UDC: 616.31:616.36; 616.31; 616-092; 616-08; 612

ANTIOXIDANT AND STRESS-PROTECTIVE MARKERS IN PATIENTS WITH CORONARY HEART DISEASE UNDERGOING CORONARY ARTERY BYPASS GRAFTING UNDER CARDIOPULMONARY BYPASS

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Abstract. *The study assessed antioxidant and stress-protective markers in patients with coronary heart disease undergoing coronary artery bypass grafting under cardiopulmonary bypass. Serum superoxide dismutase and Klotho protein levels were determined before surgery, on the first day, and on the seventh day after surgery. Before surgery, patients showed reduced antioxidant and stress-protective potential: superoxide dismutase was 980.3±0.57 pg/ml, 1.53 times lower than in the control group, while Klotho protein was 6.54±0.33 pg/ml versus 32.8±0.29 pg/ml in healthy individuals. On the first postoperative day, superoxide dismutase increased to 1290.4±5.21 pg/ml and Klotho protein to 10.3±0.06 pg/ml. By the seventh day, superoxide dismutase reached 1451.7±3.26 pg/ml, approaching control values, while Klotho protein increased to 26.2±0.06 pg/ml. These findings indicate that patients with coronary heart disease have a pronounced preoperative deficiency of antioxidant and stress-protective mechanisms. The postoperative increase in superoxide dismutase and Klotho protein reflects compensatory activation of protective systems after surgical myocardial revascularization.*

Key words: *coronary heart disease, coronary artery bypass grafting, cardiopulmonary bypass, superoxide dismutase, Klotho protein, oxidative stress, antioxidant protection, myocardial revascularization.*

Introduction. Coronary heart disease remains one of the leading causes of morbidity and mortality worldwide. In patients with multivessel coronary artery disease, coronary artery bypass grafting is one of the most effective methods of surgical myocardial revascularization. However, despite the high clinical efficacy of this intervention, the use of cardiopulmonary bypass is associated with a number of pathophysiological changes, including systemic inflammatory response, endothelial dysfunction, oxidative stress and reperfusion injury (3,6,7).

During cardiopulmonary bypass, blood contact with artificial surfaces, ischemic myocardial damage and subsequent reperfusion lead to the formation of reactive oxygen species. Under these conditions, the antioxidant system becomes one of the key protective mechanisms aimed at limiting cellular damage. Superoxide dismutase is considered an important enzymatic component of antioxidant protection, since it participates in the neutralization of superoxide radicals and reflects the functional state of the antioxidant defense system (1,2,4,9).

In recent years, special attention has also been paid to Klotho protein, which is involved in the regulation of cellular aging, mineral metabolism, endothelial function and anti-inflammatory mechanisms. A decrease in Klotho protein may be associated with endothelial dysfunction, progression of atherosclerosis and increased sensitivity to oxidative stress. Therefore, simultaneous assessment of superoxide dismutase and Klotho protein in patients with coronary heart disease may provide additional information about the adaptive reserve of the organism before and after coronary artery bypass grafting (5,8,10,11).

Purpose of the study. To evaluate the dynamics and clinical significance of superoxide dismutase and Klotho protein as antioxidant and stress-protective markers in patients with coronary heart disease undergoing coronary artery bypass grafting under cardiopulmonary bypass.

Materials and methods of research. The study was carried out in patients with coronary heart disease who underwent coronary artery bypass grafting under cardiopulmonary bypass. The study group included patients with verified coronary heart disease and indications for surgical myocardial revascularization. The control group consisted of practically healthy individuals of comparable age.

Blood samples were collected from the cubital vein. The serum levels of superoxide dismutase and Klotho protein were determined before surgery, on the first day after surgery and on the seventh day after surgery. The study of immunobiochemical markers was performed by solid-phase enzyme-linked immunosorbent assay using appropriate test systems. Statistical processing of the obtained data was carried out using variation statistics. Differences were considered statistically significant at $p<0.05$.

Research results. The study of antioxidant and stress-protective markers showed that patients with coronary heart disease had a pronounced decrease in adaptive defense mechanisms before coronary artery bypass grafting under cardiopulmonary bypass. The most informative changes were found in the dynamics of superoxide dismutase and Klotho protein, which reflected different but interrelated components of the organism's response to chronic myocardial ischemia, surgical trauma, extracorporeal circulation, and reperfusion stress.

Before surgery, the serum level of superoxide dismutase in patients with coronary heart disease was 980.3±0.57 pg/ml, while in the control group it was 1502.3±0.37 pg/ml. Thus, the preoperative level of this enzyme was 1.53 times lower than in practically healthy individuals. This indicates that even before surgical intervention, patients with coronary heart disease had a significant weakening of enzymatic antioxidant protection. Such a decrease may be associated with long-term ischemia, chronic inflammatory activity, endothelial dysfunction, and increased consumption of antioxidant enzymes under conditions of oxidative stress.

After coronary artery bypass grafting, the superoxide dismutase level showed a gradual increase. On the first postoperative day, it reached 1290.4±5.21 pg/ml, which was 1.32 times higher than the preoperative value. This increase indicates early activation of antioxidant mechanisms in response to surgical myocardial revascularization. However, despite this positive trend, the value remained lower than the control group, which suggests that oxidative stress persisted during the early postoperative period.

By the seventh postoperative day, the level of superoxide dismutase increased to 1451.7±3.26 pg/ml. This value approached the control level and was 1.48 times higher than the preoperative indicator. Therefore, the dynamics of superoxide dismutase demonstrated a clear tendency toward restoration of antioxidant defense by the end of the first postoperative week. This may reflect the gradual stabilization of redox balance after restoration of coronary blood flow.

A more pronounced impairment was observed in the stress-protective marker Klotho protein. In the control group, the Klotho protein level was 32.8±0.29 pg/ml. Before surgery, its concentration in patients with coronary heart disease was only 6.54±0.33 pg/ml. This indicates a severe reduction in stress-protective reserve and may reflect the negative influence of chronic coronary insufficiency, vascular aging, endothelial dysfunction, and systemic inflammation.

On the first day after surgery, the Klotho protein level increased to 10.3±0.06 pg/ml. Although the value remained considerably lower than in the control group, it exceeded the preoperative level by 1.57 times. This change can be interpreted as an early adaptive response to myocardial revascularization and reperfusion. However, the incomplete recovery of Klotho protein on the first postoperative day indicates that stress-protective mechanisms were still insufficient at this stage.

By the seventh postoperative day, the Klotho protein concentration increased to 26.2±0.06 pg/ml. Compared with the preoperative value, this indicator increased approximately 4.0 times. Nevertheless, it did not fully reach the level of the control group, which suggests that the restoration of stress-protective mechanisms occurs more slowly than the recovery of enzymatic antioxidant activity.

Table 1.

Dynamics of superoxide dismutase and Klotho protein levels in patients with coronary heart disease undergoing coronary artery bypass grafting under cardiopulmonary bypass, M±m

Indicator	Control group	Before surgery	1st day after surgery	7th day after surgery
Superoxide dismutase, pg/ml	1502.3±0.37	980.3±0.57	1290.4±5.21	1451.7±3.26
Klotho protein, pg/ml	32.8±0.29	6.54±0.33	10.3±0.06	26.2±0.06

The comparative analysis showed that the preoperative deficiency of superoxide dismutase was less pronounced than the deficiency of Klotho protein. Superoxide dismutase before surgery corresponded to 65.3% of the control level, while Klotho protein corresponded to only 19.9% of the control level. This difference indicates that in patients with coronary heart disease, stress-protective mechanisms are more deeply suppressed than enzymatic antioxidant defense.

On the first postoperative day, superoxide dismutase reached 85.9% of the control value, whereas Klotho protein reached only 31.4%. By the seventh day, superoxide dismutase reached 96.6% of the control level, while Klotho protein reached 79.9%. Therefore, antioxidant recovery was faster and almost complete by the seventh day, while Klotho protein recovery remained incomplete.

The increase in superoxide dismutase after surgery was consistent and gradual. Compared with the preoperative level, the marker increased by 310.1 pg/ml on the first postoperative day and by 471.4 pg/ml on the seventh postoperative day. In relative terms, this corresponded to an increase of 31.6% and 48.1%, respectively. These data confirm that the antioxidant system actively responds to cardiopulmonary bypass and reperfusion stress.

Table 2.

Comparative assessment of marker recovery relative to the control group

Indicator	Before surgery	1st day after surgery	7th day after surgery
Superoxide dismutase, % of control	65.3%	85.9%	96.6%
Klotho protein, % of control	19.9%	31.4%	79.9%

The increase in Klotho protein was also progressive, but its dynamics had a different pattern. On the first postoperative day, the concentration increased by 3.76 pg/ml compared with the preoperative level. By the seventh day, the increase reached 19.66 pg/ml. In relative terms, Klotho protein increased by 57.5% on the first day and by approximately 300.6% by the seventh day compared with the preoperative value. This pronounced increase indicates mobilization of stress-protective mechanisms after restoration of myocardial blood supply.

Table 3.

Postoperative increase in antioxidant and stress-protective markers compared with the preoperative level

Indicator	Increase on the 1st postoperative day	Increase on the 7th postoperative day
Superoxide dismutase, pg/ml	+310.1	+471.4
Superoxide dismutase, %	+31.6%	+48.1%
Klotho protein, pg/ml	+3.76	+19.66
Klotho protein, %	+57.5%	+300.6%

The obtained results show that coronary artery bypass grafting under cardiopulmonary bypass is accompanied by a two-phase adaptive response. The first phase, observed on the first postoperative day, is characterized by early activation of antioxidant protection and partial restoration of Klotho protein. This phase reflects the immediate biological response to surgical trauma, extracorporeal circulation, ischemia-reperfusion injury, and systemic inflammatory activation.

The second phase, observed by the seventh postoperative day, is characterized by more pronounced recovery of both markers. Superoxide dismutase almost reached the control values, which indicates compensation of enzymatic antioxidant mechanisms. Klotho protein also increased significantly, but remained lower than in healthy individuals. This may indicate persistent endothelial, metabolic, and stress-related disturbances in the early postoperative period.

From a pathogenetic point of view, the simultaneous decrease in superoxide dismutase and Klotho protein before surgery reflects the formation of a combined antioxidant and stress-protective deficiency in patients with coronary heart disease. This condition may reduce the patient's resistance to cardiopulmonary bypass and increase vulnerability to postoperative complications. Therefore, these markers should not be considered separately; their combined assessment provides a more complete view of the adaptive reserve of the organism.

The dynamics of the studied markers also demonstrate that superoxide dismutase and Klotho protein have different diagnostic meanings. Superoxide dismutase mainly reflects the enzymatic component of antioxidant protection and the ability to neutralize reactive oxygen species. Klotho protein characterizes a broader stress-protective reserve associated with endothelial protection, anti-inflammatory regulation, and vascular homeostasis. The incomplete normalization of Klotho protein by the seventh day suggests that this marker may be more sensitive to prolonged postoperative stress.

Table 4.

Clinical and pathogenetic interpretation of antioxidant and stress-protective marker dynamics

Marker	Preoperative change	Postoperative dynamics	Clinical interpretation
Superoxide dismutase	Decreased compared with control	Gradual increase by the 1st and 7th postoperative days	Restoration of enzymatic antioxidant protection
Klotho protein	Markedly decreased compared with control	Slow but pronounced increase after surgery	Mobilization of stress-protective and endothelial-protective mechanisms
Combined assessment	Simultaneous deficiency of both markers	Compensatory postoperative activation	Indicator of adaptive reserve and recovery potential

Thus, the results indicate that patients with coronary heart disease before surgical myocardial revascularization have a pronounced deficiency of antioxidant and stress-protective mechanisms. Coronary artery bypass grafting under cardiopulmonary bypass is followed by compensatory activation of these systems, which becomes most evident by the seventh postoperative day. The combined determination of superoxide dismutase and Klotho protein may therefore be useful for assessing the adaptive capacity of patients, monitoring early postoperative recovery, and identifying individuals with persistent stress-protective deficiency.

Conclusions. Patients with coronary heart disease before coronary artery bypass grafting under cardiopulmonary bypass have a significant decrease in antioxidant and stress-protective potential, manifested by reduced levels of superoxide dismutase and Klotho protein. After surgery, a compensatory increase in these markers is observed, with the highest values recorded on the seventh postoperative day.

Superoxide dismutase reflects the state of enzymatic antioxidant protection, while Klotho protein characterizes the stress-protective and endothelial-protective reserve of the organism. The combined determination of these markers may be recommended as an additional tool for assessing the adaptive capacity of patients with coronary heart disease before surgical myocardial revascularization and for monitoring the early postoperative period.

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