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Original article

Prognostic value of type 2 diabetes mellitus and visfatin level in patients after coronary artery bypass grafting

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Abstract: *Objective* — Our study aimed to evaluate the prognostic value of type 2 diabetes mellitus (DM) and the level of visfatin in patients undergoing coronary artery bypass grafting (CABG).
Methods — Our study included 103 patients with chronic heart failure and stable coronary artery disease. The clinical outcomes and adverse cardiovascular events were analyzed 12 months after the CABG.
Results — The patients were distributed between two groups: Group 1 (without registration of composite endpoints, n=71) and Group 2 (patients with the development of composite endpoints, n=32). In Group 1, 22.5% of patients were diagnosed with DM vs. 31.2% in Group 2 (p=0.346). Kaplan-Meier estimator demonstrated that patients with duration of DM over 5 years experienced significantly earlier and more frequent adverse cardiovascular events after CABG vs. patients without DM or with duration of DM less than 5 years. The visfatin level before CABG did not differ between the groups (p=0.416), whereas 10 days after CABG it was higher in Group 2. Correlation between the difference in visfatin levels before and after CABG and duration of type 2 DM was calculated (r=0.54, p=0.041).
Conclusion — In patients after CABG, the duration of DM had a negative impact on the development of cardiovascular events. With a duration of DM exceeding 5 years, the risk of adverse events increased significantly. An increase in visfatin level 10 days after CABG was associated with the duration of DM and the development of adverse cardiovascular events in patients.

Keywords: heart failure, coronary artery disease, diabetes mellitus, coronary artery bypass grafting, visfatin.

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Introduction

It is known that type 2 diabetes mellitus (DM) and coronary artery disease (CAD) are comorbid illnesses [1]. According to traditional concepts and common prognosis scales (Framingham Risk Score and SCORE), DM is an important risk factor for cardiovascular complications [2]. DM has a major impact on prognosis in patients with multivessel atherosclerosis after revascularization. Large randomized trials demonstrated a preference for coronary artery bypass grafting (CABG) over percutaneous interventions and conservative strategy in patients with DM [3-5]. At present, the search for new biomarkers predicting adverse cardiovascular events in patients after CABG is relevant. Visfatin/NAMPT (nicotinamide phosphoribosyltransferase) is an adipocytokine associated with metabolic disorders, endothelial dysfunction, and systemic inflammation [6]. It was previously shown that high levels of visfatin may contribute to vascular inflammation and destabilization of atherosclerotic plaques [7-9].

In connection with the aforementioned, our study aimed to evaluate the prognostic value of type 2 DM and visfatin level in blood serum in patients undergoing CABG.

Material and Methods

Study sample and design

A total of 103 patients with chronic heart failure (CHF) and stable multivessel CAD hospitalized for elective CABG were included in the study. The inclusion criteria were patients with CHF, triple vessel CAD revealed by invasive coronary angiography, atherosclerotic plaques ≥ 50% of the vessel lumen in the anterior descending, circumflex and right coronary arteries, or the presence of left coronary artery stenosis in combination with damage to the right coronary artery. The exclusion criteria were as follows: severe respiratory failure (exacerbation of chronic obstructive pulmonary disease, uncontrolled course of bronchial asthma), diagnosed cancer, acute or aggravated chronic infectious disease, and myocardial infarction or progressive angina less than three months ago.

All patients were examined according to the algorithm including the review of the anamnesis, and clinical examination with determination of body mass index (ratio of body weight in kilograms to the square of height in meters), as well as the symptoms, and signs of heart failure. The instrumental examination included 12-lead electrocardiography (ECG) and transthoracic echocardiography performed by a trained professional [10]. All tests were done before the surgery.

In addition, routine blood tests were performed. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI equation. Coronary angiography was conducted according to clinical indications within two months of inclusion in the study.

DM was diagnosed in compliance with the guidelines [11]. The duration of DM history was analyzed from medical records.

The study was approved by the local institutional Ethics Committee (Protocol No. 188 of September 18, 2018), and all patients signed the written informed consent prior to the study.

The clinical outcomes and adverse cardiovascular events were analyzed 12 months after CABG: the median duration of the follow-up period (Me[IQR]) was (16 [13; 22]) months. The composite endpoints were represented by death due to a cardiovascular event, decompensated heart failure, the need for intravenous diuretic therapy or doubling of the loop diuretics dose, acute ischemic stroke requiring unplanned revascularization, and acute cerebrovascular accident. The patients were distributed between two groups based on registration of composite endpoints: Group 1 (without registration of composite endpoints, n=71), and Group 2 (with the development of composite endpoint, n=32).

Biomarker quantification

The concentration of the N-terminal pro-B-type natriuretic peptide (NT-proBNP) was determined via enzyme immunoassay method using the diagnostic kit by Biomedica Medizinprodukte GmbH (Austria) before CABG and 10 days after it. Creatine kinase myocardial band (CK-MB) activity was determined before CABG and on the first day after it.

The concentration of serum visfatin (ng/mL) was determined by enzyme-linked immunosorbent assay technique using RayBio® Human/Mouse/Rat Visfatin Enzyme Immunoassay Kit before CABG and 10 days after it in all patients. The difference in visfatin levels before and after CABG was calculated using the following formula:

$$\Delta Visfatin\ (\%) = ((Visfatin\ after\ CABG - Visfatin\ before\ CABG)/ Visfatin\ before\ CABG)) * 100\%. \quad (1)$$

Table 1. Main characteristics of patients with chronic heart failure and multivessel atherosclerosis of coronary arteries depending on the development of composite endpoints

Parameter	*Group 1 (n=71)*	*Group 2 (n=32)*	*p-value*
Men/women, n (%)	64/7 (90.1; 9.9)	27/5 (84.4/15.6)	0.389
Age, years	63 (59; 68)	91 (58; 64)	0.282
Smokers, n (%)	20 (28.1)	10 (31.3)	0.750
Previous acute cerebrovascular accident, n (%)	3 (4.2)	2 (6.2)	0.658
Previous myocardial infarction, n (%)	43 (60.1)	26 (81.2)	0.039
Time since last myocardial infarction, months	32.5 (4.25;158.5)	20 (5; 131)	0.889
Duration of CAD, years	3 (1; 12)	3 (1.5; 11)	0.792
Angina pectoris, Class I, n (%)	5 (7)	1 (3.1)	0.353
Angina pectoris, Class II, n (%)	32 (45.1)	11 (34.4)	
Angina pectoris, Class III, n (%)	34 (47.9)	20 (62.5)	
Angina pectoris, Class IV, n (%)	0	0	
Heart failure, I sensu NYHA, n (%)	8 (11.3)	2 (6.2)	0.422
Heart failure, II sensu NYHA, n (%)	39 (54.9)	14 (43.8)	
Heart failure, III sensu NYHA, n (%)	24 (33.8)	16 (50)	
Heart failure, IV sensu NYHA, n (%)	0	0	
Heart failure with reduced ejection fraction (LVEF ≤40%)	21 (29.5)	13 (40.6)	0.249
Heart failure with mildly reduced ejection fraction (LVEF 41-49%)	11 (15.5)	3 (9.4)	
Heart failure with preserved ejection fraction (LVEF≥50%)	39 (55)	16 (50)	
Arrhythmias, n (%)	36 (50.7)	11 (34.4)	0.123
Body mass index, kg/m2	28 (25,1; 31,2)	29 (25.3;31.8)	0.491
Obesity, Grade I	23 (32.4)	9 (28.1)	0.454
Obesity, Grade II	2 (2.8)	2 (6.2)	
Obesity, Grade III	1 (1.4)	2 (6.2)	
Diabetes mellitus, n (%)	16 (22.5)	10 (31.2)	0.346
Duration of diabetes mellitus, years	2 (1.5; 5.75)	9 (5.5;14.5)	0.001
Glomerular filtration rate before CABG (CKD-EPI), mL/min/1.73m^2	72 (60.5; 79.8)	67.5 (55.3;75)	0.204
Glomerular filtration rate after CABG (CKD-EPI), mL/min/1.73m^2	74 (64; 85)	73.2 (58;80.6)	0.318
Left ventricular ejection fraction, %	55 (38; 63.5)	50 (30.75; 64)	0.562
NT-proBNP before CABG, pg/mL	187.5 (128; 397.2)	225 (130;626)	0.321
NT-proBNP after CABG, pg/mL	248 (155;461)	280 (180;650)	0.409
Creatine kinase myocardial band before CABG, unit/L	17 (13; 22.5)	14 (16.5; 18)	0.645
Creatine kinase myocardial band after CABG, unit/L	25.6 (18;48)	24.8 (16.3; 51)	0.782
Visfatin concentration before CABG, ng/mL	10.1 (9.49;20.1)	12.3 (9.7; 26.4)	0.416
Visfatin concentration after CABG, ng/mL	9.49 (9.59; 15.5)	16.7 (14.4; 21.9)	0.015
Δ Visfatin, %	0.83 (-6; 19.7)	21.4 (0.03; 45.5)	0.022

CAD, coronary artery disease; NYHA, New York Heart Association functional classification; CABG, coronary artery bypass grafting; Δ Visfatin, difference in visfatin levels before and after CABG calculated by the formula (1); p – significance level.

Statistical data processing

Data were analyzed using the STATISTICA 10.0 and demo version of IBM SPSS software. Continuous variables are presented as median (Me) and interquartile range (IQR) considering their non-normal distributions. Categorical data are presented in absolute and relative values (n [%]). Continuous variables in the independent samples were analyzed using Wilcoxon rank sum test. For categorical variables, statistical significance of differences was determined using Pearson's χ2 test and the two-sided Fisher's exact test. The correlation between variables was assessed by calculating the Spearman's rank correlation coefficient. The survival analysis in the studied groups was carried out using the Kaplan-Meier estimator, and the comparison of the two curves was performed using the log-rank test. The predictive power was calculated using the ROC analysis. Receiver operating characteristic (ROC) curves were drawn for visfatin level and registration of the composite endpoints. The area under the curve (AUC) was measured. The statistical significance was assumed at p <0.05.

Results

Main characteristics of the patients are presented in *Table* 1. The studied groups did not differ significantly in terms of main clinical characteristics and medical history. However, the patients of Group 2 more often had a history of myocardial infarction (and 81.2% vs. 60.1%, p=0.039).

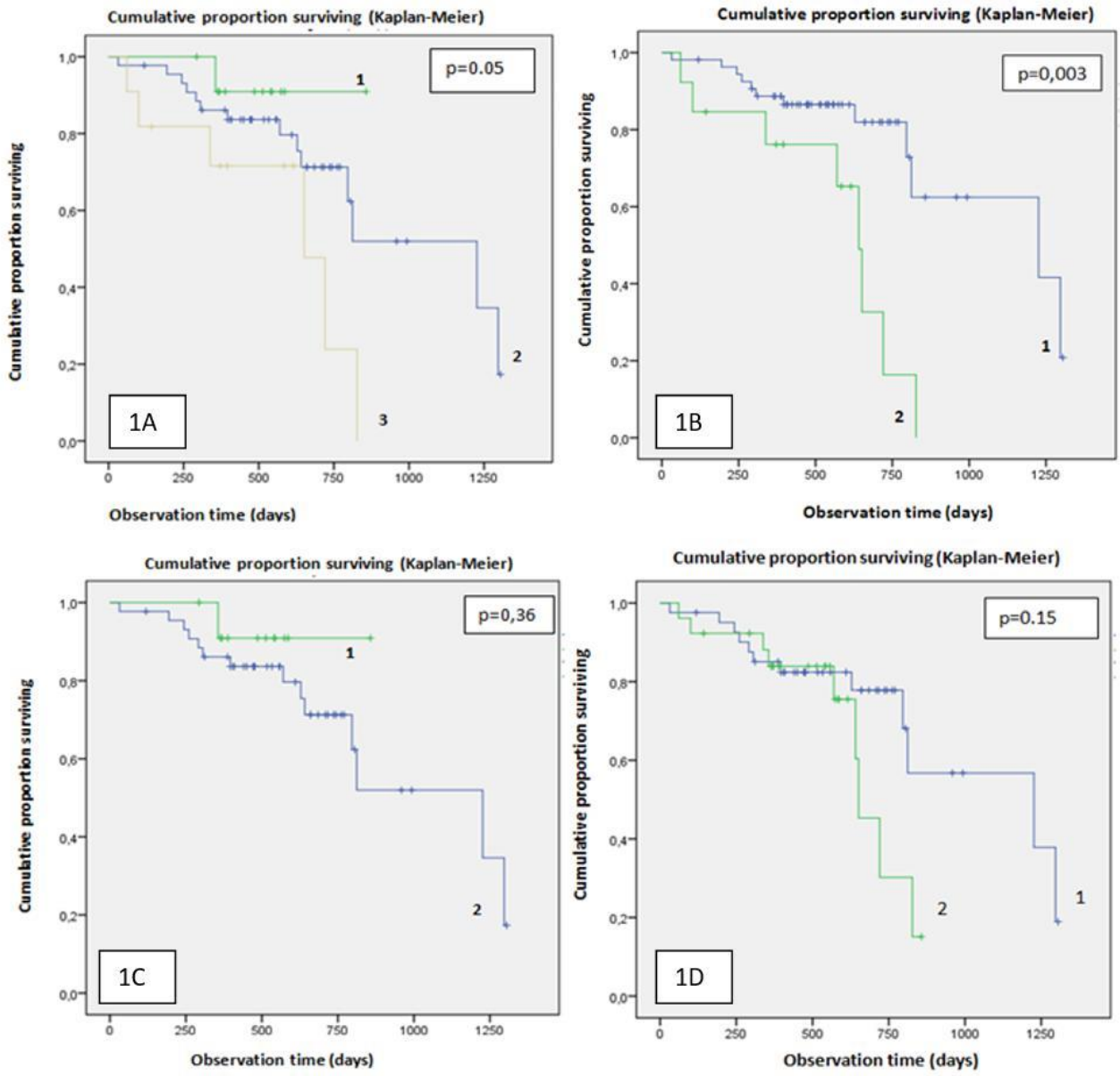

Figure 1. Survival rate of patients after CABG versus the duration of type 2 diabetes mellitus.

1A: 1 – patients with duration of DM less than 5 years (n=13); 2 – patients without DM (n=77); 3 – patients with duration of DM more than 5 years (n=13) (p=0.049).1B: 1 – patients without DM and patients with duration of DM less than 5 years (n=90); 2 – patients with duration of DM more than 5 years (n=13) (p=0.003). 1C: 1 – patients with duration of DM less than 5 years (n=13); 2 – patients without DM (n=77) (p=0.362). 1D: 1 – patients without DM (n=77); 2 – patients with DM (n=26) (p=0.154).

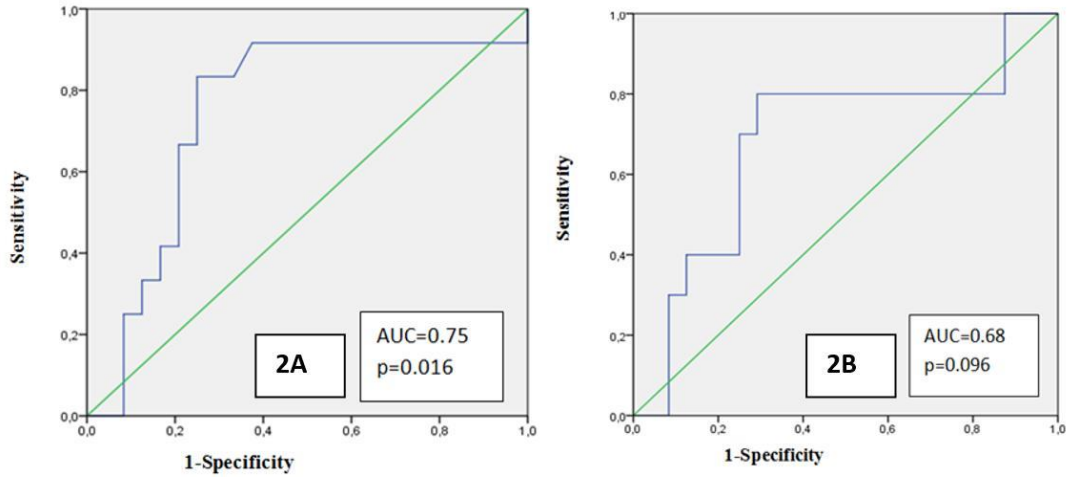

Figure 2. ROC curve for visfatin level and registration of a composite endpoint.

2A: ROC curve of visfatin concentration after CABG and development of endpoints in prospective observation (AUC=0.75; p=0.016); 2B: ROC curve of difference in visfatin concentrations before and after CABG and development of endpoints in prospective observation (AUC=0.68; p=0.096).

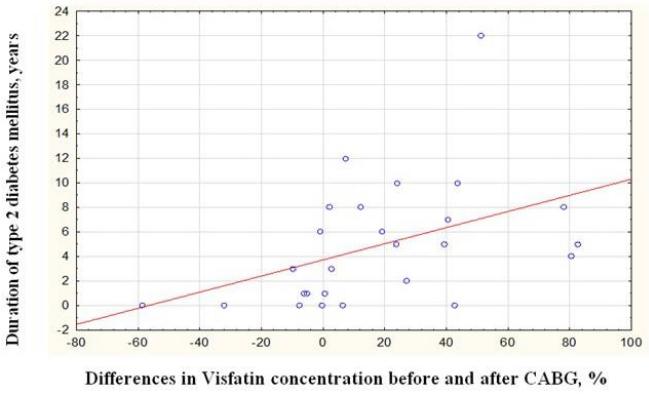

Figure 3. Correlation between difference in visfatin concentrations before and after CABG and duration of type 2 diabetes mellitus (r=0.54, p=0.041).

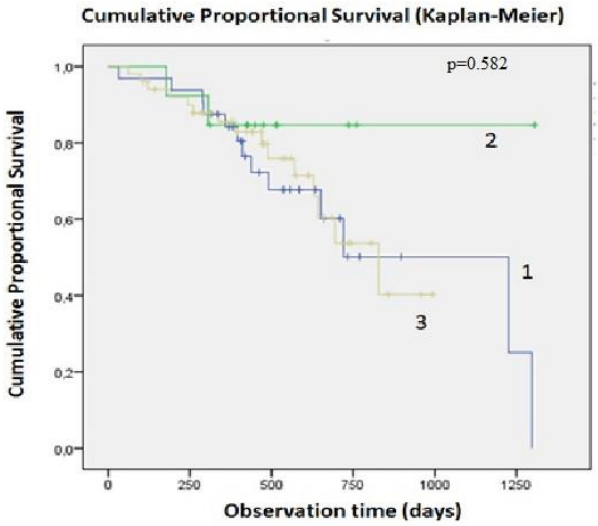

Figure 4. Survival rate of patients after CABG based on left ventricular ejection fraction

1 – Heart failure with reduced ejection fraction (LVEF ≤40%); 2 – heart failure with mildly reduced ejection fraction (LVEF 41-49%); 3 – heart failure with preserved ejection fraction (LVEF ≥50%).

Table 2. Visfatin concentration and its dynamics depending on the presence of diabetes mellitus.

Parameter, Me (IQR)	*DM-*	*DM+*	*p*
Visfatin level before CABG, ng/mL	11.8(9.8;26.7)	10.4(9.4;14.8)	0.184
Visfatin level after CABG, ng/mL	9.8(9.5;19.8)	13.4(9.9;16.8)	0.526
Δ Visfatin, %	-2.5(-23;6.8)	9.6(-0.9;41.7)	0.021

CABG, coronary artery bypass grafting; DM+, patients with diabetes mellitus; DM-, patients with diabetes mellitus; Δ Visfatin, difference in visfatin concentrations before and after CABG calculated by the formula (1); p – significance level.

The diagnosis of DM was established in 22.5% (n=16) of Group 1 patients vs. 31.2% (n=10) of Group 2 subjects (p=0.346). DM was first diagnosed during the current hospitalization in 6 patients of Group 1 vs. none in Group 2. The duration of DM differed significantly between study groups: 2 (1.5; 5) years in Group 1 and 9 (5.75; 14.5 years) in Group 2 (p=0.001). Kaplan-Meier time-to-event endpoint analysis demonstrated that patients with duration of DM over 5 years experienced significantly earlier and more frequent adverse cardiovascular events after CABG vs. patients without DM and patients with duration of DM less than 5 years (*Figures* 1A, 1B). At the same time, the endpoint frequencies did not differ between patients without DM and patients with duration of DM less than 5 years (*Figure* 1C), as well as between all patients with DM and subjects without DM (*Figure* 1D).

The levels of visfatin in the blood serum before CABG did not differ between the groups (p=0.416), whereas its concentration 10 days after CABG was significantly higher in Group 2 (*Table* 1). The dynamics of the visfatin level (Δ visfatin) differed significantly between the groups: *Δ visfatin* indicator was 0.83 (-6; 19.7) % in Group 1 vs. 21.4 (0.03; 45.5) % in Group 2 (p=0.022). ROC analysis revealed that the AUC of visfatin level 10 days after CABG was 0.748 (p=0.016) (*Figure* 2A), while it was 0.68 (p=0.096) for the *Δ visfatin* indicator (*Figure* 2B).

The correlation between DM duration and *Δ visfatin* indicator was calculated (r=0.54, p=0.041) (*Figure* 3).

At the same time, the visfatin level did not depend on the presence of DM in the general cohort (*Table* 2). Furthermore, visfatin levels before and after CABG were not associated with the

body mass index (r=-0.07, p=0.653; r=-0.15, p=0.368) and age (0.18, p=0.2; -0.81, p=0.611).

There was no association of the ejection fraction with endpoint development between groups of patients with different values of left ventricular ejection fraction (p=0.582) (*Figure 4*).

Discussion

Visfatin is an adipocytokine with some additional properties that are not fully understood yet [6]. The extracellular form of visfatin was shown to be associated with metabolic disorders including obesity and DM. T. Dogru et al. demonstrated that visfatin concentrations increased in patients with DM, but not in patients with impaired carbohydrate tolerance. The authors concluded that visfatin levels did not increase at the early stages of insulin resistance [12]. This finding was confirmed by our results, since the level of visfatin after CABG increased to a lesser extent in patients with DM less than 5 years. There are conflicting data on the relationship between the level of visfatin and the degree of obesity [6]. We did not obtain data on the relationship between the body mass index and visfatin concentration before and after CABG.

It is known that visfatin is one of the key factors in the synthesis of nicotinamide adenine dinucleotide (NAD^+). It participates in the pathways of cellular metabolism [13] and possesses proinflammatory effects, including mediating the inflammasome activation [14]. H. Duman et al. established that the level of visfatin, along with the presence of DM, was associated with the severity of coronary atherosclerosis in patients with CAD [15]. In our study, all patients had multivessel coronary artery disease, and therefore their levels of visfatin were initially higher than in the group with less pronounced atherosclerosis, as was shown by H. Duman et al. (8.6 ± 4.2 ng/mL) [15]. However, the dynamics of visfatin level in patients after CABG was not studied to date. According to our results, a significant increase in the concentration of visfatin after CABG is a predictor of adverse cardiovascular events.

Besides, we demonstrated an adverse effect of a longer DM duration on the development of a composite endpoint after CABG, which was consistent with previous data from a cohort of patients with myocardial infarction [16, 17].

At the same time, the concentrations of NT-proBNP and CK-MB did not differ between the groups and were not associated with the endpoint one year after CABG. There was no association of ejection fraction with endpoint development between groups of patients with different values of left ventricular ejection fraction. According to the study by A. Marui et al. (2015) performed on 1,877 patients undergoing CABG (CREDO-Kyoto registry), 236 patients had left ventricular ejection fraction (LVEF) of ≤50% and 152 patients with heart failure had preserved ejection fraction (LVEF>50%). After adjusting for confounding factors, the risk of cardiac arrest and sudden cardiac death did not differ between the groups [18].

The limitation of our study was a small sample size of the patient group with DM, which could affect the level of statistical significance of the assessed differences. Also, we had no data on cardiac troponin concentrations after CABG.

Conclusion

In patients after CABG, the duration of DM had a negative impact on the development of cardiovascular events. With a duration of DM of over 5 years, the risk of adverse events increased significantly. An increase in visfatin level 10 days after CABG was associated with the duration of DM and the development of adverse cardiovascular events in patients. Hence, monitoring the visfatin levels before CABG and 10 days after it and assessing its dynamics can help predicting adverse cardiovascular events in patients.

Data availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare that they have neither apparent or potential conflicts of interest related to the publication of this article.

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References

1. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J* 2020; 41(3): 407-477. Erratum in: *Eur Heart J* 2020; 41(44): 4242. https://doi.org/10.1093/eurheartj/ehz425.
2. Vesa CM, Popa L, Popa AR, Rus M, Zaha AA, Bungau S, et al. Current data regarding the relationship between type 2 diabetes mellitus and cardiovascular risk factors. *Diagnostics (Basel)* 2020; 10(5): 314. https://doi.org/10.3390/diagnostics10050314.
3. Farkouh ME, Domanski M, Dangas GD, Godoy LC, Mack MJ, Siami FS, et al. FREEDOM Follow-On Study Investigators. Long-term survival following multivessel revascularization in patients with diabetes: The FREEDOM Follow-On Study. *J Am Coll Cardiol* 2019; 73(6): 629-638. https://doi.org/10.1016/j.jacc.2018.11.001.
4. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease: The Bypass Angioplasty Revascularization Investigation (BARI). *Circulation* 1997; 96(6): 1761-1769. https://doi.org/10.1161/01.cir.96.6.1761.
5. Howlett JG, Stebbins A, Petrie MC, Jhund PS, Castelvecchio S, Cherniavsky A, et al. STICH Trial Investigators. CABG improves outcomes in patients with ischemic cardiomyopathy: 10-year follow-up of the STICH trial. *JACC Heart Fail* 2019; 7(10): 878-887. https://doi.org/10.1016/j.jchf.2019.04.018.
6. Dakroub A, Nasser SA, Younis N, Bhagani H, Al-Dhaheri Y, Pintus G, et al. Visfatin: a possible role in cardiovasculo-metabolic disorders. *Cells* 2020; 9(11): 2444. https://doi.org/10.3390/cells9112444.
7. Auguet T, Aragones G, Guiu-Jurado E, Berlanga A, Curriu M, Martinez S, et al. Adipo/cytokines in atherosclerotic secretomes: Increased visfatin levels in unstable carotid plaque. *BMC Cardiovasc Disord* 2016; 16(1): 149. https://doi.org/10.1186/s12872-016-0320-5.
8. Li B, Zhao Y, Liu H, Meng B, Wang J, Qi T, et al. Visfatin destabilizes atherosclerotic plaques in apolipoprotein E-deficient mice. *PLoS One* 2016; 11(2): e0148273. https://doi.org/10.1371/journal.pone.0148273.
9. Zheng LY, Xu X, Wan RH, Xia S, Lu J, Huang Q. Association between serum visfatin levels and atherosclerotic plaque in patients with type 2

diabetes. *Diabetol Metab Syndr* 2019; 11: 60. https://doi.org/10.1186/s13098-019-0455-5.

10. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: Recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2019; 32(1): 1-64. https://doi.org/10.1016/j.echo.2018.06.004.
11. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J* 2020; 41(2): 255-323. Erratum in: *Eur Heart J* 2020; 41(45): 4317. https://doi.org/10.1093/eurheartj/ehz486.
12. Dogru T, Sonmez A, Tasci I, Bozoglu E, Yilmaz MI, Genc H, et al. Plasma visfatin levels in patients with newly diagnosed and untreated type 2 diabetes mellitus and impaired glucose tolerance. *Diabetes Res Clin Pract* 2007; 76(1): 24-29. https://doi.org/10.1016/j.diabres.2006.07.031.
13. Yoshino J, Baur JA, Imai SI. NAD^+ intermediates: The biology and therapeutic potential of NMN and NR. *Cell Metab* 2018; 27(3): 513-528. https://doi.org/10.1016/j.cmet.2017.11.002.
14. Koka S, Xia M, Zhang C, Zhang Y, Li PL, Boini KM. Podocyte NLRP3 inflammasome activation and formation by adipokine visfatin. *Cell Physiol Biochem* 2019; 53(2): 355-365. https://doi.org/10.33594/000000143.
15. Duman H, Özyıldız AG, Bahçeci İ, Duman H, Uslu A, Ergül E. Serum visfatin level is associated with complexity of coronary artery disease in patients with stable angina pectoris. *Ther Adv Cardiovasc Dis* 2019; 13: 1753944719880448. https://doi.org/10.1177/1753944719880448.
16. Afanasiev SA, Garganeeva AA, Kuzheleva EA, Andriyanova AV, Kondratieva DS, Popov SV. The Impact of Type 2 Diabetes Mellitus on Long-Term Prognosis in Patients of Different Ages with Myocardial Infarction. *J Diabetes Res* 2018; 2018: 1780683. Erratum in: *J Diabetes Res* 2019; 2019: 8347891. https://doi.org/10.1155/2018/1780683.
17. Rana JS, Liu JY, Moffet HH, Jaffe M, Karter AJ. diabetes and prior coronary heart disease are not necessarily risk equivalent for future coronary heart disease events. *J Gen Intern Med* 2016; 31(4): 387-393. https://doi.org/10.1007/s11606-015-3556-3.
18. Marui A, Nishiwaki N, Komiya T, Hanyu, Tanaka S, Kimura T, et al. CREDO-Kyoto CABG Registry Cohort-2 Investigators. Comparison of 5-year outcomes after coronary artery bypass grafting in heart failure patients with versus without preserved left ventricular ejection fraction (from the CREDO-Kyoto CABG Registry Cohort-2). *Am J Cardiol* 2015; 116(4): 580-586. https://doi.org/10.1016/j.amjcard.2015.05.020.

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