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Hydroxyethyl Starch vs Saline for Volume Expansion After Abdominal Surgery-Reply

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In Reply Dr Mascha argues that the between-group difference in KDIGO stages of AKI in the trial¹ might have resulted from incorrect analysis of ordinal variables. However, rather than a comparison of each KDIGO stage with all other stages of severity, the absence of kidney dysfunction (stage 0) was used as a reference. The omnibus *P* value from the χ^2 test is .17. The same result is obtained with a multinomial (polytomous) logistic regression, which allows comparison of groups overall and vs a reference modality, taking into account the ordinal nature of the variable. *P* values for each comparison are unchanged, irrespective of whether $2 \times 2 \chi^2$ comparisons (with-out correction for type I error, as indicated in the statistical analysis section) or multinomial logistic regression is used.

Dr Markow raises concern about the sex distribution in the study population and its connection to outcome. We agree that use of the acute kidney injury index¹ for patient risk stratification in the trial may have contributed to the sex ratio imbalance, as well as overrepresentation of other components of the risk index (eg, hypertension) compared with the general surgical population. Data from the American College of Surgeons-National Surgical Quality Improvement Program² showed that male sex doubles the risk of AKI after general surgery. However, in the FLASH trial, male sex was not associated with the primary outcome (odds ratio, 1.42; 95% CI, 0.87-2.31).

We agree with Dr Xue and colleagues that larger amounts of intravenous fluids resulting in positive cumulative fluid balance may artificially lower serum creatinine and influence the diagnosis of AKI. No adjustment for the effect of fluid balance was made given that our assessment of fluid balance was a post hoc analysis and the findings were only hypothesis generating.

Xue and colleagues are also concerned about missing information on preoperative anemia and hypoalbuminemia. We did not collect serum albumin data, but the 2 treatment groups did not differ with regard to hemoglobin levels at baseline (mean, 13.1 [SD, 1.9] g/L in the HES group and 13.3 [SD, 1.8] g/L in the saline group; *P* = .30).

The possible influence of intraoperative hypotension on outcomes is important to consider.³ The recommendation was made to maintain mean arterial pressure of 60 mm Hg or higher during surgery, but possible imbalance between groups cannot be excluded. Nevertheless, no between-group differences were noted in mean arterial pressure at the end of surgery or in mean doses of intraoperative vasopressor.

Xue and colleagues question the duration of monitoring of kidney function in the trial. We presented data on kidney function up to 28 days in the article. Nevertheless, we concur that an increased need for renal replacement therapy has been reported up to 90 days after HES administration.

Drs De Backer and Michiels are concerned about the administration of fluids other than study fluids in the trial. The protocol restricted the use of study fluids to intravascular volume expansion to a maximum daily dose of 30 mL/kg, beyond which open-label fluids were given for fluid therapy. Although the use of study fluids as a single therapy (including as maintenance intravenous fluids) might have enhanced the trial design, this methodology could be criticized from a clinical perspective.⁴

De Backer and Michiels point out the possible confounding effect of the co-administration of HES in a significant amount in the 2 groups, thus minimizing differences in outcomes. In practice, the co-administration of HES during the study period was noted in 2 patients in the HES group and in 4 patients in the saline group (*P* = .17), without a difference in the dose administered (median, 300 [interquartile range, 100-500] mL in the HES group and 500 [interquartile range, 500-750] mL in the saline group; *P* = .45).

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