

UNIVERSITY OF MEDICINE, PHARMACY, SCIENCE AND TECHNOLOGY
"GEORGE EMIL PALADE" FROM TÎRGU MUREȘ

DOCTORAL SCHOOL

ABSTRACT OF THE PhD THESIS

INVESTIGATIONS ON MYOCARDIAL PROTECTION USING HISTIDINE- TRYPTOPHAN- KETOGLUTARATE CARDIOPLEGIA IN AORTIC VALVE INTERVENTIONS

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INTRODUCTION:

Cardioplegia is essential solution used in cardiac surgery to achieve an motionless and bloodless operating field, which is important for the success of heart surgery. Histidine-Tryptophan-Ketoglutarate (HTK) solution is one of the most widely used cardioplegia solutions, which provides prolonged cardioprotection time and is thus useful in complex operations with prolonged ischemic time. However, recent research highlights controversies regarding the efficacy of HTK in aortic valve surgery due to microvascular malperfusion secondary to left ventricular hypertrophy/dilation. These morphopathologic changes may result in inappropriate cardioplegia distribution. Further research is needed to optimize current cardioprotective protocols and to better understand the complex mechanisms involved in the action of cardioplegic agents.

OBJECTIVE:

The current research started from the hypothesis that HTK cardioplegia provides high myocardial protection. Based on the fact that the ideal cardioplegic solution is currently unknown and the effects of different types of cardioplegia are not fully understood, this study aims to objectify the effects of HTK cardioplegia on postoperative outcome in patients who have undergone aortic valve replacement. It also elucidates some unknowns regarding the use of HTK in cardiomyopathy secondary to aortic valve pathology. To this end, preoperative data of patients with indication for surgical cure of aortic valve pathology were analyzed; intraoperative technical data were evaluated; the degree of myocardial protection was quantified and the systemic effects of HTK cardioplegia were identified; perioperative data were correlated with the evolution of patients in the short term (<30 days post-procedural); then, a comparative analysis of the parameters reported in the literature was performed with the data resulting from this thesis.

GENERAL METHODOLOGY:

The studies described in this paper were retrospective and prospective and were composed of data extracted from a group of 302 patients hospitalized between June 2022 and June 2024 for surgical treatment of aortic valve pathology in the Clinic of Cardiovascular Surgery for Adults and Children, within the Emergency Institute for Cardiovascular Diseases and Transplantation, Tîrgu Mureş. The study inclusion criteria were: age > 18 years, patients undergoing elective surgery for aortic valve replacement (mechanical/biologic valve prosthesis) due to congenital/acquired significant valvular stenosis/insufficiency according to current guidelines, using HTK cardioplegia. Exclusion criteria were: concomitant surgical procedures, age under 18 years, cardioplegia administered retrograde or combined cardioplegia, and emergency cardiac surgery. Data collection involved taking blood samples from all patients at four key time points: one day before surgery (T1), at the time of patient entry to the operating room (T2), at the time of transfer to the ICU (T3) and on the day after surgery (T4). Transthoracic echocardiographic transthoracic echocardiographic assessment was performed at the time of admission to the Adult and Pediatric Cardiovascular Surgery ward, on the first postoperative day, 24 hours later, and at different intervals thereafter, depending on the patient's progress, with the last measurement being performed 30 days after surgery. Intraoperatively, transesophageal echocardiography was performed before and after aortic valve replacement. The study was approved by the Ethics Committee of the University of Medicine, Pharmacy, Science and Technology "George Emil Palade", Tîrgu Mureş (no. 3103 of 29.04.2024). All procedures in the study were performed in accordance with the ethical standards laid down in the Declaration of Helsinki, and the analysis protocol was approved by the Ethics Committee of the Emergency Institute for Cardiovascular Diseases and Transplantation, Tîrgu Mureş (no. 3240 of 15.04.2024).

RESULTS:

STUDY 1: DOES THE USE OF HTK CARDIOPLEGIA LEAD TO DIFFERENT RESULTS AFTER AORTIC VALVE REPLACEMENT DEPENDING ON THE SEX OF THE PATIENT ?

Given the adaptive changes in the ventricular myocardium secondary to volume/pressure overload in aortic valve disease, there is currently uncertainty regarding the efficacy of this type of cardioplegia for myocardial protection during the surgical cure of aortic valve disease. Studies have demonstrated that there is a difference in myocardial adaptability between genders, which could lead to different postoperative outcomes. In this study it was found that men are more likely to develop aortic valvulopathy, but the gender of the patients does not significantly influence postoperative mortality rate. Although some studies indicate higher mortality in women due to factors such as higher body mass, comorbidities and valvular anatomy, the present study did not confirm a significant gender difference. The study also analyzed postoperative cardiac biomarkers such as CK-MB and troponin. Higher levels of these biomarkers correlate with higher risks of complications and mortality. The postoperative decrease in left ventricular ejection fraction was more pronounced in men, while female patients were able to maintain myocardial function for a longer period of time both preoperatively and postoperatively due to possible hormonal influences. Neurological complications associated with open-heart surgery were also analyzed and it was found that patients' gender did not significantly influence their incidence. In conclusion, the use of HTK cardioplegia in aortic valve surgery provides similar results between genders, effectively overcoming gender differences in myocardial adaptability to this pathology. The influence of cardioplegic solution on postoperative outcome is multifactorial. The use of HTK cardioplegia for myocardial protection in adult patients undergoing aortic valve replacement can be considered a safe and effective method.

STUDY 2: CONSEQUENCES OF HYPONATREMIA IN AORTIC VALVE SURGERY UNDER THE PROTECTION OF HISTIDINE-TRYPTOPHAN-KETOGLUTARATE CARDIOPLEGIA

This study analyzed the relationship between HTK cardioplegia administration and postoperative hyponatremia. The impact of perioperative hyponatremia on short-term mortality in patients undergoing valve surgery was also examined. Hyponatremia affects between 1% and 24% of patients with cardiac pathology. According to the literature, the presence of hyponatremia is associated with increased mortality and increased risk of postoperative adverse events. Patients in this study who had preoperative hyponatremia required surgery with prolonged cardiopulmonary bypass. Although a mean postoperative decrease of 2.9 mmol/L in Na⁺ concentration was observed, this variation did not have a significant impact on patient outcome. In contrast to other studies that have reported greater decreases in postoperative Na⁺ concentrations and an increased incidence of complications, this study suggests that ultrafiltration used during cardiopulmonary bypass prevented the development of severe hyponatremia. By removing excess fluid, ultrafiltration maintained blood osmolarity, reducing associated risks. HTK cardioplegia, due to its high osmolarity (310 mOsm/kg compared to 275-300 mOsm/kg for blood), may help prevent electrolyte imbalances. In conclusion, the results of the study show that the occurrence of postoperative complications is not associated with the presence of postoperative hyponatremia, but with preoperative hyposodemic status, even when there are minor deviations from normal serum Na⁺ values.

ORIGINALITY OF THE THESIS:

This thesis is notable for being the first study to analyze the implementation methods and effects of HTK cardioplegia in aortic valve interventions. The morphopathologic effects of aortic valve pathology involved in the cardioplegic process are also described. This research offers insights that elucidate certain pivotal aspects of the utilisation of HTK cardioplegia, which have hitherto been elucidated in medical practice.