

Peer Review File

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Reviewer #1

Overall: A very well written article summarizing a topic that doesn't receive the attention it deserves and should be better understood by all oncologists and physicians dealing with patients with brain metastases. I only have very minor mostly language points described below.

Abstract: An excellent and succinct abstract.

We are grateful of the reviewers' suggestions. Please see our response below.

Comment 1: Intro: May want to rephrase the first line; any metastases transitions patients from curative to palliative treatment, this sentence implies otherwise. Otherwise no issues.

This sentence had been rephrased to: "Brain metastases affect 20% to 40% of all cancer patients and are associated with poor outcomes, **as with any form of metastases**, the patient transitions from curative to palliative management (1, 2)"

Comment 2: Neurocognitive measures: The line 79 "MMSE only detected 50% of those patients as abnormal" – 50% of which patients? Those with neurocognitive decline on some other test? Please clarify

The patient's group has been specified to: "The MMSE underperforms when compared a battery of neuropsychological tests, as the MMSE only detected 50% of **patients which the test battery found to be functioning abnormally** (13). This suggests that the MMSE is an insensitive measure on par with chance (13)."

Comment 3: Quality of life measures: Can you please briefly define what "role functioning" means. Line 291: rephrase "survive on the longer term"

Role functioning has been defined as: "role functioning (the patient's ability to perform their occupational and social roles)."

Line 291 was rephrased from our initial submitted manuscript.

It now reads "Nonetheless, the results are still very encouraging especially in the subgroup of patients who survive longer and it is imperative to report on reasons for dropout to properly interpret study results." – Line 323

Discussion:

Comment 4: Line 302, rephrase “has come with a battery of validated tests” – do you mean “has suggested”?

Changed to “has suggested a battery of validated test”.

Comment 5: Line 306 “future study should be analysed over time” – what do you mean?

Clarified by: “In regard to HRQoL, **future studies should consider the results over a longer period of time following** treatment, with incorporation of both individual changes HRQoL and influencing factors.”

Comment 6: Line 308 please rephrase “Assessment of HRQoL...” as this sentence is confusing.

Comment 6 was rephrased from initial submitted manuscript

It now reads: To obtain accurate assessments of this patient population, brain cancer-specific self-report HRQoL questionnaires should be utilized to capture different aspects of HRQoL (41). - Line 340

Comment 7: Line 321: I agree that these studies would facilitate communication, but how would that actually improve outcomes? Or do you mean something other than improving outcomes?

This has been rephrased to: “In the clinical context this facilitates patient-physician communication, which improves patients’ access to the necessary supports to cope with changes to their quality of life.”

Reviewer #2

The authors in the present manuscript presents a comprehensive review and summary of neurocognitive and health-related quality of life assessment tools used in prospective clinical trials of brain metastases. The manuscript is well written and discusses the nuances/limitations which exist in the application of assessment tools in patients treated with radiotherapy for brain metastases. The discussion highlights the inherent challenges in designing trials which incorporate appropriate neurocognitive and HRQoL assessment and attempts to provide a framework for implementation.

This work represents a useful addition to the literature.

Comment 1: One minor suggestion would be for the authors to consider providing a table to highlight key recommendations on the incorporation/implementation of the reviewed assessment tools.

Table 5 has been added to the end of the manuscript, which summarizes the authors recommendations for assessment tools used in neurocognitive and quality of life assessments.