

RISK FACTORS FOR HEART FAILURE IN CHILDREN WITH TYPE 1 DIABETES WHO HAVE HAD COVID-19

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Abstract. Study GLS parameters as an early indicator of heart failure in children with type 1 diabetes who have undergone Covid-19. Research 65 children with diabetes of 1 type of the transferred COVID-19 which underwent treatment in children's office of RSNPMTs of endocrinology aged from 2 up to 18 years were attracted to our research. The group of comparison was made by 114 children with diabetes of 1 type, who are picked up for age and sex without any symptoms or symptoms of cardiovascular diseases was used. In work are used, biochemical researches (HbA1c, brain natriuretic peptide - NT-proBNP), tool methods of the research GLS and statistical methods of a research. Subclinical LV dysfunction in patients with DM 1 occurs already in childhood, while even EF persists. The longitudinal function of the heart changes, but not the circumferential function. GLS can be used to detect subclinical LV systolic dysfunction in the pediatric population.

Keywords: type 1 diabetes mellitus, children, heart failure, COVID-19.

Relevance. The prevalence of type 1 diabetes (DM 1) is growing worldwide, even among the pediatric population, quickly becoming an urgent public health problem [4,]. The International Diabetes Federation estimates that DM 1 affects more than 1,100,000 children and adolescents, with an annual incidence of about 128,900 worldwide. The prevalence of SD1 reaches 34% [5, 8, 10]. A recent study was conducted among 708 children who tested positive for one of the circulating diabetes autoantibodies but did not have diabetes. The study showed that children with a negative test result for HLA haplotypes predisposing to DM 1, and with an increased body mass index (BMI), showed progression to multiple positive autoantibody results and an increased risk of DM 1.

Cardiovascular risk factors in children and adolescents with diabetes. Cardiovascular dysfunction is a well-recognized complication of DM 1 and contributes to one of the most frequent causes of death in these children. HbA1c is associated with a 30% increase in heart failure. Diabetic cardiomyopathy (DCM) is a well-identified complication of diabetes, with a prevalence of 19-26%. DCM is defined as myocardial dysfunction in the absence of coronary heart disease, valvular defects and other cardiovascular risk factors (hypertension, dyslipidemia) in a diabetic [9]. Given its clinical significance and close association with glycemic control, early detection of DCM is vital in the pediatric DM 1 population.

Currently, SARS-CoV-2 infection is also a potential trigger for the development of type 1 diabetes mellitus in children, which is the most frequent chronic metabolic disorder in the pediatric population [1, 2]. There is growing evidence that many patients with COVID-19 may experience a wide range of post-acute consequences, including cardiovascular complications. [6, 12].

Purpose of the study. Study GLS parameters as an early indicator of heart failure in children with type 1 diabetes who have undergone Covid-19.

Materials and methods research. 65 children with diabetes of 1 type of the transferred COVID-19 which underwent treatment in children's office of RSNPMTs of endocrinology aged

from 2 up to 18 years were attracted to our research. The group of comparison was made by 114 children with diabetes of 1 type, who are picked up for age and sex without any symptoms or symptoms of cardiovascular diseases was used. In work are used, biochemical researches (HbA1c, brain natriuretic peptide - NT-proBNP), tool methods of the research GLS and statistical methods of a research.

Table 1.

Clinical characteristics of examined children with type 1 DM

Indicators	Primary group (n=65)	Comparison group (n=114)
Mean age (years)	12,85±0,7	12,76±3,9
Gradation by gender		
Boys	53%	39,5%
Girls	47%	60,5%
DM experience (years)	3,6±0,58	4,69±2,89

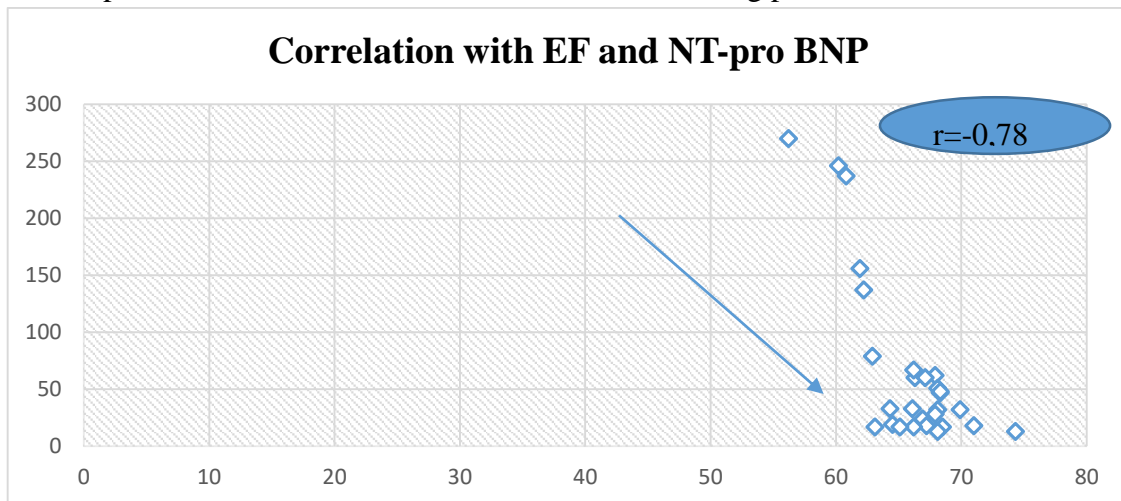
Diagnosis of chronic heart failure (CHF) in patients with type 1 diabetes mellitus (DM) at the compensation stage can prevent the development of cardiovascular complications, reduce the disability and mortality of patients from cardiovascular complications. In our study, we studied the level of the N-terminal fragment of brain natriuretic peptide (NT-proBNP) and also assessed the possibility of using this marker for the diagnosis of chronic heart failure in children with T2DM. When we studied the NT-proBNP indicator, it was significantly increased in children with DM 1 who had a COVID-19 infection.

Diabetic cardiomyopathy (DCM) is a serious complication that often occurs in patients with type 1 diabetes mellitus (T1DM), which requires early diagnosis. Based on this, in our studies, we identified subclinical DCM in children with DM 1 who underwent COVID-19 infection and assessed the effect of antioxidants on myocardial dysfunction. Serum N-terminal brain natriuretic peptide prohormone (NT-proBNP) was evaluated in addition to conventional echocardiography and speckle-tracking echocardiography.

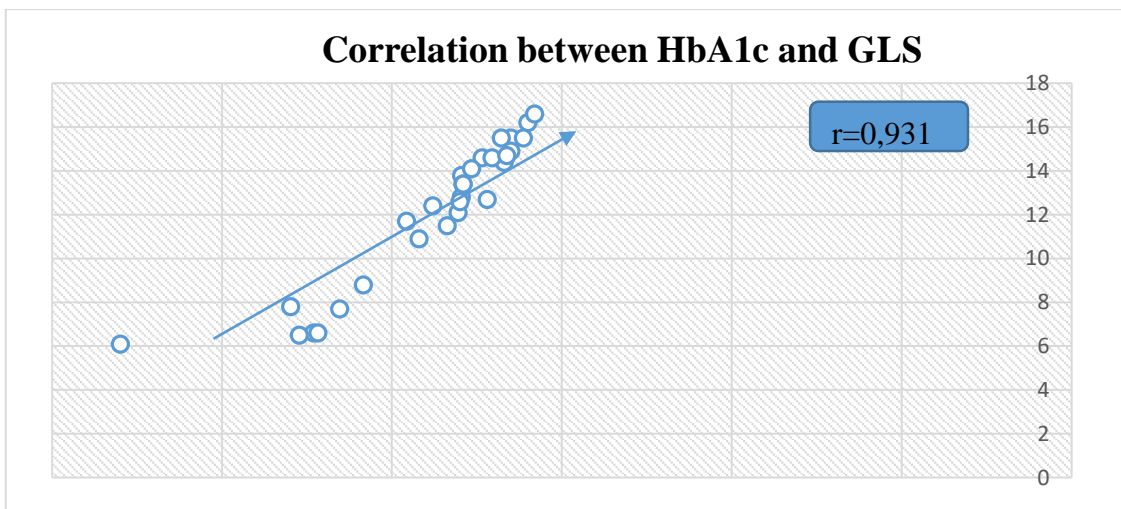
Heart failure with a reduced ejection fraction is observed in children with type 1 diabetes who have had a COVID-19 infection and is often overlooked and misdiagnosed. Left ventricular hypertrophy, left atrial dilation, diastolic dysfunction, and subclinical systolic dysfunction, listed as decreases in global longitudinal myocardial contractility, are the main echocardiography abnormalities in patients with diabetic cardiomyopathy. These structural and functional changes are also common in children with type 1 diabetes mellitus who have undergone COVID-19 infection, and these patients with these disorders have a higher incidence of heart failure than without COVID-19 infection. Glycemic control may improve some of these abnormalities on echocardiography, but it is still unclear whether their improvement may be due to a reduced risk of heart failure. We also found an inverse strong correlation ($r = -0.78$) between left ventricular EF and NT-pro BNP.

Patients and controls were comparable in age, sex. LV EF was significantly higher in T1DM patients with COVID-19 infection compared to the comparison group. However, this difference was clinically significant. More negative GCS values indicated improved longitudinal contractility of the LV myocardium. In contrast, LV GLS values indicate a worse disease outcome. Mean S and e'mitral ring values were significantly lower, whereas the E/e'LV ratio was

significantly higher in patients with DM1, but usually within the normal range. Mitral e'values indicated impaired relaxation. Patients had undefined LV filling pressure.



Hyperglycemic condition responsible for increased vascular complications and heart failure in patients with type 1 diabetes who have had COVID-19 infection. It is well known that glucose levels are directly associated with CVD risk. According to the investigators, each 1% decrease in baseline HbA1c levels reduces the incidence of myocardial infarction by 5%. We found a direct strong correlation ($r = 0.931$) between HbA1c and GLS. Conventional echocardiographic methods may not be effective, but speckle-tracking echocardiography appears to be useful for recognizing subclinical myocardial involvement in this population. The presence of COVID-19 infection and the quality of glycemic control are known as the most important factors responsible for the development of cardiovascular complications in DM 1. Significant correlations between disease duration, glycemic control and new myocardial mechanics parameters have already been reported.



We also revealed a positive weak correlation between the LV EF and LV GLS, which says that in the initial stages there are no signs of chronic heart failure, but at the same time there is a subclinical myocardial lesion.

CONCLUSIONS. Subclinical LV dysfunction in patients with DM 1 occurs already in childhood, while even EF persists. The longitudinal function of the heart changes, but not the circumferential function. GLS can be used to detect subclinical LV systolic dysfunction in the pediatric population. Our data suggest that the quality of glycemic control has a significant impact

on subclinical myocardial involvement in patients with DM 1. Therefore, strict glycemic control should be a high priority therapeutic target for diabetic patients to minimize the risk of myocardial injury and subsequent heart failure.

REFERENCES

1. American Diabetes Association. 13. Children and Adolescents: Standards of Medical Care in Diabetes-2020. *Diabetes Care* 2020, 43 (Suppl. S1), S163–S182.
2. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. *Diabetes Care* 2020, 43 (Suppl. S1), S14–S31.
3. Bogdanović, J. et al. Impact of acute hyperglycemia on layer-specific left ventricular strain in asymptomatic diabetic patients: An analysis based on two-dimensional speckle tracking echocardiography. *Cardiovasc. Diabetol.* 18, 68. (2019).
4. Breyer, M.K.; Ofenheimer, A.; Altziebler, J.; Hartl, S.; Burghuber, O.C.; Studnicka, M.; Purin, D.; Heinzle, C.; Drexel, H.; Franssen, F.M.E.; et al. Marked differences in prediabetes- and diabetes-associated comorbidities between men and women-Epidemiological results from a general population-based cohort aged 6–80 years-The LEAD (Lung, hEart, sociAl, boDy) study. *Eur. J. Clin. Investig.* 2020, 50, e13207
5. Ferrara-Cook, C.; Geyer, S.M.; Evans-Molina, C.; Libman, I.M.; Becker, D.J.; Gitelman, S.E.; Redondo, M.J.; Type 1 Diabetes TrialNet Study Group. Excess BMI Accelerates Islet Autoimmunity in Older Children and Adolescents. *Diabetes Care* 2020, 43, 580–587.
6. Flokas, M.E.; Zeymo, A.; Mete, M.; Anhalt, H.; Rother, K.I.; Gourgari, E. Overweight and obese children with optimal control in the T1D Exchange Registry: How are they different from lean children with optimal control? *J. Diabetes Complicat.* 2020, 34, 107513.
7. Ifuku, M. et al. Left atrial dysfunction and stiffness in pediatric and adult patients with Type 1 diabetes mellitus assessed with speckle tracking echocardiography. *Pediatr. Diabetes* 22, 303–319. (2021).
8. Jones, S.; Khanolkar, A.R.; Gevers, E.; Stephenson, T.; Amin, R. Cardiovascular risk factors from diagnosis in children with type 1 diabetes mellitus: A longitudinal cohort study. *BMJ Open Diabetes Res. Care* 2019, 7, e000625.
9. Kim, G.; Divers, J.; Fino, N.F.; Dabelea, D.; Lawrence, J.M.; Reynolds, K.; Bell, R.A.; Mayer-Davis, E.; Crume, T.; Pettitt, D.J.; et al. Trends in prevalence of cardiovascular risk factors from 2002 to 2012 among youth early in the course of type 1 and type 2 diabetes. The SEARCH for Diabetes in Youth Study. *Pediatr. Diabetes* 2019, 20, 693–701.
10. Maffei, C.; Birkebaek, N.H.; Konstantinova, M.; Schwandt, A.; Vazeou, A.; Casteels, K.; Jali, S.; Limbert, C.; Pundziute-Lycka, A.; Toth-Heyn, P.; et al. Prevalence of underweight, overweight, and obesity in children and adolescents with type 1 diabetes: Data from the international SWEET registry. *Pediatr. Diabetes* 2018, 19, 1211–1220.
11. Miller, R.G.; Costacou, T.; Orchard, T.J. Risk Factor Modeling for Cardiovascular Disease in Type 1 Diabetes in the Pittsburgh Epidemiology of Diabetes Complications (EDC) Study: A Comparison With the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT/EDIC). *Diabetes* 2019, 68, 409–419
12. Rakha, S. & Aboelenin, H. M. Left ventricular functions in pediatric patients with ten years or more type 1 diabetes mellitus: Conventional echocardiography, tissue Doppler, and two-dimensional speckle tracking study. *Pediatr. Diabetes* 20, 946–954. (2019).