Author’s response to reviews

Title: Point-of-care ultrasound defines gastric content in elective surgical patients with type 2 diabetes mellitus: a prospective cohort study

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Response sheet

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Manuscript title: Point-of-care ultrasound defines gastric content in elective surgical patients with diabetes mellitus: a prospective cohort study

Dear Editor:

We would like to thank you and reviewers for the time spent on our manuscript, for your encouragement and your constructive suggestions. We have thoroughly modified the text according to reviewers' comments, and below we provide point-by-point responses to those
comments. We have also modified the manuscript according to the formatting requirements of the journal.

We hope the revised manuscript can now be judged suitable for publication in BMC Anesthesiology.

Sincerely,

Chunling Jiang, M.D., Ph.D.
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Response to the first reviewer’s comments

Reviewer reports:

Rita Cataldo (Reviewer 1): the topic of the paper is interesting and the study well conducted

Some criticisms appears:

1. It should be better to declare from the beginning what type of population you studied (diabetes type 2) and duration of the disease (6 years). personally I'd choose to insert the "type 2" even in the title

Reply: Thank you for the comments and your advice. We have revised the manuscript accordingly and added the “type 2” in the title. Since the results of median duration of type 2 diabetes were generated through our analysis, we would like to emphasize this point in the first sentence of the discussion section. We wish it is acceptable.

2. Did you explain to yourselves why your percentage of full stomach is so higher than in literature? (see recent Ohashi Y.2018 for example)
Reply: Thank you for the comments on this point. We read the article you mentioned and analyses the differences. We speculate this may partly be explained by the different diagnosis criteria of full stomach. In our study, a full stomach was defined as Perlas Grade 2, which is the content was detected in both semi-recumbent and right lateral decubitus positions regardless of the antral cross-sectional area (CSA)1, 2. While in Ohashi Y's study3, gastric residual content volume (GRV) were calculated by Volume = 27.0 + (14.6 x CSA) – (1.28 x age), and a high-risk GRV is defined as measured value >1.5 ml/kg. Therefore, the criteria used in our study tends to find more positive cases. Additionally, our results are similar to the recently published study, in which the percentage of full stomach in diabetic patients is 60%4.

References:


3. Despite your data fortunately aspiration is quiet infrequent. In clinical practice, when do you think your US data can justify a postponement of an elective surgery or the use of a prokinetic drug or RSI? this answer can enrich the discussion.

Reply: Thank you for the suggestion. We have added this content in the revised manuscript. In clinical practice, we propose that preoperative ultrasound assessment of gastric content should be performed for patients with type 2 diabetes duration of 6 years or more. Moreover, a prokinetic drug and rapid sequence induction is recommended for such cases.

4. I read in page 5 line 52 that you detected the presence of diabetic nephropaty, but I cannot find this data in the Tables. It should be interesting to know if gastroparesis can be related to
some degree of chronic renal failure (see recent Garima Sharma 2018). What is in your opinion the role of the age in your population?

Reply: Thank you for the comments. In our study, none of the patients had diabetic nephropathy. That’s may partly because of the duration of diabetes in our study is not long enough, with only 6 years (IQR 2-10 years). The mean age of our subjects was $60.67 \pm 10.34$ years old, and we did not find the association of age and delayed stomach emptying in our study.

5. Regarding Tables anf Figures, I'd like to summarise in just one table Table 2/S1/S2; Probably Figure 1 S1 can be deleted

Reply: Thank you for the comments. We have deleted Figure S1 and summarised Table 2/S1/S2 in one table (Table 2).

6. In Table I: ASA I patients in diabetic patient column: n 9. There is an error?

Reply: Thank you for the comments. There is an error. we have corrected it.

7. Page 1 line 21 Changhai is is that right? or Shanghai?

Reply: Changhai Hospital is correct.

8. Page 5 line 24: mm instead mm2

Reply: Thank you for the comments. We have corrected it.

9. In the conclusions I think that use "recommend" can be too loud..

Reply: Thank you for the comments. We agree with your comment and we have changed it to "suggest". We wish our revision is acceptable.
Response to the second reviewer’s comments

Stefano Falcetta (Reviewer 2): I want to congratulate to all the authors because this study is well designed and conduct and the manuscript is written clearly and fluently.

The topic is of crucial interest for the anesthesia practice: the use of Point of care Ultrasounds to detect a delayed gastric emptying and the resultant "full stomach" as a risk factor for perioperative regurgitation and aspiration in patients undergoing general anesthesia.

In particular the authors demonstrated that diabetic patients have a higher prevalence of delayed gastric emptying (as previously reported in literature) but also the usefulness of ultrasounds as a simple non-invasive and bedside technique to use before anesthesia induction for the assessment of gastric emptying status especially when ASA fasting guidelines may be not suitable.

I found very interesting the finding that diabetes-related eye disease could be an independent risk factor of full stomach.

Abstract

Ok

Introduction

Page 3/23, Line 33-37: "ultrasound sonography allows anesthesiologists to evaluate a patient's gastric content and volume at the bedside, and helps guide anesthetic and airway management"… for example, the doubt of the usefulness of cricoid pressure during direct laryngoscopy. Please, Refer to..."Sorbello M. Aristotle, Galileo and Sellick: The unsolved dilemma of cricoid pressure. Trends in Anaesthesia and Critical Care 2016; 6: 1-2. DOI: 10.1016/j.tacc.2015.11.001"

Reply: Thank you for the comments. We have supplemented this reference and cited it.

Material and Methods

Ok

Ultrasound Examination

Page 5/23, Line 20: Please refer to the correspondent figure
Reply: Thank you for your suggestion. We have supplemented Figure 1.

Page 5/23, Line 24: "Grade 1 with CSA <340 mm." Please correct with < 340 mm2
Reply: Thank you for the comments. We have corrected it.

Sample size and Statistical analysis
Ok

Results
I think it could be appropriate to represent the data in the table 2 and table 3 also on a graphic diagram.

Reply: Thanks for your advice. In the revised version, we have summarised the original Table 2, S1, and S2 into the new Table 2. The Table 3 was still reserved. Since Table 2 and 3 present different characteristics and features of the included patients, we then did not combine the two tables into a new one table. We wish our revision is acceptable.

Page 7/23, Line 22-27: "As shown in table 2, diabetic patients have a higher prevalence of full stomach when compared to non-diabetic patients (48.1% vs. 8.00%, P= 0.000), which is 44.0 % vs. 8.0% (P=0.000) for 2-hour fast after clear fluid and 51.9% vs. 8.0 % (P=0.000) for 6-hour fast after a light meal, respectively (S1Table - S2 Table).” Could you insert these 2 subgroups (44.0% vs 8.0% for clear fluid and 51.9% vs 8.0% after light meal) in the table 2?

Reply: We are grateful to the reviewer for this good comment on our study. We have revised it accordingly. The 2 subgroups shown in S1 and S2 were inserted into Table 2 in the revised version.
Nevertheless, others showed it was the acute changes in the glucose concentration, not glucose concentration affect gastric emptying. Please correct with … that affects gastric emptying.

Reply: Thank you for the comments. We have revised it accordingly.

Page 10/23, Line 25: "our findings might possibly not represent the condition before anesthetic induction". This could have conditioned the SAS score anxiety that was lower than 40 in both groups of patients.

Reply: Thank you for the comments. We are in complete agreement with your opinions. In clinical practice, there were not any fasting guidelines in elective surgical patients with type 2 diabetes currently. Our study may supplement the knowledge in this area. As a pilot study, our conclusions were suitable for type 2 diabetic patients without anxiety or depression. We then revised the manuscript accordingly.

Response to the third reviewer’s comments

Alessandro Di Filippo (Reviewer 3): Dear Authors,

Unfortunately I have to underline some reasons that lead me to express an unfavorable opinion on the publication of your work on BMC Anesthesiology. List below:

1. I do not believe that the work has sufficient originality as the subject has been widely discussed and promulgated in the past and even recently


Abdominal Ultrasound for the Evaluation of Gastric Emptying Revisited. Muresan C, Surdea Blaga T, Muresan L, Dumitrascu DL. J Gastrointestin Liver Dis. 2015 Sep; 24 (3): 329-38;


Reply: Thanks for your critical comments on this point. We admire your adherence to the originality of a clinical study. We carefully read the articles you raised and thought that our current study still has some merits and provided valuable information to clinicians and readers of BMC Anesthesiology. We do admit that the publication on Acta Anaesthesiol Scand. 2019 made us feel a little nervous, for that it is in the same area. However, several differences should be noted. Their study estimated the antral cross-sectional area and compared with the aspirated volume through the nasogastric tube. While our study also measures the antral cross-sectional area, and further identified risk factors through multivariate logistic regression analysis. Our study was registered at Clinicaltrials.gov(NCT03217630) at July 2017, and was carried out from July 2017 to April 2018. We updated the trial and tagged it with “Completed” this April. Their study was also registered, but was carried out later than ours. Although their results have been published, the trial was still tagged with “Not yet recruiting”. We do admit that preparation and language editing of the manuscript costed us a lot of time, which made us a delay to submit it to BMC Anesthesiology at May 2019. Apart from the reasons above, we divided patients included into light meal and clear liquid, providing further information on the topic. Thus, we revised our manuscript according to comments from all reviewers and wish it is much more acceptable. We would like to make further revision as requested.

2. The method of randomisation is not declared, in my opinion.

Reply: Thank you for the comments. We have supplemented the methods of randomization and wish it is much more acceptable. We randomized patients into clear fluid or light meal subgroup.

3. The statistical method of identifying the number of cases for the multivariate survey has not been declared, in my opinion.

Reply: Based on our preliminary trial and data from literature, we calculated the samples needed. In order to investigate the risk factors for full stomach, we also enlarged sample size to 108 patients for multivariate logistic regression analysis in our study.

4. In my opinion, it is not sufficiently discussed the reason why neuropathy does not appear to be a risk factor in the univariate investigation but it should be such as an element that underlies the presence of ocular alterations.

Reply: Thank you for the comments. We agree with your comment and admit this is the limitation in our study. That’s partly because of the diabetic patients in our study were not severe enough, and the potential relationship between ocular alterations and neuropathy may be underestimated, which may need further studies to evaluate.
5. The cut off used for obesity (BMI 35) is a confounding factor; in fact, you are forced to argue that obesity does not appear to be a risk factor for reasons related to the selection of cases. It would be necessary to resume enrollment by inserting only non-obese patients.

Reply: Thank you for the comments. We use BMI 35 as criteria for obese patients according to the recent published study, which found obesity was a risk factor for delayed stomach emptying. (Kruisselbrink R, Arzola C, Jackson T, Okrainec A, Chan V, Perlas A: Ultrasound assessment of gastric volume in severely obese individuals: a validation study. British journal of anaesthesia 2017, 118(1):77-82.)

Response to the fourth reviewer’s comments

Silvia De Rosa (Reviewer 4): The manuscript by Li Zhou, et al. is prospective cohort study of point-of-care ultrasound defines gastric content in elective surgical patients with diabetes mellitus: a prospective cohort study. One hundred and eight patients (54 diabetic patients and 54 non-diabetic controls) admitted for elective surgery were enrolled in this study between July 2017 and April 2018. The research question is interesting and highly clinically relevant.

The introduction

Please add in the introduction section that gastric emptying is delayed in 30%-50% of patients with longstanding diabetes mellitus. The prevalence of disordered gastric emptying in patients with "early" Type 2 diabetes is controversial, but it has been suggested that gastric emptying is often accelerated. Acute changes in the blood glucose concentration have a major effect on gastric motor function and gastric emptying.

Reply: Thank you for the comments. We have revised it accordingly. We also added the point you mentioned in the discussion section and the revision is highlighted in blue.

The authors defined the research question at the end of the background section:

"Using this non-invasive technique for the assessment of gastric content, we aimed to determine the prevalence of full stomach following the present fasting guidelines in elective adult surgical patients with diabetes mellitus, and to investigate associated risk factors for delayed gastric emptying, in this prospective cohort study".
I miss a PICO-diagram specifying the research question:

Population: elective adult surgical patients with diabetes mellitus

Intervention: the prevalence of full stomach following the present fasting guidelines or the associated risk factors for delayed gastric emptying

Comparator: Not mentioned?

Outcome: Not mentioned?

In addition, you did not explain the reason of your prospective study. Which is you hypothesis? Please, consider the pico question

Reply: Thank you for the comments. We tried your PICO-diagram method as follows.


Intervention: use ultrasound to evaluate the gastric emptying under the current fasting guideline.

Comparator: elective adult surgical patients with or without type 2 diabetes.

Outcome: the prevalence of full stomach under current fasting guideline for elective surgical patients.

Your PICO-diagram made us much clearer about the objective and hypothesis of our study. We have revised the introduction accordingly.

Methods: authors stated that the primary outcome was the prevalence of full stomach in diabetic elective surgical patients. The secondary outcome was the gastric emptying time of clear liquids and light retrospectively examined. Methods were well described

Reply: Thanks to your appreciation on our methods.

Discussion and Results: 102 patients (52 diabetic and 50 non-diabetic patients) completed the study and were included in the final analysis, with the dropout rate at 5.56%. Diabetic patients have a higher prevalence of full stomach when compared to non-diabetic patients (48.1% vs. 8.00%, P= 0.000), which is 44.0 % vs. 8.0% (P=0.000) for 2-hour fast after clear fluid and 51.9% vs. 8.0 % (P=0.000) for 6-hour fast after a light meal, respectively. The average time to empty stomach was significantly longer in diabetic patients than that of non-diabetic patients. Surprisingly, was not detect significant correlation between BMI with delayed stomach
emptying. I am not agree with the statement that "Surprisingly, we did not detect significant correlation between BMI with delayed stomach emptying, inconsistent with previous studies, which showed obesity was a risk factor for delayed stomach emptying. This is possibly due to the fact that a relatively small sample size of obese patients was recruited"

Data in literature showed that overall 3 h gastric emptying rate was similar in obese (BMI=38.7 kg/m2) and normal weight males, and unaffected by a major weight loss. The anesthetic risks in the obese should be attributed to factors other than delayed gastric emptying (i.e., anatomic variation, increased rates of hiatal hernia and reflux). So, your data are consistent with data present in literature.

Reply: Thanks for your comment on this point. We agree with you that a relatively small sample size of obese patients should not be neglected. We have revised relevant section accordingly and wish it is much more acceptable. We also appreciate your explanation on this issue we raised in the discussion.

Conclusions: data should be confirmed in diabetic patients with complications

? ?

Reply: We are grateful to the reviewer for the comment on this point. We have revised it accordingly.