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[MSB-24]

Metabolomic Signatures of Hypothermia Under Cardiopulmonary Bypass: A Systematic Evaluation of Mild and Moderate Hypothermia on Urinary Metabolome Profiles

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Türk Gogus Kalp Dama 2024;32(Suppl 2):MSB-24

Doi: 10.5606/tgkdc.dergisi.2024.msb-24

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Received: September 09, 2024 - Accepted: September 29, 2024

Objective: This study aimed to investigate the differential impacts of mild (32 to 35°C) and moderate (26 to 31°C) hypothermia on urinary metabolome profiles during cardiopulmonary bypass (CPB) in adult cardiac surgery.

Methods: This randomized study included 32 patients who underwent CPB under hypothermic conditions (mild, n=16; moderate, n=16) using only the Bretschneider solution. Urine samples were collected at two time points: immediately before CPB initiation and 1 h after rewarming and termination of CPB. Urinary metabolomic analyses were conducted using gas chromatography-mass spectrometry and liquid chromatography-quadrupole time-of-flight mass spectrometry. Metabolite changes were evaluated using statistical methods, including the Mann-Whitney U test, principal component analysis, and partial least squares discriminant analysis.

Results: Significant differences in urinary metabolites were observed between the two hypothermia groups. Mild hypothermia resulted in increased levels of creatinine and 5,6-DHET and decreased levels of 2-methylbutyrylcarnitine and S-adenosylhomocysteine, suggesting a more favorable metabolic response with reduced stress. In contrast, the moderate hypothermia group exhibited increases in metabolites such as C17-sphinganine and ceramide (t18:0/16:0), indicating heightened metabolic stress and potential cellular damage. Principal component analysis and partial least squares discriminant analysis revealed distinct separations between the groups, highlighting greater metabolic perturbations with moderate hypothermia.

Conclusion: Mild hypothermia is associated with a more stable urinary metabolomic profile, whereas moderate hypothermia is linked to significant metabolic disruptions, necessitating careful monitoring and management. These findings provide valuable insights for optimizing hypothermia protocols during CPB.

Acknowledgements: Supported by TÜBİTAK, project number: 123S448.

Ethics approval: Ankara University School of Medicine, January 13, 2022 (İ01-12-22).

Keywords: Cardiac surgery, cardiopulmonary bypass, hypothermia, metabolomics, urinary metabolome,