Peer Review File

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Reviewer A

Evaluation of cancer pain management techniques is a laudable target. However, this article falls far short of achieving this goal.

This article is essentially a catalogue of loco regional procedures of pain treatment without real literature review and analysis of evidence in cancer pain management including the evidence base medicine for each procedure.
Moreover, the article often only describes the techniques. No data is provided on long term follow up and induced opioid savings.
Finally, this article does not mention recommendations like those of ESMO (2018)

In addition, for some procedures, the evaluation is mainly on non-cancer pain (Epidural steroid injections, join and bursa injections, etc.) and for others like celiac block the evaluation is almost 30 years old!
Moreover, for the Superior Hypogastric Plexus Block you interpret the outcomes, in fact the authors confirm the modest efficacy in advanced cancers.

For neurostimulation you forgot to mention the huge majority of cancer patients suffer mixed pain and cannot be treated by neurostimulation effective only on neuropathic pain, specifically for pelvic cancers therefore neurostimulation is rarely a good option for cancer pain management.

Finally, it is astounding that you would recommend epidural analgesia for these patients, while it is recognized the procedure has a higher rate of complications than IDDS. At the same time, you describe a negative aspect of intrathecal pumps, despite many publications on evidence including several randomized prospective studies (the last one Ma ke Pain 2020). To suggest that the process is more complex is not true, it's just a matter of training.

Dear Reviewer A,
Thanks for your kind feedback. We really appreciate all your time in the review of the manuscript, and your helpful comments and the recommendations to make this review more effective. We have made all the changes on your suggestions and added more data and references as recommended. The changes are as follows.

Comment 1: this article does not mention recommendations like those of ESMO (2018)
Reply 1: ESMO recommendations were an excellent suggestion. We have added ESMO 2018 recommendations in multiple places, especially in the section for Intrathecal pumps, and Celiac plexus blocks.
Changes in the text: Line 304-306, and Line 474-475– Added Reference #77 (Line 885-886)

Comment 2: Data for celiac plexus is 30 years old.
Reply 2: You are correct, the data for celiac plexus by Eisenberg is almost 30 years old. Meta-analysis by Eisenberg is one of the most detailed and extensive works ever done on Celiac plexus blocks for cancer pain. And it continues to be one of the most valid pieces of research for this plexus block. But your point is very valid, and we have added a few new studies for celiac plexus, especially relating to newer techniques like cryoablation, EUS with RFA for neurolysis with this version of edits. This data is from the last 3 years, and tries to balance out the older and newer data.
Changes in the text: Line 302-305. Added Reference #75-76 (Line 878-883)

Comment 3: There is modest response to Sup Hypogastric block in advanced cancers
Reply 3: Yes, there is modest response in advanced cancers to SHPB. We have updated the language to refer to modest effects rather than significant improvements as stated earlier.
Changes in the text: Lines 332-339 have been updated with recommended changes.

Comment 4: Data for opioid savings is needed
Reply 4: Data for opioid savings for Celiac plexus block, SHPB, GIB, and Intercostal nerve blocks for cancer has been added along with references.
Changes in the text: Celiac plexus block Lines 301-302, SHPB Lines 339, GIB Lines 369-370, and Intercostal Nerve block Lines 199-200

Comment 5: SCS works for mostly neuropathic pain, while cancer pain is mixed pain.
Reply 5: Yes, we updated to make the neuropathic elements of pain more prominent, and noted the part about cancer pain being mostly mixed.
Changes in the text: Lines 254-257

Comment 6: Temporary epidural analgesia vs IDDS
Reply 6: You are correct. Temporary epidural analgesia section was added since often cancer patients are very sick, and unable to undergo GA at EOL for IDDS placement, so epidural analgesia is provided in these cases for a few days of prognosis. Often in hospice settings.
Your recommendation on the newer data from Ke Ma was very helpful to add, so it was added with its reference and ESMO 2018 guidelines.
Changes in the text: Lines 475-477, and reference 115 Lines 1014-1016

Thanks again. We really appreciate all your kind feedback.

Reviewer B

Your review is comprehensive with regard to pain management interventions for cancer pain. Cancer pain indications for epidural injections and medial branch blocks, especially vertebral augmentation, such as metastasis to the neuroforamen, paraspinal regions, and vertebral bodies, should be included and discussed.

Dear Reviewer B,
We really appreciate your kind remarks and suggestions. We have made all the recommended suggestions.

Comment 1: Cancer pain indications for epidural injections and medial branch blocks, especially vertebral augmentation, such as metastasis to the neuroforamen, paraspinal regions, and vertebral bodies, should be included and discussed.

Reply 1: The recommended changes to the Epidural injections for spinal malignancies and mets has been added along with references.
Also, for other intervention of vertebral augmentation for metastasis to the neuroforamen, paraspinal regions, and vertebral bodies has been included and discussed along with references.

Changes in the text: Line 223-225 with reference 58 for epidural injections for spinal mets. Line 155-157 with reference 38 has been added for vertebral augmentation for specific neuroforamen and paraspinal regions.

Thanks.

Reviewer C

I understood that this manuscript is a scoping review on the interventional pain management in cancer patients and that it is an easy-to-understand summary.

Major comments are as follows;

Although this manuscript describes many positive results with respect to Vertebral Augmentation, some representative systematic reviews and meta-analyses (e.g.,

Buchbinder R, et al. Cochrane Database Syst Rev. 2018) have reached negative conclusions. This manuscript should at least mention the studies with negative conclusions and give an unbiased view of the possible benefits.

Dear Reviewer C,
We really appreciate your kind remarks and suggestions. We have made all the recommended suggestions.

Comment 1: Addition of studies with negative conclusions should also be added.
Reply 1: Thanks for recommending the Buchbinder paper on vertebroplasty and its equivalence to sham procedures. This was very helpful, and we added it as a negative study as recommended.

Changes in the text: Line 230-233, Reference #60 is added

Thanks.

Minor comments are as follows

Comment # There are subheadings with the same numbering (i.e., "5 - Intercostal Nerve Block and Neurolysis:" and "5 - Vertebral Augmentation”), and "6 - Spinal Cord Stimulation" would be "7 - Spinal Cord Stimulation".
Reply: Yes, it has been corrected. Thanks for the suggestion/ correction.

Comment # Is it unnecessary to list Diskitis in the adverse effects section of Celiac Plexus in table 3?
Reply: Thanks. Discitis has been added to table 3, and also to the main article in line 311 along with reference #72.

Comment # It would be better to indicate where the Table in the text applies.
Excellent point. Table # in the main headings have been added. Thanks.