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### Reply to the comment on “Effects of norepinephrine alone and norepinephrine plus dopamine on human intestinal mucosal perfusion.”

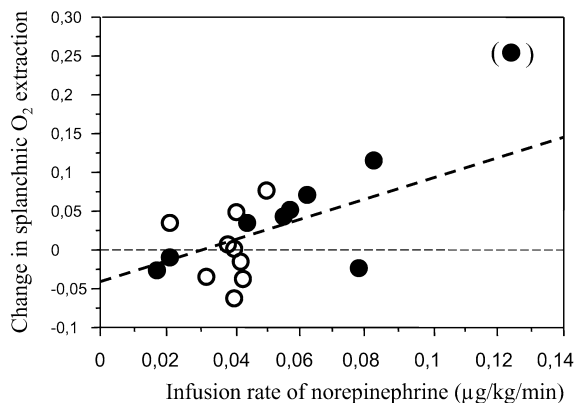
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Sir: We thank Drs. Spronk, Zandstra and Ince for their comments and interest in our study [1]. First, Spronk and co-workers claim “that a single (outlying) observation seems responsible for the reported conclusion”. Thus, by excluding the patient receiving the highest infusion rate of norepinephrine (a procedure which, by itself, is questionable), they suggest that “no significant change in splanchnic oxygen extraction in relation to the norepinephrine infusion rate can be demonstrated after correction for this outlier”. To illustrate this they have added an alternative regression line (dashed line of their modification of our Fig. 1), “describing an alternative relationship” when this proposed “outlier” is omitted. How this “alternative line” was constructed is not described and its appearance is obscure to us. It is, however, evident, from visual inspection that this “alternative line” does not fit to our data, with or without the proposed “outlier”. Indeed, when performing a correlation analysis for non-parametric data (Spearman rank correlation), with the outlier excluded, there is still a significant ( $p < 0.05$ ) positive correlation (Spearman coefficient of correlation,  $\rho = 0.57$ ) between norepinephrine infusion rate and the change in splanchnic oxygen extraction (Fig. 1).

Second, Spronk et al. claim that, by excluding the patient receiving the highest infusion rate of norepinephrine, “jejunal mucosal perfusion appears to be inversely related to increasing norepinephrine infusion rates”. Once again, they have illustrated this by an alternative regression line (dashed line of their modification of our Fig. 2) excluding the “outlier”. Exactly how they reached this conclusion is obscure to us, as a correlation analysis for non-parametric data (Spearman rank correlation), with the outlier excluded, reveals a Spearman coefficient of correlation ( $\rho$ ) of  $-0.48$  (n.s., Fig. 2). In other words, there is no apparent correlation between the dose of infused norepinephrine

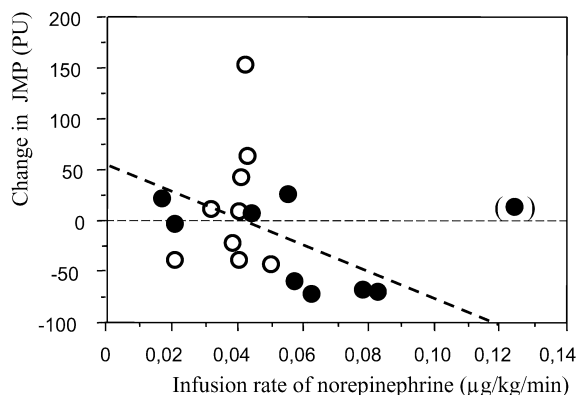
and the change in jejunal mucosal perfusion, even after excluding the “outlier”.

In conclusion, the statement by Spronk et al. that completely opposite conclusions from our study can be drawn simply by excluding data from one “outlying” patient is incorrect. On the contrary, re-analysing our data, with the “outlier” excluded, leads us to the same conclusions as those which were put forward in our article: Vasopressor therapy with norepinephrine, when used in postoperative patients, does not necessarily jeopardise intestinal mucosal perfusion, in spite of a dose-dependent global splanchnic oxygen demand-supply mismatch. This, in turn, suggests that vasopressor therapy with norepinephrine is ac-



**Fig. 1** The relationship between the individual dose of norepinephrine, to an increase in mean arterial pressure from 60 to 90 mmHg, and the change in splanchnic oxygen extraction after uncomplicated cardiac surgery. The dashed line is the regression line after exclusion of a proposed

“outlier”. The Spearman rank correlation analysis for non-parametric reveals a significant ( $p < 0.05$ ) positive correlation ( $\rho = 0.57$ ) between the individual dose of norepinephrine and the change in splanchnic oxygen extraction



**Fig. 2** The relationship between the individual dose of norepinephrine, to an increase in mean arterial pressure from 60 to 90 mmHg, and the change in jejunal mucosal perfusion (JMP) after uncomplicated

cardiac surgery. After exclusion of the proposed “outlier”, there is still no significant correlation (Spearman rank,  $\rho = -0.48$ ) between the individual dose of norepinephrine and the change in JMP

companied by an intramural redistribution of flow to the intestinal mucosa.

### References

1. Nygren A, Thorén A, Ricksten S-E (2003) Effects of norepinephrine alone and norepinephrine plus dopamine on human intestinal mucosal perfusion. *Intensive Care Med* 29:1322–1328

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