Peer Review File

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Reviewer Comments

Reviewer A

General Comments:

- This is a well written narrative review however it is unclear how the literature search impacted the writing of the manuscript. For a search that included 109 articles, were all of these relevant to the topic at hand? The authors only reference 38 citations, leaving some question about the content of the other 71 manuscripts.

Reply: This article has been substantially rewritten to include much more detail about the literature search. PRISMA flow chart and inclusion/exclusion criteria have been added.

- The search strategy was incredibly basic and leaves a significant amount of room for missed literature and bias given that the authors performed a simple keyword search without a more comprehensive search strategy. For example, much of the endoscopic and interventional radiology literature frequently does not include the phrase "palliative" in manuscript titles though these sub-specialty interventionalists certainly characterize and publish results of palliative interventions for this patient population.

Reply: Limitations have been added to Conclusion section.

- Methods: No inclusion and exclusion criteria are reported to have been applied to the 109 identified articles- as above, this would indicate that all articles were read in full and found to be relevant and therefore included in the discussion. If any article(s) was excluded from inclusion in the synthesis of the narrative review, the criteria used to exclude this study should be outlined. It is abnormal for all studies using a given search criteria to be included in a narrative review. If inclusion and exclusion criteria were applied to the results, this should be explicitly noted. Additionally, only the abstract (and not the body) of the article state "our search returned 109 articles." Would include this information in the body of the text.

Reply: This article has been substantially rewritten to include much more detail about the literature search. PRISMA flow chart and inclusion/exclusion criteria have been added.

- The rationale/background section is a bit jumbled as this should be a reflection of the rationale for writing a narrative review on this topic and for this patient population; perhaps discussion of life-prolonging treatment advances can be summarized more succinctly.

Reply: This section has been heavily edited to address this comment.

- Do the authors believe that their conclusion "specific needs for specialty palliative care in the GEJ cancer population… include complex symptom management starting at diagnosis" is supported by the literature presented? Based on the articles included in this review, do we have good enough data to support the claim that early specialty PC consultation improves QOL in patients with early gastric cancers and that patients with early GEJ cancers require complex symptom management?

Reply: This language has been softened and the article has been substantially rewritten.

- Many citations are missing/absent; do the authors have access to uncited literature to support many of their unreferenced statements? For any claims that are unsupportive by the literature, these impressions would best fit in a Summary/Conclusions section, which allows for professional commentary on the available evidence (or lack thereof).

Reply: Citations have been added throughout and specific statements as below have been edited or removed.

- What are the limitations of this study? What are the remaining questions that clinicians and researchers need to address to better understand how to best to care for the gastric cancer patient population? Are there any gaps in the current literature?

Reply: Limitations have been added to Conclusion section.

- If in fact the authors agree with themselves that all patients diagnosed with gastric cancer should receive a palliative care specialty referral, I would love to hear their input (in the Summary/Conclusions) about how whether or not it would even be feasible to achieve this goal given the shortage of PC specialty providers and the barriers that the healthcare system might face should every patient with said diagnosis be expected to see a PC specialist.

Reply: Strongly agree with this comment, and respectfully respond that this is outside the scope of this review. This sentence has been added to the Conclusion section: "Acknowledging that specialty palliative care is a scarce resource both in the United States and internationally, efforts are needed to improve palliative care access for this population."

- "Gastroesophageal junction (GEJ) cancer"- At almost all points in this manuscript it is written GEJ cancer, could consider making this abbreviation just GEJC.

Reply: We favor to keep this as is.

Specific Comments:

1) Line 81- “Histology may be adenocarcinoma or squamous cell carcinoma (SCC), with unique risk factors for each type of cancer.” – Would consider making this sentence more accurate by saying “the two most common histologies are…”
   Reply: done

2) Line 86- “Risk factors for both types of GEJ cancer can be modifiable and are based on an individual’s lifestyle…”– This is a bit overstated. Both BMI and Barrett’s esophagus have known genetic components, and to suggest that a person’s weight (or the development of Barrett’s) “can be modifiable” is to ignore systemic circumstances that are often far outside an individual patient’s sphere of influence/control- including but not limited to early childhood eating patterns, access to healthy food choices, and time/financial resources to pursue self-care related behaviors such as exercise.

Reply: point well taken! Changed to “Because these risk factors are perceived as modifiable to some degree, the psychological impact of this cancer can be complex.”

3) Line 88- “…which add complexity to the psychological impact of this cancer.” If you are claiming that there is an increased psychological impact of this cancer, this requires a citation. Is it true that patients with gastric cancer are at increased risk of self-blame for the development of cancer? Are their baseline psychological features or outcomes different as compared to patients with other types of cancer?

   Reply: language softened as above, see 2a.

4) Line 95- “which is a highly morbid procedure”- what is your definition of highly here?, please include a citation to make this more objective. You mention that esophagectomy “has long-term ramifications for functional status and symptoms”; the tone of this sentence downplays or disregards the potential for symptomatic improvement s/p surgical intervention. For patients at an early stage with minimal or no surgical complications, surgically resected patients have an opportunity to preserve an ability to maintain PO intake and overall QOL. This reads as a high-level of author bias, especially when no citations are offered and blanket statements are made to support these claims.

   Reply: this phrase has been deleted and the section substantially rewritten.

5) Line 116- “Early specialty palliative care consultation addresses the

physiologic effects of GEJ cancer"- Is this true? Though this might be somewhat true, I again think that this is overstated. Palliative care specialists don't/can't help with bleeding, or really obstruction, and as outlined in lines 199 and beyond, interventionalists (not PC specialists) are offering interventions that allow relief for dysphagia. How do PC specialists facilitate these referrals, do these referrals normally come via PC instead of oncologists? *How* are PC specialists leading the multidisciplinary approach to gastric cancer, and why are PC specialists "better" at stepping in to this role as compared to oncologists or other members? Are there publications to support these claims within the searched timeframe?

Reply: edited to "Early specialty palliative care consultation, recommended for all patients with a new cancer diagnosis (Farrell), should address the effects of GEJ cancer and its treatment at all stages of disease and include care coordination with interventionalists as appropriate."

6) Line 185- "A percutaneous endoscopic gastrostomy (PEG) tube may be offered if the patient continues to lose weight despite these interventions. This is one circumstance in which a PEG tube may provide significant value and enhance QOL, particularly as a short-term intervention when treatment is anticipated to reduce tumor and obstruction." - I would be careful putting this here. If a PEG is placed in the stomach on a patient who may respond to neoadjuvant therapy or be a candidate for resection, the future gastric conduit can be injured and this can limit or impair surgical reconstruction options. Most surgeons would not favor PEG placement in this scenario. Is the point of this comment to highlight options of preoperative enteral nutrition? In practice, J-tubes are preferred if needed. Again, this section lacks citations.

Reply: Yes, the goal of this sentence is to highlight options. Text changed to "Temporary pre-operative jejunostomy or percutaneous endoscopic gastrostomy (PEG) tube may be offered if the patient continues to lose weight despite these interventions."

7) Line 300- "…or endoscopic clips may be helpful"- I'm not sure what this means.

   Reply: this entire section has been removed

8) Line 303- "Acute and chronic bleeding may also cause emotional distress."- please cite.

   Reply: this entire section has been removed

9) Line 312- “Having these conversations upfront can alleviate anxiety and help patients and caregivers prepare for potential complications.”- please cite

Reply: “alleviate anxiety” has been removed and this sentence has otherwise been moved to the section on prognostic awareness in the context of appropriate citation.

10) Line 317- “Patients facing GEJ cancer experience high rates of anxiety and depression in light of their symptom burden, poor prognosis, and increased touch points with the medical system.”- please cite

Reply: this sentence has been removed.

11) Line 322- “and may contribute to attrition in completion of curative-intent therapy.” – please cite

Reply: this sentence has been removed.

12) Line 326- “Frequent assessments of mood using validated tools should be used to screen GEJ cancer patients for acute needs and indication for referral to psychosocial oncology.”- Do we have data to support this? Did a publication identified using the stated search strategy provide good evidence to support wide adoption of this practice?

Reply: this sentence has been rewritten: “Specialty palliative care physicians assess mood using validated tools.”

13) Line 346- “1 year” → one year

Reply: done

14) Line 386- The summary in the body of the text states “Early referral to specialty palliative care should *be considered*…” this rings much more true and likely is more supported by the available data than compared to the claim in the abstract that “Early specialty palliative care intervention *is indicated* for patients with all stages of GEJ cancer to improve quality of life (QOL)…”

Reply: abstract updated to reflect this language

Tables/Figure:

- Tables 1 and 2 are helpful and will be of use to readers

Reply: these are now tables 2 and 3

- There are no included Figures

Reply: there is now a Figure 1

Reviewer B

Thank you for the opportunity to review this article. It was a very interesting ready and I think has the potential to make a useful contribution to the literature. However I think it needs major revision to do so, particularly with regard to the methods

Introduction
There are several sentences in the introduction that require references: line 85-88, line 100-102, line 115-116, 118-122.

Reply: References have been added.

Methods
It would be useful to see the full search strategy as an appendix to the article. It would also be beneficial to reference a protocol if there was one registered. I also think that this requires a widening of the search. Only searching PubMed is likely to miss articles that may have been identified if other databases were included. I would suggest also looking at Medline, Embase, and CINHAL and rerunning the search. It would also be useful to include a table or figure with the full inclusion and exclusion criteria using PICOS.

Reply: Text has been added to describe the search strategy and show there was no protocol for this study. Single database search has been added as a limitation in the Conclusion section. A table and figure have been added.

Results
A PRISMA diagram or similar would be useful here to see where and why articles were excluded. A Table with a summary of the included articles would also be of benefit here.

Reply: A PRISMA diagram has been added and a table of the included articles has been added.

Reviewer C

Appropriate review of practical clinical palliative care concerns for gej cancer.

Reply: N/A

Reviewer D

This is a well-organized review article on the palliative care of gastroesophageal junction cancer.

1. Line 140. Approximately 25% of gastric cancers are resectable at the time of diagnosis. – Te overall resectability of gastric cancer seems to be higher than this, and I do not know exactly what it means. It would be better to remove this sentence.

Reply: done

2. Table 2

Class of drug – misclassification of opioid and opiate. It can be distinguished as follows, or it can be changed to opioid.

Opiate – narcotic analgesic derived from an opium poppy (natural). Ex : morphine, codeine, heroin

Opioid – narcotic analgesic that is at least part synthetic, not found in nature. Ex : oxycodone, meperidine, methadone, fentanyl…

Reply: all instances changed to opioid