ISA Journal of Multidisciplinary (ISAJM)

Homepage: https://isapublisher.com/isajm/
Email: office.isapublisher@gmail.com
Volume 2, Issue 1, Jan-Feb ISSN: 3049-1851

Early Complications and Changes in Iron Levels, Markers of Oxidative Stress, and Nitric Oxide Levels in Surgery

Maksimovich Yelizaveta

Department of Propaedeutics of Internal Medicine, Grodno State Medical University, Grodno, Belarus

Received: 01.01.2025 | **Accepted:** 05.01.2025 | **Published:** 10.01.2025

***Corresponding Author:** Maksimovich Yelizaveta

DOI: 10.5281/zenodo.14932809

Abstract **Original Research Article**

Reconstructive heart surgeries, like coronary artery bypass grafting (CABG), carry a risk of significant complications, including death. These complications encompass a range of cardiovascular issues, including CABG-related myocardial infarction, worsening heart failure, arrhythmias, stroke, and pericarditis. This study aimed to develop a method for predicting these early postoperative complications in patients with ischemic heart disease undergoing CABG. The prediction model was based on the relationship between hemolysis (blood breakdown during surgery), changes in iron levels, markers of oxidative stress, and nitric oxide levels.

Keywords: Bypass Grafting, Oxidative, Complications, Iron, Nitric Oxide, Hemolysis

1. RELEVANCE.

The study enrolled 123 patients undergoing coronary artery bypass grafting (CABG). Patients were categorized into three groups based on the degree of intraoperative hemolysis (IOH). Blood samples were collected pre- and post-operatively to assess various parameters related to iron metabolism, oxidative stress, and nitric oxide [1]. These included indicators of iron transport (serum iron, transferrin, total and latent iron-binding capacity), iron storage (ferritin) [2], nitric oxide metabolites (NO_x) [3], and oxidative stress markers (malondialdehyde (MDA), diene conjugates, α-tocopherol, and retinol) [4]. Using statistical analyses (multiple logistic regression and receiver operating characteristic (ROC) curve analysis), the researchers found that levels of MDA, transferrin, and NO_x were significantly associated with the development of early postoperative complications. Critically, the study observed a strong correlation between the severity of intraoperative hemolysis and the rate of complications [5]. The high hemolysis group exhibited a substantially higher incidence of complications (57.9%) compared to the low hemolysis group (11.9%) and the no hemolysis group (4.7%). The proposed method offers a valuable tool for predicting early postoperative complications in patients undergoing CABG for IHD [6]. The predictive model incorporates MDA, NO_x, and transferrin levels. These markers reflect oxidative stress, free iron levels, and potentially, endothelial dysfunction – all factors implicated in the development of post-operative complications [7] [8] [9]. This predictive capability can assist in making timely decisions regarding patient management, potentially enabling the implementation of preventative measures or specific interventions to address oxidative processes and endothelial dysfunction in high-risk individuals. This study investigated the early cardiac complications that can arise after CABG surgery in patients with coronary artery disease [10]. Previous research has explored the link between the frequency of these

complications and factors such as the degree of intraoperative hemolysis (blood breakdown during surgery), changes in iron metabolism, oxidative stress levels, and nitric oxide metabolites.

The primary goal of this research was to develop a method for predicting the probability of developing cardiovascular complications in the early postoperative period following CABG. The prediction method focuses on how changes in iron levels, oxidative stress, and nitric oxide levels are influenced by the degree of intraoperative hemolysis. The researchers aimed to identify indicators that could be used to anticipate the risk of these complications. The study's approach draws upon earlier investigations, which looked at the relationship between complications following CABG and: intraoperative hemolysis [11], changes in iron transport and storage [12], oxidative stress levels, and stable nitric oxide metabolites [13]. This research built on that foundation to create a more comprehensive understanding and prediction method. This study employed a multi-faceted approach to investigate the relationship between intraoperative hemolysis and the development of early postoperative cardiac complications after CABG.

2. RESEARCH METHODS

A total of 123 patients with coronary artery disease (CAD), who underwent CABG, were categorized into three groups based on the degree of IOH, measured by free hemoglobin (Hb) levels in blood plasma at the conclusion of the CABG procedure using a HemoCue Plasma/Low Hb analyzer. Groups were: no significant intraoperative hemolysis (n=43), low intraoperative hemolysis (n=42), and high intraoperative hemolysis (n=38). Comprehensive clinical evaluations were conducted, including electrocardiography (ECG), coronary angiography, echocardiography, and monitoring of blood pressure and pulse. Biochemical analyses of blood samples were performed before surgery and within 5-7 days post-surgery. These analyses included a complete blood count, complete urinalysis, lipid profile, protein profile, C-reactive protein, and levels of residual nitrogen (creatinine and urea). The researchers meticulously tracked cardiac complications during the first month after surgery (including the perioperative period), specifically noting myocardial infarction, stroke, arrhythmias, and death. Assessment of iron metabolism, nitric oxide, and oxidative stress: blood samples were collected from the cardiopulmonary bypass machine at the start and end of the CABG procedure to evaluate various markers. These markers included indicators of iron transport (serum iron, transferrin, total and latent iron-binding capacity), iron storage (ferritin), nitric oxide metabolites (nitrite/nitrate ions [NO_x]), and oxidative stress parameters (malondialdehyde, diene conjugates, α-tocopherol, and retinol) [14]. The collected data were analyzed statistically using non-parametric methods in the Statistica 10.0 software package. The researchers also employed logistic regression analysis within the R programming environment, utilizing the Borute package to identify significant predictors of cardiac complications [15].

3. RESULTS AND DISCUSSION

123 of the patients examined with ischemic heart disease and coronary artery bypass grafting, cardiovascular complications of varying severity were observed in 29 (23.6%) patients: arrhythmia (atrial fibrillation, paroxysms of ventricular tachycardia, supraventricular and ventricular extrasystoles) in 27 patients (21.95%), progression of heart failure (decrease in ejection fraction) in 13 patients (9.8%), myocardial infarction in 5 patients (4.1%), acute cerebrovascular accident in 2 patients (1.6%). The highest incidence of complications was observed in the group with high IOH ($p<0.001$) – 57.9%, which is more than in the group with low IOH – in 11.9% of patients ($p<0.001$) and in the group without IOH – in 4.7% of operated patients ($p<0.001$) [4].

Based on the analysis, a formula was obtained for assessing the probability (p) of complications after CABG surgery, which has the general form:

(1)

$$\rho = \frac{1}{1 + \exp^{-(b0+b1\times X1+b2\times X2)}}$$

Where: exp is the base of the natural logarithm (exp = 2.718);
$z = b_0 + b_1 X_1 + b_2 X_2 + b_3 X_3$,
b_0 is the free term (intercept);
b_1, b_2 , b_3 – logistic regression coefficients
X_1, X_2, X_3 – values of the variables [MDA], [$_{\Delta}NO_x$] and [Tr] selected in the equation, respectively.
As a result,
z= 0.799 x [MDA] + 0.192 x [$_{\Delta}NO_x$] - 0.062 x [Tr], where
[MDA] is the concentration of malondialdehyde in blood plasma, μm/l;
[$_{\Delta}NO_x$] is the difference between the 2-nd and 1st samples of nitrate/nitrite levels in blood plasma, μmol/l;
[Tr] is the level of transferrin in blood plasma, mg/dl.

As a result, the equation for determining the probability of developing complications after CABG surgery took the following form:

(2)

$$\rho = \frac{1}{1 + \exp^{-(0.799\times[MDA]+0.192\times[\Delta NOx]-0,062\times[Tr]}}$$

With a calculated value of p≥0.54, patients with coronary artery disease after CABG are at high risk of developing complications in the early period.

Assessments of the quality of the multiple logistic regression model: Hosmer-Lemeshow test (χ^2 = 11.1; p = 0.194); the sensitivity of the method is 96.5%, the specificity is 100%, the PPV (positive predictive value) = 100%, the NPV (negative predictive value) = 98.9%, the area under the ROC curve (AUC) = 0.992. The odds ratio (OR) for MDA = 2.22, for $_{\Delta}$NOx – 1.21, for Tr – 0.94.

Based on the results obtained using the multiple logistic regression method and ROC analysis, the possibility of using the values of MDA, transferrin (Tr), changes in nitrites and nitrates (NO_x) in the blood plasma in assessing the risk of complications of CABG surgery in the early period is shown. The use of MDA and NO_x indicators in the model reflects the relationship of CABG complications with the development of oxidative and nitrosative stress, while the transferrin level indirectly reflects the involvement of free iron in the mechanisms of complication development. The revealed dependence of the occurrence of complications on changes in these indicators in the blood plasma is consistent with the literature data on the development of heart failure under oxidative and nitrosative stress.

4. CONCLUSIONS

1. A statistical model for assessing the likelihood of developing cardiac complications in the early period in patients with coronary heart disease after CABG has been obtained, which involves determining malondialdehyde, changes in stable metabolites of nitric oxide and transferrin in the blood plasma of operated patients.
2. The proposed method allows determining the risk of developing cardiovascular complications in patients with coronary heart disease after CABG in the early period, based on the values of indicators characterizing the

activity of oxidative stress, the level of free iron, the degree of endothelial dysfunction, which is important for timely management decisions.

3. The possibility of predicting the development of complications in high-risk patients suggests, along with generally accepted therapeutic measures, supplementing them with correction of the activity of oxidative processes and endothelial dysfunction.
4. The proposed method has high sensitivity and specificity, and therefore can be recommended for use in practical healthcare to predict CABG complications in patients with coronary heart disease in the early period, which will reduce the likelihood of their development by carrying out therapeutic and preventive measures in the intra- and postoperative periods.

ABBREVIATIONS:

CABG: coronary artery bypass grafting
IOH: intraoperative hemolysis
NOx: nitric oxide metabolites
MDA: malondialdehyde
ROC: receiver operating characteristic
CAD: coronary artery disease
ECG: electrocardiography

Conflict of Interest: The authors declare that there are no conflicts of interest

REFERENCES

[1] Adelborg, K. Thirty-year mortality after coronary artery bypass graft surgery: a Danish nationwide population-based cohort study/ K. Adelborg, E. Horváth-Puhó, M. Schmidt, et al. // Circ. Cardiovasc. – Qual. Outcomes. – 2017. – V.10. – P.1-9.

[2] Åström A. Risk of ischemic stroke after acute myocardial infarction in patients undergoing coronary artery bypass graft surgery / Åström A., Söderström L., Mooe T. // Scientific Reports. – 2020. – V. 10. – №. 1. – P. 1-9.

[3] Bagheri F. et al. Reactive oxygen species-mediated cardiac-reperfusion injury: mechanisms and therapies/ Bagheri F. et al. // Life sciences. – 2016. – T. 165. – P. 43-55.

[4] Bi Y. et al. Dysregulation of iron metabolism in cardiovascular diseases: From iron deficiency to iron overload / Bi Y. et al. // Biochemical Pharmacology. – 2021. – V.190. – P.114 – 661.

[5] Maksimovich Ye. Early complications after coronary bypass operation/ Maksimovich Ye., Chmara N.// Abstr. the 16th International congress of medical sciences (ICMS) for students and young doctors 11-14 May 2017. – Bulgaria. – P.254.

[6] Afrasiabirad, A. On-pump beating coronary artery bypass in high risk coronary patients/ A. Afrasiabirad, N. Safaie, H. Montazergaem // Iran J. Med. Sci. – 2015. – V. 40. – P. 40 – 44

[7] Cavalcante, R. Outcomes after percutaneous coronary intervention or bypass surgery in patients with unprotected left main disease/ R. Cavalcante, Y. Sotomi, C.W. Lee, J.M. Ahn, V. Farooq, H. Tateishi // J. Am. Coll. Cardiol. – 2016. – V.68.–P.999 – 1009.

[8] Bagheri F. et al. Reactive oxygen species-mediated cardiac-reperfusion injury: mechanisms and therapies/ Bagheri F. et al. // Life sciences. – 2016. – T. 165. – P. 43-55.

[9] Bi Y. et al. Dysregulation of iron metabolism in cardiovascular diseases: From iron deficiency to iron overload / Bi Y. et al. // Biochemical Pharmacology. – 2021. – V.190. – P.114 – 661.

[10] Chikwe, J. Long-term outcomes after off-pump versus on-pump coronary artery bypass grafting by experienced surgeons / Chikwe J., Lee T., Itagaki S. et al. // J. Am. Coll Cardiol. – 2018. – V. 72. – P.1478 –1486.

[11] Maksimovich, Ye.N. Endothelial vasoactive properties in patients after coronary artery bypass surgery with different level of hemolysis / Ye.N. Maksimovich, T.P.

Pronko: abstract // Pathophysiology, 2018. – Vol. 25(3). – P.177.

[12] Maksimovich, Ye. N. Association of hemolysis with the incidence of heart rhythm disturbances following coronary artery bypass graft surgery/ Ye.N. Maksimovich, T.P. Pronko, V.A. Yanushko, Yu. A. Kashcheyeu, V.A. Snezhitski // Journal of Arrhythmology, 2019;26(2):29-36. (In Russ. https://doi.org/10.35336/VA-2019-2-29-36

[13] Maksimovich Y. Nitrites and nitrates concentration in patients with coronary artery bypass/ Maksimovich Y., Stelmakh A., Dubovik A., ChmaraN., Kashcheua Y. // International Scientific Conference SCIENCE4HEALTH 2017 13-15.04.2017 RUDN. – University, Moscow, Russia – P.137.

[14] Chikwe, J. Long-term outcomes after off-pump versus on-pump coronary artery bypass grafting by experienced surgeons / Chikwe J., Lee T., Itagaki S. et al. // J. Am. Coll Cardiol. – 2018. – V. 72. – P.1478 –1486.

[15] Daniel, J.F. Improving coronary artery bypass grafting: a systematic review and meta-analysis on the impact of adopting transit-time flow measurement / J.F. Daniel, Thuijs M., Margreet W.A. David P. Taggart // Eur. J. Cardiothorac. – 2019. – V.56(4). – P. 654 – 663.