

Reviewer #1:

Well written. Please look into attached file for comment.

Within the attached file title: 20221013_79762-Manuscript File.docx

1. In reference to severity of hypoxia defined as mild (SpO₂ 91-94%), moderate (SpO₂ 90-76%) and severe (SpO₂ ≤75%) the reviewer asked is this a standard way of classifying hypoxemia? If yes, please provide reference.

Thank you for your kind words. With regards to the severity of hypoxia, there is no standard approach to defining the severity of hypoxaemia. We had chosen these values in reference to Lin et al. 2019.^[1] In addition, the severity of the hypoxaemia has been revised and the data re-analyse using mild (SpO₂ **90**-94%), moderate (SpO₂ **89**-76%) and severe (SpO₂ ≤75%).

Reviewer #2:

This manuscript presents a randomised trial of whether the incidence of hypoxaemia in patients undergoing upper GI endoscopy receiving supplemental oxygen using an oxygenating mouthguard at 20L/min flow is inferior to standard nasal cannula at 2l/min flow. The trial is approved by ethics committees, registered in a public trial register, and performed in accordance with the principles of the Helsinki Declaration. I have some methodological comments.

1. Major: The lexicon for endoscopic adverse events (ASGE, 2010) defined hypoxia as SpO₂ <85%. Why did you use the cut-off of 90%? The results are the same for the cut-off of 85%? I suggest an analysis using this standardised cut-off.

Thank you for your constructive feedback. A post-hoc analysis using **SpO₂ <85** as a secondary outcome has been performed and is included in the manuscript. The use of SpO₂ <90% is consistent with other randomized controlled trials using high-flow nasal cannula in endoscopy.^[1-3]

2. Minor: Can you explain why did you use the rate of 20l/min by the HFMG?

The choice of 20L/min via the high-flow mouthguard was based on the experience of our esteem anaesthetists.

3. Minor: The sample size calculation should be better defined.

Further detail has been included in the manuscript. Specifically, a treatment effective of 8.4% based on Lin et al 2019.^[1] The incidence rate used for the sample size calculation were 9.4% and 1.0% in the control and interventional group, respectively.

Reference:

- 1 Lin Y, Zhang X, Li L, Wei M, Zhao B, Wang X, Pan Z, Tian J, Yu W, Su D. High-flow nasal cannula oxygen therapy and hypoxia during gastroscopy with propofol sedation: a randomized multicenter clinical trial. *Gastrointest Endosc* 2019; **90**(4): 591-601 [PMID: 31278907 DOI: 10.1016/j.gie.2019.06.033]

- 2 Riccio CA, Sarmiento S, Minhajuddin A, Nasir D, Fox AA. High-flow versus standard nasal cannula in morbidly obese patients during colonoscopy: A prospective, randomized clinical trial. *Journal of Clinical Anesthesia* 2019; **54**: 19-24 [DOI: <https://doi.org/10.1016/j.jclinane.2018.10.026>]
- 3 Doulberis M, Sampsonas F, Papaefthymiou A, Karamouzos V, Lagadinou M, Karampitsakos T, Stratakos G, Kuntzen T, Tzouvelekis A. High-flow versus conventional nasal cannula oxygen supplementation therapy and risk of hypoxia in gastrointestinal endoscopies: a systematic review and meta-analysis. *Expert Review of Respiratory Medicine* 2022; **16**(3): 323-332 [DOI: 10.1080/17476348.2022.2042256]