



## Reply to the authors

Hang-Cheng Xu<sup>1</sup> · Ying-Chang Pang<sup>1</sup> · Jing-Wen Chen<sup>1</sup> · Jia-Yu Cao<sup>1</sup> · Zhi Sheng<sup>1</sup> · Jun-Hua Yuan<sup>2</sup> · Rui Wang<sup>2</sup> · Cai-Shun Zhang<sup>2</sup> · Liu-Xin Wang<sup>2</sup> · Jing Dong<sup>2,3</sup> 

Published online: 7 November 2019

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We are very glad that the authors are interested in our research. And we appreciate their further investigation on this issue very much which is still full of controversy. Here is our reply to the authors. In this reply, we want to clarify the following questions.

1. Why number of the studies included in our meta-analysis was fewer than the authors'?

Firstly, the due date of literature search was April 2018. Therefore, we didn't included studies (Jingge Yang et al., Svane et al., and Tsouristakis et al.) after that. Secondly, we have stated the inclusion and exclusion criteria clearly in our meta-analysis. The authors have obtained 26 articles for their meta-analysis (16 articles for ours). However, in our searching progress, we also collected them all (except the three articles mentioned above). After screening by three reviewers, we only included the studies which reported the levels of total ghrelin (not acylated or des-acylated ghrelin). And we also limited the data expression form, only data of the studies presented as mean ± standard deviation (SD) were collected. The Fig. 1 of our meta-analysis has shown concrete screening process.

In this reply, we have presented the reasons for literature exclusion (10 articles) in Table 1.

2. Why we didn't conduct detail subgroup analysis of follow-up time as the authors did?

The original intention of the subgroup analysis was to find the source from which heterogeneity generated. By sorting the studies based on the time course ( $\leq 3$  months and  $> 3$  months), the heterogeneity partially reduced ( $I^2 = 0\%$  or  $42\%$ , respectively). However, in the authors' subgroup analysis, they didn't eliminate the heterogeneity sufficiently ( $I^2 = 0\%$ ,  $62.8\%$ ,  $70.8\%$ , or  $66.3\%$ , respectively). We might not draw a conclusion based on results with  $I^2 > 50\%$ . In the process of conducting our meta-analysis, we had tried many ways to do the subgroup analysis (including the detail time course as the authors did). At last, using 3 months as a time node was probably the most appropriate choice.

In our meta-analysis, we admitted that limitation existed. For instance, the studies included in this research were inadequate. More clinical trials related to this issue might be conducted in the future, and the results of our meta-analysis would change accordingly. However, based on the current evidence, we could draw the conclusion that fasting total ghrelin levels decreased in the short term ( $\leq 3$  months) and increased in the long term ( $> 3$  months) after RYGB.

Thank the authors for their work again.

**Table 1** Reasons for literature exclusion

Item	Data expression (not mean ± SD)	Ghrelin status (not total ghrelin)	Publication date (after April 2018)
Yousseif et al.	Mean ± SEM	Acyl-ghrelin	/
Ramón et al.	Median (IQR)	/	/
Jingge Yang et al.	Median (IQR)	Unknown	Jun 14, 2018
Nannipieri et al.	Median (IQR)	Des-acyl ghrelin	/
Alamuddin et al.	Mean ± SEM	Unknown	/
Malin et al.	Median (IQR)	Acyl-ghrelin	/
Svane et al.	Mean ± SEM	/	Feb 8, 2019
Borg et al.	Mean ± SEM	Unknown	/
Tsouristakis et al.	Mean ± SEM	/	Aug 3, 2019
Stoeckli et al.	Mean ± SEM	Unknown	/

SEM, standard error of the mean; IQR, interquartile range; /, meet the inclusion criteria

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Hang-Cheng Xu, Ying-Chang Pang and Jing-Wen Chen contributed equally to this work.

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✉ Jing Dong  
dongjing6@hotmail.com

<sup>1</sup> Clinical Medicine Department, Medical College, Qingdao University, Shandong, China

<sup>2</sup> Special Medicine Department, Medical College, Qingdao University, Shandong, China

<sup>3</sup> Physiology Department, Medical College, Qingdao University, Shandong, China