Cardiometabolic Health: The Missing Piece in Most Cardiovascular Evaluations

Position Paper

What the GLP-1 Era Is Revealing About the Limits of Standard Monitoring

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DOI: 10.5281/zenodo.19986186

Abstract

The rapid adoption of glucagon-like peptide-1 receptor agonists as cardiometabolic therapeutics has produced meaningful improvements in standard metabolic markers and demonstrated landmark reductions in major adverse cardiovascular events. Yet the monitoring infrastructure surrounding these medications has not kept pace with the physiologic complexity they introduce. Analysis of 63.4 million GLP-1 prescriptions over a six year period reveals that cardiologists write 0.4 percent of all prescriptions, while primary care physicians and advanced practice providers manage the overwhelming majority of patients on these potent metabolic agents within monitoring frameworks designed for glycemic and weight management oversight. Three significant physiologic gaps remain unaddressed within the current standard of care: sarcopenic metabolic compromise affecting lean muscle mass preservation, autonomic disruption evidenced by measurable reductions in heart rate variability and elevations in resting heart rate, and progressive micronutrient depletion during sustained appetite suppression. This paper presents a systems based physiologic framework for comprehensive cardiovascular monitoring and management of patients receiving GLP-1 receptor agonist therapy, grounded in published peer reviewed evidence and applied through the clinical model of Advanced Functional Cardiovascular Care. The position advanced is that true cardiometabolic care in the GLP-1 era requires evaluation of the vascular, autonomic, body composition, and cellular substrate dimensions of cardiovascular health that current guidelines and standard monitoring frameworks were not designed to reach.

Keywords: *GLP-1 receptor agonists, cardiometabolic health, cardiovascular monitoring, heart rate variability, autonomic dysfunction, sarcopenia, visceral adiposity, insulin resistance, micronutrient depletion, functional cardiology, preventive cardiovascular medicine, semaglutide, tirzepatide, SELECT trial, body composition, DEXA, VO2 Max, soft plaque, coronary CT angiography, parasympathetic tone, baroreflex, Zone 2 conditioning, cardiometabolic gap, GLP-1 cardiovascular physiology, systems based cardiovascular medicine*

What Cardiometabolic Health Actually Means

Cardiometabolic health is not a number on a laboratory report. It is the state of the body's most fundamental biological systems operating in concert: cellular energy production running efficiently, the endothelium maintaining its protective integrity, the autonomic nervous system regulating cardiovascular function with precision, and metabolically active muscle tissue preserving the body's capacity to process glucose efficiently. When these systems are aligned, the cardiovascular system operates with resilience. When any one of them is under sustained biological pressure, the others absorb that pressure and eventually express it.

The standard metrics used to monitor cardiometabolic health; body weight, hemoglobin A1c, and a routine lipid panel, are lagging indicators. They measure the shadows of a biological process that has been advancing long before any number crosses a clinical threshold. True cardiometabolic health requires a deeper standard of evaluation, one that reads the body as one interconnected biological system and investigates the origin of dysfunction rather than monitoring its surface expressions.

The Physiologic Connection

The cardiovascular system and the metabolic system are one interconnected biological web, governed by the same hormonal signals, the same inflammatory pathways, and the same autonomic regulatory architecture. When a powerful metabolic force enters that web, its effects do not stay contained within a single organ or specialty domain. They ripple across every system simultaneously.

Insulin resistance is the organizing force through which metabolic dysfunction reaches the cardiovascular system. As insulin sensitivity declines, visceral adipose tissue accumulates around the abdominal organs and begins to function as an active endocrine organ, releasing pro-inflammatory cytokines directly into the portal circulation. Those cytokines damage the endothelial lining of blood vessels, promote the formation of soft unstable plaque within the coronary and cerebral vasculature, and create the systemic inflammatory environment that advances silently for years before producing a visible cardiovascular consequence.

The same inflammatory burden reaches the atrial myocardium, altering its electrical environment and creating the substrate for rhythm disturbance. It engages the autonomic nervous system, progressively impairing its ability to regulate blood pressure, heart rate, and cardiovascular recovery with precision. It disrupts the hormonal architecture that governs vascular tone and cardiac resilience. It also impairs the kidney's capacity to maintain normal uric acid clearance, producing hyperuricemia as a metabolic signal that the system has exceeded its physiologic tolerance.

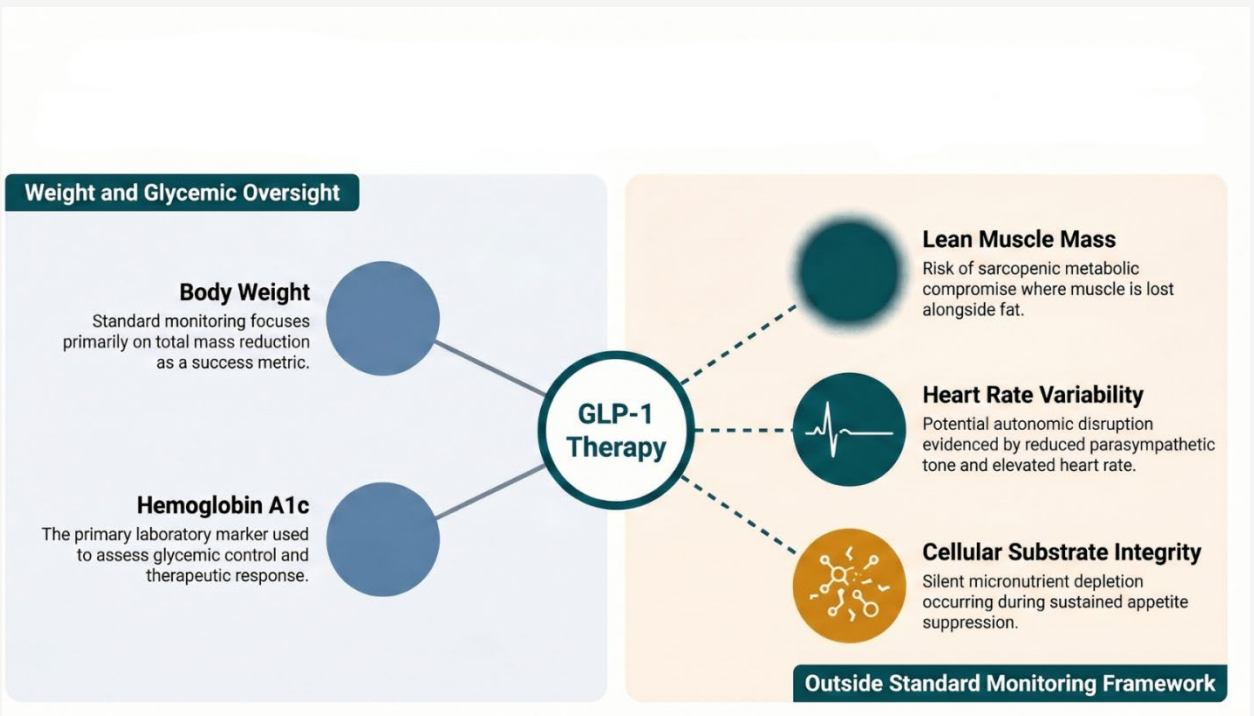

Figure 1. *The Three Unmonitored Physiologic Gaps of GLP-1 Receptor Agonist Therapy. Standard care monitoring frameworks track body weight and hemoglobin A1c as primary therapeutic endpoints. Three physiologic dimensions, sarcopenic metabolic compromise, autonomic disruption, and micronutrient depletion remain outside mandated monitoring protocols and may advance concurrently during treatment. Illustration created by the author based on evidence presented herein.*

The GLP-1 Era and the Gap It Has Exposed

Glucagon-like peptide-1 receptor agonists represent one of the most significant pharmacological advances in cardiometabolic medicine in a generation. The evidence is compelling and must be stated with the precision it deserves. The SELECT trial demonstrated a 20 percent reduction in major adverse cardiovascular events in patients with obesity and established cardiovascular disease. Clinical trials have demonstrated hemoglobin A1c reductions of 1.5 to 2.0 percent, weight loss of 7 to 24 percent, and improvements in standard lipid parameters proportional to weight loss. These are

genuine, landmark benefits supported by robust peer reviewed evidence. The medications work.

The question that cardiometabolic medicine has not yet fully answered is what is happening across the broader physiologic landscape during treatment, and whether the monitoring infrastructure currently in place is equipped to see it.

A 2022 analysis published in the Journal of the American Heart Association by Eberly and colleagues audited 63.4 million GLP-1 receptor agonist prescriptions over a six year period using IQVIA's National Prescription Audit, which captures approximately 90 percent of all United States retail prescriptions. The prescribing distribution was striking. Primary care physicians and internists wrote 53 percent of all prescriptions. Advanced practice providers wrote 22.9 percent. Endocrinologists wrote 21.1 percent. Cardiologists wrote 0.4 percent, representing 258,290 prescriptions of the 63.4 million total.

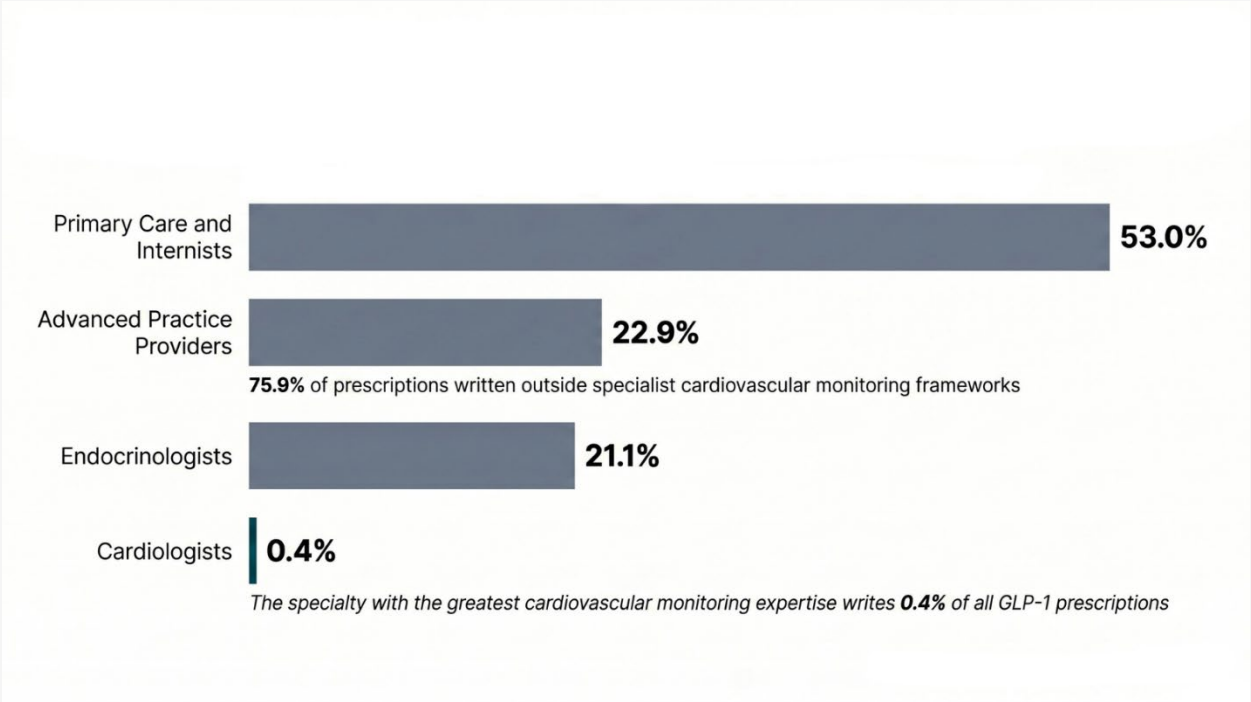

Figure 2. *GLP-1 Receptor Agonist Prescribing Distribution by Physician Specialty, 2015 to 2020. Analysis of 63.4 million prescriptions from the IQVIA National Prescription Audit demonstrates that cardiologists wrote 0.4 percent of all GLP-1 prescriptions during the study period. Primary care physicians, internists, and advanced practice providers collectively wrote 75.9 percent of all prescriptions within monitoring frameworks designed for glycemic and weight management oversight. Source: Eberly LA et al. Journal of the American Heart Association. 2022;11(9):e023811.*

More recent data from IQVIA in 2025 documents a 900 percent surge in GLP-1 prescribing by cardiologists following landmark cardiovascular approvals. That growth

reflects a significant and appropriate recognition by the cardiovascular establishment that metabolic dysfunction and arterial disease are expressions of the same underlying pathology viewed through different clinical lenses. Yet despite this historic growth, cardiologists represent between 1.5 and 3 percent of total GLP-1 prescribing volume. The overwhelming majority of patients undergoing these potent metabolic interventions remain managed within monitoring frameworks that were designed for glycemic and weight management oversight, not for comprehensive cardiovascular physiologic surveillance.

The American Diabetes Association, the American Heart Association, and the American College of Cardiology guidelines for GLP-1 therapy monitoring require hemoglobin A1c assessment, body weight, blood pressure, kidney function, and standard lipid panels at intervals of 3 to 6 months. These are appropriate parameters for the purposes those guidelines were designed to serve. They were not designed to characterize what is happening inside the vessel wall, within the atrial myocardium, across the autonomic nervous system, or within the body composition profile during rapid metabolic change. We have entered a highly complex era of medicine where the pharmacological tools have rapidly evolved, yet the clinical infrastructure tasked with monitoring their systemic impact has not kept pace.

Three significant physiologic gaps exist within the current standard of care for patients on GLP-1 therapy, each with direct cardiovascular implications that standard monitoring does not reach.

I. Sarcopenic Metabolic Compromise

The American Association of Clinical Endocrinology 2025 Obesity Algorithm defines successful obesity management as the improvement of Adiposity-Based Chronic Disease through the preservation of lean body mass. Within this specialist framework, body composition assessment using bioelectrical impedance analysis or DEXA scanning, protein titration at 1.2 to 1.5 grams per kilogram of body weight, and resistance training as a non-negotiable component of the therapeutic prescription represent the gold standard of care for patients receiving GLP-1 receptor agonist therapy. The AACE framework explicitly identifies sarcopenic obesity, the condition in which a patient loses muscle mass while remaining at an elevated adiposity burden, as a distinct and serious clinical risk of GLP-1 therapy that mandates active monitoring and prevention.

The prescribing reality that surrounds this gold standard tells a different story. Of the 63.4 million GLP-1 prescriptions audited by Eberly and colleagues, endocrinologists, the specialty most aligned with AACE guidance, wrote 21.1 percent. The remaining 75.9 percent were written within clinical environments where body composition assessment, protein titration, and resistance training prescription are not mandated components of the monitoring framework. Scale weight and hemoglobin A1c remain the primary measures of therapeutic success across the majority of GLP-1 prescribing. A patient who loses 40 pounds, 15 of which represent lean muscle mass, meets every standard metric of success. The metabolic consequence of that lean mass depletion, a collapse in basal metabolic rate, accelerated insulin resistance, diminished cardiovascular resilience, and a body composition trajectory that makes weight regain almost inevitable upon

medication discontinuation, remains outside the scope of what standard monitoring is designed to detect.

Prescribing a GLP-1 receptor agonist without a mandated muscle preservation protocol carries a clinical risk profile analogous to prescribing an anticoagulant without a falls prevention strategy. The therapeutic benefit is real. The physiologic vulnerability it introduces, when left unmonitored and unaddressed, is equally real.

The standard of care as practiced across the majority of GLP-1 prescribing environments has not yet incorporated what the science already requires. At Advanced Functional Cardiovascular Care, body composition assessment, lean mass monitoring, and individually calibrated metabolic conditioning are integrated components of the physiologic evaluation for every patient on GLP-1 therapy.

II. Autonomic Disruption

GLP-1 receptors are expressed not only in the gut and pancreas but densely throughout the central nervous system and within the sinoatrial node of the heart. A peer reviewed study published in the American Journal of Physiology, Heart and Circulatory Physiology by Grosicki and colleagues tracked 66 individuals using wearable technology across 12 weeks of GLP-1 receptor agonist initiation. Patients achieved significant weight loss of 10 percent alongside a statistically significant increase in resting heart rate of 3.2 beats per minute, a change mediated by a reduction in heart rate variability of 6.2 milliseconds, reflecting a measurable withdrawal of parasympathetic autonomic tone. Current monitoring guidelines from all major national bodies require no assessment of autonomic function or heart rate variability during GLP-1 therapy. This physiologic shift advances undetected and unaddressed within the standard of care.

III. Micronutrient Depletion

GLP-1 medications suppress appetite without discriminating between adequate and inadequate nutritional intake. Patients consume less without necessarily consuming better. Deficiencies in the micronutrients and cellular substrates upon which the heart's electrical system, mitochondrial function, and vascular integrity depend, develop silently. No standard monitoring protocol requires assessment of the intracellular biochemical environment during GLP-1 therapy.

What a Physiologic Systems Based Cardiovascular Investigation Looks Like

At Advanced Functional Cardiovascular Care, the standard of care for a patient on GLP-1 receptor agonist therapy begins where the current monitoring framework ends. Every dimension of the physiologic landscape that standard guidelines leave uncharacterized becomes the starting point for a comprehensive, physician directed investigation that reads the body as one interconnected biological system.

The Vascular Assessment

The vascular environment is assessed with a precision that standard lipid panels cannot provide. Advanced lipid particle analysis, including apolipoprotein B, lipoprotein particle number and size, and oxidized low density lipoprotein, characterizes atherogenic burden at the biological level where cardiovascular risk is actually produced. AI assisted coronary CT angiography with soft plaque characterization answers the question that every patient on weight loss therapy deserves to have answered. That question is whether the arterial burden is stabilizing, regressing, or advancing despite the improvements in standard metabolic markers. This is the difference between monitoring the shadow of cardiovascular risk and measuring the fire itself.

Body Composition and Metabolic Structural Integrity

Body composition is evaluated through DEXA scanning, which distinguishes visceral adipose tissue from subcutaneous fat and quantifies lean muscle mass with the precision that scale weight cannot approximate. This establishes whether weight loss is structurally sound, whether the metabolic foundation is being preserved or depleted, and whether the sarcopenic risk that GLP-1 therapy introduces is being actively monitored and addressed. A patient who appears lighter on the scale and improved on standard metabolic markers may simultaneously be losing the metabolic architecture that determines long term cardiovascular resilience. DEXA makes that trajectory visible.

Cardiovascular Fitness and Exercise as Clinical Intervention

Cardiovascular fitness is measured through VO2 Max and cardiopulmonary exercise testing, establishing aerobic reserve as the single strongest longitudinal predictor of cardiovascular survival as supported by medical literature. This assessment enables exercise to be prescribed as a targeted physiologic clinical intervention, individually calibrated to each patient's measured capacity and autonomic response, rather than applied as a generic lifestyle recommendation. For the patient on GLP-1 therapy whose lean mass and autonomic tone are both under physiologic pressure, the precision of this prescription carries direct and measurable therapeutic significance.

Autonomic Characterization and Recalibration

The autonomic dimension of GLP-1 therapy receives the rigorous evaluation the published evidence demands. Longitudinal heart rate variability monitoring through physician directed rhythm analysis characterizes the autonomic shift that GLP-1 receptor agonist therapy introduces at the level of the sinoatrial node and the parasympathetic nervous system. Where autonomic disruption is identified, AFCC applies a targeted recalibration strategy built around four validated physiologic pathways as characterized below:

I. Resonance Frequency Biofeedback

Resonance frequency biofeedback restores vagal tone through the synchronization of respiratory rhythm with baroreflex activity. The physiologic effect is confirmed by objective longitudinal rhythm monitoring that tracks the autonomic response to

intervention over time, providing a measurable and reproducible marker of parasympathetic restoration.

II. Zone 2 Metabolic Conditioning

Zone 2 metabolic conditioning is prescribed individually based on each patient's measured cardiovascular capacity and aerobic threshold. Sustained low intensity aerobic work at this physiologic zone builds mitochondrial density, increases stroke volume, and engages the parasympathetic nervous system in ways that higher intensity exercise does not. For the patient whose autonomic tone has been measurably diminished by GLP-1 therapy, this precision of prescription is a targeted clinical intervention.

III. Targeted Thermal Stress Interventions

Targeted thermal stress interventions activate the vagus nerve through well established physiologic mechanisms, engaging the parasympathetic nervous system through pathways that pharmacologic intervention does not address. The physiologic response to controlled thermal stress produces measurable autonomic recalibration that complements the other elements of the restoration protocol.

IV. Cellular Substrate Optimization

Cellular substrate optimization evaluates the intracellular biochemical environment upon which the cardiac conduction system, mitochondrial energy production, and vascular integrity depend. This is an environment that standard laboratory panels do not assess and that GLP-1 induced appetite suppression places under silent and progressive attrition. Restoring this environment is a prerequisite for sustainable autonomic recalibration and long term cardiovascular resilience.

Nutritional and Cellular Substrate Assessment

The nutritional foundation is assessed through comprehensive micronutrient and cellular substrate profiling, identifying specific deficiencies that develop beneath the surface of improved metabolic markers. This ensures the heart's biological environment is restored rather than depleted during weight loss. While appetite suppression produces visible metabolic improvement, it does not guarantee nutritional adequacy. At AFCC, metabolic optimization and nutritional integrity are treated as two distinct, equally critical clinical priorities.

Every finding from this investigation is interpreted by the physician across all systems simultaneously, integrated into a single biological picture, and translated into a personalized plan of care that addresses what that picture has revealed. The investigation is precise because the thinking that precedes it is precise. The care that follows is comprehensive because it is built on a complete biological story.

Who This Applies To

The physiologic gaps that GLP-1 therapy exposes belong to a broad and growing population whose biology is advancing through a profound metabolic transition without

the cardiovascular physiologic oversight that transition demands. The following portraits represent the patients whose stories deserve to be read completely.

The Vulnerable Legacy Patient

An adult with longstanding hypertension, borderline lipid values, and a family history of premature coronary artery disease is on GLP-1 therapy with improving standard metabolic markers. While these surface metrics stabilize, the vascular environment that preceded and produced those original risk factors continues to evolve during treatment. Its current status remains uncharacterized, leaving the underlying legacy of disease unaddressed despite visible metabolic progress.

The Hollowed Success Story

This patient has achieved dramatic weight loss on GLP-1 therapy. Standard metrics reflect clinical success by every conventional measure, yet the structural integrity of the metabolic foundation beneath that transformation has not been evaluated. What the body lost alongside the weight remains an open question that standard monitoring protocols are not designed to investigate.

The High-Performing Dysautonomic

A high-performing executive or athlete reports increased fatigue and recurring early morning palpitations since initiating therapy. Their wearable device reveals a persistently elevated resting heart rate that deviates significantly from their baseline. Despite these clear clinical signals, the specific physiologic dimension of the cardiovascular response producing this pattern remains unassessed and unaddressed. Within the current standard of care, these vital signs are often dismissed as benign side effects rather than being recognized as markers of autonomic dysregulation or cardiac substrate depletion.

The Normalized Numbers Patient

This patient presents with a normalized A1c and a reassuring standard cardiovascular profile. Yet, the deeper layers of physiologic function remain unexamined. A success in one clinical framework does not guarantee safety in another; standard tools were simply not designed to detect the silent attrition occurring beneath the surface.

The Symptomatic Success

A patient six months into GLP-1 therapy presents with progressive fatigue, cognitive dulling, and diminished physical stamina despite a standard metabolic profile that suggests clinical improvement. While the surface metrics stabilize, the internal biological environment governing mitochondrial energy production, cardiac electrical stability, and vascular integrity remains entirely unmonitored. This represents a dangerous clinical blind spot where rapid physiologic change and sustained appetite suppression occur without a roadmap of the cellular substrates required to sustain them.

The Proactive Patient

This individual is cardiovascular health-conscious, asymptomatic, and performing at a high level. Within the conventional monitoring framework, they present no clinical concern. However, they pose a sophisticated question that standard care is not equipped to answer: Is GLP-1 therapy producing genuine physiologic improvement, or is it merely optimizing the specific metrics the current system is designed to track? Answering this requires a depth of evaluation that transcends the original design and intent of standard clinical protocols.

The Standard This Era Demands

GLP-1 receptor agonists represent a genuine and significant advance in cardiometabolic medicine. The landmark evidence from the SELECT trial is compelling, the metabolic benefits are real, and the cardiovascular event reduction data marks a turning point in our understanding of the relationship between metabolic dysfunction and arterial disease. That progress deserves full acknowledgment.

What the GLP-1 era has also revealed, with equal clarity, is that the monitoring infrastructure surrounding these medications has not kept pace with the physiologic complexity they introduce. Standard metrics offer only a pinhole view of a vast underlying terrain. The vascular, autonomic, body composition, and cellular substrate dimensions of a patient's response to profound metabolic change require a depth of evaluation that standard care was never designed to provide.

At Advanced Functional Cardiovascular Care, this level of evaluation is the foundation of every patient relationship. The cardiovascular environment is assessed across every system simultaneously by a physician whose singular focus is decoding the biological reality beneath the surface. For the patient on GLP-1 therapy, this means the transformation is not simply celebrated. It is verified, protected, and optimized across every dimension that determines whether that success is genuinely durable.

The investigation reveals the origin. The protocol addresses it there.

Advanced Functional Cardiovascular Care

For further information regarding the AFCC framework and clinical protocols:
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Conflict of Interest Disclosure

The author declares no conflicts of interest regarding the publication of this paper.

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