Peer Review File

Article information: https://dx.doi.org/10.21037/ajo-21-31

Reviewer #1 Comments:

Thank you for your contribution to the journal.

This study aims to look at the incidence of refeeding phenomena (as opposed to refeeding syndrome) in a clearly defined head and neck cancer population.

As pointed out in the manuscript, there is limited data available regarding this.

While clinical inference are not able to be made from this study, my opinion is that it is an important first step in qualifying how this can be managed in the post-operative setting and merits publication. This will hopefully act as a building block to further study in this regard.

Reply to Reviewer #1:

Thank you for your support and comments.

Reviewer #2 Comment #1:

This is a well written paper that presents a contemporary review of large series of an important condition that can occur in postoperative head and neck cancer patients. It also highlights two important predictive factors for this condition that will allow such patients to be anticipated.

Could the authors define how the final cohort of patients were included. For instance, it is assumed that there were 187 oral cancer patients who were treated during a five year period. However only 104 patients were included because these had the defined serum phosphate levels. Did the authors review those patients who were excluded from the study and how were they different from the included criteria.

Reviewer #2 Reply #1:

Thank you for your comments.

To determine our final cohort of patients, we reviewed the serum phosphate levels (on the electronic results system) for all 187 patients who were identified from the cancer database as having surgical treatment for their oral cavity cancer. However, not all patients had their serum phosphate levels checked consistently in the acute post-operative period. Therefore, in order to detect a trend / a change in phosphate levels over time, we only included patients who had their serum phosphate level checked at least twice in the post-operative period, of which one of the two levels, had to be within the first four days post-operatively.

We found that 83 out of the 187 patients either did not have their phosphate checked at least twice, or did not have phosphate checked at all from day 1 to day 4 post operatively and were hence excluded. Whilst formal statistical analysis of the excluded group was not performed, it was noted that the majority of the excluded patient group had early stage T1 / T2 tumours and they were patients who were treated from the earlier half of the 5-year study period. This could potentially reflect the change in clinical practice over time, with refeeding phenomena becoming an increasingly important post-operative complication to be aware of.

Changes in the text: Please see modified text on page 6 line 89 – 95 in blue font clarifying how we defined our final cohort of included patients. Please see added text on page 12 line 222-223 in blue font describing the excluded cohort.

Reviewer #2 Comment #2:

The authors refer to bias and confounding in the discussion section (line 213). Could the authors further expand on this?

Reviewer #2 Reply #2:

The criteria of selecting patients to be included in the study depended on patients having had their serum phosphate levels checked sufficiently. Therefore, for the excluded cohort of 83 patients, we noted that they were largely clinically earlier stage cancers and could have been

at lower risk of RFP. Hence this could explain why a majority of our cohort of included patients were of advanced T4 stage. This could explain why we were unable to demonstrate T classification as a statistically significant risk factor in the present study. It could also have influenced a higher refeeding phenomena rate.

Changes in the text: Please see modified / additional text on page 11&12, lines 219-226 in blue font.

Reviewer #2 Comment #3:

Could the authors justify their definition for refeeding syndrome? Has this been used in other manuscripts and if so, could these be referenced? Are there any other bio markers of RFS and were these assessed?

Reviewer #2 Reply #3:

Our definition for refeeding phenomena is an 'isolated decline in phosphate levels following refeeding', to a level below 0.75mmol/L. Refeeding syndrome is the development of clinical symptoms as a result of the decline in the phosphate levels. We adopted this definition because it is commonly used in other manuscripts.

Changes in the text: References to support this definition has been added to page 6 line 100.

Other biomarkers of RFS include potassium and magnesium however phosphate has been attributed to be the most common electrolyte abnormality. We did not assess potassium and magnesium levels post operatively as these more commonly replaced electrolytes could have already been supplemented or influenced by other factors such as common medications (eg. Diuretics) or background medical conditions such as kidney disease.

Changes in the text: Please see added text on page 11,12 line 210-216 in blue font.

Reviewer #2 Comment #4:

Could the authors explain why some patients did not have their phosphate levels checked?

Reviewer #2 Reply #4:

Due to the retrospective nature of our study, we are unable to definitively say why phosphate was not checked in all patients. However, we hypothesize that it was not checked in patients who were deemed to be low risk of refeeding phenomenon (and this may therefore introduce a selection bias into our study). It is also probable that the test was simply forgotten in some cases. The increase in multidisciplinary dietetic support over the period of the study could be expected to reduce the frequency of this occurrence.

Changes in the text: Please see text on page 12 line 226-229, text highlighted in blue font

Reviewer #2 Comment #5:

In the conclusion, the authors recommend routine testing of phosphate levels. This conclusion is somewhat misleading because the paper is based on a cohort of patients where phosphate levels were tested retrospectively as opposed to prospectively

Reviewer #2 Reply #5:

Thank you for your comment. We agree with your point and we have re-worded the statement accordingly.

Changes in the text: Please see modified text on page 2, line 47-49 and on page 13, line 232 -235.