Competing Interests

The authors declare no competing interests.

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Fasting Duration and Blood Pressure in Children: Comment

To the Editor:

We read with interest the article by Simpao *et al.*[1] regarding the association between clear fluid fasting duration and postinduction low blood pressure in anesthetized children. In this retrospective analysis, the authors reported that, among children (0 to 18 yr) who underwent inhalational induction of anesthesia for elective surgical procedures, longer duration of clear fluid fasting was associated with increased risk of postinduction low blood pressure during the surgical preparation. Despite the clinical relevance of the topic and the elegant study design, certain methodologic issues require clarification.

First, although the exposure (fasting duration) was collected as a continuous variable, the authors transformed this continuous variable into categorical groups using some clinically useful, though arbitrary, cutpoints. The statistical limitations of this approach must be highlighted. As elegantly assessed by the authors, the association between clear fasting time and low blood pressure was not linear. In this setting, percentile categorizations can misrepresent the dose–response relationship between the exposure and outcome because instead of accounting for the nonlinearity, the cutpoints are merely identified according to the distribution of the primary predictor.[2,3] This may result in the lumping together of subjects with different risks of low blood pressure, thus violating the assumption of no differences in risk of the outcome between groups. For instance, children in the 6- to 8-h group had a 22% (1.55/1.27) relative higher odds of low blood pressure, relative to children in the 4- to 6-h group, yet both groups have been lumped into the 4- to 8-h category. Similarly, children in the 10- to 12-h group had a 17% (1.16/0.99) relative higher odds of low blood pressure, relative to children in the 8- to 10-h group, yet both groups have been lumped into the 8- to 12-h category. These departures of 22% and 17% appear to be meaningful, given the context of the study, because the highest relative excess in the odds ratio was 33%. In addition, the authors adopted an open-ended categorization of patients with clear fasting time greater than 12 h (alternatively greater than 14 h in the sensitivity analysis). This cutpoint of 12 h (14 h in the sensitivity analysis) may be too far from the most extreme value and may hide important effects. For example, the risk of low blood pressure among children with clear fasting time greater than 18 h (corresponding to about 2.5% of the study population) is unknown because it was averaged with those of the other children in the greater than 12-h group.

Second, it appears that about 60% of the study cohort received coinduction of anesthesia with propofol or an intravenous opioid, and 12% of subjects received a neuraxial block (type not stated). Given that propofol coinduction and neuraxial anesthesia are known causes of hypotension under anesthesia, the observed associations do not disambiguate the effect of fasting from the expected hypotensive effects of propofol and/or neuraxial anesthesia. Therefore, the interpretation of the authors' findings would benefit from a sensitivity analysis by separating patients who received propofol from their counterparts who did not receive propofol.

In conclusion, we applaud Simpao *et al*. for adding to the literature on the association of preoperative fasting with intraoperative hypotension. However, the limitations of their exposure and outcome variables must be considered when interpreting the findings of their report.

Competing Interests

The authors declare no competing interests.

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Fasting Duration and Blood Pressure in Children: Comment

To the Editor:

We read with interest the article by Simpao *et al.*[1] on fasting times and incidence of low blood pressures. The study found that prolonged clear fluid fasting was associated with increased odds of low blood pressure during the preincisional phase in anesthetized children, interestingly, in a nonlinear fashion. The definition of hypotension was based on the percentile reference curves from intraoperative blood pressure nomograms, reported by de Graaff *et al.*[2] These reference curves were derived from the electronic anesthetic records of healthy American Society of Anesthesiologists (ASA; Schaumburg, Illinois) physical status I, II children.[2] The study identified 889 patients with low systolic blood pressure during the surgical preparation phase, and 697 patients during the anesthesia preparation phase. Although ASA III, IV comprised only 9.2% (n = 1,433) of the entire study cohort (n = 15,543), we do not know if they contributed disproportionately to the hypotension results, as might be expected from a greater incidence of hemodynamic instability in ASA IV adult patients.[3] This might affect the interpretation of the study results, and be of interest to journal readers.

Competing Interests

The authors declare no competing interests.

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Fasting Duration and Blood Pressure in Children: Reply

In Reply:

We thank Dr. Chen and Dr. Mpody[1] for their interest in our article[2] and for highlighting important

aspects of our study for readers. We concur with the authors regarding percentile categorizations, the nonlinear dose–response relationship, and the identification of cutpoints based on the distribution of the primary predictor. This point was raised during the process of manuscript review, and in response, we provided a sensitivity analysis using a 2-h fasting duration interval to complement the 4-h quartile analysis. Analysis with smaller time intervals could certainly have been performed, yet we eschewed that option because of word count limitations and because the results would likely have remained consistent with the nonlinear relationship shown in the locally estimated scatterplot smoothing curve on the scatterplot.[2] As mentioned in the article, we weighed fractional polynomial transformation *versus* fasting time categorization during the analysis. Our goal was to take into account the nonlinearity of the relationship between clear fluid fasting duration and low blood pressure while providing an interpretable result. While fractional polynomial modeling might have been a more appropriate approach to the nonlinearity, the challenge of a straightforward clincial interpretation remained, as the regression coefficient became difficult to interpret after the transformation.

The authors raise a valid point concerning the open-ended categorization of clear fluid fasting time at a cutpoint of 12 h. Insight might have been gained by extending the sensitivity analysis to greater than 16 or 18 h as long as the sample size in the category remained adequate to provide a reliable estimate of the odds ratio. This relationship between extreme clear fluid fasting durations and low blood pressure may be a topic that we examine more closely in future work.

With regard to anesthesia medications, we agree that propofol, opioid, and neuraxial anesthesia were potential confounders of the association between the fasting duration and low blood pressure during induction. To control for the confounding, anesthesia medications were included in the final multivariable model in table 2 of our article.[2] This was done to ensure independence of the primary exposure–outcome relationship from the controlled confounders, such as propofol. A sensitivity analysis separating patients who received propofol from their counterparts who did not receive propofol would indeed allow us to assess whether the association of fasting with blood pressure varied across these two groups of patients. With two different stratum-specific odds ratios, propofol would likely be an effect modifier, suggesting a potential interaction between fasting duration and propofol.[3,4] We again thank the authors for sharing their insightful comments, and we look forward to their and other researchers' efforts to improve our understanding of the relationship between clear fluid fasting duration and blood pressure in children undergoing anesthesia.

We also thank Dr. Sharma and Dr. Naik[5] for their interest in our article. We included the American Society of Anesthesiologists (Schaumburg, Illinois) physical status III and IV patients in our analysis to enhance our study's generalizability, and the results of this analysis are shown in table 2 of our article.[2] However, the authors make an excellent point regarding the possible impact of the differences between our study population and the population that was used to generate the blood pressure reference normograms.[6] We thank the authors for sharing their astute observation of the discrepancy between the two study populations, which is a limitation that is worth highlighting to readers of our article.

Competing Interests

The authors declare no competing interests.

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