To the Chairman of the Scientific Jury

According to the Decision of the Scientific Council (protocol No. 65/ 08.04.2026)

Order No. 15-03-96#2/16.04.2026 of the Executive Director and the Procurator

of Acibadem City Clinic UMBAL Tokuda EAD

OPINION

on the dissertation for the award of the educational and scientific degree "Doctor" in the field of higher education 7.3 Health and Sports, Professional field 7.1 Medicine, doctoral program "Internal Medicine"

by Dr. Desislava Ivanova Gorcheva

on the topic: "ROLE OF GDF-15 AS A PROGNOSTIC MARKER FOR DIABETIC CARDIOMYOPATHY IN PATIENTS WITH TYPE 2 DIABETES AND DIABETIC KIDNEY DISEASE"

by Assoc. Prof. Dr. Alexander Ivanov Osichenko, MD,

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The parallel development of CKD and heart failure significantly increases the cardiovascular risk and mortality in patients with Diabetes mellitus type 2 (DM type 2). This determines the relevance of the presented dissertation work of Dr. Desislava Ivanova Gorcheva, who aims to analyze and evaluate some cardiovascular risk factors and metabolic abnormalities in patients with DM type 2 (with and without diabetic kidney disease), to determine the frequency of diabetic cardiomyopathy and the importance of GDF-15 in the diagnostic algorithm for early myocardial dysfunction in these patients, with a view to its wider implementation in clinical practice.

To achieve the set goal, 7 main tasks have been clearly and precisely formulated.

The dissertation work contains 158 pages and is illustrated with 31 figures and 29 tables. The literature reference includes 203 literary sources, of which 5 are in Cyrillic and 198 are in Latin.

Dr. Desislava Ivanova Gorcheva knows the essence of the problem well and has presented a creative assessment of the analyzed literary material.

The dissertation work covers 131 patients: 110 with type 2 diabetes, divided into 4 groups according to the presence of albuminuria and diastolic dysfunction and 21 - healthy controls. The study was conducted in 2 directions: 1) Comprehensive blood examination of all patients:

biochemical laboratory tests to assess metabolic status, renal function, cardiac status; 2) Imaging studies to assess diastolic dysfunction: ECG and ultrasound examination of the heart. Statistical data were processed using SPSS v.22.

The results obtained have been interpreted in depth and compared with data from studies published in the literature: 1) Patients with DM type 2 have a clearly pronounced metabolic, inflammatory and cardiorenal profile of damage compared to healthy controls. Cardiorenal "aging" is observed with the progression of diabetes; 2) Diastolic dysfunction is a frequent first manifestation of diabetic cardiomyopathy - up to 60% in patients with type 2 diabetes without other cardiovascular diseases; 3) There is a relationship between diastolic dysfunction and the degree of albuminuria; 4) The occurrence of diastolic dysfunction depends on age and duration of diabetes; 5) The combination of albuminuria >30mg/24h and elevated hsTroponin I may be an early predictor of subclinical myocardial damage; 6) Elevated GDF-15 and IL-6 in diastolic dysfunction signal progression of systemic damage; 7) GDF-15 in patients with type 2 diabetes may be associated with: myocardial damage and diabetic cardiomyopathy, higher albuminuria or reduced renal function, increased inflammatory markers, heart failure; 8) GDF-15 is an indicator of systemic stress and damage, not metabolic control; 9) Nephropathy has a stronger effect on GDF-15 than myocardial damage; 10) GDF-15 values are highest in the combination of diastolic dysfunction and diabetic nephropathy - a prognostic marker for cardio-renal metabolic syndrome; 11) It can be used for risk stratification in patients with diabetes, hypertension or CKD without known vascular pathology.

The contributions of the dissertation work are of a certain scientific-theoretical and applied-practical nature: 1) For the first time in Bulgaria, an in-depth clinical study has been conducted on the role of GDF-15 in the diagnosis and prognostic assessment of diabetic cardiomyopathy in patients with type 2 diabetes, depending on the degree of albuminuria; 2) An association has been proven between elevated levels of GDF-15 and the presence of diastolic dysfunction, as well as with the severity of albuminuria, which confirms its role as a biomarker for early combined cardiorenal injury in individuals with diabetes; 3) It has been shown that GDF-15 has a stronger dependence on nephropathy than on isolated myocardial injury. The discovery supports the concept of a cardiorenal continuum and the role of GDF-15 as an integrative indicator of systemic stress and injury; 4) The combination of albuminuria >30 mg/24 h and elevated GDF-15 may be an early predictor of cardiorenal dysfunction, even before the clinical manifestation of diastolic dysfunction; 5) The correlation between GDF-15 and markers of inflammation, heart failure and renal function has been confirmed, which establishes GDF-15 as a multisystem biomarker reflecting the degree of systemic damage in diabetes; 6) A new approach for risk stratification is proposed by including GDF-15 in a diagnostic algorithm for diabetic cardiomyopathy, which builds on classical biomarkers and allows for a more precise assessment of subclinical damage, applicable in clinical practice; 7) The dissertation represents the first systematic study of GDF-15, performed by an endocrinologist in Bulgaria, with a contribution to the introduction of modern biomarkers in the assessment of diabetic complications

In relation to the topic of the dissertation, Dr. Desislava Ivanova Gorcheva has 6 publications in scientific journals.

The materials submitted under the procedure meet the requirements of the Regulation on the Development of the Academic Staff of the Republic of Bulgaria and the Regulations on the Development of the Academic Staff of Acibadem City Clinic UMBAL Tokuda EAD for the award of the scientific degree "doctor".

In conclusion, I believe that the dissertation work of Dr. Desislava Ivanova Gorcheva is complete, modern, thorough, well-structured and designed, with clear and precisely formulated and implemented tasks, with certain conclusions and contributions to both modern science and practice. All this gives me reason to recommend to the members of the esteemed scientific jury to award Dr. Desislava Ivanova Gorcheva the educational and scientific degree of "Doctor" in the field of higher education 7.3 Health and Sports, Professional field 7.1 Medicine, doctoral program "Internal Medicine"

05.05.2026

Sofia

Assoc. Prof. Dr. Alexander Ivanov Osichenko, D.M.