Letter: dose-response analysis revealed closer relationship between obesity and perioperative outcomes in patients after liver transplantation

Citation for the original published paper (version of record):
Liu, Z., Mardinoglu, A., Que, S. (2018). Letter: dose-response analysis revealed closer relationship between obesity and perioperative
outcomes in patients after liver transplantation. Alimentary Pharmacology and Therapeutics, 47(2): 310-312. http://dx.doi.org/10.1111/apt.14425

DOI: 10.1111/apt.14425

WILEY AP&T Alimentary Pharmacology & Therapeutics

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EDITORS,

We read with great interest the article by Barone et al[1] about the impact of obesity on clinical outcomes after liver transplantation (LT). The authors evaluated the risk of different levels of obesity on post-operative mortality and related complications in more than 100 000 orthotopic liver transplant recipients. An association was observed with obesity when pre-operative body mass index (BMI) was considered as a categorical variable, however this conclusion seems dependent on the selection of BMI cut-off value. In addition, the risk trend of obesity-related mortality cannot be compared in groups with different survival time. To help avoid these limitations, a dose-response analysis is worth performing to estimate the risk of increasing BMI on post-transplant survival and related complications.

Based on available data presented in Barone's meta-analysis,[1] we have evaluated pooled dose-response odd ratios (ORs) for the impact of increasing BMI on 30-day, 1-, 2-, 5-year mortality and post-transplant complications. Dose-response risk was calculated by the generalised least squares method.[2] Nonlinearity was evaluated by the Wald test (testparm command).[3] Intersubgroup comparison was performed by Metan.[4] As shown in Figure 1, BMI was associated with all indicators in a linear manner ($P > .05$ for nonlinearity test). Only 30-day (pooled OR = 1.16, 95% CI: 1.09-1.22) and 2-year mortality (pooled OR = 1.06, 95% CI: 1.02-1.10) were significantly increased per 5 kg/m^2 of BMI increment. Compared to 30-day mortality, the influence of pre-transplant obesity was decreased regarding longer-term mortality (exceeded 1 year, $P < .05$); and stable ($P < .05$) for survival from 1 to 5 years, with low intergroup heterogeneity. Post-operative complications also correlated with BMI per 5 kg/m^2 increment (pooled OR = 1.56, 95% CI: 1.17-2.08).

Obesity, as a consequence of its associations with chronic inflammation,[5] and co-morbidities like diabetes, metabolic syndrome and cardiovascular disease might contribute to higher mortality in patients after LT.[6,7] In the paper by Barone et al,[1] preoperative obesity was assessed as a risk factor without adjustment of potential threshold effects caused by an arbitrarily defined BMI cut-off. Our re-analysis based on calculation of a dose-response shows that although obesity impacted on short-term perioperative outcomes it had only a limited impact on long-term survival.

Pre-operative weight control might have benefits for better recovery of patients after liver transplantation.

ACKNOWLEDGEMENTS

Declaration of personal interests: None.

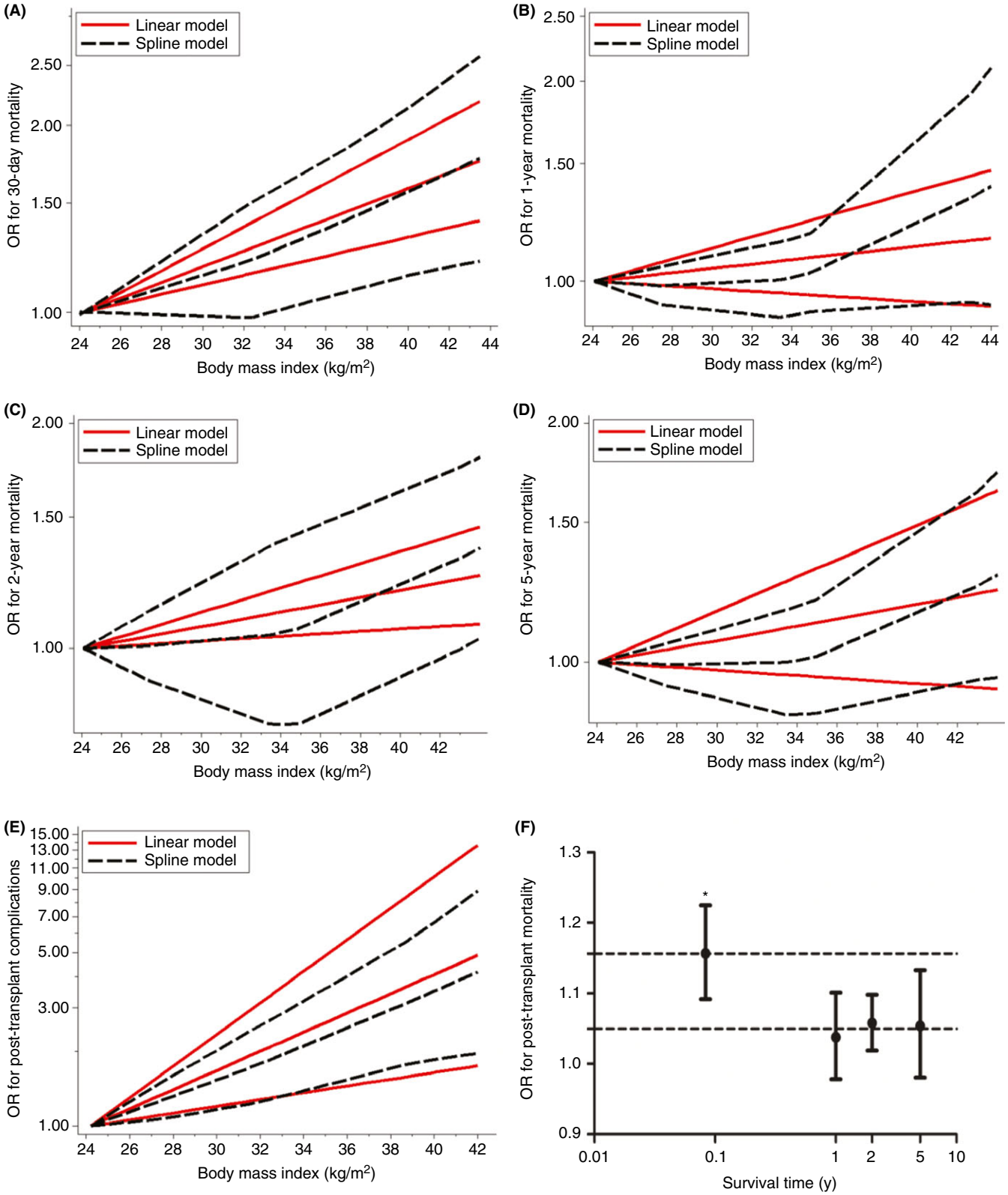
FUNDING INFORMATION

None.

AUTHORSHIP

Author contributions: Zhengtao Liu designed the research, Shuping Que collected and analysed the data, Zhengtao Liu wrote the paper,

FIGURE 1 Dose-response impact of body mass index (BMI) on post-transplant mortality and complications. Solid line in red represents fitted linear trend and corresponds to upper/lower limits; lines with long dashes in black represent fitted linear trend and correspond to upper/lower limits. (A) Dose-response association between BMI and 30-day mortality. *P* for nonlinearity test = .56, OR = 1.16 per 5 kg/m^2 of BMI increment, 95%CI: 1.09-1.22; (B) dose-response association between BMI and 1-year mortality. *P* for nonlinearity test = .21, OR = 1.04 per 5 kg/m^2 of BMI increment, 95%CI:0.98-1.10; (C) dose-response association between BMI and 2-year mortality. *P* for nonlinearity test = .26, OR = 1.06 per 5 kg/m^2 of BMI increment, 95%CI: 1.02-1.10; (D) dose-response association between BMI and 5-year mortality; *P* for nonlinearity test = .13, OR = 1.05 per 5 kg/m^2 of BMI increment, 95%CI: 0.98-1.13; (E) dose-response association between BMI increment and risk of post-transplant complications. *P* for nonlinearity test = .77, OR = 1.56 per 5 kg/m^2 of BMI increment, 95%CI: 1.17-2.08; (F) Comparison of dose-response risk for BMI increment on short-term (30-day) and long-term (1-, 2-, 5- year) mortality. *represents significant elevation on risk of 30-day mortality followed with BMI increment compared to 1-, 2- and 5-year mortality (all $P < .05$)



Adil Mardinoglu and Shuping Que reviewed the paper. All authors approved the final version of the article, including the authorship list.

Guarantor of article: Shuping Que is the author who is acting as the submission's guarantor.

Competing financial interests: The authors declare no competing financial interests.

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LINKED CONTENT

This article is linked to Barone et al papers. To view these articles visit https://doi.org/10.1111/apt.14139 and https://doi.org/10.1111/apt.14446.

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DOI: 10.1111/apt.14446

Letter: dose-response analysis revealed closer relationship between obesity and perioperative outcomes in patients after liver transplantation—Authors' reply

EDITORS,

We thank Drs. Liu and Que for their comments reported in their letter[1] concerning our recent meta-analysis on post-operative complications and mortality risk in liver transplant candidates with obesity.[2] Interestingly, even if at the beginning they appear to criticise our work, at the end, they conclude reinforcing our data. In fact, using a different statistical approach (Wald test, and inter-subgroup comparison by Metan),[3,4] their additional analysis suggests an even higher risk on perioperative mortality in obese liver transplant (LT) recipients. Moreover, as previously reported by us,[2] they suggest that it would be desirable to plan a reduction in body weight in LT candidates.

In addition, we will try to give a more exhaustive answer to each of their considerations. Since the WHO grades subjects with obesity in three BMI classes in consideration of their different risk of developing several pathological conditions, it was obvious to us to evaluate the outcome of liver transplanted patients on the basis of their BMI class. We agree with the authors[1] that the risk trend of obesity-related mortality cannot be compared in groups with different survival time, however, we did not pretend to calculate this statistical parameter but limited our analysis to the OR, which is just a "picture" taken at a specific time period, which does not even consider other potential factors that can influence mortality. As far as the latter aspect, in our previous work[2] we already discussed the importance of diabetes as one of the major contributor to the higher mortality in these patients, and therefore we agree with the comments that reinforce our opinion on the possibility that obesity-related comorbidities more that obesity itself could negatively influence post-transplant mortality. However, as previously stated, for theoretical reasons, a meta-analytic approach is based on raw data unless all studies included report OR or HR adjusted for the same parameters. Therefore, we could not evaluate the role of diabetes or other confounding factors as post-operative risk factors.