) limited range of motion of an associated joint; (e) pain that worsens with stress; and (f) palpation of a taut band and/or nodule associated with a tender spot (1).”

“(b) patients with rheumatoid pathologies (e.g., fibromyalgia, polymyalgia rheumatica)”

Comment 5: *Line 137 (procedure): please explain the method of treatment with more details. If caregivers are using ischemic compression on Myofascial Trigger Points, use a valid reference of this method. Again, the treatment of myofascial trigger points*

may vary from one location to another (is not the same to treat a trigger point on the masseter muscle compared to upper trapezius fibres) so this is biasing your study. Table 2 in results specify that trigger points are located on lower or upper back, but this should be indicated on the text.

Response: We have added the relevant text to the Methods and Results sections as follows: (page 10, lines 144–151; page 16, lines 261–262):

“In all groups, the patients were marked with ink at the location of the MTrPs by the clinicians. All groups were given a pamphlet with specific intervention details. The method of ischemic compression in this pamphlet was based on previous studies (14-17). For the ischemic compression and sham compression groups, direct instruction on the technique was given by the clinicians to family caregivers for approximately 5 minutes on day 0 (T0, the day before the start of the intervention). Patients were assessed by clinicians to ensure that they had been treated as indicated and properly on day 14 (T1, 14 days after the start of the intervention).”

“The MPS sites were found only in the upper and lower back, but not in other areas”

Comment 6: *On the procedures, was there any method to check that caregivers were doing the intervention (when indicated and properly)? This is not indicated on the manuscript.*

Response: We have added the relevant text to the Methods and Results sections as follows: (page 10, lines 150–151; page 16, lines 255–257):

“Patients were assessed by clinicians to ensure that they had been treated as indicated and properly on day 14 (T1, 14 days after the start of the intervention).”

“On T1, all patients who were followed up were confirmed by clinicians to have received appropriate interventions when indicated.”

Comment 7: *Line 176 (personalized pain goals) "the PPG among cancer patients was 3"; does this refer to the reference added? Please specify.*

Response: The three in this number do not represent the reference. We have revised this sentence from "PPG" to "PPG score" (page 12, lines 188):

"The median PPG score of patients with cancer was 3."

Comment 8: *Same as on the introduction, I think this discussion lacks of information related to the caregivers self-esteem. I wonder if authors could find other manuscripts that check this outcome with other treatment, in order to reduce pain in patients. They state that there are not other publications with this kind of application, but maybe if their outcome is to check self-esteem, comparison with other interventions may be indicated.*

Response: We thought this point was very important, but we could not find suitable manuscripts. Therefore, we have added it to the Limitations section as follows: (page 22, lines 369–373):

"(f) there is no previous study on the interventions by family caregivers to improve the patient conditions for their self-esteem, and we were unable to compare the results of our study with others."

Comment 9: *Also, ischemic compression has been evidenced to reduce the pain produced by myofascial trigger points. Please refer to other authors that have already evidenced these changes. To improve it, I would explain the way ischemic compression helps reduce the nociception generated by myofascial trigger points.*

Response: We have added the relevant text to the Discussion and References sections as follows: (page 17, lines 309–310; page 19, lines 316–317):

“A systematic review of ischemic compression by clinicians for shoulder pain showed immediate and short-term positive effects (33).”

[29] da Silva AC, De Noronha M, Liberatori-Junior RM, et al. The effectiveness of the ischemic compression technique on pain and function in individuals with shoulder pain: a systematic review. *J Manipulative Physiol Ther.* 2020;43(3):234–46.

“The mechanism of PPT-related inactivation is unknown, but it may reduce the nociception generated by MTrP.”

Comment 10: I would deep on the difference between groups related to the self-esteem of caregivers. Your results evidence that the fact of doing something that may help the patient, even if it is a sham intervention, helps improve their self-esteem when compared to doing nothing, so I would reccomend to look for other publications that also evidence this fact.

Response: We appreciate your thoughtful feedback. We have added the relevant text to the Discussion and References sections as follows: (page 21, lines 344–347):

“One study reported that the holding of the hands of patients with cancer by family caregivers did not significantly increase the patient's autonomic functioning, but significantly increased the family caregiver's autonomic functioning, resulting in family self-care (35).”

[31] Sakuma H, Hasuo H, Fukunaga M. Effect of handholding on heart rate variability in both patients with cancer and their family caregivers: a randomized crossover study. *Biopsychosoc Med* 2021;15(1):14. doi: 10.1186/s13030-021-00217-y.

Comment 11: I think your major limitation is the huge difference between patients. Most of them are cancer patients, but there are different locations, and therefore, pain may be perceived on many different regions. This bias your results, even if one of your main outcomes is to check the self-esteem of caregivers. I would enhance this

manuscript by making a body map of the pain perceived by patients and the different locations, so maybe you could reduce this bias.

Response: We have added the relevant text to the Results and Limitations sections as follows: (page 16, lines 261–262; page 22, lines 369–371):

“The MPS sites were found only in the upper and lower back, but not in other areas (Figure 2).”

“(e) it was not possible to compare the effects on different sites of MPS due to the small number of cases in this study”

Comment 12: Also on your limitations you specify that most of your population were cancer patients, so maybe it would be interesting of focusing on this population, and thus the results would be only related to this population (indeed, this would make your manuscript more homogeneous)

Response: We have added the relevant text to the Results and Limitation sections as follows: (page 17, lines 274–278; page 18, lines 292–296; page 20, lines 364–366):

“When limited to cancer patients (70 patients), the rate of improvements of 50% or more in the NRS score for patients 14 days after the intervention was 60.9% (90% CI, 43.8–78.0) for the ischemic compression group, 8.7% (90% CI, –0.9–18.3) for the sham ischemic compression group, and 4.2% (90% CI, –2.6–11.0) for the control group ($p < 0.001$).”

“When limited to cancer patients (70 family caregivers), the ischemic compression and sham compression groups showed significantly lower caregiver self-esteem scores (higher caregiver self-esteem) at T1 than the control group ($p < 0.001$ and $p = 0.005$), but there was no significant difference between the ischemic compression and sham compression groups ($p = 0.349$).”

“(b) the results cannot be generalized because homecare patients are mostly cancer patients (however, the results of the main outcome were similar even when the study was limited to cancer patients and their family caregivers)”