Answering Reviewers

As our revision was started as soon as we received the very first comment, we were able to finish this process not along after the revision was finally required, we would like to thank all the reviewers for their time and patience, and here are our responses to the questions raised:

1. Reviewers' comments

Reviewer #1: The study is very interesting with potentially important clinical implications. However, I must raise some points that should be addressed by authors:

1- both Introduction and Discussion sections are too long and should be shortened.

Response: Some superfluous statements have been deleted and both the Introduction and Discussion sections are pruned as requested.

2- in Materials and Methods section you have stated "Based on the differences in mortality among groups estimated with our previous experience, animals were unequally and randomly divided into the following three groups."; please explain based on which data you can claim this.

Response: We are sorry for making this indistinct and poorly described. In order to improve the postoperative survival rate of study subjects, few modifications were made on the perioperative management, plus considering the learning curve of the operation induces on the survival rate, a preliminary experiment involved sham-surgery group and SG group (healthy controls were considered safe and therefore not included since no interventions would be taken)was designed and conducted exactly the same with a smaller sample size to assess the postoperative mortality: 15 obese and diabetic rats for each group(modeled successfully as described), none of them were sacrificed or executed after surgeries, and here is how the survival rates were finally estimated:

Among the 15 sham-operated rats, 12 survived until the 12^{th} week after the operation while 1 died at the 8^{th} week, and 2 died at 10^{th} week, so a survival rate of 80% was calculated. And by what we observed, the deterioration of hyperglycemia increased the mortality rate over time. In order to ensure the sample size, we decided to set the postoperative week 12 as the appropriate end-point of our study.

For the 15 SG rats, 8 of them survived. We noticed that there was a high probability of survival after the postoperative week 2. Among the 7 rats that died after surgery, 6 of them died within the first 2 weeks, in which 4 died in the first week, and the remaining one died at the 4^{th} week after surgery. Thus, a survival rate of nearly 50% was estimated, and with the improvement in the surgical proficiency, we assumed that the mortality may drop slightly.

To clarify, it is now stated in the first paragraph of the Material and Methods section. Thank you.

3- please, correct the following sentence in the Materials and Methods section: "Eighteen rats in the SG group survived, while 30 died of the following causes: gastric leakage (n = 3), infection (n = 3), intestinal obstruction (n = 4), and unknown cause (n = 2; inconclusive

on autopsy). "
Response: We feel deeply embarrassed for this mistake. As reminded, the number is now corrected as 12.

4- please, explain more clearly how you came up with number of 15 subjects in each study group.
Response: Thank you. This is truly a key point that should be explained further. Though great and caring effort was made to increase the survival of study subjects, considering the mortality estimated in our preliminary experiment, we were aware of the fact that the interventions we took may endanger the lives of the operated animals, so instead of performing an analysis to look for the statistical sample size, which we think, could have probably been larger, we decided to set an appropriate number which is not statistically too "small" and is ethically acceptable. Therefore, 5 animals were included in each sub-group that was divided by the postoperative time points. Frankly speaking, we have to admit that our artificially determined sample size may not be totally rigorous in statistics, but we believe the current sample size with up to 15 rats in each group is enough to perform an inter-group comparison and produce convincing results. After all, it is a moral thing to reduce the animals used out of humanity when we knew that many of them may die.
For readers, a simpler statement is now added in the first paragraph of the Material and Methods section. Thank you.

5- please, explain the meaning of the "...significant reduction to oral glucose tolerance..." appearing in the Abstract.
Response: We are terribly sorry for this sloppy mistake. Actually the results indicated a reduction in the values of OGTT which refers to an improved oral glucose tolerance and insulin sensitivity. This reverse and false statement is now corrected.

6- please, revise the list of references and make it uniform in style.
Response: The references are reformatted and revised throughout as requested, few missing PMIDs and DOIs are added if available.

7- the whole manuscript requires the language polishing, mainly due to frequent typographical errors.
Response: Following above revisions, the manuscript was carefully read and the language is polished with existed errors revised.

Reviewer #2: Very interesting study. The manuscript is well written. I only suggest the authors to remove the abbreviations in the figure 1, and list them at the figure legend.
Response: The Figure 1 is revised as suggested. Thank you.

Reviewer #3: Well done study. Bariatric surgeries are universally adopted and performed as an effective treatment for severe obesity, T2DM, and other related comorbidities. In addition, whether in clinical trials or animal studies, they have been shown to prevent or

lower the risk of cancers, including lung cancer. Compared to these apparent effects, little is known about the underlying mechanisms of lowered cancer risk after bariatric surgery. Thus, considering the scarcity of relevant studies and the negative impacts of obesity and T2DM on endothelial function, tumor development, and the essential role of ET-1 axis in tumor pathogenesis of lung, we inferred that there may be some kind of correlation between the ET-1 axis with ameliorated endothelial function and lowered risk of cancer following bariatric surgery. The authors design the study, to find the role and effect of sleeve gastrectomy in obese and diabetic rats. The study is very interesting, and the manuscript is well written. The results are very useful in the clinicals. I have no specific comments.
Response: No specific revision was required. Thank you.

Reviewer #4: This is an interesting study of the sleeve gastrectomy in preventing lung cancer in obese and diabetic rats. The experiment of the study is designed very well, aims are very clear. Methods are reasonable. Data in figures and tables are very good, and well discussed. I have no specific comments.
Response: No specific revision was required. Thank you.

Reviewer #5: This study of effect of sleeve gastrectomy in preventing lung cancer in obese and diabetic rats, is very interesting. By using an obese and diabetic rat model induced by high-fat diet and streptozotocin, the authors investigated the potential effect of SG in improving endothelial function and lowering the risk of carcinogenesis by normalizing the ET-1 axis and ameliorating DNA damage using γ-H2AX, as a widely accepted biomarker of cancer. The design of the study is very good, and the results are excellent. I recommend to accept this manuscript for publication after a minor editing.
Response: The readability of the whole manuscript is improved and it is revised according to the comments received. Thank you.

2. Editorial Office's comments
The author must revise the manuscript according to the Editorial Office's comments and suggestions, which listed below:
(1) Science Editor: Recommend for potential acceptance. 1 Scientific quality: A,3B,C. The article is about sleeve gastrectomy ameliorates endothelial function and prevents lung cancer by normalizing endothelin-1 axis in obese and diabetic rats, within the scope of WJG. Summary of peer-review report: This study of effect of sleeve gastrectomy in preventing lung cancer in obese and diabetic rats, is very interesting. The design of the study is very good. The results are excellent and very useful in the clinicals. 1 table and 5 figures. 61 references were cited, including 17 latest references from 2017-2020. No self-citation. 2 Language quality: 3A,2B. Edited by Filipodia language editing services. 3 Academic norms and rules: Basic Study. Copyright license agreement, The ARRIVE Guidelines, IRB, BRC and Conflict-of-Interest statement files are complete and qualified. Bing search and CrossCheck are eligible. 4 Others: With National Natural Science Foundation of China financial support. Corresponding author has not published articles in WJG. Unsolicited manuscript.

Response: No specific revision was required. Thank you.

(2) Editorial Office Director: Recommend for potential acceptance. 1. Scientific quality: I have checked the comments written by the science editor, and I basically agree with the science editor. The topic of the paper is the sleeve gastrectomy ameliorates endothelial function and prevents lung cancer, and is within the scope of the WJG. The reviewers stated that the study is very interesting with potentially important clinical implications, well written and very useful in the clinical. The questions raised by the reviewers should be answered. 2. Language quality: 3A2B. The language certificate is provided by Filipodia, but the reviewer 03490943 pointed out that whole manuscript requires the language polishing, especially the typographical errors. 3. Academic norms and rules: I have checked the documents, including biostatistics review certificate, The ARRIVE Guidelines, institutional review board approval form or document, conflict-of-interest disclosure form, and copyright license agreement, all of which are qualified. The institutional animal care and use committee approval form or document is not qualified, the authors need to check and revise it. No academic misconduct was found in the CrossCheck investigation and the Bing search. 4 Supplementary comments: (1) Unsolicited manuscript. (2) With 1 national financial support. (3) Corresponding author has not published articles in BPG journals.
Questions:
1)The language certificate is provided by Filipodia, but the reviewer 03490943 pointed out that whole manuscript requires the language polishing, especially the typographical errors.
Response: The language is polished throughout the whole manuscript and the existing errors are corrected. Thank you.

2) The institutional animal care and use committee approval form or document is not qualified, the authors need to check and revise it.
Response: As requested, we have carefully looked through the submitted document and we are deeply sorry for the disqualification of our form. Since no exact reason for disqualification was stated, we would like to kindly make the following explanation. First, the difference between the name of the project in the form and the title of the manuscript was caused due to our concern that the original title may be too long to meet the requirement of the journal, which we decided to shorten with a slight modification right before the final submission while the document had been obtained from our institution few days ago. Second, according to the regulations of the ethics committee of The First Affiliated Hospital of Shandong First Medical University, the submitted form, which is exactly same as the document of Institutional Review Board Approval Form, is the one and only official approval that can be provided on granting medical research, it was filled and given by the institutional review board after considerately evaluating our project. Today, we have consulted our institution about this issue and we were suggested to resubmit the original form with a further explanation on its validity under current situation though the file may seem too brief. Please, check our form again. And sincerely, we like to apologize for our defective document and kindly ask for an approval. Thank you.

(3) Company Editor-in-Chief: I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report and the Criteria for Manuscript Revision by Authors.

Response: Thank you for reviewing our manuscript, a diligent revision has been made.