

## Answering Reviewers

Reviewer #1:

This is a well written minireview that updates the interplay between NAFLD and SAS. Some typos: the authors wrote - "Nonalcoholic fatty liver disease (NAFLD) is strongly associated and sleep apnea syndrome (SAS)". Please correct the sentence and substitute "and sleep apnea" for "with sleep apnea". "NAFLD can progress into nonalcoholic steatohepatitis (NASH)" - include the extension: with or without fibrosis.

Re: Many thanks for the suggestions. We have revised the description and thoroughly checked the whole context.

"NAFLD patients are prone to sleep apnea syndrome (SAS), a common respiratory disease." How common is it? What is the overall prevalence?

Re: Many thanks for your questions. We have supplemented the epidemic description of SAS as well as NAFLD with SAS, and added 2 citations in the revised manuscript.

Figure 1: Include abbreviation's legends I would suggest the inclusion of a table with the studies that show the improvement of SAS after NAFLD intervention with lifestyle measures, medications and bariatric surgery studies cited in the manuscript. This may help the reader to evaluate the design of the studies, the number of patients included and their conclusions.

Re: We appreciated the suggestions. We have prepared a table to summarize the effects of current strategies (lifestyle measures, medications and bariatric surgery intervention) on NAFLD patients with SAS (Table 1).

Reviewer #2:

This is a concise, carefully-undertaken narrative review on the connection between NAFLD and sleep apnea, with clinical correlations. Overall, it is scientifically sound, informative and easy to read. Here are my specific comments and suggestions:

Introduction-paragraph 1: One is the "two-hit" hypothesis proposed by James et al in 1998, the first strike...--> ...by James et al. in 1998: the first strike...

Re: Thanks for your detailed comments, we have corrected the punctuation mark in the sentence.

Hypoxia and oxidative stress: It would be useful to add a comment in the last paragraph regarding the genetic associations of NAFLD and SAS, as per Bhatt et al. (doi: 10.1371/journal/pone.0199599).

Re: Many thanks for the suggestions. We have added the comments regarding the genetic associations of NAFLD and SAS in the last paragraph of "Hypoxia and oxidative stress" section.

Diagnosis: (regarding the role of MRI in the non-invasive diagnosis and grading of NAFLD) although there are practical restrictions for patients suffering from severe obesity.

Re: Many thanks for the suggestions. The role of MRI in the non-invasive diagnosis and grading of NAFLD has been discussed in the revised version.

Bariatric Surgery: i) As per IFSO, the correct term that has been adopted is Metabolic Bariatric Surgery (MBS), exactly because of the sequelae of this kind of operations on conditions such as T2DM and NAFLD. Consequently, I would suggest changing "bariatric surgery" into "metabolic bariatric surgery" throughout the text.

Re: Many thanks for the suggestions. We have changed "bariatric surgery" into "metabolic bariatric surgery" throughout the text.

ii) As per the 6th IFSO Global Registry Report (<https://www.ifso.com/pdf/ifso-6th-registry-report-2021.pdf>), MBS leads to a reduction of SAS ranging 58-65%, depending on the type of operation (LSG, RYGB, OAGB). Consequently, SAS is among the comorbidities with the greatest response rate to MBS and this is something worth mentioning.

Re: Many thanks for the reminding. We have supplemented this important information in the revised manuscript.

iii) Last paragraph-last period (It is important...by a specialist): This statement is not absolutely true. On the one hand the indications for MBS are constantly expanding. On the other hand, it has been estimated that only 1% of patients

who are candidates for MBS are eventually being operated. The reasons for this discrepancy are multiple and include (but are not limited to) suboptimal patient information about the indications and benefits of MBS, fear of surgery, reduced referrals by colleagues of related specialties etc.

Re: Many thanks for the reminding. We may have not fully evaluated the current literature, and made too absolute declaration. To be concise and rigorous, we decided to delete the inappropriate sentences in this paragraph.

iv) There are at least two important original papers that have studied the clinical correlation of NAFLD and SAS before and after MBS and are worth mentioning: (1) Lesailly et al., doi: 10.1053/j.gastro.2015.04.014; (2) Zhang YX et al., doi: 10.1007/s11695-020-04696-w.

Re: Thanks for the suggestions. We have added the text to show the effects of MBS on NAFLD and SAS before and after the surgery, and added the refs accordingly.

Conclusions: obese patients--> patients living with obesity (politically and pathophysiologically correct term encouraged by IFSO).

Re: Thanks for the suggestions. We have modified the term.

Figure 1 i) In the "Drugs" bubble, and specifically in the anti-obesity medications, I would suggest adding "including GLP1RAs (semaglutide, liraglutide)", as per Seghieri et al., doi: 10.3390/fendo.2018.00649. ii) I would suggest a ramification in the NAFLD-SAS continuum, as well as briefly mentioning potential responsible mechanisms, as per Ahmed and Byrne, doi: 10.3748/wjg.v16.i34.4243 (also see attached file).

Re: Thank you very much for your constructive suggestions. We have updated the figure, added the corresponding information in the context accordingly.