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CARDIOMETABOLIC STRATEGIES IN HEART FAILURE AND CHRONIC KIDNEY DISEASE: FROM GLP-1 RECEPTOR AGONISTS TO IMPROVED QUALITY OF LIFE AND TECHNOLOGY-ENABLED CARE

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ABSTRACT

Heart failure (HF) and chronic kidney disease (CKD) frequently coexist and interact in a way that worsens prognosis, increases hospitalization risk, and reduces quality of life. This overlap is increasingly understood within the cardiovascular-kidney-metabolic (CKM) framework, which recognizes obesity, insulin resistance, type 2 diabetes, kidney dysfunction, and cardiovascular disease as interconnected components of a shared pathophysiological continuum rather than isolated disorders. In this context, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have attracted growing clinical interest because their actions extend beyond glycemic control and include body weight reduction, metabolic improvement, and favorable effects on selected cardiovascular and renal outcomes. The aim of this narrative review is to summarize the current evidence on GLP-1-based therapies in patients with HF and CKD, with particular emphasis on semaglutide, liraglutide, and tirzepatide. The review focuses on biological rationale, major clinical trials, practical implications, and the emerging role of precision phenotyping, digital health, wearable monitoring, and artificial intelligence in long-term CKM care. The structure of the review was informed by general scoping review principles, although it was not designed as a formal systematic review or meta-analysis. Available evidence suggests that GLP-1-based therapies may offer clinically meaningful benefits, particularly in patients with obesity, type 2 diabetes, HF with preserved ejection fraction (HFpEF), and CKD. Semaglutide has shown the strongest and most consistent evidence, improving symptoms, physical limitations, exercise capacity, and body weight in obesity-related HFpEF, while also reducing clinically important kidney outcomes in patients with CKD and type 2 diabetes. Liraglutide remains historically important because it helped establish cardiovascular benefit for the GLP-1 RA class, whereas tirzepatide represents a promising next-generation option in patients with a marked metabolic phenotype and obesity-related HFpEF. In conclusion, GLP-1-based therapies are becoming an important component of modern CKM care. Their relevance extends beyond glucose lowering and includes symptom improvement, better physical functioning, cardiovascular risk reduction, and kidney protection in selected populations. Future progress in this field will likely depend on more precise patient selection, better integration with existing cardiorenal therapies, and wider use of digital and phenotype-guided approaches to support individualized long-term care.

KEYWORDS

Heart Failure, Chronic Kidney Disease, Cardiovascular-Kidney-Metabolic Syndrome, GLP-1 Receptor Agonists, Semaglutide, Liraglutide, Tirzepatide, Hfpef, Digital Health, Wearable Devices, Precision Medicine

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1. Introduction

Heart failure (HF) and chronic kidney disease (CKD) are two of the most common and clinically significant chronic disorders in contemporary medicine. Their coexistence is not accidental. Cardiac dysfunction may reduce renal perfusion, worsen venous congestion, and promote neurohormonal activation. Declining kidney function, in turn, contributes to sodium and water retention, hypertension, inflammation, and difficulty maintaining optimal cardiovascular therapy. The result is a bidirectional interaction that increases symptom burden, hospitalization frequency, treatment complexity, and mortality risk. This interaction is particularly important because both conditions are highly prevalent, frequently coexist in older and metabolically burdened populations, and are associated with high residual risk even when guideline-directed treatment is used.

This relationship has traditionally been described as cardiorenal syndrome. More recently, however, clinical thinking has moved toward a broader cardiovascular-kidney-metabolic (CKM) framework. This model is more useful because it recognizes that obesity, insulin resistance, type 2 diabetes, CKD, and cardiovascular disease often arise from interconnected biological mechanisms rather than independent disease pathways. Chronic inflammation, endothelial dysfunction, altered adipose tissue biology, metabolic stress, neurohormonal imbalance, and maladaptive hemodynamics all contribute to disease progression across organ systems (Ndumele et al., 2023a, 2023b; Sebastian et al., 2024). In practical terms, this means that many patients are no longer best understood by a single diagnostic label, but rather by a broader, overlapping phenotype that spans several specialties at once.

This broader view is clinically important because it changes the way treatment is approached. Instead of targeting a single organ system, current management increasingly aims to address several interacting processes at once. In this context, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have become especially relevant. Initially introduced for the treatment of type 2 diabetes and later obesity, these agents are now recognized for effects that may also include cardiovascular benefit, renal protection, and improvement in symptom burden and functional status (Lincoff et al., 2023; Perkovic et al., 2024). Their clinical significance lies not only in lowering glycated hemoglobin, but in modifying the broader metabolic environment in which HF and CKD progress.

Their role appears particularly important in patients with obesity-related heart failure with preserved ejection fraction (HFpEF). This phenotype is often marked by severe exercise intolerance, high symptom burden, metabolic dysfunction, systemic inflammation, reduced physical capacity, and reduced daily functioning. In such patients, meaningful weight reduction and symptomatic improvement may have major practical value (Kosiborod et al., 2023, 2024). Importantly, this is one of the few areas in HF research where improvement in symptoms, functional performance, and patient-reported quality of life has emerged as a central signal of benefit rather than a secondary observation.

Among currently available agents, semaglutide, liraglutide, and tirzepatide are of particular interest. Semaglutide has the strongest current evidence for improving symptoms and quality of life in obesity-related HFpEF, as well as for reducing clinically important kidney outcomes in chronic kidney disease with type 2 diabetes (Kosiborod et al., 2023, 2024; Perkovic et al., 2024). Liraglutide was one of the first drugs in this class to demonstrate cardiovascular benefit in a major outcomes trial (Marso et al., 2016). Tirzepatide, as a dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 (GIP/GLP-1) receptor agonist, represents a newer therapeutic option for patients with a pronounced metabolic phenotype, especially obesity and HFpEF (Packer et al., 2025). Together, these drugs illustrate how cardiometabolic pharmacotherapy is evolving from glucose-centered treatment toward phenotype-oriented treatment.

Another reason this field is moving quickly is the rise of new technologies in chronic disease management. HF and CKD are both long-term disorders characterized by variability, recurrent destabilization, and substantial patient-to-patient heterogeneity. This makes them particularly suitable for digital monitoring, precision medicine, and artificial intelligence (AI)-supported care. Increasingly, researchers and clinicians are

exploring multimodal approaches that combine clinical data, imaging, biomarkers, remote physiologic signals, and machine learning-based pattern recognition to improve patient selection and long-term management (Abedi et al., 2025; Li et al., 2025; Rosano et al., 2024). In this sense, the future of CKM care is not only pharmacological, but also computational, personalized, and longitudinal.

2. Aim of the Review

The primary aim of this review is to summarize the current evidence on GLP-1-based therapies in patients with HF and CKD, with emphasis on semaglutide, liraglutide, and tirzepatide. The review focuses on biological rationale, major trial data, practical clinical implications, and the potential effect of these therapies on symptom burden, functional capacity, kidney outcomes, and quality of life. This objective is especially relevant because the expansion of GLP-1-based therapy into cardiorenal medicine has outpaced the ability of many clinicians to integrate the evidence into a coherent clinical framework.

A secondary aim is to broaden the discussion toward emerging technologies that may refine patient selection and support long-term monitoring. These include phenotype-guided treatment in HFpEF, biomarker and multimodal risk stratification, digital health interventions, wearable-based monitoring, and AI-assisted data interpretation. These additions are important because modern CKM care is increasingly shaped not only by new drugs, but also by new ways of measuring disease burden, functional limitation, and response to therapy over time.

A third aim is practical. The manuscript is written in a scientific but accessible style so that it can be used not only by subspecialists, but also by clinicians and researchers who need a clear overview of how modern CKM therapeutics and technology-enabled care may increasingly converge. Since HF, CKD, obesity, and diabetes are often managed across several disciplines, a review of this type should ideally support communication across specialties rather than reinforce academic silos.

3. Materials and Methods

This paper is a narrative literature review with elements of a scoping review. Its structure was informed by general reporting principles used in scoping reviews, although the goal was not to perform a formal systematic review or meta-analysis (Tricco et al., 2018). The emphasis was on synthesizing clinically relevant evidence rather than estimating pooled effect sizes. This approach was chosen because the topic spans several partially overlapping fields, including cardiovascular outcomes research, obesity pharmacotherapy, nephrology, digital medicine, and precision cardiology.

The review prioritized large randomized clinical trials, guideline-shaping scientific statements, and recent review articles relevant to the intersection of HF, CKD, obesity, and GLP-1-based therapy. Particular attention was given to the STEP-HFpEF, STEP-HFpEF DM, FLOW, LEADER, SELECT, and SUMMIT trials because these studies provide the most important contemporary evidence on symptom improvement, exercise capacity, body weight, cardiovascular outcomes, and kidney outcomes with semaglutide, liraglutide, and tirzepatide (Kosiborod et al., 2023, 2024; Lincoff et al., 2023; Marso et al., 2016; Packer et al., 2025; Perkovic et al., 2024). These trials were selected not only because of their size and visibility, but because they address the central clinical question of whether incretin-based therapy can modify more than one part of the CKM phenotype at the same time.

To address the technological dimension of the topic, the review also incorporated current work on CKM syndrome, precision phenotyping in HFpEF, digital health interventions for cardiometabolic disease, wearable-based cardiovascular monitoring, and AI-enabled remote care (Liang et al., 2024; Ndumele et al., 2023a, 2023b; Qi et al., 2025; Rosano et al., 2024; Xie et al., 2025). These sources were selected because they provide clinically meaningful frameworks rather than purely theoretical or technical commentary. In a field increasingly shaped by data streams and algorithmic stratification, it is not enough to discuss drug efficacy in isolation from the technologies that may eventually determine who receives those drugs and how response is tracked.

Because this is a narrative review, the manuscript should be interpreted as a structured synthesis of current knowledge and future directions rather than a definitive pooled quantitative evaluation of treatment effect. This also means that the review intentionally prioritizes coherence and translational usefulness over exhaustive enumeration of every available publication. Such an approach is particularly suitable for a rapidly evolving topic where several influential developments are very recent and where mechanistic and clinical literatures are still converging.

4. The Cardiovascular-Kidney-Metabolic Framework

The CKM framework is more than a new label. It provides a clinically useful way to understand why patients with obesity, type 2 diabetes, CKD, and HF often do poorly despite standard organ-specific management. Instead of viewing each condition as separate, CKM syndrome highlights cumulative biological stress across multiple systems. Excess adiposity, insulin resistance, systemic inflammation, endothelial dysfunction, altered substrate use, abnormal hemodynamics, and kidney impairment all interact over time and move the patient toward overt cardiovascular disease (Ndumele et al., 2023a, 2023b; Sebastian et al., 2024). This concept is particularly helpful because it explains why isolated, organ-centered care can leave major residual risk untreated.

This approach is highly relevant to HFpEF, which increasingly appears to be one of the most characteristic cardiovascular expressions of CKM disease. In many patients, HFpEF develops in the setting of central obesity, diabetes, sleep-disordered breathing, hypertension, reduced exercise capacity, and low-grade inflammatory activation. Rather than a single left ventricular problem, this phenotype reflects multisystem stress that includes vascular dysfunction, skeletal muscle deconditioning, renal impairment, altered body composition, and impaired metabolic flexibility. This explains why some patients with relatively preserved systolic function remain profoundly symptomatic and why therapies directed only at conventional hemodynamic targets may be insufficient.

CKM thinking also matters therapeutically. It encourages clinicians to use therapies that can target multiple parts of the syndrome simultaneously. Sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors) are one example. GLP-1 receptor agonists are another. Anti-obesity pharmacotherapy, blood pressure control, rehabilitation, and digitally supported lifestyle management all fit naturally within this model. The value of GLP-1-based therapy becomes much easier to understand when the patient is viewed through a CKM lens rather than a narrow disease-specific lens. This is one of the most important conceptual shifts in current medicine: drugs are increasingly judged not only by whether they improve one disease endpoint, but by whether they improve the overall syndrome phenotype.

Another strength of the CKM framework is that it emphasizes prevention and disease trajectory. It allows clinicians to think not only about late-stage HF or advanced CKD, but about earlier metabolic and vascular abnormalities that precede overt organ failure. This matters because interventions such as weight reduction, blood pressure control, early renoprotection, and metabolic therapy may have very different impact if introduced before irreversible remodeling is established. In this sense, the CKM framework provides both a descriptive and strategic model of care.

5. Mechanistic Rationale for GLP-1-Based Therapies

5.1. Metabolic and Systemic Effects

GLP-1 receptor agonists influence appetite regulation, energy intake, body weight, glycemic control, and broader metabolic function. In patients with obesity, type 2 diabetes, HF, and CKD, these effects may have direct and indirect clinical benefits. Reduction in body weight can reduce hemodynamic load, decrease blood pressure, improve insulin sensitivity, and reduce inflammatory burden. These changes are especially important in obesity-related HFpEF, where symptoms and exercise intolerance may be driven as much by systemic metabolic dysfunction as by classic cardiac impairment.

This is one reason GLP-1-based therapy has attracted so much interest in HFpEF. A treatment that reduces body weight while also improves symptom burden may have a more noticeable patient-level effect than therapies that primarily affect long-term risk but produce only modest changes in daily function. In clinical terms, this means patients may not only live longer or remain more stable, but also feel better and function better. For chronic diseases with high symptom burden, that distinction is not secondary; it is central.

GLP-1-based therapies may also have broader metabolic consequences beyond weight and glucose alone. In patients with obesity-related HFpEF, altered adipose tissue function, ectopic fat deposition, systemic inflammation, and impaired skeletal muscle metabolism likely contribute to reduced exercise capacity. Even if all mechanisms are not fully understood, the clinical response seen in recent trials suggests that modifying the metabolic milieu can alter the lived expression of heart failure. This is important because it supports a syndrome-based rather than chamber-based view of HFpEF.

5.2. Cardiovascular Effects

The cardiovascular relevance of GLP-1-based therapies extends beyond glycemic control. Weight loss, lower blood pressure, improved endothelial function, reduced inflammatory activity, and lower atherosclerotic risk may all contribute to benefit. In obesity-related HFpEF, these effects may reduce the mismatch between physiologic demand and limited reserve. In patients with established atherosclerotic cardiovascular disease, they may also reduce recurrent event risk. The clinical importance of this broader cardiovascular signal is that it suggests GLP-1-based therapies are not confined to the diabetology domain.

The SELECT trial is particularly important because it showed that semaglutide reduced major adverse cardiovascular events in people with overweight or obesity and established cardiovascular disease, even without diabetes (Lincoff et al., 2023). That result strongly supports the view that GLP-1-based benefit is not simply a consequence of glucose lowering, but rather reflects broader metabolic and vascular effects. This helps explain why enthusiasm for semaglutide expanded rapidly from metabolic medicine into preventive cardiology and heart failure research.

Another relevant point is that cardiovascular benefit may not look identical across all phenotypes. In some patients, the primary gain may be symptomatic and functional. In others, it may be risk reduction. In still others, benefit may lie in the ability to stabilize several risk pathways simultaneously. This reinforces the need to understand GLP-1 receptor agonists not only as drugs with one dominant endpoint, but as therapies whose value may differ depending on the biological and clinical profile of the patient.

5.3. Renal Effects

Renal benefit appears to involve several pathways, including better metabolic control, reduced albuminuria, lower inflammatory burden, and possibly hemodynamic or tubular effects that slow CKD progression. In patients with HF and CKD, this matters because preserving kidney function can stabilize the overall treatment plan. Worsening kidney function often leads to therapeutic compromises, especially in patients taking multiple cardiovascular medications. It can also intensify congestion, accelerate frailty, complicate diuretic use, and narrow the therapeutic window for several evidence-based interventions.

The FLOW trial provided a major step forward by showing that semaglutide reduced clinically important kidney outcomes in patients with type 2 diabetes and CKD (Perkovic et al., 2024). That finding makes semaglutide highly relevant not only to diabetology, but also to broader cardiorenal care. Additional analyses from FLOW suggest that semaglutide may remain beneficial irrespective of baseline SGLT2 inhibitor use, which is clinically relevant because future practice will often involve combination therapy rather than drug-class isolation.

Renal protection is especially valuable in CKM patients because it has implications far beyond the kidney itself. Stabilizing renal function may support more consistent use of decongestive therapy, renin-angiotensin system modulation, and other core cardiovascular treatments. It may also reduce clinical fragility and improve the feasibility of longitudinal multimodal management. In that sense, renal benefit should be interpreted as a systems-level advantage, not just a nephrology endpoint.

5.4. Symptom Burden and Quality of Life

The effect of GLP-1-based therapy on how patients feel is one of the strongest arguments for its relevance in HFpEF. For many patients, quality of life depends more on walking farther, feeling less breathless, and functioning better day to day than on changes in a single biomarker. In the STEP-HFpEF trials, semaglutide improved heart-failure-related symptoms, physical limitations, and exercise capacity in patients with obesity-related HFpEF (Kosiborod et al., 2023, 2024). These are meaningful outcomes because they directly reflect lived disease burden.

This feature is particularly important in HFpEF because one of the frustrations in the field has been the gap between traditional endpoints and patient experience. A therapy that alters symptoms, effort tolerance, and well-being may be especially relevant in a syndrome where disability and fatigue dominate the patient's perception of illness. This is one reason why semaglutide and tirzepatide have generated so much attention beyond conventional cardiovascular outcome discussions.

5.5. Safety, Tolerability, and Therapeutic Positioning

A more complete publication should also address safety and practical tolerability. GLP-1 receptor agonists are generally well known for gastrointestinal adverse effects, including nausea, vomiting, reduced appetite, abdominal discomfort, and sometimes diarrhea or constipation. In metabolically fragile patients with HF and CKD, these side effects can matter more than in standard obesity populations because they may affect oral intake, hydration, adherence, and willingness to continue treatment. This does not negate the value of these drugs, but it means their implementation requires practical skill, gradual titration, and realistic follow-up.

Therapeutic positioning also matters. GLP-1-based therapies should not be framed as replacements for established HF therapies, especially in patients who clearly meet criteria for agents with proven heart failure benefit. Instead, they are better understood as phenotype-oriented additions, particularly useful in obesity-related HFpEF, CKD with type 2 diabetes, and broader CKM overlap. This framing makes the treatment paradigm more rational and reduces the risk of exaggerated claims.

6. Clinical Evidence for Key Agents

6.1. Semaglutide

Semaglutide currently has the strongest evidence base across several clinically relevant CKM domains. In the STEP-HFpEF trial, semaglutide 2.4 mg improved heart-failure-related symptoms and physical limitations assessed by the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score, increased 6-minute walk distance, and produced substantial weight loss in patients with obesity-related HFpEF (Kosiborod et al., 2023). These findings were important because they showed that a metabolic therapy could produce significant symptom-level and functional benefits in a syndrome where patients often remain very limited despite conventional care.

The STEP-HFpEF DM trial extended these findings to patients with obesity-related HFpEF and type 2 diabetes. Semaglutide again improved symptoms, physical limitations, and body weight over one year (Kosiborod et al., 2024). The consistency across these two trials strengthened the case for semaglutide as a meaningful option in metabolic HFpEF. It also reduced the concern that the original positive result might have been overly dependent on a narrowly selected metabolic subgroup.

In the FLOW trial, semaglutide reduced the risk of clinically important kidney outcomes and death from cardiovascular causes in patients with CKD and type 2 diabetes (Perkovic et al., 2024). This trial broadened the significance of semaglutide beyond obesity or symptom management and positioned it as a drug with true cardiorenal implications. It also helped connect semaglutide with a clinically important question: whether one therapy can modify symptom burden, cardiovascular risk, and kidney trajectory at the same time.

The SELECT trial expanded its importance further by showing reduced major adverse cardiovascular events in patients with overweight or obesity and established cardiovascular disease, even in the absence of diabetes (Lincoff et al., 2023). Taken together, these data suggest that semaglutide sits at a clinically powerful intersection of obesity management, cardiovascular prevention, HF symptom relief, and kidney protection. That combination of domains is one reason semaglutide now occupies such a prominent role in CKM discussions.

Additional analyses also suggest that semaglutide's symptomatic benefit in HFpEF may persist across left ventricular ejection fraction categories within the studied obesity-related spectrum and may be accompanied by reduction in inflammatory burden. Although these analyses do not change the primary trial message, they strengthen the biological plausibility of the observed benefit and make the result feel less accidental.

6.2. Liraglutide

Liraglutide remains a landmark therapy because it helped establish cardiovascular benefit for the GLP-1 receptor agonist class. In the LEADER trial, liraglutide reduced major adverse cardiovascular events in patients with type 2 diabetes and high cardiovascular risk (Marso et al., 2016). Although LEADER did not specifically target the HF-CKD overlap, it shifted the field by showing that incretin-based therapy could improve hard cardiovascular outcomes. That shift was foundational for everything that followed.

This matters historically and clinically. It laid the foundation for later trials and helped transform GLP-1-based agents from drugs used mainly for glucose lowering into cardiometabolic therapies. Even though liraglutide is now often overshadowed by semaglutide and tirzepatide, it remains an essential reference point in the evolution of the field. A serious review should acknowledge this historical continuity, because current therapeutic enthusiasm did not emerge from nowhere; it developed stepwise through outcome trials that gradually redefined the class.

6.3. Tirzepatide

Tirzepatide is a dual GIP/GLP-1 receptor agonist and has generated substantial interest because of its potent effect on body weight and metabolic control. In the SUMMIT trial, tirzepatide reduced the risk of a composite outcome of cardiovascular death or worsening HF and improved health status in patients with HFpEF and obesity (Packer et al., 2025). These findings suggest that dual-pathway incretin therapy may be especially effective in patients with a marked metabolic phenotype.

Tirzepatide may therefore represent a next-generation step in phenotype-guided treatment. If future studies confirm long-term benefit across broader CKM populations, it may become an important option in patients whose disease burden is strongly linked to obesity and metabolic dysfunction. Post hoc and subgroup analyses from SUMMIT also suggest beneficial effects across important complementary domains, including health status and functional outcomes, which is especially relevant in HFpEF.

One of the most interesting implications of tirzepatide is conceptual. It suggests that deeper metabolic intervention may sometimes produce stronger heart-failure-relevant benefit in carefully selected phenotypes than older frameworks would have predicted. This does not mean obesity is the only driver of HFpEF, but it strongly supports the view that in some patients it is one of the dominant drivers.

6.4. Anti-Obesity Therapy in HF More Broadly

Beyond individual trial results, the growing use of GLP-1-based therapies reflects a broader change in the management of obesity in HF. Anti-obesity treatment used to be viewed as secondary or optional. That is no longer tenable in patients whose symptom burden and systemic risk are clearly driven by excess adiposity. Recent practical guidance has started to frame anti-obesity pharmacotherapy as a potentially important part of HF management in selected patients, especially when obesity is central to disease expression (Harrington et al., 2024).

This is not just about body weight as a number. In many patients, obesity affects hemodynamics, ventilation, mobility, sleep quality, inflammatory tone, and the ability to engage in physical activity. Effective anti-obesity therapy may therefore change the whole disease environment. It may alter not just risk but also what the patient can do, how the patient feels, and how intensively the patient can participate in rehabilitation or lifestyle change.

7. Precision Phenotyping and Personalization in HFpEF

HFpEF is increasingly understood as a syndrome made up of overlapping biological subtypes rather than a single condition. Some patients are predominantly hypertensive and elderly. Others are more strongly characterized by obesity, diabetes, systemic inflammation, and renal dysfunction. Still others show major atrial dysfunction, pulmonary hypertension, or skeletal muscle limitation. This heterogeneity is one reason broad therapeutic results in HFpEF have often been mixed.

Precision phenotyping aims to address that problem by identifying which subgroup a patient most closely resembles and then selecting therapies accordingly. Rosano et al. (2024) emphasized the growing importance of phenotype-targeted therapy in HF with mildly reduced ejection fraction (HFmrEF) and HFpEF. Rasalam et al. (2025) further argued that the field has entered a new therapeutic age in which precision medicine is becoming increasingly relevant in HFpEF. Machine learning-based phenotyping has also begun to show that patient clusters may differ not only in baseline biology, but also in treatment response (Li et al., 2025).

This is especially relevant to GLP-1-based therapy. These agents are unlikely to be equally useful across every HF phenotype. Their greatest value may lie in patients with a clear obesity-metabolic-inflammatory profile, especially when HFpEF coexists with type 2 diabetes, reduced exercise tolerance, and CKD. In this sense, the future of GLP-1 receptor agonist therapy in HF may depend less on universal use and more on identifying the right phenotype. This also makes the technology discussion more relevant, because better phenotyping may become one of the main determinants of appropriate prescribing.

A strong publication should also note that precision medicine in HFpEF is not simply a fashionable idea. It is a practical response to a problem that has limited therapeutic progress for years. If phenotypes are too biologically mixed, trial signals dilute and clinical decision-making becomes vague. By contrast, phenotype-oriented studies such as those focusing on obesity-related HFpEF may offer more actionable results and more reproducible symptom-level benefit.

8. Digital Health, Remote Monitoring, and Wearables

8.1. Digital Health in CKM Disease

Digital health approaches are becoming increasingly relevant in cardiometabolic prevention and chronic disease management. Liang et al. (2024) described how digital health tools can support disease prevention, self-management, and continuity of care across cardiometabolic conditions. Qi et al. (2025) similarly highlighted the growing role of digital interventions in cardiovascular prevention. These approaches matter because CKM care is inherently longitudinal and behavior-dependent. Patients do not deteriorate only in clinics; they deteriorate between visits.

For patients with HF and CKD, digital tools may help with medication adherence, symptom tracking, weight monitoring, blood pressure management, glycemic control, and behavior change. These interventions are particularly relevant in long-term diseases where success depends not only on prescribing the right therapy, but on maintaining it safely and consistently over time. In this sense, digital health is not merely a convenience layer; it may become part of the therapeutic architecture itself.

8.2. Wearable Devices

Consumer-grade and clinical wearables are becoming increasingly useful in cardiovascular care. They can now provide continuous or semi-continuous information about heart rate, rhythm irregularity, physical activity, sleep, and, in some settings, even hemodynamic trends. Jamieson et al. (2025) provided a practical guide to the role of wearables in cardiovascular care, while Nazir et al. (2025) and Xie et al. (2025) reviewed their broader value in cardiovascular monitoring and wearable sensor development.

In the context of GLP-1-based therapy, wearables could become especially useful for tracking functional response. Patients started on semaglutide or tirzepatide may improve gradually over months. Conventional follow-up may miss important changes in activity level, resting heart rate, exercise tolerance, or sleep behavior. Wearables could therefore provide a more continuous picture of whether the patient is actually functioning better. This may be especially useful in HFpEF, where changes in daily life often matter more to patients than isolated laboratory measures.

8.3. AI-Supported Care Pathways

AI-based systems are being explored as tools for pattern recognition, risk stratification, remote monitoring, and clinical decision support. Abedi et al. (2025) reviewed AI-driven real-time cardiovascular monitoring using wearable technologies. In chronic disease management, AI may eventually help detect subtle signs of decompensation, identify adherence problems, or cluster patients into more meaningful phenotypes. These possible uses are especially appealing in HF and CKD because both diseases evolve over time and produce complicated data that are difficult to interpret manually at scale.

In HF and CKD, this could be particularly useful because both conditions fluctuate over time and generate large volumes of longitudinal data. If these data can be integrated intelligently, clinicians may be able to intervene earlier and tailor therapy more effectively. That possibility remains partly aspirational, but the direction of the field is increasingly clear. Even if today's systems remain imperfect, the larger trajectory is toward more continuous, data-supported, individualized management.

8.4. Why Technology Matters Specifically for GLP-1-Based Therapy

A useful addition to a modern review is to explain why technology matters not just in general, but specifically in relation to GLP-1-based therapy. These drugs often require gradual titration, side-effect monitoring, weight tracking, adherence support, and attention to functional response. They are therefore unusually compatible with digital follow-up models. A therapy that changes symptoms, appetite, activity, and body weight over time is particularly suitable for remote and multimodal monitoring. This is another reason why the future of incretin-based therapy may be tightly linked to digital medicine rather than limited to prescription habits alone.

9. Practical Clinical Implications

From a practical standpoint, GLP-1-based therapies appear especially relevant in several patient profiles. The first is the patient with obesity-related HFpEF who remains highly symptomatic despite standard therapy. In this setting, semaglutide or tirzepatide may offer meaningful improvements in symptoms, exercise tolerance, and weight-related disease burden (Kosiborod et al., 2023, 2024; Packer et al., 2025). For clinicians, this is one of the most immediately actionable scenarios because the phenotype is recognizable and the clinical problem is often dominated by functional limitation.

The second is the patient with type 2 diabetes and CKD who also has high cardiovascular risk. In such patients, semaglutide may have value not only for glycemic control and weight reduction, but also for kidney protection and cardiovascular risk reduction (Lincoff et al., 2023; Perkovic et al., 2024). Here, the attraction lies in domain overlap: one therapy may contribute to renal stabilization, cardiometabolic improvement, and long-term event reduction at the same time.

The third is the broader CKM patient with multimorbidity, where the challenge is less about a single diagnosis and more about integrating several partial syndromes into one treatment strategy. Here, GLP-1-based therapy may function as one part of a layered approach that also includes SGLT2 inhibition, blood pressure control, rehabilitation, and digitally supported self-management. Clinical practice is therefore moving toward a model in which the key question is not merely whether these agents work, but which patient should receive them, at what stage, alongside which other therapies, and under what type of monitoring.

A fuller publication should also mention implementation barriers. Cost, access, reimbursement, therapeutic inertia, fragmented specialty care, and patient concerns about adverse effects can all limit real-world uptake. This matters because successful translation of trial evidence depends on more than efficacy; it depends on whether the health system can actually deliver the therapy to the right patients in a sustainable way.

10. Future Directions

Several future directions are likely to shape the field. First, more work is needed to define which CKM phenotypes derive the greatest benefit from GLP-1-based therapy. Precision phenotyping and machine learning may help identify these subgroups more clearly (Li et al., 2025; Rasalam et al., 2025). This is not just an academic refinement; it may directly determine treatment efficiency and outcome reproducibility in HFpEF research.

Second, digital monitoring needs to move from novelty to integration. Wearables, remote symptom capture, and AI-supported analysis are promising, but they will only matter if they fit into real clinical workflows and improve meaningful outcomes (Abedi et al., 2025; Jamieson et al., 2025; Xie et al., 2025). The next challenge is therefore not inventing more devices, but integrating them intelligently into routine longitudinal care.

Third, the field needs more long-term data. Current trials strongly support the role of semaglutide and increasingly support tirzepatide in carefully defined populations, but important questions remain unresolved. Clinicians still need clearer answers regarding when to introduce GLP-1-based therapy relative to SGLT2 inhibitors and other CKM therapies, which patient phenotype should trigger earlier use, and how to monitor and support therapy over the long term. Additional evidence is also needed in more diverse populations, including patients with more advanced frailty, different CKD severities, and broader real-world multimorbidity.

Fourth, future work will likely focus increasingly on combination strategies. The clinically relevant question is not whether semaglutide or tirzepatide works in isolation, but how incretin-based therapy interacts with SGLT2 inhibitors, diuretics, rehabilitation, obesity counseling, and digital follow-up. This systems-oriented view better reflects how real patients are treated.

11. Discussion

The current evidence base suggests that GLP-1-based therapies are moving from the edges of cardiology and nephrology into the core of CKM care. This shift is happening because these drugs align unusually well with the biology of metabolic HFpEF and diabetic CKD. They reduce body weight, improve metabolic control, improve symptoms in obesity-related HFpEF, and, in the case of semaglutide, improve clinically important kidney outcomes in diabetic CKD (Kosiborod et al., 2023, 2024; Perkovic et al., 2024). This combination of symptomatic, metabolic, renal, and cardiovascular relevance is difficult to ignore.

Semaglutide currently has the strongest overall profile because its evidence spans multiple clinically relevant domains: symptom and functional improvement in HFpEF, kidney benefit in CKD with diabetes, and cardiovascular event reduction in obesity-related atherosclerotic disease (Kosiborod et al., 2023, 2024; Lincoff

et al., 2023; Perkovic et al., 2024). Liraglutide remains foundational because it established cardiovascular benefit for the class (Marso et al., 2016). Tirzepatide is especially important because it suggests the next phase of incretin-based therapy may produce even larger effects in carefully defined phenotypes (Packer et al., 2025). These developments collectively suggest that obesity-directed metabolic therapy has become a serious part of cardiovascular and renal therapeutics rather than an external adjunct.

However, the larger story is not just about drugs. It is about a change in care logic. CKM syndrome has encouraged clinicians to think across organ systems rather than within traditional specialty silos (Ndumele et al., 2023a, 2023b). Precision phenotyping in HFpEF has challenged the field to stop treating heterogeneous populations as if they were biologically uniform (Rasalam et al., 2025; Rosano et al., 2024). Digital health and wearable monitoring have highlighted the possibility of continuous, patient-centered, longitudinal care rather than episodic care based only on clinic visits (Jamieson et al., 2025; Liang et al., 2024; Xie et al., 2025). These changes reinforce one another. Better phenotyping enables better prescribing, and better monitoring may enable better long-term persistence and response assessment.

When these developments are viewed together, a more coherent future begins to appear. In that future, a patient with obesity, type 2 diabetes, HFpEF, and CKD is not treated by four disconnected pathways. Instead, the patient is recognized as having a CKM phenotype, stratified more precisely, started on phenotype-relevant therapy, and followed with a smarter combination of symptom assessment, laboratory monitoring, and digital support. That future is not fully here yet, but the evidence increasingly points in that direction.

This review has several limitations. First, it is a narrative review and does not provide a formal systematic synthesis of evidence. Second, some of the discussed trials focused on specific patient phenotypes, particularly obesity-related HFpEF or type 2 diabetes with CKD, which may limit generalizability. Third, long-term comparative data across different GLP-1-based therapies are still limited. Fourth, the technological aspects of the field are advancing quickly, which means some current concepts in AI-supported care may mature, change, or be abandoned as evidence develops. These limitations are important, but they do not weaken the overall conclusion that the field is moving toward integrated, phenotype-aware, technology-enabled CKM care.

12. Conclusions

GLP-1-based therapies are becoming an important component of treatment for patients with cardiovascular-kidney-metabolic disease. Their relevance extends beyond glucose lowering and includes body weight reduction, symptom improvement, better physical function, cardiovascular benefit, and, in selected populations, kidney protection. Semaglutide currently has the strongest evidence across HFpEF, CKD, and obesity-related cardiovascular risk. Liraglutide remains a landmark therapy in the development of this field, and tirzepatide represents a highly promising next-generation option.

The importance of these therapies lies not only in the magnitude of their effects, but in the pattern of those effects. They act across domains that clinicians have historically treated separately: body weight, symptoms, physical limitations, kidney outcomes, and cardiovascular risk. This is precisely why they fit so naturally into the CKM framework. In the setting of obesity-related HFpEF and diabetic CKD, they offer a therapeutic logic that is broader, more integrated, and often more clinically intuitive than older organ-specific models of care.

The next phase of this area will depend not only on new molecules, but also on new methods of care. Precision phenotyping, multimodal monitoring, wearables, digital care systems, and AI-supported analysis may help identify the right patient, at the right time, for the right therapy. In other words, the future of GLP-1-based treatment in HF and CKD is likely to be both more personalized and more technology-enabled. This is especially relevant in heterogeneous syndromes such as HFpEF, where better classification may be just as important as better drugs.

What matters now is disciplined implementation. The field needs practical algorithms, equitable access, careful long-term follow-up, and realistic integration with existing cardiorenal therapy. It also needs honesty about what is already well supported and what still remains uncertain. Overstatement would weaken, not strengthen, the credibility of this area. The current data are already strong enough to justify serious clinical attention, especially for semaglutide and increasingly for tirzepatide in selected metabolic phenotypes.

A final and broader conclusion is that CKM care is no longer just about adding one more drug to a crowded treatment list. It is about rethinking the patient as a whole biological system. In that model, the most valuable therapies are not necessarily those that fit neatly into one specialty, but those that address the interactions between specialties. GLP-1-based therapies increasingly appear to be such agents. If future work continues to support their benefits across symptoms, kidney outcomes, cardiometabolic risk, and patient-centered functioning, they may become one of the central therapeutic bridges between endocrinology, nephrology, cardiology, obesity medicine, and digital chronic care.

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