SMJ Saratov Medical Journal

ISSN 2712-8253, Saratov Medical Journal

2026. Volume 7. Issue 3. Article CID e0301
DOI: 10.15275/sarmj.2026.0301

Original article

Reprint

Prognostic value of Galectin-3 for long-term cardiovascular outcomes in COVID-19 survivors without prior heart disease

Tatyana V. Kanaeva ✉, Ekaterina A. Popova, Nina A. Karoli, Natalia M. Nikitina
✉ tatyanakanaeva7795@gmail.com

Razumovsky State Medical University of Saratov, Saratov, Russia

Received 22 January 2026, Accepted 19 June 2026

© This article is an open access publication. Russian Text published in the *Saratov Journal of Medical Scientific Research,* 2026; 22(3): 344-348. https://doi.org/10.15275/ssmj2203344 ISSN 1995-0039.

Abstract:
Objective: To determine the prognostic significance of galectin-3 (Gal-3) and other biomarkers for major adverse cardiovascular events (MACEs) in patients without prior cardiovascular disease (CVD) who recovered from a novel coronavirus infection (COVID-19).
Materials and methods: This prospective study collected data on 112 patients without a history of CVD who were hospitalized with confirmed COVID-19. On the day of admission, levels of traditional and promising Gal-3 biomarkers were additionally determined.
Results: During long-term follow-up (over two years), 14 cases (12.5%) of MACEs were recorded. Individuals with MACE had higher values of body mass index (BMI) (p=0.017), interleukin 6 (p=0.019), D-dimer (p=0.001), high-sensitivity troponin T (p=0.003) and Gal-3 (p=0.001) than the corresponding parameters in patients without MACE. According to the results of multivariate logistic regression, independent predictors of MACEs were Gal-3 concentration 5.1 ng/mL (sensitivity 96%, specificity 90%; p=0.001) and BMI>27 kg/m² (sensitivity 85%, specificity 78%; p=0.022).
Conclusion: According to the results of the study, predictors of MACEs after COVID-19 are the concentration of Gal-3 and the BMI value.

Keywords: galectin-3 (Gal-3), cardiovascular diseases, major adverse cardiovascular events, COVID-19.

Cite as: Kanaeva TV, Popova EA, Karoli NA, Nikitina NM. Prognostic value of Galectin-3 for long-term cardiovascular outcomes in COVID-19 survivors without prior heart disease. *Saratov Medical Journal* 2026; 7(3): e0301. https://doi.org/10.15275/sarmj.2026.0301

Introduction

The novel coronavirus disease (COVID-19) has become a global pandemic, involving over 590 million cases and more than 6 million deaths worldwide [1]. Following the pandemic, there has been an increase in new cardiovascular diseases (CVD) in patients with no prior history of cardiac pathology, which underscores the critical importance of further studying the complex association between COVID-19 and the cardiovascular system (CVS) [2]. Direct viral invasion mediated by the angiotensin-converting enzyme 2 (ACE2) receptor, cytokine storm, endothelial dysfunction, hypercoagulability, and atherothrombosis are key factors causing the destabilization of preexisting CVD and primary cardiovascular injury in individuals without previously diagnosed cardiac pathology [3, 4].

Identifying CVS dysfunction markers prior to the onset of clinical symptoms (i.e., during the stage of subclinical injury) could facilitate the development of novel strategies for the early detection and prevention of major adverse cardiovascular events (MACEs) [4]. Galectin-3 (Gal-3) is a protein reflecting the severity of myocardial inflammation and fibrosis; hence, it is considered a promising marker in this regard [5]. Gal-3 has previously been investigated as a prognostic and risk-stratification marker in chronic heart failure (CHF), indicating the extent of cardiac chamber remodeling [6]. Recent studies have demonstrated that Gal-3 is a novel proinflammatory biomarker involved in processes such as intravascular inflammation, lipid endocytosis, atherogenesis, foam cell formation, macrophage activation, cell proliferation (including that of myofibroblasts), and the chemotaxis of monocytes and cell adhesion molecules to the site of inflammation [7].

The proinflammatory effects of Gal-3 are not limited to its participation in the pathogenesis of CVD alone. In severe cases of COVID-19, an increase in Gal-3 receptors on immune cells is observed, with the highest concentrations detected in infected macrophages responsible for the development of a cytokine storm [5].

According to studies conducted in the USA and Spain, patients with severe COVID-19 exhibit statistically significantly higher serum Gal-3 levels vs. healthy individuals (28.7 [17.5-42.0] and 9.6 [8.2-14.7] ng/mL, respectively; p<0.001) [8]. Elevated levels are also associated with an increased likelihood of adverse in-hospital outcomes, such as the development of acute respiratory failure or transfer to the intensive care unit (odds ratio [OR] 3.68; 95% confidence interval [CI] 1.47-9.20; p<0.01) [9].

Published data regarding new cases of CVD following COVID-19 highlight the need for research aimed at developing accurate models to predict MACEs. Such models

© Kanaeva T.V., Popova E.A., Karoli N.A., Nikitina N.M., 2026

expand the range of sensitive and specific predictors for these events, incorporating both standard markers, such as high-sensitivity troponins T (hs-TnT) and I (hs-TnI), N-terminal prohormone of brain natriuretic peptide (NT-proBNP), and D-dimer, as well as promising novel markers (e.g., Gal-3).

The *objective* of this study was to determine the predictive value of Gal-3 and other biomarkers concerning the development of MACE in patients without significant preexisting CVD who have recovered from COVID-19.

Materials and methods

In this prospective single-center study, data were collected on 112 patients with no documented history of prior CVD who were hospitalized with a confirmed diagnosis of COVID-19 between September 2021 and February 2022. Patient selection criteria are presented in *Table* 1. The study was approved by the local ethics committee of the Razumovsky State Medical University of Saratov, Russia.

Standard clinical examination included measurements of blood pressure, heart rate, oxygen saturation (SpO_2) while breathing ambient air, along with anthropometric data.

The following assessments were performed on the day of hospital admission: complete blood count (CBC) with white blood cell differential, comprehensive metabolic panel, electrocardiography, and chest computed tomography (CT). Additionally, levels of conventional biomarkers (hs-TnT, hs-TnI, NT-proBNP, D-dimer) and the promising serum marker (Gal-3) were measured.

Standard clinical examination included measurements of blood pressure, heart rate, oxygen saturation (SpO_2) while breathing ambient air, along with anthropometric data.

The following assessments were performed on the day of hospital admission: CBC with white blood cell differential, comprehensive metabolic panel, electrocardiography, and chest CT. Additionally, levels of conventional biomarkers (hs-TnT, hs-TnI, NT-proBNP, D-dimer) and the promising serum marker (Gal-3) were measured.

Table 1. Patient selection criteria for the study

Criteria	Characterization
Inclusion	• Age: 40–70 years • Patient consent to participate in the study • Confirmed SARS-CoV-2 infection via polymerase chain reaction • Pulmonary damage upon admission (Grades 1–4), based on chest CT results
Non-inclusion	• History of any CVD (except Grade 1 hypertension); • Type 1 or type 2 diabetes mellitus • Heart failure (NYHA functional classes I–IV) • Malignancy in anamnesis • Need for mechanical ventilation upon admission • Pregnancy • Early postpartum period • Lactation period
Exclusion	• Patient death during hospitalization • MACE development during hospitalization

Interleukin 6 (IL-6) (pg/mL) and C-reactive protein (mg/L) levels were measured using a Cobas® C 311 automated analyzer. D-dimer levels (μg/mL) were determined using the Immulite® 2000 XPi Immunoassay System (Siemens Healthineers, USA) via an immunochemiluminescent assay. Serum Gal-3 concentrations (ng/mL) were measured using the RayBiotech® Human Galectin-3 ELISA Kit (RayBiotech, USA). NT-proBNP levels (pg/mL) were determined by enzyme-linked immunosorbent assay (ELISA) using kits from Biomedica (Austria); hs-TnI level (ng/L) was measured using the Abbott ARCHITECT STAT High-Sensitive Troponin-I kit (Abbott, USA), while hs-TnT concentrations (ng/L) were determined on a rapid analyzer using the Elecsys test (Roche Diagnostics, Germany).

During hospitalization, patients received standard pharmacotherapy in accordance with the *Interim Guidelines for the Prevention, Diagnosis, and Treatment of Novel Coronavirus Infection* [10] in effect at the time.

Patients received dynamic follow-up for 24 months after the infection with monitoring for the occurrence of the primary endpoint in the form of MACE (specifically, acute cerebrovascular accident, myocardial infarction, or cardiovascular death). During a two-year follow-up of patients who had recovered from COVID-19 during the pandemic, 14 (12.5%) cases of MACE were recorded: myocardial infarction (n=9), acute cerebrovascular accident (n=3), and pulmonary embolism (n=2). We stratified patients into subgroups based on the occurrence of the primary endpoint (MACE).

Statistical analysis was performed using Statistica 8 (StatSoft Inc., USA) and StatTech v. 4.6.3 (StatTech LLC, Russia) software. Normality of data distribution was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Variables with non-normal distributions were reported as median and interquartile range (*Me* [*Q25*; *Q75*]). Intergroup differences were examined using nonparametric methods (Mann-Whitney U test and Kruskal-Wallis test). Categorical data were presented as counts and percentages. Proportions were compared using Pearson's chi-squared (χ^2) test. Potential predictors of MACE were identified via logistic regression with a forward stepwise variable selection procedure. Prediction strength was expressed as the OR with a 95% confidence interval (CI). Receiver operating characteristic (ROC) analysis was performed to determine cut-off values of quantitative variables (including biomarkers) for predicting MACE and to calculate sensitivity, specificity, and the area under the ROC curve (AUC). Differences were considered statistically significant at $p<0.05$.

Results

A comparative clinical and demographic analysis demonstrated that patients in Subgroup 1 (with MACE) and Subgroup 2 (without MACE) were similar in terms of their age and gender, smoking history, SpO_2 level, COVID-19 severity, and the extent of pulmonary damage on chest CT ($p\geq0.05$ for all parameters). No statistically significant differences were found between the subgroups regarding CBC values (leukocytes, neutrophils, lymphocytes, monocytes, platelets, hemoglobin, erythrocytes, and erythrocyte sedimentation rate), the majority of biochemical markers (C-reactive protein, creatinine, urea, glomerular filtration rate,

alanine aminotransferase, aspartate aminotransferase, total cholesterol, non-high-density lipoprotein cholesterol, and glucose), or coagulation profile results (fibrinogen, international normalized ratio, activated partial thromboplastin time, and prothrombin time) ($p \geq 0.05$ for all listed parameters).

Patients with and without MACE differed in terms of their body mass index (BMI) (28.7 [25.1; 36.2] kg/m² vs. 24.9 [22.9; 29.3] kg/m²; $p=0.017$), IL-6 level (16 [8; 58] pg/mL vs. 3 [0.5; 29] pg/mL; $p=0.019$), and D-dimer (1.2 [0.8; 1.9] μg/mL vs. 0.56 [0.38; 0.92] μg/mL; $p=0.001$) concentration, respectively.

The MACE subgroup was characterized by higher concentrations of hs-TnT (6 [4; 6] ng/mL vs. 3 [2; 5] ng/mL; $p=0.003$) and Gal-3 (7.5 [2.2; 10.1] ng/mL vs. 2.4 [0.5; 7.8] ng/mL; $p=0.001$).

Yet, we established no statistically significant differences in hs-TnI and NT-proBNP levels ($p \geq 0.05$ for both).

We identified cut-off values for quantitative parameters (BMI, IL-6, D-dimer, hs-TnT, and Gal-3) via ROC analysis and subsequently converted them into binary variables. ORs for the occurrence of MACEs were calculated for each factor using univariate logistic regression. Based on the results of multivariate logistic regression, independent predictors of MACEs were a BMI >27 kg/m² (sensitivity 85%, specificity 78%; $p=0.022$) and a Gal-3 concentration >5.1 ng/mL (sensitivity 96%, specificity 90%; $p=0.001$) (*Table* 2).

Discussion

Patients with a history of novel coronavirus infection are characterized by the destabilization of previously diagnosed CVD, the onset of new CVD cases, and an increased incidence of MACEs during the post-hospitalization period [11].

Hyperactivation of the immune system and cytokine-mediated damage to the CVS are key factors in the development of delayed MACEs following COVID-19 [12]. A major challenge in the early identification of patients with high cardiovascular risk but no prior history of CVD is the lack of universally accepted prognostic markers. Our study evaluated the prognostic value of Gal-3 and other biomarkers for the development of MACEs in patients who had recovered from moderate to severe COVID-19. Multivariate analysis established that BMI >27 kg/m² and a Gal-3 concentration >5.1 ng/mL are factors associated with late-onset MACEs.

Table 2. Results of univariate and multivariate logistic regression analysis for predicting major

Parameter	OR	95% CI	*p*
Univariate model			
BMI>27 kg/m²	1.145	1.028-1.274	0.012
IL-6>8.8 pg/mL	1.110	0.955-1.153	0.055
вчTnT>9.6 ng/mL	1.257	1.107-1.373	0.041
Gal-3>5.1 ng/mL	2.318	1.610-3.340	0.0
D-dimer>0.41 μg/mL	1.409	1.400-4.053	0.045
Multivariate model			
Gal-3>5.1 ng/mL	1.409	1.400-4.053	0.001
BMI>27 kg/m²	1.115	1.008-1.194	0.022

The prognostic potential of Gal-3 in the context of novel coronavirus infection may stem from its pivotal role in the complex pathophysiological processes underlying proinflammatory alterations of CVS. Gal-3 is a member of the lectin family capable of binding β-galactosides [13]. It actively regulates key cellular processes (including inflammation, proliferation, and apoptosis) acting as a chief mediator in acute and chronic inflammatory responses. A significant aspect of biological activity of Gal-3 is its capability to stimulate the release of major proinflammatory cytokines – IL-1, IL-6, and tumor necrosis factor-alpha (TNF-α) – which are known to play a major role in the pathogenesis of severe COVID-19 [14].

In In their 2020 study, M. Barutaut et al. state that elevated Gal-3 levels correlate with an increased risk of developing CVD [15]. A serum Gal-3 concentration exceeding 17.8 ng/mL has been established as the threshold for distinguishing between low and high risk of cardiovascular complications in patients with COVID-19 [14]. Serum Gal-3 level can serve as a marker of myocardial fibrosis severity and help assess the prognosis of MACEs in patients with either CHF or COVID-19 [6, 14, 15]. Differences in Gal-3 threshold values between the study by M. Barutaut et al. (Gal-3 >17.8 ng/mL) and our study (Gal-3 >5.1 ng/mL) may stem from variations in study populations and the timing of biomarker measurement (we measured Gal-3 concentration on the day of admission to a specialized clinic). The lower Gal-3 threshold observed in our study may be attributed to the absence of preexisting CVD in our patient cohort.

Spanish researchers discovered that Gal-3 levels in patients with COVID-19 are significantly higher than in healthy controls (28.7 [17.5-42.0] vs. 9.6 [8.2-14.7] ng/mL, respectively; $p<0.0001$). High Gal-3 levels are an independent predictor of adverse in-hospital outcomes, such as the development of acute respiratory failure and transfer to the intensive care unit (OR 3.68; 95% CI 1.47-9.20; $p<0.01$) [9].

However, we found no published studies evaluating Gal-3 as a potential prognostic marker for MACE after COVID-19. We established that a 1 ng/mL increase in Gal-3 levels raised the risk of CVD during the post-hospital period by 40.9% ($p<0.001$).

In our study, we did not identify any prognostic value for standard biomarkers of cardiovascular lesions (hs-TnT, hs-TnI, NT-proBNP) regarding the likelihood of MACEs ($p \geq 0.05$ for all parameters). This finding contrasts with the results of T. Guo et al. and S. Shi et al., whose independent studies were published in 2020 [16, 17]. These Chinese researchers demonstrated that elevated levels of biomarkers such as high-sensitivity troponins and NT-proBNP correlate with the severity of acute myocardial injury and in-hospital cardiovascular complications [16, 17].

The direct link between inflammatory injury of the CVS associated with COVID-19 and elevated serum levels of the novel biomarker Gal-3 accentuates the need for further research into its role in the early identification of patients at risk for cardiovascular pathology. Given the limited and scarce data regarding the prognostic value of Gal-3 in patients without a history of CVD, it is crucial to continue research aimed at identifying an optimal biomarker panel capable of predicting MACEs after COVID-19 or other infections characterized by systemic hyperinflammation.

Study limitations

When interpreting the study results, its single-center design and small sample size (112 patients) should be considered. Furthermore, serial measurements of traditional biomarkers and Gal-3 were not performed; such data could have expanded the list of prognostic laboratory markers and strengthened the prognostic model. We found no prognostic value for NT-proBNP, hs-TnT, or hs-TnI, even though large international studies indicate otherwise. This is likely attributable to the small sample size and methodology employed in our study.

Conclusion

The development of MACEs after COVID-19 involves complex pathophysiological mechanisms likely driven by the inflammatory nature of the CVS injury. Our study has identified two independent predictors of MACEs: Gal-3 concentration >5.1 ng/mL (sensitivity 96%, specificity 90%; p=0.001) and BMI >27 kg/m² (sensitivity 85%, specificity 78%; p=0.022).

Author contributions

All authors contributed equally to the preparation of this manuscript.

Conflict of interest

None declared.

Informed consent for publication

Patients signed a voluntary informed consent form for the publication of medical information.

Funding

The authors declare no external funding for the study or the publication of its results.

Compliance with ethical standards

The study protocol was approved by the local ethics committee. Approval and protocol implementation adhered to the principles of the Declaration of Helsinki.

References

1. Avdeev SN, Adamyan LV, Alekseeva EI, et al. Prevention, Diagnosis, and Treatment of Novel Coronavirus Infection (COVID-19). Interim Guidelines. Version 19 (27 May 2025). Moscow: Ministry of Health of the Russian Federation, 2025; 246 p. (In Russ.). https://elibrary.ru/zhuaax.
2. Shlyakhto EV, Konradi AO, Arutyunov GP, et al. Guidelines for the diagnosis and treatment of circulatory diseases in the context of the COVID-19 pandemic. *Russian Journal of Cardiology*. 2020; 25(3): 3801. (In Russ.) https://doi.org/10.15829/1560-4071-2020-3-3801.
3. Xiong TY, Redwood S, Prendergast B, Chen M. Coronaviruses and the cardiovascular system: acute and long-term implications. *Eur Heart J* 2020; 41(19): 1798-1800. https://doi.org/10.1093/eurheartj/ehaa231.
4. Podzolkov VI, Tarzimanova AI, Bragina AE, et al. Damage to the Cardiovascular System in Patients with SARS-CoV-2 Coronavirus Infection. Part 1: Predictors of the Development of an Unfavorable Prognosis. *Rational Pharmacotherapy in Cardiology*. 2021; 17(6): 825-830. (In Russ.) https://doi.org/10.20996/1819-6446-2021-11-03.
5. Reddy K, Nichol A, McAuley DF. Galectin-3 inhibition in COVID-19. *Am J Respir Crit Care Med* 2023; 207(2): 118-120. https://doi.org/10.1164/rccm.202209-1758ED.
6. Gehlken C, Suthahar N, Meijers WC, Boer RA. Galectin-3 in heart failure: An update of the last 3 years. *Heart Fail Clin* 2018; 14(1): 75-92. https://doi.org/10.1016/j.hfc.2017.08.009.
7. Gao Z, Liu Z, Wang R, et al. Galectin-3 is a potential mediator for atherosclerosis. *J Immunol Res* 2020; 2020: 5284728. https://doi.org/10.1155/2020/5284728.
8. Schroeder JT, Bieneman AP. The S1 subunit of the SARS-CoV-2 spike protein activates human monocytes to produce cytokines linked to COVID-19: Relevance to galectin-3. *Front Immunol* 2022; 13: 831763. https://doi.org/10.3389/fimmu.2022.831763.
9. Cervantes-Alvarez E, Limon-de la Rosa N, Salgado-de la Mora M, et al. Galectin-3 as a potential prognostic biomarker of severe COVID-19 in SARS-CoV-2 infected patients. *Sci Rep* 2022; 12(1): 1856. https://doi.org/10.1038/s41598-022-05968-4.
10. Avdeev SN, Adamyan LV, Alekseeva EI, et al. Prevention, Diagnosis, and Treatment of Novel Coronavirus Infection (COVID-19). Interim Guidelines. Version 16 (18 August 2022). Moscow: Ministry of Health of the Russian Federation, 2022; 249 p. (In Russ.) https://static-0.minzdrav.gov.ru/system/attachments/attaches/000/060/193/original/BMP_COVID-19_V16.pdf.
11. Bunova SS, Okhotnikova PI, Skirdenko YuP, et al. COVID-19 and cardiovascular comorbidity: novel approaches to reduce mortality. *Cardiovascular Therapy and Prevention* 2021; 20(4): 2953. (In Russ.) https://doi.org/10.15829/1728-8800-2021-2953.
12. Alsaidan AA, Al-Kuraishy HM, Al-Gareeb AI, et al. The potential role of SARS-CoV-2 infection in acute coronary syndrome and type 2 myocardial infarction (T2MI): Intertwining spread. *Immun Inflamm Dis* 2023; 11(3): e798. https://doi.org/10.1002/iid3.798.
13. Boza-Serrano A, Ruiz R, Sanchez-Varo R, et al. Galectin-3, a novel endogenous TREM2 ligand, detrimentally regulates inflammatory response in Alzheimer's disease. *Acta Neuropathol* 2019; 138(2): 251-273. https://doi.org/10.1007/s00401-019-02013z.
14. Cannavo A, Liccardo D, Gelzo M, et al. Serum galectin-3 and aldosterone: Potential biomarkers of cardiac complications in patients with COVID-19. *Minerva Endocrinol (Torino)* 2022; 47(3): 270-278. https://doi.org/10.23736/S2724-6507.22.03789-7.
15. Barutaut M, Fournier P, Peacock WF, et al. sST2 adds to the prognostic value of Gal-3 and BNP in chronic heart failure. *Acta Cardiol* 2020; 75(8): 739-747. https://doi.org/10.1080/00015385.2019.1669847.
16. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020; 5(7): 811-818. https://doi.org/10.1001/jamacardio.2020.1017.
17. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; 5(7): 802-810. https://doi.org/10.1001/jamacardio.2020.0950.

Authors:
Tatyana V. Kanaeva – PhD (Medicine), Instructor, Department of Internal Medicine, Razumovsky State Medical University of Saratov, Saratov, Russia. https://orcid.org/0000-0002-9451-9318;
Ekaterina A. Popova – Student, Institute of Clinical Medicine, Razumovsky State Medical University of Saratov, Saratov, Russia. https://orcid.org/0009-0005-3302-4345;
Nina A. Karoli – DSc (Medicine), Professor, Department of Internal Medicine, Razumovsky State Medical University of Saratov, Saratov, Russia. https://orcid.org/0000-0002-7464-826X;
Natalia M. Nikitina – DSc (Medicine), Professor, Chair of the Department of Internal Medicine, Razumovsky State Medical University of Saratov, Saratov, Russia. https://orcid.org/0000-0002-0313-1191.