

Peer Review File

Article Information: <http://dx.doi.org/10.21037/jgo-20-193>

Review Comments:

Major concerns

1. The old term “carcinoid” should be replaced by current terminology according to WHO using the term “neuroendocrine tumor” or “neuroendocrine carcinoma”. In particular, the description of “colonic carcinoid... with poorer differentiation” is difficult to interpret. Are the authors referring to poorly differentiated NEC or to well differentiated high grade NET (eg NET G3)?

Reply 1: Thank you for the information. The relevant text in the manuscript has been changed to use the terms Neuroendocrine tumors (NETs) or Neuroendocrine Carcinoma (NEC) where indicated as per the current WHO classification.

Changes to text: The term ‘carcinoid’ has been replaced with the appropriate terminology in all the relevant headings including the abstract and the body of the manuscript.

2. Use of chemotherapy has been identified as a risk factor for radical resection. As no chemotherapy has been established for use in NET, there is concern, that patients treated with chemotherapy actually suffer from NEC rather than NET. Again, using current terminology would greatly help to understand data.

Reply 2 : The term ‘carcinoid’ has been replaced with the terms NETs and NECs as appropriate to better describe the use of chemotherapy in patients with high grade NETs or poorly differentiated NECs

Changes to text: Page 14, line 318 now describes the use of chemotherapy for the patients with the high grade NETs or poorly differentiated NECs.

3. How is the high rate of missing data for TNM staging explained? As more than 50% of data are missing, the authors should reflect this in the discussion.

Reply 3: The TNM staging were not consistently documented for all patients in the database leading to the high rate of missing data. These patients were however included in the study due to availability of other data pertinent to the study objectives. This has been explained in the limitation section of the paper.

Changes to text: We have included this as a limitation in our study on Page 16, line 350.

4. The authors state, that the current study represents a population-based study. As nearly 90% of cases are from metro areas, this should at least be critically discussed.

Reply 4: Thank you for pointing this out. The text now highlights this caveat mentioning it as one of the limiting factors for generalizability.

Changes to text: We have discussed this limitation in our study on Page 15, line 338.

Minor concerns

1. Is there a correlation between T and N stage?

Reply 1: Please pardon us if we find it unclear what this comment means. Although our study did not specifically analyze correlation between T and N stage, anecdotally our results showed that the T and N stages had similar trends i.e higher T and N stages in colon NETs, and lower T and N stages in rectal NETs. These data are not discussed further for space considerations.

2. To better understand age-related incidence and mortality a more detailed description of this relevant information would be helpful.

Reply 2: Thank you. We have expanded this discussion additional studies supporting our findings bearing in mind space limits.

Changes to text: In Page 12, line 254, we have expanded on the discussion about age related incidence and mortality.