

## **REVIEW**

**By Prof. Valeri Lyubenov Gelev, MD, PhD  
Head of the Clinic of Cardiology,  
Acibadem City Clinic Tokuda University Hospital, Sofia**

*Regarding:* Dissertation thesis for acquisition of the educational and scientific degree “PhD” in the field of higher education 7. Healthcare and Sports, professional field 7.1. Medicine, doctoral program “**Internal Diseases**”.

**Author: Dr. Desislava Ivanova Gorcheva**

**Form of doctoral study: Independent training**

**Structural unit: Clinic of Internal Diseases**

**Topic: “Role of GDF-15 as a Prognostic Marker for Diabetic Cardiomyopathy in Patients with Type 2 Diabetes Mellitus and Diabetic Kidney Disease”**

**Scientific Supervisor: Assoc. Prof. Lachezar Boyanov Lozanov, MD, PhD**

### **1. General Presentation of the Procedure and the Doctoral Candidate**

The requirements concerning the dissertation procedure, including dissertation eligibility, topic selection, internal defense, and appointment of the Scientific Jury, have been fulfilled.

Dr. Desislava Gorcheva was enrolled as a doctoral student in independent training by Order No. 15-03-192#2 dated 07.06.2023 of the Executive Director and Procurator of Acibadem City Clinic Tokuda University Hospital. She completed her individual doctoral plan and successfully passed the doctoral minimum examination. On 25.03.2026, the completed dissertation thesis was presented and successfully defended before an extended Scientific Collegium of the Clinic of Internal Diseases. Subsequently, at a meeting of the Scientific Council (Protocol No. 65/08.04.2026), the doctoral candidate was granted the right to public defense. By Order No. 15-03-96#2 dated 16.04.2026, I was appointed as an internal member of the Scientific Jury in relation to the dissertation thesis of Dr. Desislava Ivanova Gorcheva. At the first remote meeting of the Scientific Jury, I was assigned to prepare the present review.

The dissertation thesis, abstract, and accompanying documents submitted by the doctoral candidate fully comply with the requirements of the Academic Staff Development Act in the Republic of Bulgaria, its implementing regulations, and the Regulations for Academic Staff Development at Acibadem City Clinic Tokuda University Hospital.

No plagiarism was identified according to the StrikePlagiarism.com metadata report.

I declare that I have no conflict of interest with the author of the dissertation thesis.

Dr. Desislava Gorcheva graduated in Medicine from the Higher Medical Institute – Sofia in 1994. From 1995 to 1999, she specialized in Internal Diseases at the Medical University – Sofia. Between 2003 and 2005, she specialized in Endocrinology and Metabolic Diseases at the Medical University – Sofia. In April 1995, she started work as a district physician in the village of Gorni Okol at the Municipal Hospital in Samokov. From 19.06.1995 to 29.08.1998, she worked as an emergency physician in the Internal Diseases Office at the Emergency Unit of the VIII Polyclinic in Sofia. From March 2001 to August 2005, she worked in the Internal Diseases Department at DCC “Dr. I.S. Greenberg” Ltd. Between August 2005 and December 2006, she served as a resident physician in the Endocrinology Department of the Fifth MHAT, Sofia. Since 05.12.2006, she has been working at the Department of Endocrinology within the Clinic of Internal Diseases at Acibadem City Clinic Tokuda University Hospital, and since August 2021 she has been Head of Department. Since October 2019, she has also been a part-time assistant lecturer in Propedeutics of Internal Diseases and Internal Diseases – Endocrinology for Bulgarian-language medical students at the Faculty of Medicine of Sofia University “St. Kliment Ohridski”.

At the Medical University – Sofia, she obtained postgraduate qualifications in “Abdominal Ultrasound and Superficial Structures” (2008), “Neck Ultrasound” (2010), and “Fine Needle Aspiration Biopsy in the Neck Region” (2015).

Dr. Gorcheva is a member of the Bulgarian Medical Association, the Bulgarian Society of Endocrinology, the Bulgarian Association of Thyroid and Parathyroid Diseases, and the Bulgarian Diabetes Association.

## **2. Relevance of the Topic**

Approximately one-third of patients with type 2 diabetes mellitus (T2DM) suffer from cardiovascular disease, while the prevalence of chronic kidney disease reaches up to 40%. Diabetic cardiomyopathy is a frequently underestimated complication leading to heart failure due to early diastolic dysfunction. Despite the known metabolic changes in the myocardium associated with diabetes, there is still no unified and effective diagnostic approach. Diabetic kidney disease is also an established risk factor for cardiovascular complications, yet the relationship between the degree of renal impairment and cardiovascular risk remains insufficiently clarified.

In recent years, new biomarkers for early myocardial injury have been investigated, including GDF-15 – a factor associated with tissue injury, increased cardiometabolic risk, and cardiovascular, renal, and diabetic diseases. Data regarding its diagnostic and prognostic value in patients with T2DM without overt cardiac pathology, as well as its application in Bulgarian clinical practice, remain limited.

The presented dissertation thesis focuses on the evaluation of diabetic cardiomyopathy and the role of GDF-15 in patients with T2DM and diabetic kidney disease. The topic is relevant and of clear practical significance.

### 3. Knowledge of the Problem

The doctoral candidate demonstrates excellent knowledge of the subject and approaches the reviewed literature analytically and creatively.

### 4. Structure and Content of the Dissertation

The dissertation thesis consists of 158 pages and includes 31 figures and 29 tables. Its structure comprises: Contents – 2 pages; Abbreviations and Symbols – 2 pages; Introduction – 3 pages; Chapter One: Literature Review – 45 pages; Chapter Two: Methodology of the Study – Objectives and Tasks – 2 pages; Materials and Methods – 14 pages; Chapter Three: Results – 30 pages; Chapter Four: Discussion – 29 pages; Chapter Five: Conclusions and Recommendations – 5 pages; Contributions – 2 pages; Bibliography – 23 pages; Publications and Scientific Forum Participation – 1 page. The bibliography contains 203 references, including 5 in Cyrillic and 198 in Latin script.

The *Introduction* clearly formulates the problem and justifies the purpose of the dissertation.

**Chapter One. The Literature Review** is competently written and demonstrates comprehensive knowledge of the topic in its various aspects. It presents an overview of cardiovascular and renal complications in patients with T2DM and discusses the mechanisms underlying their development. Particular emphasis is placed on the need to introduce novel biomarkers into clinical practice for the diagnosis and prognosis of renal damage and diabetic cardiomyopathy, one of which is GDF-15. Additional studies in different patient cohorts with strictly defined criteria are necessary to clarify the diagnostic and prognostic significance of GDF-15 and its independent role in cardiovascular risk stratification and early assessment of diabetic complications.

**Chapter Two describes the methodology** of the study, including aims, objectives, materials, and methods.

The *aim* of the dissertation is clearly formulated and consistent with both the dissertation topic and the literature review. Through analysis of cardiovascular risk factors and metabolic abnormalities in patients with T2DM, with and without diabetic kidney disease, the study aims to evaluate the prevalence of diabetic cardiomyopathy and the role of GDF-15 as a marker of early myocardial dysfunction and its potential clinical application.

Seven clearly formulated and feasible *tasks* have been set to achieve this objective.

A cross-sectional study was conducted. The section describes in detail the 131 patients treated between 2022 and 2025 at the Department of Endocrinology of Acibadem City Clinic Tokuda University Hospital, as well as 21 healthy controls. The sample size is sufficient to meet the study aims and objectives. Patients were divided

into five groups: Group A (diabetic patients without complications, n=32); Group B (diabetic nephropathy only, n=13); Group C (combined damage – diastolic dysfunction and diabetic nephropathy, n=26); Group D (diastolic dysfunction only, n=39); and Group E (healthy controls, n=21). Inclusion and exclusion criteria, as well as the applied methods, are clearly defined.

Appropriate statistical methods and SPSS version 22 software were used, ensuring the reliability of the obtained results.

The chosen *methodology* allows achievement of the stated objectives and provides adequate answers to the research questions addressed in the dissertation.

**Chapter Three: Results** The dissertation is distinguished by precision and clarity. The obtained results are well illustrated with statistically processed tables and graphs and correspond to the aims of the study. The most significant findings are as follows:

- Patients with T2DM demonstrate a pronounced metabolic, inflammatory, and cardiorenal profile, with progressive cardiorenal impairment observed as the disease advances.
- Diastolic dysfunction is a frequent early manifestation of diabetic cardiomyopathy and is associated with albuminuria, age, and duration of diabetes.
- The combination of albuminuria and elevated hsTroponin I, GDF-15, and IL-6 may serve as a marker of early subclinical myocardial injury.
- GDF-15 is associated with myocardial injury, renal dysfunction, inflammation, and heart failure, with the highest levels observed in patients with both diastolic dysfunction and diabetic nephropathy.
- The data identify GDF-15 as a potential diagnostic and prognostic marker for cardiorenal risk stratification in patients with T2DM, hypertension, and chronic kidney disease.

In **Chapter Four: Discussion and Analysis of Results**, the study results are discussed and analyzed in the context of the available literature and existing data. The results and their relevance for clinical practice are reviewed.

**Chapter Five: Conclusions and Recommendations.** Based on the results obtained, Dr. Gorcheva logically makes 11 conclusions and recommendations for the clinical application of the obtained data, which correspond to the tasks set. An Algorithm for the application of GDF-15 in practice for the assessment of cardio-renal risk in patients with type 2 diabetes without vascular pathology has been developed in 6 steps.

## **5. Main scientific contributions**

The main scientific contributions of the dissertation are 6, of which 3 are original. I accept that the first and seventh contributions overlap. The most important contributions are:

- For the first time in Bulgaria, the role of GDF-15 in patients with T2DM was investigated for the diagnosis and prognostic assessment of diabetic cardiomyopathy according to the degree of albuminuria.
- A relationship was established between elevated GDF-15 levels, diastolic dysfunction, and renal impairment.
- It was demonstrated that the combination of albuminuria and elevated GDF-15 may serve as an early predictor of cardiorenal dysfunction.
- Based on these findings, an algorithm for risk stratification and early detection of subclinical damage in diabetic patients was proposed.

**6. The abstract** is 54 pages long and reflects what is written in the dissertation work. According to the requirements, the contributions and available publications of the dissertation candidate on the presented topic are included in the abstract.

## **7. Assessment of the publications and personal contribution of the doctoral candidate**

The doctoral candidate has submitted 2 publications in national journals and 4 scientific communications in national and international scientific forums, 1 of which has a published summary in a journal with IF. In both of the submitted publications, Dr. Gorcheva is the first author, and in two of the scientific communications she is an independent author. This scientific activity is sufficient to show that the doctoral candidate meets the national minimum requirements for the educational and scientific degree "PhD".

## **8. Critical Remarks and Recommendations**

The following remarks may be made without diminishing the scientific value of the dissertation:

- Foreign words and expressions are used in certain parts of the text.
- Some references in the bibliography do not fully comply with the Vancouver citation style adopted by Acibadem City Clinic Tokuda University Hospital.

## **CONCLUSION**

The dissertation thesis of Dr. Desislava Ivanova Gorcheva is relevant and scientifically valuable. The work is written in an academic style and complies with the requirements of the Academic Staff Development Act in the Republic of Bulgaria, its

implementing regulations, and the regulations of Acibadem City Clinic Tokuda University Hospital.

Dr. Desislava Gorcheva is an experienced clinician with extensive professional practice in internal diseases and endocrinology, possessing strong theoretical knowledge and professional competence.

**Based on the above, I give my positive evaluation and recommend that the members of the Scientific Jury approve the dissertation thesis entitled “Role of GDF-15 as a Prognostic Marker for Diabetic Cardiomyopathy in Patients with Type 2 Diabetes Mellitus and Diabetic Kidney Disease” and award Dr. Desislava Ivanova Gorcheva the educational and scientific degree “PhD” in the field of higher education 7. Healthcare and Sports, professional field 7.1. Medicine, doctoral program “Internal Diseases”.**

05/26/2026

City of Sofia

Reviewer:

Prof. Dr. Valeri Gelev, PhD

