Peer Review File

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Review Comments

Reviewer A

Comment 1

Dear authors. Thank you for the opportunity for reviewing this excellent pilot study. Please see my comments listed below.

Abstract:

In line 23, the first paragraph in the abstract, is the "(9)" a reference? In this case, it should be deleted from the abstract. If this is referring to something else, I am unsure of the meaning of it.

Response 1

Many thanks for this. An error on our part. This has now been removed.

Comment 2

Introduction:

First paragraph in introduction, line 79-80. "it is more common in cancers that tend to spread to the spine such as breast, prostate and lung. The incidence in these cancers may be as high as 19% (4)." This sentence is a bit unclear. When reading it, I am unsure if this refers to the incidence of MSCC for these cancer types, or these cancer types represent 19% of MSCC, or perhaps something else. Could this be clarified?

Response 2

We have now deleted the sentence "the incidence maybe as high as 19% in some cancers"

Comment 3

In the last paragraph on page 3, line 99, the words "fit" and "young" are used. Consider the choice of words, as they to the reader can sound a bit biased. Consider using more clinical terms, such as age and performance status.

Response 3

We have changed "fit and young" to good performance status (page 3, line 99)

Comment 4

Page 4, line 115, second paragraph, here "metastatic spinal cord compression (MSCC)" should be replaced by only "MSCC", as this has been explained previously.

Response 4

This has been updated accordingly.

Comment 5

Methods and materials:

Page 5, first paragraph, line 145-148, as well as second paragraph, line 156-158. In this section, both hospitals and sample is listed with the use of (i), (ii), (iii). The same kind of listing is used on page 10, results and page 13, discussion. It confuses the reader, when the same kind of listing is used for different things and makes the text harder to read. I would suggest using different ways of listing, e.g. (a), (b), (c) or (1), (2), (3), etc and be consistent in only using one form of listing for each in order to make the text easier to read and avoid mix up.

Response 5

Many thanks for this. We have now updated this. Using a numbered list for names of hospitals and alphabetical list for types of data collected. Page 5 line 161-165, 172-174)

Comment 6

Results:

Page 11, Figure 2. This figure shows the Kaplan-Meier analysis of survival probability. Since the study population is rather small and it is explained previously that the 6 months survival was 90%, it is worth considering if this figure adds to any further explanation. If not, I would suggest rather deleting this figure.

Response 6

Many thanks for this suggestion, we have now deleted this figure

Comment 7

Discussion:

Page 14, section "Main clinical implications", line 336, "which positively impacted patient care." This part would be nice to clarify, in which way it positively impacted patient care. Do you have data on this? Perhaps some quality of life or reduced adverse effects due to quicker onset of treatment. If so, maybe this could replace figure 2 to illustrate or be clarified in the sentence.

Response 7

Many thanks. We have added to this section:

"the centres involved in this study are more likely to meet national standards for time from imaging to MSCC treatment (≤24 hours) as a result of this intervention". This could be seen as positively impacting patient care at these centres. Unfortunately, due to the nature of disease presentation, split hospital and community-based management of these patients, it was quite challenging to collect follow-up or quality of life data. We plan to make this a priority in planned, subsequent larger studies." Page 13 line 391-393

Comment 8

Page 15, line 345-351. Last couple of sentences in last paragraph in the discussion should be re-read and some small grammatical and spelling errors corrected, such as "an" should probably be "and" and "be part of a future prospective studies" should either be singular or plural instead of both.

Response 8

Thanks for this. The sentences have now been reviewed and corrected. Page 14, line 419-423

Reviewer B

This is a very well-written article on a very interesting and important topic. My comments/suggestions are as follows:

Comment 1

It would have been helpful to see information on the time from presentation with symptoms to imaging/treatment. You addressed this in the Discussion.

Response 1

Many thanks for your kind feedbacks. We tried really hard to collect this data (i.e., presentation of symptoms to imaging), unfortunately, there were a lot of missing data. The main reasons we identified were (i) Some of these patients were seen by multiple care teams and health practitioners before a final diagnosis of MSCC was made. Some other patients were asymptomatic and were only diagnosed with MSCC on planned interval CT scans to assess their disease burden or treatment response. Collection of imaging to treatment data was much better and reliable as date of scans and date of treatment could be easily verified regardless of the centre were scan was done.

Comment 2

Please include the 6 month overall survival prior to introduction of the MSCC for comparison. Also, please add the number of patients for which survival data was available in the paragraph with this information on page 10.

Response 2

Following discussions within the team and with senior clinicians within the group, we decided to de-emphasize/remove the results on impact of the MSCC intervention on OS. Reasons being (i) small sample size (ii) short follow-up time interval (6 months) (iii) limited number of patients for which follow-up data was available (iv) nature of the study as proof of concept. A much larger, well-powered study with adequate time for follow up, will be the next steps, to further confirm findings from this small study.

Comment 3

Please expand upon the information regarding referrals made to hospital palliative care physiotherapy/occupational health, and hospice palliative care teams. Why were only 7 referrals made to each- should it be more? What percentages of patients were referred? Please add this to the pertinent paragraph on page 10.

Response 3

Thanks for this comment. Our local and national guidelines recommend early referral to the physiotherapy team. Unfortunately, documentation of these referrals and patient functional improvement/outcomes have not been clear in the information available for this study. In addition, some of these patients were referred to either the hospital-based or community-based physiotherapy and palliative care teams. Further studies will look into how best to navigate and gather study data across these groups in different settings to further enrich our patient outcomes data.

Thanks for this comment

Comment 4
If there is information on the number of patients who experienced symptom improvement with treatment and/or regained ambulation, both pre and post introduction of the MSCC, this should be included.
Response 4
Many thanks for this. Unfortunately, as with other systemic challenges faced in some aspects of data availability or access, accurate follow-up data on functional recovery was difficult to gather as patients were managed by different teams and discharged to community palliative care teams. The palliative care team referral will depend on the patient's postal/zip code or in some cases, patient's preference. Other factors include if the patient has been known to a particular community care team in the past, or if patient will be moved closer to the location of their next of keen/family for end-of-life care and comfort.

Reviewer C
Comment 1
This is a well-done study looking at the impact of adding an MSCC coordinator in reduction of treatment times and in improving patient outcomes. This study poses an important question, and is well done particularly within the confines of a very challenging population to enroll and follow.
Response 1
Many thanks for your kind comments

Comment 2
A few recommendations
Main clinical implications Line 332 – "hightlights o significant differences between centers", however earlier in the paper mentions one center had longer treatment times due to the need for further communications/ round discussions. Please clarify.
Response 2
Many thanks for this comment. DVH had the lowest number of patients(n=4) enrolled into the study. Also, only one patient experienced a prolonged treatment time in this centre, which likely skewed the result in an already small sample size. Other than this one outlier, we felt all the centres had similar patient population and characteristics. This proof-of-concept study was able to show promising data that the implementation of the MSCC coordinator is feasible and could potentially translate to patient benefit which we hope to assess in more detail in future, larger studies.

Comment 3
Please elaborate on potential challenges implementing this program in a community center – ie need for expedited communication with a tertiary center, could result in delays if rounds discussion required

Response 3
As the four hospitals evaluated in this study are general hospitals based outside of major cancer centres in London, there will always be some level of dependence on the big cancer institutes for super-specialist care. However, what we hope to demonstrate is the need to have a dedicated communication channel between the local hospitals and the academic healthcare institutions. Such channel could enable a fast and clear communication with the surgical services to allow prompt clinical decisions to be made. Other factors which could have an impact on the implementation of this program is availability of funding or staff to run the service on an ongoing basis. Having a cross-cover MSCC coordinator to support during annual leave or sick leave will ensure continuity and maintain standard of care

Comment 4
Line 337 – states MSCC coordinator might have an impact on overall survival. Earlier it was reported OS over 90%. What was the OS of patients prior to implementation of MSCC coordinator? What is the basis for this
Response 4
Many thanks for this comment. The question on overall survival was a recurring theme across all the reviewers. After further evaluation, we think we do not have enough data (especially data prior to the implementation of the MSCC coordinator) to provide a comparative analysis of impact of the service on overall survival. We have removed OS as endpoint from this study.

Editorial Comments
By comparing relevant data in 2020 and 2021, this non-randomized controlled trial shows that MSCC coordinators can improve the time from imaging to treatment for MSCC patients. We consider the manuscript to be of some clinical value. Below are some minor suggestions from the editorial office.

Comment 1: Title
Indicating non-randomization in the title will help the readers to initially understand the type of this trial.
Response 1
This has now been added to the title

Comment 2: Author
Please add the corresponding author information in the text, including name, institution, and email address
Response 2
These have now been added. Page 1 line 2

Comment 3: Abstract
(1) Line 23, the abstract should not contain any citations.

(2) For enriching the abstract information, we kindly suggest the authors state the study sample (2020 and 2021) and briefly describe the eligibility criteria for participants.
(3) After the Abstract, 3-5 keywords should be provided. Authors can add it according to the PICO principles of evidence-based medicine.
(4) Line 47, please add the FULL name of EKH in the Abstract.

Response 3

All of the above have now been edited. Thanks
Eligibility criteria Page 5, line 174-177
Keywords Page 2 line 61 and 62
2020 and 2021 study sample Page 2 line 48
Full name of EKH Page 2 line 51

Comment 4: Introduction

Lines 131-138:
(1) To better highlight the objective of this article, authors can use these statements, i.e. we aim to /our objective is... It is just a kind suggestion.
(2) This paragraph described the objective of this study, how about hypotheses? For example, the hypothesis of this study was that the time from imaging to radiotherapy is shorter for patients with MSCC in 2021 than in 2020. (just an example). We kindly suggest authors provide testable hypotheses.

Response 4

Many thanks for these suggestions. We have now added the aim, objective and hypothesis for the study
Study aim Page 4 line 132
Study objective Page line 133-135
Hypothesis Page 5 135-136

Comment 5: Methods

(1) The author should indicate whether it was carried out at the group or individual level in each analysis.
(2) $p \leq 0.05$ should be revised to $P \leq 0.05$. And, we will report P-values to 2 decimal places if P-values ≥ 0.01. Please check the FULL text to make sure uniform.
(3) Please add statistical software or programs used in the Statistical analyses section.

Response 5

Many thanks for these comments/suggestions. These have now been implemented. Page 6 line 221 to 223

Comment 6: Results

(1) We propose to put the inclusion/exclusion criteria of participants in Table 1 so that the reader will have a clear idea of the study's recruitment criteria simply by reading the table.

Response 6 (1)

Thanks for this suggestion. This has now been done. Page 5 line 176-177

(2) It's good to provide baseline clinical characteristics of patients in each group, how about baseline demographic, e.g. gender and age, and baseline characteristics relevant to MSCC? We recommend adding them.

Response 6 (2)

Many thanks for this suggestion. We agree with the editor in providing this information. However, we might be able to provide the post-intervention cohort age and gender but unfortunately, similar data is not available for the pre-intervention cohort.

(3) We suggest the authors add P-value in Table1, including imaging to treatment times and baseline data. If there is a baseline difference, please state the statistical method used to control this difference.

Response 6 (3)

We have now added the p values. There were no significant differences between the groups. Page 7 line 245-248, table 2

(4) Line 220, we have a bit of confusion about the P=0.045, is this value based on the median time or the mean time in Table 1? And, if possible, please add the confidence interval.

Response 6 (4)

Many thanks for the comments. These have now been added Page 7 line 245, table 2

(5) A little question: why does the number of patients in Table 2 (36 and 13) not match the final number in Table 1 (40 and 20)? We kindly suggest the authors clarify it in the previous text.

Response 6 (5)

This difference comes from patients where the hospital of referral wasn't recorded. We have tried to clarify this in the results section.

In the results section, in the subsection 'difference within hospitals', we have added a sentence "4 patients in the pre-intervention phase and 7 patients in the post-intervention phase had missing data for their hospital, so were not included in this analysis."

Page 9, line 280-281

(6) As Fig1 and Fig 2 are not prespecified analyses, to better distinguish exploratory from prespecified analyses in the text, authors can utilize this statement, e.g., an exploratory analysis shows that.

Response 6 (6)

These changes have now been made. Page 9 line 288

(7) We suggest that the authors add to Table 1 the follow-up times associated with Fig 2 and the missing data.

Response 6 (7)

Figure 2 has now been removed based on some of the reasons earlier described.

(8) Were there any adverse events or unintended effects during the study? If so, please summarize and, if not, also need to state in the text.

Response 6 (8)

Many thanks for this suggestion. We have now added in the results section
"There were no adverse events or unintended side effects reported during the study"
Page 7 line 242-243

Comment 7: Discussion

We have learned about the benefits of MSCC coordinators according to the paper, but we also wonder if there are any obstacles or phenomena that still need to be addressed if MSCC coordinators are to be promoted more widely. Would you please add these reflections to the Discussion?

Response 7

Many thanks. A paragraph some of these obstacles or phenomena has now been added.
Page 13 line 381-387

Comment 8: Ethical Statement

Please provide the name of the ethics committee or institutional review board, the number/ID of the approval, and a statement that the participants gave informed consent before taking part (or a statement that it was not required and why). Authors should also state that the study conformed to the provisions of the Declaration of Helsinki (as revised in 2013).

Response 8

The ethics approval number and statement regarding participants informed consents have been added.
Page 5 line 159-161

Comment 9: Editorial Policy

According to the author instruction, please add the following information:
(1) For articles written in accordance with specific reporting guidelines, the author must include the "Reporting Checklist" section in the footnote and indicate, "The authors have completed the TREND reporting checklist."

Response 9 (1)

Many thanks. This has been added
Page 14 line 440

(2) Original articles should include a section describing the contribution made by each author to the manuscript. See the "3.4 Author Contributions" sections for details. (https://apm.amegroups.com/pages/view/guidelines-for-authors#content-3-4)

Response 9 (2)
Please see author contribution. This has also been added to the manuscript
Conception and design: Rubyyat-A Hakim and Sola Adeleke
Administrative support: Rubyyat-A Hakim, Huma Zahid, Mariya Karova, Zartaj Ahmad, Katy Taylor, Charlotte Moss, Kathryn Less and Sola Adeleke
Provision of study materials or patients: All authors
Collection and assembly of data: All authors
Data analysis and interpretation. Tamir Sirkis, Woojin Chae, Rubyyat-A Hakim, Russell Burcombe, Charlotte Moss, Kathryn Less and Sola Adeleke
Manuscript writing: All authors
Final approval of manuscript: All authors

(3) All authors will be asked to fill in the ICMJE's unified disclosure form (the latest version). The form could be downloaded at: https://cdn.amegroups.cn/static/public/coi_disclosure.docx. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The corresponding author should use the information in the form completed by each author to create the COI statement for the manuscript.

Response 9 (3)
Now completed. Thanks