

Peer Review File

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Reviewer A

Comment 1: It's unclear which country this review is from. However, there is no mention or discussion of multi-disciplinary team - based decision making, or post-procedural care. These are essential for any successful palliative procedure. Locally our MDT is made up of oncologists, gastroenterologists, surgeons, radiologists, palliative care physicians, cancer nurse specialists, and PEG community nurses. In this regard, it is also important to include discussion/comment/a paragraph about the services available to patients. Not all regions have the same services and this is essential. There is little point in offering a patient (or performing) a venting gastrostomy if the support services are not available. It's also likely that given the lower frequency of these procedures, they may need to be done in a tertiary centre by an experienced surgeon/physician – but data are needed. As well as data, the appropriate supportive structures/ organisations/ services/ training/ professionals are needed.

Reply 1: Thank you for the suggestion. We agree with the importance of MDT thus included a paragraph at the end (line 351-361).

Changes in the text: “Lastly, it is paramount to involve a multi-disciplinary team consisting of surgeons, oncologists, gastroenterologists, interventional radiologists, palliative care team, oncologists, and nurse specialists. While more data is needed to compare the effect of hospital settings on PGT outcomes, much research on PGT has been performed at tertiary care centers (1-3). Given the complexity of the decision-making process and support staff needed, tertiary referral center is often required as a place for palliative patients to receive care (2). Unmet psychosocial needs often arise, thus early, multi-disciplinary consultations of social work and palliative care are indicated (3, 4). If support services are unavailable, primary care providers should consider facilitating early palliative care consultation to begin the decision-making process.”

Comment 2: Venting gastrostomy tubes may be well understood by physicians and surgeons. However, APM reaches a wide professional demographic. A helpful diagram of what a venting gastrostomy is / how it is placed/ different types of gastrostomies (PEG pull-through versus gastropexy-assisted push PEG versus RIG +/- extension feeding tubes) may be helpful.

Reply 2: We agree that details regarding the technique and different types of PEG would help reach a wider professional audience. Thus, we added a paragraph in the Introduction. Please see lines 58-64.

Changes in the text: “The pull technique is the most common method in which an endoscope is passed through the mouth into the stomach to insufflate and transilluminate the abdominal wall, through which the needle is inserted along with the guidewire that is brought out through the mouth. Then the gastrostomy tube is guided down the wire from the mouth to the stomach

then pulled through the abdominal wall (5). Less commonly, gastrostomy tube can also be pushed down from the mouth to the stomach via a guidewire (push technique) or can be directly inserted through the abdominal wall via gastropexy and fluoroscopic guidance in a technique called radiologically-inserted gastrostomy (RIG) (6, 7).”

Comment 3: Overall, I would avoid using the term ‘physician-based outcomes’ as these are not necessarily anything to do with physicians, but traditional ‘hard’ data points. It is important to consider mortality data (and traditional outcome measures) too: they are not mutually exclusive! E.g. Do patient’s survive long enough to get benefit; what’s the length of benefit; is there benefit but a substantial mortality risk? For example in the text, in the introduction, there is an argument presented against using outcomes measures such as mortality and overall survival. This needs justified by evidence (at present it is presented as the authors’ opinion) – there is also confounding between ‘time spent at home’ and ‘overall survival’. I’d argue that mortality outcomes are absolutely important to discuss with patients when performing procedures that carry a reasonable mortality rate (up to 5.6% at 7 days and 22% at 30 days and 48% at 1 year, reported by Smith et al in Surg End 2008 22(1):74-80 – for ALL indications) – it does matter to patients and it’s important for them to weight up procedure-related mortality versus perceived symptomatic benefit; particularly when they are in a higher risk group. Your review also discussed palliative tube feeding which absolutely must take these ‘traditional’ outcome measures into account. They are not mutually exclusive.

Reply 3: Thank you for your comment. We agree that data such as mortality and overall survival are absolutely paramount in palliative surgery and patients can immensely benefit from such data. What we intended to communicate is the imbalance of the available data in palliative surgery research in which *only* the mortality and overall survival are measured as palliative outcomes *with minimal* inclusion of palliative measures such as symptom resolution and quality of life. Again, we agree that they are not mutually exclusive but rather should be dually emphasized in a balanced way in palliative research. Thus, we changed the syntax and our diction to reflect the nuance. Please let us know if this is clear. Our goal is not to disparage the traditional outcome measures such as mortality and overall survival, but rather to increase the awareness of the patient-centered outcome measures such as symptom resolution and quality of life. Please see lines 45-49.

Changes in the text: “Thus, whenever surgery is deemed palliative, the *intent* and *individualized* care are paramount. If the intent is to relieve symptoms such as nausea or vomiting, then the outcome ought to be evaluated by the success of symptom relief weighed against treatment toxicity **in addition to** overall survival. Often, physician-based outcomes (e.g. mortality, length of stay, complications, cost) are the **sole** primary endpoints of clinical and translational research, while patient-based outcomes (e.g. symptom resolution, QOL, time at home, functional status) are de-emphasized. **Given that they are not mutually exclusive, adequate representation of both physician-based and patient-based outcomes are required** in palliative research, as the very intent of palliative surgery is to relieve patient-reported symptoms and improve their QOL.”

Comment 4: In lines 96 and 239, it is important to make sure we do not advocate for unjustly biasing certain groups based on their demographics. E.g. perhaps we need to be offering better community support to those ‘over 66 [or with] lack of family support’, to maximise their benefit from PGT, rather than using these as risk factor metrics to exclude them from potentially helpful interventions.

Reply 4: We agree that instead of framing them as risk factors, changing the language to providing additional support for optimal care is more appropriate. Please see lines 170-173 and 349.

Changes in the text: “Other factors **associated with** prophylactic PGT included regional instead of local cancer, no surgical treatment, and patients who were unmarried, divorced or widowed (8). **While this study provides helpful data, it is important not to introduce bias into our care based on patients’ demographics but rather be more attentive and aware to provide additional social support to facilitate maximal benefit from PGT (lines 170-173)”**

“Thus, these factors **can help facilitate additional social support** when selecting for patients whose value would be maximized with PGT (line 349).”

Comment 5: Gastrostomy tubes are inserted by surgeons, gastroenterologists, endoscopists, and radiologists. Therefore gastrostomy tube insertion is not necessarily a surgical procedure. It would be worth softening the language – not deeming it a strictly surgical procedure. Much of the stigma surrounding palliative venting gastrostomies may, in part, come from concern that it is an invasive procedure and branding it as a surgical procedure may precipitate and bias this.

Reply 5: We agree that “surgery” can pose unwarranted stigma of “invasiveness”. Thus we removed “surgical” in lines 52, 67, 180, 282.

Changes in the text: **Removed “surgical”** in lines 52, 67, 180, 282.

Comment 6: In line 35, I would change to “...provide artificial enteral nutrition AND/OR decompression...”

Reply 6: Thank you. Please see line 53.

Changes in the text: **Changed to “and/or”** in line 53.

Comment 7: In line 39 (and possibly 50), it would be important to clarify there are different types of ‘PEG’ tubes. For example there are traditional pull-through PEG tubes, gastropexy-assisted gastrostomy tubes, surgically created gastrostomies, and radiologically inserted gastrostomies (RIGs). I.e. does your review exclude radiologically inserted gastrostomy tubes which are the standard of care in many centres. Does it exclude PEJ or PEG-J tubes?

Reply 7: Thank you for the suggestion. We do not exclude RIG or extended PEG tubes as our literature included these techniques. Thus, we have expounded on the types of PEG in line 58-64.

Changes in the text: **“The pull technique is the most common method in which an endoscope is passed through the mouth into the stomach to insufflate and transilluminate the abdominal**

wall, through which the needle is inserted along with the guidewire that is brought out through the mouth. Then the gastrostomy tube is guided down the wire from the mouth to the stomach then pulled through the abdominal wall (5). Less commonly, gastrostomy tube can also be pushed down from the mouth to the stomach via a guidewire (push technique) or can be directly inserted through the abdominal wall via gastropexy and fluoroscopic guidance in a technique called radiologically-inserted gastrostomy (RIG) (6, 7).”

Comment 8: In line 51, I think the authors mean ‘compromised per oral (PO)’ rather than ‘compromised per os (PO)’

Reply 8: Thank you. Please see line 75.

Changes in the text: **Changed to “per oral”** in line 75.

Comment 9: For lines 56-61, it would be helpful to reference the original articles rather than/ in addition to review (5).

Reply 9: Included the original articles. Please see lines 89-90.

Changes in the text: **Citations added** in lines 89-90.

Comment 10: When discussing optimal time for PEG insertion and tumour seeding risk in head and neck cancers, it is may also be important to discuss ‘traditional pull’ technique versus gastropexy ‘push’ technique.

Reply 10: We included that the importance of techniques has been suggested in regard to tumor seeding risk in lines 130-158.

Changes in the text: **“In order to prevent tumor seeding, some reports have suggested radiologic placement of gastrostomy tube instead of traditional push or pull-technique, thereby avoiding direct contact with tumors (7).”**

Comment 11: Please insert a reference to evidence the statements in line 122.

Reply 11: Included a reference to line 199 (new version) .

Changes in the text: **“Thus, patients suffer intractable nausea, vomiting, bloating, and inability to take PO, all of which dramatically affect QOL along with decreased nutritional and functional status (9).”**

Comment 12: In paragraph beginning 171, it is important to clarify how this works. I.e. a venting gastrostomy is created then a secondary e.g. jejunal extension feeding tube is inserted for feeding. It’s important we characterise and clearly define the additional risks these tubes may place (e.g. perforation, dislodgement etc). If a patient has MBO, then it is unlikely that nutritional support will be appropriate in the vast majority of circumstances. A multi-disciplinary nuanced approach again is needed. However, there is a lack of data (given the above) to help informed decision making regarding 'feeding AND venting' approaches.

Reply 12: We have included a paragraph discussing all the points you mentioned. We also revised the language to indicate a “suggestive” nature of the paragraph, rather than a “factual” nature, since more data are needed on this matter. Our intention was to encourage healthcare professionals to engage in MDT discussions, rather than shying away from discussing the possibility of procedure in MBO patients. Please see lines 272-278.

Changes in the text: “Thus, when deemed appropriate by the multidisciplinary team, it is important to consider PGT as a feeding tube (e.g. via jejunal extension) after a forthright discussion with patients and families regarding risks and benefits of the procedure. It may be helpful to cite 90-99% successful PEG insertion rate in MBO population with 0-24% risk of major complications (i.e. major bleeding, peritonitis, revision) (5), though further studies are needed in the area of dual approaches of feeding and decompressive use of PGT.”

Comment 13: I would remove ‘valuable’ from line 194. We cannot always assume time at home = better in the context of symptom relief. While we use ‘time at home’ as a positive marker, patients may be more symptomatic compared to those who have easier access to a physician; patients may put up with symptoms at home to try and avoid hospitalisation. Studies are needed to evaluate ‘symptoms at home’ as well as ‘time’ at home.

Reply 13: Thank you. Please see line 294.

Changes in the text: Removed “valuable” from line 294.

Reviewer B

Comment 1: In the head and neck surgery section, the definitions of palliative surgery and PGT needs to be clarified and applied appropriately. By the looks of the included studies most patients would have been treated with curative intent rather than palliative intent treatment protocols. So patients undergoing surgery in this context are not having palliative surgery. The primary intention for these patients is cancer cure/control rather than, as the authors define in the introduction, with the primary intention of relieving symptoms or improving quality of life (QOL). In patients treated with curative intent surgery, the PEG tube would be inserted, generally, as a temporary measure to allow nutrition in the face of significant treatment-related side-effects. It is not to relieve symptoms but to allow them to tolerate treatment. The decision-making in this context is greatly different from decisions made in the palliative setting where a focus on symptom relief and QOL improvements is paramount. The placement of PGTs in palliative surgery is very different. I think the authors need to review the head and neck literature they have cited with this in mind and make appropriate adjustments to the text. The authors need to separate out the use of feeding tubes in the context of curative-intent treatment vs palliative intent treatment.

Reply 1: **Thank you for your comment. We agree that curative versus palliative intent is extremely important in determining the nature of PGT and that the decision-making process in each context is not identical. Our intention in the head/neck cancer section was to emphasize that despite such difference, there is a lack of research pertinent to the use of gastrostomy tube in palliative head/neck cancer patients. Most research pertains to the use of PEG in patients undergoing curative treatments. Perhaps palliative patients may have been included in these studies, but palliative intent is not mentioned. Thus, our goal is three-fold: 1) affirm the status quo of the lack of dedicated PGT data in head/neck cancer literature; 2) include available palliative data and principles from curative intent literature that can be applied when considering PGT; 3) emphasize the limitation of such approach and encourage further PGT research efforts. Ultimately, we aim to validate healthcare professionals' challenges when making decisions regarding PGT in head/neck cancer and facilitate a way forward in palliative patient care utilizing available data. To this end, we have made the following changes: 1) included a paragraph explaining the above nuances; 2) reframed the included literature in the context of palliative patients; 3) added relevant references to support the premise. For the specifics of our revision, please see lines 94-189.**

Changes in the text: **The entire head/neck cancer section has been revised to reflect the Reviewer's recommendations.**