

## Peer Review File

Article information: <https://dx.doi.org/10.21037/apm-22-1380>

### Reviewer Comments

Thank you for providing a manuscript that capture the clinical relevance in TPN use in palliative GI cancer patients in a well written manner.

Minor comments include:

Comment 1: key words: reconsider these to leave out terms that overlap with the title and introduce other relevant synonymes and abbreviations.

Reply 1: We appreciate this feedback. Keywords are now: “artificial nutrition, peripheral nutrition, cancer cachexia, palliative care, gastrointestinal malignancy, malignant bowel obstruction, malnutrition”.

Comment 2: the interchange use of artificial/perpheral/parenteral words may be confusing for readers not well known in the field of clinical nutrition. Please use “parenteral” throughout the manuscript whenever relevant to avoid confusion

Reply 2: The manuscript has been updated with the word “parenteral”, rather than “artificial” or “peripheral”. The abbreviation “TPN” has been in some cases used to avoid redundancy in language. The word “artificial” was left in the first sentence of the introduction but is further categorized as “parenteral” vs. “enteral”.

Comment 3: - line 40: please mention the reason why the patient was not a candidate for PEG tube.

Reply 3: To clarify why the patient was not a candidate for a PEG tube, the following phrase was added to the line: “due to distal obstruction of the gastrointestinal tract”.

Comment 4: - line 55-56: please rephrase, the sentence makes no sense. onto me as reader.

Reply 4: We agree that this is a confusing sentence. It has been revised to read as: “Anorexia and cachexia are striking manifestations of advancing cancer, impacting a patient’s functional status, mood, and appearance. These changes often invoke emotional responses from the patient, caregivers, and clinicians.”

Comment 5: -line 126: please provide reference to commonly used indications mentioned

Reply 5: References are added after this line.

Comment 6: line 224: you do state the study is old, but it would be beneficial to provide reasons as to how progress in tpn composition, administration and hygiene has improved since then (to guide readers novel to the field of clinical nutrition).

Reply 6: Added the following clarifying sentences:

Line 216- “Education about line hygiene and handling, as well as daily inspection of line sites, are tools that have led to the reduction of infection rates.<sup>16,17</sup> International guidelines exist to guide site selection, sterile technique for insertion, and the development of line maintenance protocols.”

Line 237- “Most nutritional solutions now contain all amino acids in sufficient amounts. Studies in critically ill patients have demonstrated that high protein nutrition has been associated with decreased mortality.<sup>19</sup> Soy bean oils, olive oil, and fish oil have been introduced to increase patients’ antioxidant levels and decrease omega-6 fatty acids, which may contribute to inflammation and immune system activation.<sup>16</sup> Nutritional solutions are now tailored to meet patients’ needs, and nutritionists consider insulin-resistance and other comorbidities when guiding treatment. One systematic review found metabolic complications were reported in 3 studies with a range of 0.32 to 1.37 per 1000 days.<sup>9</sup> Newer formulations are “all-in-one” admixtures instead of separate components administered separately. This reduces likelihood of contamination, line infections, and cost.<sup>16”</sup>

Comment 7: -line 245-247: you mention the range is wide, but only present one example. Please provide more data on the size of the range.

Reply 7: The paragraph starting with line 243 now reads: “Hepatobiliary dysfunction in patients receiving long-term TPN has been well-documented. Associated complications include hepatic steatosis, fibrosis, cholelithiasis, and acalculous cholecystitis.<sup>20</sup> The reported incidence of liver-related complications in patients receiving TPN ranges widely and it is often unclear if alterations in liver function are clinically significant. The incidence of abnormal liver function tests following TPN initiation, ranges from 25-100% of patients across early studies.<sup>20</sup> Many of these studies included heterogenous groups of patients with varying degrees of liver dysfunction and disease burden at baseline. <sup>20</sup>The abnormal liver function tests in these patients are predominately correlated with steatosis of the liver. Of note, malnutrition itself can predispose patients to the development of liver steatosis. The steatosis associated with the use of peripheral nutrition is thought to be reversible and mild, especially as nutritional formulations have been made to be more protein-balanced and less glucose-rich. The consequences of biliary stasis, a byproduct of parenteral nutrition, include the development of cholelithiasis and cholecystitis.<sup>20</sup>The duration of TPN is associated with the degree of biliary stasis that results, with patients receiving TPN over a longer period of time experiencing the development of more biliary sludge. For many patients, especially those with limited-life expectancy, the risk of likely minor hepatobiliary complications may be outweighed by the benefits of receiving nutrition.

Comment 8: -line 292: please state the type of study (observational or rct, selection of patients) to aid reader comprehens the results of this study.

Reply 8: Line 289-291 now reads: “In another prospective study of 414 palliative cancer patients receiving TPN at home and with a life-expectancy of > 6 weeks at time of initiation, 50% of patients survived for 3 months while 22.9% of patients survived to 6 months. These patients had incurable solid-tumor cancer of variable types and were malnourished at time of enrollment.”