

Heart-brain axis: low blood pressure during off-pump CABG surgery is associated with postoperative heart failure

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Dear Editor,

The primary objective of the letter is to emphasize the importance of personalized management of arterial blood pressure (ABP) in the context of off-pump coronary artery bypass grafting (CABG) surgery. Coronary artery disease, a leading global cause of mortality, necessitates a substantial number of cardiac surgeries, with approximately 400,000 CABG operations conducted annually in the United States. Postoperative heart failure (HF) is a common occurrence after CABG surgery, with readmission rates within 30 d due to HF ranging from 12% to 16%. Researchers have highlighted the critical role of HF management before, during and after CABG surgery, identifying hemodynamic instability, perioperative myocardial injury, and low cardiac output syndrome as predictive factors for postoperative HF. In 2023, Han *et al.*[1] found that factors such as pulse index failure and composite grafting are independent predictors of CABG failure. Additionally, a study reported by Loncar *et al.*[2] revealed a significant relationship between reduced cerebral blood flow (CBF) and the severity of HF in elderly males. Moreover, Hartono *et al.*[3] pointed out that perioperative myocardial injury and pre-existing left ventricular systolic dysfunction can contribute to post-CABG HF. In the surgical setting, the reduction of mean arterial pressure (MAP) to minimize collateral bleeding and enhance surgical

visualization often leads to low systemic perfusion. Currently, the prevailing approach in CABG surgeries involves a uniform MAP management strategy, typically targeting a range of 60 mmHg to 70 mmHg for most patients. However, given the varying clinical backgrounds of patients and their diverse tolerance to low MAP levels, there is an urgent need for personalized MAP management during CABG surgery to ensure adequate blood flow and prevent postoperative complications.

The brain maintains stable perfusion through cerebral autoregulation (CA), which allows it to regulate CBF despite changes in ABP. Rhee *et al.*[4] have previously demonstrated that under severe hypoperfusion, the body may prioritize protecting the brain over peripheral organs such as the kidneys. By inducing continuous blood loss in piglets, they observed a reduction in kidney blood flow preceding a decrease in CBF. Previous studies by our researchers and others have established a correlation between low blood pressure and reduced cerebral perfusion during CABG and postoperative complications, including delirium, acute kidney injury, major morbidity, and operative mortality[5-7]. However, the specific MAP target most strongly associated with HF remains unknown. Therefore, the hypothesis of our current study is that low MAP and reduced cerebral perfusion to the brain might be a strong indicator of systemic ischemia and HF.

Various parameters have been developed to monitor intraoperative CA in real-time, including cerebral oxygen saturation index (COx), which is determined by the correlation between MAP and regional cortical oxygen saturation (rSO₂). COx further facilitates the promotion of personalized MAP management guideline by identifying specific MAP targets, such as the lower limit of autoregulation (LLA), the upper limit of autoregulation (ULA), and optimal mean arterial

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pressure (MAPopt). In the past several decades, these targets have been examined to prevent postoperative complications after on-pump CABG, but concerns have been raised about the reliability of these findings due to the dampening of blood pressure fluctuations during pump-driven circulation. As pointed out by Claassen *et al.*[8] and Gelpi *et al.*[9], the natural variability of MAP is extremely important in CA, emphasizing the dynamic relationship between blood pressure and CBF as a high-pass filter that may be attributed to the slow adaptation (<0.2 Hz) of cerebral arterioles in response to fast fluctuations of perfusion pressure (<0.2 Hz). Consequently, there is growing interest in off-pump CABG surgery due to the potential benefits of reduced stroke risk. Further investigation is warranted to establish personalized MAP management for off-pump CABG patients.

In this study, we have introduced a personalized approach to managing MAP during off-pump CABG surgery to address the aforementioned challenges and the whole process is shown in Fig. 1. Utilizing a sampling frequency of 1 Hz, ABP and brain oxygen saturation (rSO₂) were concurrently monitored in a group of patients undergoing off-pump CABG at Tianjin Chest Hospital (Tianjin, China), as shown in Additional file 1: Fig. S1. Individualized MAPopt, LLA, and ULA were determined by calculating COx for each patient. A previously established multi-window curve-fitting algorithm was used to construct a “U-shaped” curve (Additional file 1: Fig. S2)[10]. The relationship between the extent of MAP below a certain threshold and patient outcome was assessed by computing area under the curve (AUC) of MAP below MAPopt (or LLA). The AUC for MAP exceed in ULA was also calculated. Additionally, the percentage of time spent with MAP below MAPopt (or LLA) and above ULA was analyzed. Data integration was performed using MATLAB software and subsequent analysis was conducted using the software of Intensive Care Monitoring Plus (ICM+). For statistics, we used a logistic regression model adjusted for age, diabetes, aspartate aminotransferase/alanine transaminase (AST/ALT) and log European System for Cardiac Operative Risk Evaluation (EuroSCORE) (determined prior to possible confounding variables). For more details, please refer to Additional file 1: Material and methods.

The data from a total of 555 patients were analyzed and divided into two groups based on the presence or absence of HF, with 85 patients in the HF group and 470 patients in the non-HF group. The mean age of the cohort was 66 years (ranging from 39 years to 84 years), with 73.3% male (Additional file 1: Fig. S3; Table S1). The key findings can be summarized as follows. (1) In both the unadjusted model and the model

adjusted by age, diabetes, AST/ALT, and log EuroSCORE, a significant association was observed between the degree of MAP falling below the MAPopt and the occurrence of HF after off-pump CABG. Patients in the HF group exhibited higher AUC [24.5 (20.1–29.0) vs. 17.2 (16.1–18.2), $P<0.001$] and longer durations of low MAP [(51.1±27.3)% vs. (44.9±28.2)%, $P=0.002$] compared to those in the non-HF group (Additional file 1: Fig. S4; Table S2). However, there was no significant correlation observed between MAP<LLA and MAP>ULA with patient outcomes. (2) Compared to the non-HF group, patients in the HF group tended to exhibit higher variability in MAP ($P=0.046$) and heart rate variability ($P=0.001$), indicating a close relationship between hemodynamic instability and HF, as also noted by Hartono *et al.*[3]. (3) Furthermore, the study revealed that patients with HF tended to have lower intraoperative rSO₂ levels and reduced left ventricular ejection fraction before surgery. The degree of MAP falling below MAPopt (i.e., MAPopt-MAP) showed a negative relation with cardiac output or stroke volume (Additional file 1: Fig. S5; Table S2), suggesting that reduced cerebral perfusion is closely associated with decreased cardiac output and stroke volume.

This research underscores the significance of personalized blood pressure management in off-pump CABG surgery, with MAPopt identified as the optimal target to reduce the incidence of postoperative HF. Patients who experience longer duration and larger extent of low blood pressure are at an elevated risk of developing HF after CABG. Therefore, the implementation of a personalized MAP management strategy guided by MAPopt should be considered for off-pump CABG surgery in forthcoming clinical practice.

Abbreviations

ABP: Arterial blood pressure; ALT: Alanine transaminase; AST: Aspartate aminotransferase; AUC: Area under the curve; CA: Cerebral autoregulation; CABG: Coronary artery bypass grafting; CBF: Cerebral blood flow; COx: Cerebral oxygen saturation index; EuroSCORE: European System for Cardiac Operative Risk Evaluation; HF: Heart failure; ICM+: Intensive Care Monitoring Plus; LLA: Lower limit of autoregulation; MAP: Mean arterial pressure; MAPopt: Optimal mean arterial pressure; rSO₂: Regional cortical oxygen saturation; ULA: Upper limit of autoregulation.

Supplementary information

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Additional file 1. Material and Methods. Fig. S1 Real-time recording of intraoperative signals. **Fig. S2** Personalized MAPopt, LLA, and ULA defined a multi-window curve-fitting algorithm. **Fig. S3** Patient flowchart. **Fig. S4** Comparison of AUC and time percentage between patients based on the three ABP targets.

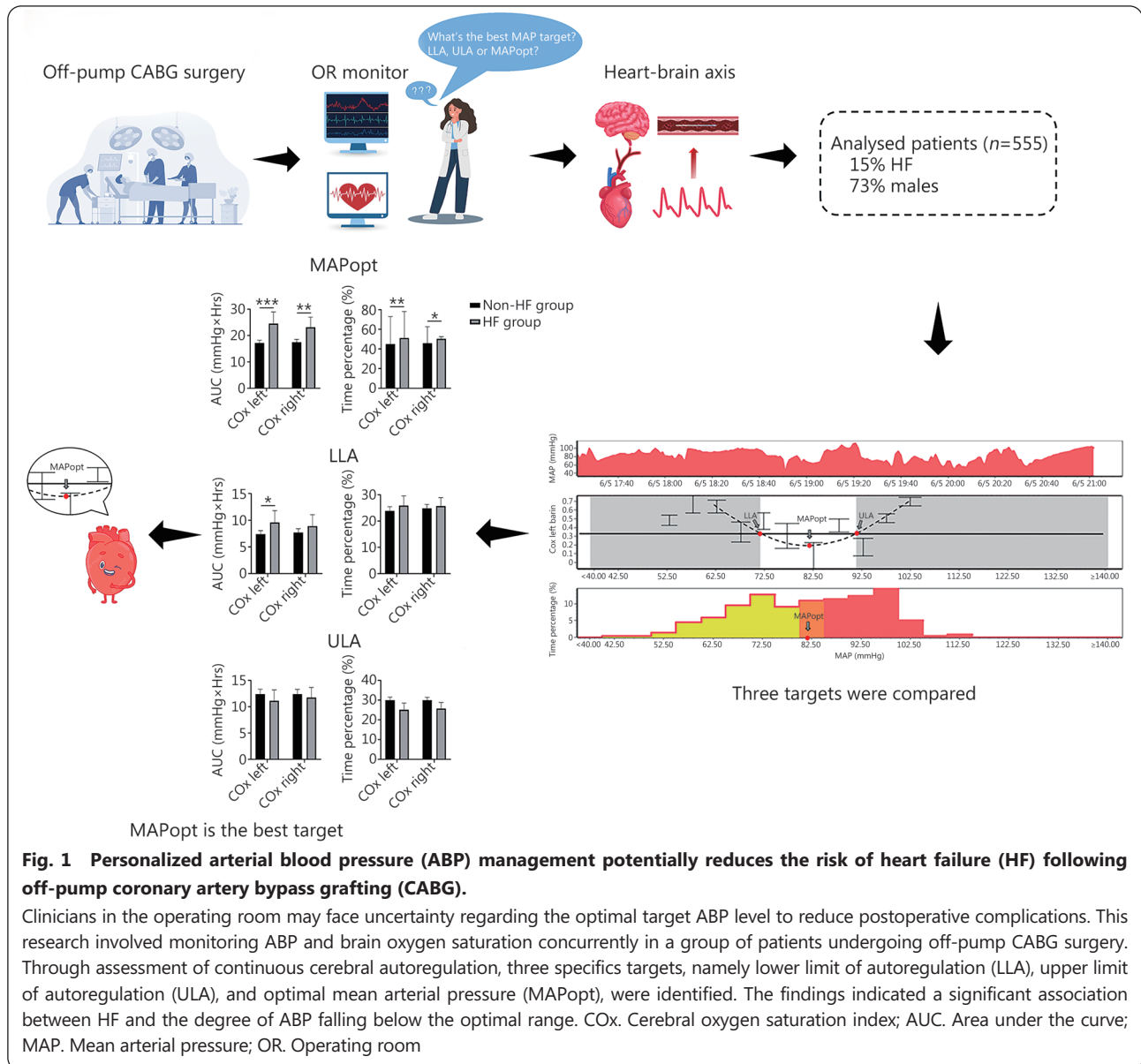


Fig. 1 Personalized arterial blood pressure (ABP) management potentially reduces the risk of heart failure (HF) following off-pump coronary artery bypass grafting (CABG).

Clinicians in the operating room may face uncertainty regarding the optimal target ABP level to reduce postoperative complications. This research involved monitoring ABP and brain oxygen saturation concurrently in a group of patients undergoing off-pump CABG surgery. Through assessment of continuous cerebral autoregulation, three specific targets, namely lower limit of autoregulation (LLA), upper limit of autoregulation (ULA), and optimal mean arterial pressure (MAPopt), were identified. The findings indicated a significant association between HF and the degree of ABP falling below the optimal range. COx. Cerebral oxygen saturation index; AUC. Area under the curve; MAP. Mean arterial pressure; OR. Operating room

Fig. S5 Relationship between MAPopt-MAP and cardiac output or stroke volume. **Table S1** Patient details. **Table S2** The association between the tested parameters and heart failure outcome.

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Authors' contributions

XYL, DM and ZGG participated in the design of the study. JJM, WQZ, and NS carried out data analysis and acquisition. JGH, MJP, KZ, GJN, and DM are involved in data interpretation. XYL and JJM wrote the original draft. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author (xiyun_liu@tju.edu.cn) on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Tianjin Chest Hospital (2020YS-022-01). A written consent form was obtained from each patient or the next of kin.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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