



Enhancing acute normovolemic hemodilution in cardiac surgery: the role of remimazolam and hemodynamic stability

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To the Editor:

We were intrigued by the work of Takahashi et al. on the effects of acute normovolemic hemodilution (ANH) in cardiac surgery under remimazolam anesthesia [1]. ANH is a method in which blood is quickly withdrawn after induction of general anesthesia in the operating room, an equal volume of extracellular fluid is transfused, and autologous whole blood is returned at the time of bleeding or before the end of surgery. One of the advantages of this method is a significant reduction in hemoglobin loss during bleeding due to hemodilution. Another advantage is that it allows the return of whole blood, including not only hemoglobin but also platelets, fibrinogen and other clotting factors. If the fibrinogen level is low, the incidence of major bleeding increases [2].

Takahashi et al. had performed ANH in 27 patients in cardiac surgery under remimazolam anesthesia [1]. The average amount of blood removed was 740 ml (12.3 ml/kg). In their study, the application of ANH was associated with decreases in the intraoperative use of allogeneic blood transfusions, number of postoperative blood transfusions, and blood loss. The volume of whole blood drawn from the patient would be key for the impact of ANH. In a randomized controlled study comparing 12–15 ml/kg of blood draw ($n=55$) with 5–8 ml/kg of blood draw ($n=55$) in ANH, it was shown that a larger volume of the blood drawn was associated with lower incidences of transfusion and postoperative excessive bleeding [3]. The clinical practice guidelines for patient blood management [4] conclude that the benefits of ANH are directly related to the volume of whole blood drawn from

the patient. Specifically, the greater is the volume of blood removed without hemodynamic instability, the greater is the benefit of ANH.

However, it is not easy to draw a large volume of blood in ANH during general anesthesia because it may cause hemodynamic instability. Takahashi et al. [1] evaluated the efficacy and safety of ANH in patients undergoing cardiac surgery under remimazolam anesthesia. Remimazolam is a short-acting benzodiazepine intravenous anesthetic that causes fewer hypotensive adverse reactions than does propofol [5–8]. Therefore, general anesthesia with remimazolam may reduce the risk of hypotension during blood withdrawal in ANH compared to that with propofol and may stabilize the patient's circulatory dynamics. In the study by Takahashi et al. [1], blood collection was completed in all of the patients in the ANH group before the start of surgery, despite the relatively large volume of ANH, low body weight, and high proportion of patients who had aortic stenosis. There were no significant differences in hemodynamic parameters, including mean arterial blood pressure between the ANH group and the group without ANH. In addition, no patients required continuous infusion of vasopressors or catecholamines before the start of cardiopulmonary bypass (CPB). Their study suggested that the choice of remimazolam as an anesthetic agent could lead to hemodynamic stability in ANH and thereby increase the amount of blood that can be removed. Consequently, this may enhance the effects of ANH such as the effects on amount of postoperative blood transfusions and overall blood loss.

There may be other than the choice of anesthetic that can enhance the effect of ANH, especially with the strategy for storing blood in ANH to maintain the quantities and quality of red blood cells, platelets and coagulation factors. Indeed, our in vitro prospective observational study suggested the potential of a bag for storing blood with good oxygen permeability [9] and cold storage temperature [10] to maintain

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high platelet function in stored blood through inhibiting platelet damage.

The efficacy of ANH has long been limited by the large heterogeneity of ANH methods among studies and institutions. To establish the validity of ANH, it is necessary to standardize the optimal ANH protocol. In addition, anesthetic management with hemodynamic stability should be one of key factors for improving the efficacy of ANH, as the study by Takahashi et al. suggested.

Data availability As this is editorial, there is no available data related with this manuscript.

References

1. Takahashi Y, Yoshii R, Amaya F, Sawa T, Ogawa S. Effect of acute normovolemic hemodilution in patients undergoing cardiac surgery with remimazolam anesthesia. *J Anesth.* 2024;38(1):98–104.
2. Kikuta M, Tobetto Y, Yamamoto K, Uraoka M, Go R. Effect of fibrinogen replacement therapy on bleeding outcomes and 1-year mortality in patients undergoing thoracic aortic surgery: a retrospective cohort study. *J Anesth.* 2023;37(1):119–29.
3. Ming Y, Zhang F, Yao Y, Cheng Z, Yu L, Sun D, Sun K, Yu Y, Liu M, Ma L, Huang Yang Y, Yan M. Large volume acute normovolemic hemodilution in patients undergoing cardiac surgery with intermediate-high risk of transfusion: a randomized controlled trial. *J Clin Anesth.* 2023;87: 111082.
4. Tibi P, McClure RS, Huang J, Baker RA, Fitzgerald D, Mazer CD, Stone M, Chu D, Stammers AH, Dickinson T, Shore-Lesserson L, Ferraris V, Firestone S, Kisson K, Moffatt-Bruce S. STS/SCA/AmSECT/SABM update to the clinical practice guidelines on patient blood management. *Ann Thorac Surg.* 2021;112:981–1004.
5. Doi M, Morita K, Takeda J, Sakamoto A, Yamakage M, Suzuki T. Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicentre, single-blind, randomized, parallel-group, phase IIb/III trial. *J Anesth.* 2020;34:543–53.
6. Doi M, Hirata N, Suzuki T, Morisaki H, Morimatsu H, Sakamoto A. Safety and efficacy of remimazolam in induction and maintenance of general anesthesia in high-risk surgical patients (ASA Class III): results of a multicenter, randomized, double-blind, parallel-group comparative trial. *J Anesth.* 2020;34:491–501.
7. Kotani T, Ida M, Naito Y, Kawaguchi M. Comparison of remimazolam-based and propofol-based total intravenous anesthesia on hemodynamics during anesthesia induction in patients undergoing transcatheter aortic valve replacement: a randomized controlled trial. *J Anesth.* 2024;38(3):330–8.
8. Hirata N. Remimazolam for cardiovascular anesthesia. *J Anesth.* 2023;37(6):825–7.
9. Murata Y, Kusudo E, Kawamoto S, Fukuda K. Effects of whole blood storage in a polyolefin blood bag on platelets for normovolemic hemodilution. *Sci Rep.* 2021;11(1):12201.
10. Kusudo E, Murata Y, Matsumoto T, Kawamoto S, Egi M. Platelet function of whole blood after short-term cold storage: a prospective in vitro observational study. *Transfusion.* 2023;63(2):384–92.

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