Author’s response to reviews

Title: The Predictive Value of Hunger Score on Gastric Evacuation after Oral Intake of Carbohydrate Solution

Authors:

Weiji Qiu (qiuweijicharles@hotmail.com)

Shitong Li (lishitongs@hotmail.com)

Yu Luo (duolan@hotmail.com)

Tianfang Hua (huatianfang@yeah.net)

Ning Kong (kongning2000@yahoo.com)

Lina Zhang (zhanglina@shsmu.edu.cn)

Version: 1 Date: 08 Dec 2017

Author’s response to reviews:

Dear Dr. Tu, Dr. Phillips, Dr. Saracoğlu and Editors:

Thank you for your consideration of our manuscript. We really appreciate your excellent and helpful comments and suggestions, which would certainly help improve the quality of our paper.

We have tried our best to make the appropriate revisions in the article and respond to the comments point to point, and have also some issues to be clarified. We hope it could be acceptable.

Thank you very much again for your time and work on our paper!

We look forward to hearing from you soon.

With Our Best Regards!

Sincerely, Weiji Qiu
Department of Anesthesia and Critical Care Medicine
Shanghai Fourth People’s Hospital
1878 North Sichuan Road, Hongkou District, Shanghai 200081, China.
qiuweijicharles@hotmail.com.

(General comments:)

Comment 1:
“The authors should comment more on what they mean by use of hunger as a second check, and clearly specify what would be the first check. Based on the findings of this current study, what liquid meal do the authors think should a patient be allowed to drink before surgery and how long before surgery should the patient safely be permitted to take the liquid meal.”

Answer 1:
Thank you very much for the suggestions.
We have re-written the text in the 9th paragraph and the last paragraph of the discussion section, and “comment more on what we mean by use of hunger as a second check, and clearly specify what would be the first check”.

We have also emphasized in the 10th paragraph of the discussion section on the composition of the liquid meal we tested (the 12.5% carbohydrate solution with a specific composition of 10 g maltodextrin and 2.5 g sucrose per 100 mL water), and we expect this would provide a reference to the readers for “what liquid meal…should a patient be allowed to drink before surgery and how long before surgery should the patient safely be permitted to take the liquid meal” based on our findings.

(Thank you in advance for the instructive Citations provided in “Comment 3”, which would help a lot in better understanding the gastric emptying process.)
Comment 2:

In the method section, support should be given to validate that the methodology used to calculate gastric volumes by MRI. Information should be provided as to the accuracy and variability of the MRI method. This information is important so that the reader can know that the gastric emptying volumes are valid. MRI validation could be a cite to prior papers that used the same MRI methodology to calculate gastric emptying volume or demonstration by the researchers that the volumes are accurate. For example, MRI imaging could be performed immediately to determine if the MRI measured gastric volumes are close to 8 ml/kg immediately upon ingestion.

Answer 2:

We have added a paragraph in the “Method- MRI Measurement” section, and 2 papers were cited to illustrate “the accuracy and variability of the MRI method” to measure the gastric emptying process. And the order of the references has also been modified accordingly.

But we are sorry that our study could not provide the immediate data “after the subjects ingest the 8ml/kg volume”, because we did not measure the immediate data during our current test.

(We learned from our previous study which was published in Chinese (Reference 1) that while MRI was used to measure the gastric emptying process, the gastric volume at T30, T60, T90, and T120 would be more stable and meaningful to illustrate the process, so we did not observe the gastric volume at T0 this time).

Comment 3:

In regards to gastric emptying volumes, in this study, normal subjects were given 8 ml/ kg of carbohydrate containing fluid. If the average weight of the subjects was 66.4 kg, they received 66.4 grams of carbohydrate which would be 265 kcal. In this paper, patients had only 4 ml/kg gastric volumes remaining in their stomachs at 30 minutes. This means that the average patient emptied 132.5 kcal in thirty minutes, or 4.4 kcal per minute. This rate of gastric emptying is very rapid for normal subjects on a kcal basis as compared to most prior reports in which average gastric emptying of kcal of protein, carbohydrate or fats is around 2.1 kcal/min.

Citation 1: Gastroenterology. 1983 Jul;85(1):76-82.
Regulation of the gastric emptying of glucose.
Brener W, Hendrix TR, McHugh PR.
Glucose assumed, soon after filling the stomach, a slow and calorie - constant emptying pattern such that 2.13 kcal of glucose were delivered per minute to the duodenum for all three concentrations of glucose.

Rapid gastric emptying of an oral glucose solution in type 2 diabetic patients.
Phillips WT1, Schwartz JG, McMahan CA.
Gastric emptying half time of 65 minutes for a 200 kcal glucose meal. Kcal/min emptying rate of 1.5 kcal
Gentilcore D1, Nair NS, Vanis L, Rayner CK, Meyer JH, Hausken T, Horowitz M, Jones KL.
The mean GE of oral glucose was 1.3 +/- 0.1 kcal/min.

One possibility is that the MRI measurements are overestimating the rate of gastric emptying. It is also possible that there are ethnic differences in the Chinese population regarding the gastric emptying of carbohydrate solutions.
Citation 4:

Answer 3:
First, I would like to thank Dr. Phillips for reminding us that there might be ethnic disparities in gastric emptying. We added the words to the limitations in discussion section and cited a reference provided by Dr. Phillips.
And as for the calorie emptying rate, I think it is a very good and interesting question to be addressed.

I agree with Dr. Phillips’ comment that there is the possibility the”MRI measurements” might be “overestimating the rate of gastric emptying” or “there are ethnic differences in the Chinese population regarding the gastric emptying of carbohydrate solutions.”

But I do have another 3 points to be addressed:

1. If we calculate the average speed of the gastric calorie emptying, the result in our report was very close to the results in these citations, and our emptying rate is within the range provided by the literatures.

We can calculate the average emptying rate of the 12.5% carbohydrate nutritional solution in our paper. The average weight of the subjects was 66.4 kg, they received 66.4 grams of carbohydrate which would be 265 kcal, the stomach was almost emptied at 120 min, this means that the average patient emptied 265 kcal in 120 minutes, or 2.2 kcal/min in our study. The result of this data is close to the previous literatures.

In the “Citation 1”, it was stated that “Glucose assumed, soon after filling the stomach, a slow and calorie-constant emptying pattern such that 2.13 kcal of glucose were delivered per minute to the duodenum for all three concentrations of glucose.”

But in the Method section, it said ”the test meals were all 400-ml solutions… the physiological glucose meals were allowed for 5-90 min emptying periods.”

And in the Result section, it said “all three glucose solutions emptied at … 1.98, 2.12, and 2.11 kcal/min”.

So I have the deduction that the author Dr. Brener might get the conclusion of “2.13 kcal of glucose were delivered per minute to the duodenum” through 90 minutes of observation, he calculates the average emptying rate of 90 minute.

In Citation 2, it was stated “Gastric emptying half time of 65 minutes for a 200 kcal glucose meal. Kcal/min emptying rate of 1.5 kcal”, but it also showed us “the extremes in calorie emptying rate varied from 1.2 to 6.9 kcal/min”.

So the gastric emptying rate in our paper is still within that range.
And in Citation 3: “the average gastric emptying rate … for the total 120 min was 1.3±0.1 kcal/min.”

As Dr. Diana Gentilcore said she got the 1.3kcal/min from a period of the total 120 min’s observation.

So we believe that although our data on gastric emptying is slightly different from previous literatures, it is still very close to the previous literatures and within the range of the previous reports.

2. There is a possibility that the different concentrations and types of liquid meal might have an influence on the gastric emptying progress.

Most citations measure the kcal/min gastric evacuation rate with the glucose solution of different concentrations, while we tested the 12.5% carbohydrate nutriental solution with the specific composition of 10 g maltodextrin and 2.5 g sucrose per 100 mL water (the use of maltodextrin has been modified in our study)( Reference 2).

The difference between the evacuation process might be attributed to the different kinds and different concentrations of these solutions.

3. In the first few minutes, the stomach will evacuate a little faster!

Last but not least, the stomach would evacuate calorie a little faster in the first few minutes.

In “Citation 1” , it was stated: “Even the most dilute glucose solution (0.2 kcal/ml) that was of comparable osmolarity to saline had emptied only 63% of the original 400ml at 20 min, as compared with 84% of saline.

The percentage and time period of the evacuation of 0.5 and 1 kcal/ml glucose was not reported in Dr. Brener’s manuscript.
When we calculate the 0.2 kcal/ml in this way: in the first 20 min, 63% of 400ml was emptied, that was a liquid meal of 252ml was emptied in the first 20 min.

\[
252\text{ml} \times 0.2\text{kcal/ml} / 20\text{min} = 2.52\text{kcal/min}
\]

In conclusion, in the first 20 min, an average of 2.52kcal/min was emptying into the stomach, which is higher than the average 2.1kcal/min.

And there are other articles showing that gastric emptying rates are faster in the first few minutes (Reference 3).

(\text{Table 2}) It shows that in the first 30 min, more than 50% gastric volume was emptied.

There was a more detailed description of the range of the calorie emptying rate in Dr. William T. Phillips’ report “Citation 2”, which was between “1.2\text{kcal/min} and 6.9\text{kcal/min}”.

In conclusion, the stomach would empty more rapid in the first few minutes, and the calorie evacuation rate of the first 30 min reported in our paper was just within a range reported before.

Comment 4:

It would be interesting to have monitored the plasma glucose levels in these patients at 30 minute time points. Generally hunger is related to blood glucose levels and it increases as blood glucose approaches fasting levels or frequently falls below fasting after a carbohydrate load. Measurement of blood glucose with a simple finger stick monitor would be another method to predict that the stomach has minimal residual volume and it would likely correlate with hunger. In these particular patients, if gastric emptying of 50% of the meal contents (265 kcal) actually occurs by 30 minutes, their postprandial glucose and insulin levels should be higher than normal.

Answer 4:

Thank you for this good suggestion. Please allow me to introduce the situation at that time:
We designed the current study and got the idea from our previous one (Reference 1). In the course of our previous research, we accidentally found that when volunteers complained of hunger at different time points, it seems to be able to suggest the emptying of their stomach.

The first driving force of our human beings to search for food is the feeling of hunger. But now, the only indicator we focus on before surgery is fasting time (Reference 4), ignoring the patient's own sense of hunger. On the other hand, the literature and reality have told us that even after a long period of fasting time, some patients still have residuals enough to cause gastric reflux (Reference 5,6). So the period of fasting time could not always be a perfect parameter to determine if the stomach has been emptied.

And we eventually confirmed that there is always a correlation between the hunger feeling and the gastric emptying through our current study. We want to tell the other doctors that to ask the patient if they feel hungry, while asking the period of fasting time at the same time, might be able to help them better judge the stomach emptying and the risk of gastric reflux.

It is truly a pity for us not to have monitor the blood glucose in our study, because in the beginning, we just wanted to design a study that could help the clinical anesthesiologists to make a rapid judgment on the gastric emptying process in a simple and noninvasive way, just like asking about the fasting time do, with no biochemical tests, and no machines. I have to admit that our design considerations were incomplete and deficient in some way.

But I still think that this study could tell the readers that to ask a second question before surgery might help them to make a better judgment.

Anyway, I do really appreciate Dr. William Phillips and all the other editors for your excellent comments and suggestions, you do really help us a lot. We planned to include the blood glucose and other biochemical monitoring programs in the near future, and we will keep on studying the factors that could have influenced the gastric emptying, such as the mood of anxiety and depression. We hope we could illustrate a more comprehensive assessment of the gastric emptying process in the near future.
Minor corrections:

1. ERAS should be defined the first time it is used in the first paragraph of the background and not in the second paragraph where it is currently defined.

2. In the discussion at the 5th paragraph, several methods of measuring gastric emptying were mentioned, but there was no mention of ultrasound which is common method used to assess gastric emptying. Ultrasound should be added as a technique as referenced in this paper #7 reference.

3. Correct the English of this sentence in the second paragraph of the discussion. "It has been reported that the gastric residual volume could be as much to cause gastric reflux even after a long time fasting."

Answer 5:

We really appreciate your meticulous work, and we feel sorry for the mistakes we have made in our writings.

We have corrected these mistakes now.

Thank you very much again and with our best regards!

Reference

1. "Qiu Weiji, Li Shitong, Bai Gang, etc. Gastric emptying time for liquids in healthy volunteers: determination by magnetic resonance imaging. Chinese Journal of Anesthesiology. 2015; 35; 1; 16-18." (Published in Chinese)

2. Ingestion of glutamine and maltodextrin two hours preoperatively improves insulin sensitivity after surgery: a randomized, double blind, controlled trial

