Author's response to reviews

Title: A longitudinal study investigating quality of life and nutritional outcomes in advanced cancer patients receiving home parenteral nutrition

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Author's response to reviews:

Reviewer 1

Minor Essential Revisions:

Abstract:
1- Result section in abstract, the P-value for the significant results should be written. AS SUGGESTED, THE P VALUES FOR SIGNIFICANT RESULTS HAVE BEEN INCLUDED IN THE ABSTRACT.

Introduction:
1- The background of PN and malnutrition in cancer patients is insufficiently illuminated. This is needed in particular for the final interpretation of the data. AS ADVISED, MORE BACKGROUND ON MALNUTRITION AND PARENTERAL NUTRITION HAS BEEN ADDED TO THE INTRODUCTION SECTION.

2- The references for the last part of first paragraph should be cited. AS SUGGESTED, THE REFERENCES HAVE NOW BEEN ADDED.

Method and Material:
1- Second paragraph, 4th line, full name of NCCN should be provided. NCCN FULL FORM PROVIDED.

Results:
1- Did the researchers observe any long-term complication of HPN? WE HAVE NOW PROVIDED THE INFORMATION ON LONG-TERM COMPLICATIONS OF HPN IN THE SECOND PARAGRAPH OF RESULTS SECTION. ONLY 1 PATIENT DEVELOPED HEPATIC DYSFUNCTION.

Tables:
1- Table 1, the units of each variable should be presented in parentheses in the
same cell of table. SUGGESTED CHANGE MADE.

2-Table1, the unit of albumin should be written according to international system of unit (SI unit). THE UNIT FOR ALBUMIN IS PROVIDED IN GRAMS/DECILITER THROUGHOUT THE MANUSCRIPT FOR THE SAKE OF CONSISTENCY. THIS IS ALSO CONSISTENT WITH PREVIOUSLY PUBLISHED STUDIES ON SERUM ALBUMIN IN CANCER.

2- It is better that table 1 and 2 are merged with each other. THANK YOU FOR THIS SUGGESTION. WE BELIEVE IT WOULD BE MORE APPROPRIATE TO KEEP THE 2 TABLES “AS IS” BECAUSE TABLE 1 PROVIDES SUMMARY STATISTICS FOR THE ENTIRE SAMPLE, WHILE TABLE 2 PROVIDES SUMMARY STATISTICS FOR THE 2 GROUPS BASED ON THE AVAILABILITY OF FOLLOW-UP DATA.

3-Table2, total number of patients in stage at diagnosis row is not 52 patients. The number of patients should be rechecked. AS INDICATED IN TABLE 1, THE “STAGE AT DIAGNOSIS” WAS UNKNOWN FOR 5 PATIENTS. THAT’S WHY IN TABLE 2, THE TOTAL NUMBER OF PATIENTS IN THE “STAGE AT DIAGNOSIS” ROW IS 47.

4- In footnote of table 1,2,3,5 and 6, the name of statistical test which has been used to analysis the data should be written. SUGGESTED ADDITIONS MADE.

5- Table 3, the unit of protein should be presented. THE UNIT GRAMS/DAY HAS BEEN ADDED TO THE TABLE.

6-Table 4 provides no additional information; therefore it can be merged with table 3. TABLE 4 WAS DELETED AS SUGGESTED. THE REMAINING TABLES WERE RE-NUMBERED.

7-Table 5 and table 6, the unit of weight and albumin should be added. SUGGESTED CHANGE MADE.

Reviewer 2

The manuscript is well-written that addresses some of the critical issues in cancer nutrition through the use of standard methodologies and robust statistical methods. I enjoyed reading the manuscript, however, found that certain details missing. The addition of the following details may improve the quality and reliability of the manuscript. THANK YOU FOR YOUR ENCOURAGING FEEDBACK. PLEASE SEE OUR RESPONSES TO YOUR COMMENTS BELOW.

Major revisions

Methodology:

1. Justification of sample size estimations in relation to the objectives of the study is missing in this manuscript. A few lines may be added to the manuscript with the precision levels. Was the final sample size enough to investigate the objectives of this study? If not, a word of caution regarding the generalisability of
the results need to be included in the limitations. THANK YOU FOR RAISING THIS POINT. NO FORMAL SAMPLE SIZE CALCULATIONS WERE CONDUCTED FOR THIS STUDY. A LIMITATION TO THIS EFFECT HAS BEEN INCLUDED IN THE MANUSCRIPT, AS RECOMMENDED.

2. Details of evaluation of compliance to HPN is missing. Were there any methods used in collecting the data on compliance and the regular intakes were assessed? THESE DETAILS HAVE NOW BEEN ADDED TO THE METHODS SECTION UNDER “HOME PARENTERAL NUTRITION”.

3. It is not clear who dispensed the HPN to the patients and whether they were trained to dispense the same alike to all the patients? Had the patients completely consume the HPN during their feedings; and was it considered during the data analysis? This information is important given that the data analysis has compared the nutrient intakes at different time points. THESE DETAILS HAVE NOW BEEN ADDED TO THE METHODS SECTION UNDER “HOME PARENTERAL NUTRITION”.

4. What was the basis for the nutrient contents (i.e. Calorie, protein etc.) of the selected HPN? Did the authors follow any guidelines or it was a random selection? Also, were the other metabolic complications of these participants considered before the quantities of calorie and protein contents were decided? Were there any other micronutrients included in the HPN? It is important to give a brief description of the composition of these HPN. THESE DETAILS HAVE NOW BEEN ADDED TO THE METHODS SECTION UNDER “HOME PARENTERAL NUTRITION”.

5. The participants were in the advanced stage of the disease, it would be important to consider the nutritive composition in relation to the tolerance to HPN, especially in participants with associated liver and kidney problems. Were there participants with liver and kidney problems? THERE WERE NO PATIENTS WITH ASSOCIATED LIVER AND KIDNEY PROBLEMS. WE HAVE CLARIFIED THIS IN THE METHODS SECTION.

6. What were the therapy goals to stop HPN in the participants? Were all the participants able to tolerate the HPN? Were there any who eventually had metabolic complications?

THESE DETAILS HAVE NOW BEEN ADDED TO THE METHODS SECTION UNDER “HOME PARENTERAL NUTRITION”. THAT SECTION HAS BECOME MUCH MORE INFORMATIVE NOW, THANKS TO YOUR VALUABLE FEEDBACK.

7. It would be good to state the follow-up duration at the beginning of the methodology for better clarity. Although the analysis considered participants with 3 months HPN and less, in the results section (Lines 253-256) the duration of follow-up was mentioned until one-half years. This is confusing. AS RECOMMENDED, WE HAVE INCLUDED THE FOLLOW-UP DURATION AT THE BEGINNING OF THE METHODS SECTION. ALTHOUGH SURVIVAL WAS NOT THE PRIMARY END-POINT OF THIS STUDY, WE INCLUDED SOME
BASIC STATISTICS ON OVERALL PATIENT SURVIVAL TO COMPLEMENT OUR PRIMARY OUTCOME OF QUALITY OF LIFE.

8. In the statistical analysis section, a brief description of various response parameters used in the GEE models and the criteria for their selection in the final multivariate model with the tests used for the model fitness should be added. THE SUGGESTED DETAILS HAVE NOW BEEN INCLUDED IN THE REVISED PAPER UNDER THE SECTION ON STATISTICAL ANALYSIS.

Results:

1. In the results section, the P value for significant differences should be reported at the relevant places. Although the authors have mentioned the significant differences it would be more meaningful to state the major findings in the text with the effect size, direction of the change with its confidence intervals (CI) ad respective P values. AS SUGGESTED, WE HAVE NOW INCLUDED THE P VALUES ALONG WITH SOME MORE DETAILS ON EFFECT SIZES THROUGHOUT THE RESULTS SECTION OF THE REVISED PAPER. HOWEVER, IN THE INTEREST OF SPACE, WE TRIED NOT TO DUPLICATE THE RESULTS PROVIDED IN TABLES.

2. The Table 3 suggests a significant difference in calorie and protein intake between the two groups of participants, however, the possible reasons and their implications were not addressed in the discussions. AS RECOMMENDED, THE REASONS FOR THIS OBSERVATION HAVE NOW BEEN INCLUDED IN THE RESULTS SECTION (PARAGRAPH 1).

3. The results from the GEE model was not well explained in the results section. Further, the unit changes (beta) or the effect size for QoL obtained from the GEE analysis may be translated to small, moderate or large change. AS RECOMMENDED, WE HAVE NOW INCLUDED A MORE DETAILED INTERPRETATION OF GEE ANALYSIS IN THE RESULTS SECTION OF THE REVISED PAPER.

4. The GEE model is adjusted for a few potential predictors, however, would be more interesting to see whether the stage of the disease, compliance to the HPN, type of cancer or SGA class (moderate vs severe malnutrition) had any influence on the QoL. Although nutritional status assessment parameters included SGA (in the statistical section) this was not mentioned in the final GEE results table (Table 6). THE CHANGES IN SGA OVER TIME HAVE ALREADY BEEN DESCRIBED IN THE RESULTS SECTION UNDER “NUTRITIONAL STATUS”. SGA BEING A CATEGORICAL VARIABLE WAS NOT (COULD NOT BE) ANALYZED USING LONGITUDINAL GEE APPROACH. LONGITUDINAL GEE APPROACH WAS ONLY USED FOR CONTINUOUS VARIABLES TO ASSESS THEIR RESPONSE PATTERNS OVER TIME. HOWEVER, AS RECOMMENDED BY YOU IN ONE OF YOUR EARLIER COMMENTS, WE HAVE NOW INCLUDED A MORE DETAILED INTERPRETATION OF GEE ANALYSIS IN THE RESULTS SECTION OF THE REVISED PAPER.
Discussion:

1. Lines: 286-288: Instead of the term "recommend" it would be more appropriate to use the term "suggest" as the study sample size is insufficient for this. **SUGGESTED CHANGE MADE.**

2. The section needs to address the implications of better nutrition through HPN on QoL, nutritional status and functional outcomes. This is not explicitly narrated in the discussion section. **WE INCLUDED A FEW SENTENCES ON CLINICAL IMPLICATIONS OF OUR FINDINGS IN THE ORIGINAL PAPER. HOWEVER, IN LIGHT OF YOUR SUGGESTION, WE HAVE ADDED MORE INSIGHTS ON THE CLINICAL IMPLICATIONS IN THE REVISED PAPER.**

Discretionary revisions:

Tables:

1. Table 1: The first half may be made more compact by combining the columns 1 & 2 and the 3 & 4 together. Footnote for the SGA classification details need to be added. The second half of the table, column 1 & 4 can be merged and 2 & 3 can be merged. **SUGGESTED CHANGES MADE.**

2. Table 2: The first half may be made more compact by combining the columns 1 & 2. Stage at diagnosis, the numbers in the column 4 are not totalling up to 15. Also, it is not clear what F/U means. Footnote for the SGA classification details need to be added. **AS INDICATED IN TABLE 1, THE “STAGE AT DIAGNOSIS” WAS UNKNOWN FOR 5 PATIENTS. THAT’S WHY IN TABLE 2, THE TOTAL NUMBER OF PATIENTS IN THE “STAGE AT DIAGNOSIS” ROW IS 47 (AND NOT 52). F/U (FOLLOW-UP) HAS BEEN SPELLED OUT IN ALL TABLES.**

3. Table 3: The units are missing for the parameters/variables. If the parameters are scores it need to be mentioned. Similarly, for energy KCal is presented, however, for protein there is no unit mentioned. In addition, it is not clear whether the nutrient intake reported from HPN was for per day? The test used to determine the P value need to be noted in the footnote section of the respective tables. **STATISTICAL TESTS ARE NOW INCLUDED IN THE FOOTNOTES OF ALL TABLES, AS APPROPRIATE. UNITS ADDED FOR ALL PARAMETERS/VARIABLES. WHEN PARAMETERS ARE SCORES, WE MENTIONED IT AS SUCH. NUTRIENT INTAKE REPORTED WAS “PER DAY”. THIS HAS BEEN CLARIFIED IN TABLE 3.**

4. Table 4: Columns 1 and 4 could be merged. The table may be excluded as the baseline scores are reported in Table 5; a few lines in the results sections may be added to emphasize the important points. **TABLE 4 WAS DELETED AS SUGGESTED. THE REMAINING TABLES WERE RE-NUMBERED.**

5. Table 5: The units are missing for the parameters/variables. The test used to determine the P value need to be noted in the footnote section of the respective tables. **UNITS ADDED. STATISTICAL TESTS INCLUDED IN THE FOOTNOTES OF ALL TABLES, AS APPROPRIATE.**
6. Table 6: The units are missing for the parameters/variables. UNITS ADDED.

Minor essential revisions:

List of abbreviations used in the text was not summarized at the end of the paper. ABBREVIATIONS ARE NOW INCLUDED AT THE END OF THE MANUSCRIPT.

Reference No: 9, 12, 13, 16, 19, 27, 33. The complete list of authors needs to be instead of et al. as observed in all the BMC articles. AS SUGGESTED, WE HAVE MADE THE DESIRED CORRECTIONS.