## REPLY, LETTER TO THE EDITOR





## "Are We Sure that Blood Transfusion is Associated with Recurrence of Hepatocellular Carcinoma After Hepatectomy?": Reply

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Thank you very much for your question about our manuscript.

Our report was a retrospective study. For ethical reasons, it is impossible to perform a randomized controlled trial, in which patients who undergo liver resection are randomized to receive or not receive blood transfusions as part of perioperative care. Patients who experience massive bleeding during or after hepatectomy must receive blood transfusions to maintain their total blood volume. Therefore, there have been no studies in which the volume of bleeding was adjusted when analyzing the impact of blood transfusion on the recurrence of hepatocellular carcinoma after hepatectomy.

As pointed out, our cohort was not free of patient selection bias, based on frequency of liver cirrhosis, rates of postoperative complication, maximum tumor diameter, extent of hepatic resection, and serum alpha-fetoprotein levels. To control for patient selection bias, we used the inverse provability of treatment weighting (IPTW) statistical method. This method balances underlying differences between transfused and non-transfused patients in distributive covariates, including rates of liver cirrhosis and postoperative complications, maximum tumor diameter, extent of hepatic resection, and serum alpha-fetoprotein levels. IPTW weighs samples using propensity scores,

reducing the confounding that frequently occurs in cohort studies testing the effects of treatment on outcomes, and enables estimation of marginal or population average treatment effects [1]. After adjusting the covariates by IPTW, we found that the selection bias between transfused and non-transfused patients became very small, with little difference in the rate of liver cirrhosis in the two groups.

Generally, propensity score matching method is one to one. This matching, however, reduces sample size, increasing the likelihood of selection bias. Therefore, we adopted the method of IPTW-adjusted analysis to control for selection bias in our study. As a result, we concluded that blood transfusion was associated with recurrence of HCC after hepatectomy in patients with HCC and Child-Pugh class A.

Future studies should address these clinical questions.

## References

 Austin PC (2012) The performance of different propensity score methods for estimating marginal hazard ratios. Stat Med 32:2837–2849



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