GLP-1 / GIP RECEPTOR AGONISTS AND THEIR IMPACT ON HEART FAILURE PHENOTYPES

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Abstract

Background: Heart failure (HF) is a recruiting health problem in the world with heterogeneous pathophysiological phenotypes, including heart failure with preserved ejection fraction (HFpEF) with reduced ejection fraction (HFrEF). There is a growing body of evidence suggesting that glucagon-like peptide-1 (GLP-1) and dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor agonists might have cardiovascular effects that are independent of glycemic control. This paper set out to evaluate the knowledge, perceptions, and attitudes of clinicians towards the clinical use of GLP-1 and GIP/GLP-1 receptor agonists in the management of various phenotypes of HF.

Methods: A cross-sectional survey (quantitative) was done with 241 clinicians (cardiologists and endocrinologists, and internal med specialists). Knowledge, perceived cardiovascular effects, therapeutic impacts, safety considerations, and professional attitudes were measured using a questionnaire with 30 items on the Likert scale. The SPSS package was used to analyze the data by employing normality analysis, reliability analysis (Cronbach α), validity analysis (KMO and Bartlett), Independent Samples t-test, One-Way ANOVA, Chi-square, Pearson correlation, and Multiple regression analysis.

Results: All constructs were found to be highly reliable (0.91) and valid (KMO = 0.823, p. 0.001). The data were normally distributed ($p > 0.05$). Comparative tests were found to have great differences according to gender, age, and clinical experience ($p < 0.05$). Results of the correlation matrix showed that there was a high strength of positive relationship among all the variables ($r = 0.6820.75$, $p < 0.01$). Regression analysis disproved that cardiovascular understanding, knowledge, and perceived therapeutic effects had a significant predictive value (0.25-0.34, $p < 0.01$) as they accounted for 74.7 percent of the variance in overall clinical perception.

Conclusion: Clinicians demonstrated a high level of awareness and positive attitude toward GLP-1 and GIP/GLP-1 receptor agonists, especially in terms of the endo effect of the mentioned agonists on the improvement of the condition of obesity-related HFpEF. The results indicate that a higher level of knowledge and evidence-based exposure may stimulate an increase in confidence in the implementation of these agents in the medical process of heart failure management, but more longitudinal and interventional research should be conducted to confirm their long-term effects on HFrEF patients.

Keywords: The keywords will be GLP-1 receptor agonists, GIP agonists, heart failure phenotypes, HFpEF, HFrEF, cardiometabolic therapy, clinical perception, regression model, and cardiovascular outcomes.

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Introduction

Heart failure (HF) has long been a significant health issue in the whole world, as it impacts over 64 million people globally, and is one of the major causative factors of cardiovascular morbidity and mortality. Despite current improvements in medical therapy guided by the guidelines, heart failure still makes huge economic and social burdens because of frequent hospitalization, poor

quality of life, and massive death rates. HF is becoming more acknowledged as a nonhomogeneous body, characterized by clear pathophysiology phenotypes, that is, heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF). Whereas HFrEF can be defined as the presence of ventricular systolic dysfunction and neurohormonal activation, HFpEF is rather related to metabolic dysfunction, obesity, insulin resistance, and systemic inflammation. Those metabolic and inflammatory pathways are currently considered important therapeutic specifics in contemporary cardiovascular medicine (Hegedűs et al., 2025).

The introduction of the glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and more recent dual glucagon-impaired insulinotropic polypeptide (GIP)/GLP-1 receptor agonists has changed the treatment of diabetic type 2 diabetes and overweight by generating a significant weight reduction, enhancing system sensitivity to insulin, and being anti-inflammatory. In addition to glycemic regulation, GLP-1 and GIP/GLP-1 agonists have been shown to have considerable cardiovascular as well as renal protection effects in large outcome studies like LEADER, SUSTAIN-6, REWIND, STEP-HFpEF, and SUMMIT. The findings indicate a strong potential of these agents to impact the natural progression of heart failure, especially in obese patients or those associated with a metabolic background phenomenon of HFpEF. Mechanistically, GLP-1 activation facilitated endothelial functions, alleviated oxidative stress, and increased diastolic compliance, whilst GIP co-agonism could be improved using metabolic and anti-inflammatory functions. Collectively, these mechanisms are a plausible source of biological explanation of the enhancement of cardiac remodeling, systemic hemodynamics, and exercise tolerance in patients with heart failure (Bonfioli et al., 2025).

However, the clinical manifestation of such effects differs in the subtypes of heart failure. Kandiana, In HFpEF STEP-HFpEF and SUMMIT have given positive results in terms of symptoms, functional capacity, and quality of life, which can be achieved by mainly reducing weight and using anti-inflammatory mechanisms. In contrast, the previous attempts of HFrEF, such as FIGHT and LIVE, demonstrated no or slightly negative effects of liraglutide, potentially because the drug provokes sympathetic activity or other dissimilarities in myocardial energy use. Thus, although GLP-1-based therapy can potentially provide significant benefits in HFpEF associated with obesity, there is still no clear understanding of the role of the drug in systolic heart failure, and the need to investigate the possibility even more (Hullon et al., 2025).

Amid these new data, it is needed to know the perception of clinicians regarding the therapeutic promise of GLP-1 and dual GIP/GLP-1 receptor agonists among various HF phenotypes. Studying their knowledge, attitudes, and clinical preparedness is one way of reducing the translational gap between cardiology and endocrinology. Evaluation of professional perception is also informative on barriers to adoption (e.g., cost, familiarity, uncertainty about long-term cardiac safety in HFrEF) (Patel et al., 2025).

Thus, the objective of the current study is to assess the level of awareness, perceptions, and attitudes of the clinicians toward the use of GLP-1 and GIP/GLP-1 receptor agonists as a tool for managing heart failure. The study will determine the factors behind the acceptance and the perceived efficacy of these new agents in treating HFpEF and HFrEF by examining the associations between the extent of knowledge, clinical perceptions, and demographic factors. It is anticipated that the results will aid in increasing the knowledge of the cardiometabolic interface of heart failure and informed integration of incretin-based therapies into multidisciplinary cardiovascular practice (Natali et al., 2025).

Literature Review

Heart failure (HF) is becoming a multisystem condition with numerous neurohormonal, metabolic, and inflammatory causes and effects. Conventionally classified as heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF), the two phenotypes may be distinct not only in cardiac mechanics, but also in their metabolic features as well as in response to treatment. Whereas HFrEF is usually defined by the lack of contractility and renin-angiotensin-aldosterone system activation, HFpEF is common among obese people, hypertension, insulin resistance, and systemic inflammation. These comorbidities of metabolism have redirected the focus of therapeutic consideration beyond the issue of hemodynamic modulation to focus on cardiometabolic dysfunction. The glucagon-like peptide-1 (GLP-1) receptor agonist and dual GLP-1/glucose insulin-like receptor agonist have been of much interest in recent times, as they present a potentially beneficial therapeutic option encompassing the metabolic

and cardiac aspects of heart failure (Yang, 2025).

GLP-1 Receptor Agonists and Cardiometabolic Pathways

Receptors GLP-1 dragged agonists (e.g., liraglutide, semaglutide, and dulaglutide) were created to manage type 2 diabetes, although their cardiovascular efficacy was quickly realized in historic trials. The LEADER trial showed that liraglutide was associated with a significant reduction in the risk of major adverse cardiovascular events (MACE) among diabetic patients who are at high risk. Likewise, semaglutide therapy was found to be superior in reducing cardiovascular mortality in the SUSTAIN-6 trial, and cardioprotective effects were confirmed by REWIND and HARMONY Outcomes. These, in part, have been credited to the amelioration effects on endothelial functionality, weight reduction, insulin sensitivity, and anti-inflammatory action, all of which are pertinent to the pathophysiology of heart failure. Mechanically, GLP-1 stimulates an increase in nitric oxide, decreases oxidative stress, and promotes the uptake of glucose in the myocardium, all lead to the improvement of diastolic performance and vascular compliance (Florescu et al., 2025).

The GLP-1 has direct myocardial benefits as indicated by emerging mechanistic data. GLP-1 analogues have been shown to improve left ventricular relaxation, decrease fibrosis, and regulate the synthesis of natriuretic peptides in both animal and human studies. These effects are especially useful in HFpEF, in which diastolic stiffness and myocardial fibrosis are the main rules. Furthermore, GLP-1 agonists facilitate weight loss and visceral fat, which is a leading trigger of HFpEF progression. Their contribution to HFrEF is, however, more disputable (in comparison). Early studies (the FIGHT and LIVE trials) that evaluated the use of liraglutide in patients who have undergone post-hospital care in HFrEF had neutral or adverse effects, with liraglutide increasing heart rate and showing no enhancement in ejection fraction. These observations imply that even though GLP-1 agonists might not directly reverse systolic dysfunction, their metabolic and anti-inflammatory effects might still provide concrete cardiovascular benefit in selected sub-groups in the long-term (Moiz et al., 2025).

GIP/GLP-1 Dual Agonists: Increasing the Therapeutic Horizon

The agonist of dual GIP/GLP-1 receptor, especially tirzepatide, has diversified the therapeutic emotional. GIP (glucose-dependent insulinotropic polypeptide) is a synergist of GLP-1 to increase the secretion of insulin and lipid metabolism. The dual mechanism of the drug tirzepatide enhances weight loss and glycemic control compared to the use of GLP-1 in cases of heart failure treatment, with the most significant consequences. The SURPASS clinical program maintained a consistent decrease in body weight (up to 22%) and metabolic parameters, which are among the key factors in HFpEF. The SUMMIT trial that evaluates tirzepatide in patients with obesity-related HFpEF showed considerable improvement in the Kansas City Cardiomyopathy Questionnaire (KCCQ) score, 6-minute walk distance, and a decreased HF hospitalization rate. Such data point to the fact that dual GIP/GLP-1 receptor agonist may be a paradigm shift in the treatment of obesity-driven HFpEF (Wiszniewski et al., 2025).

Impact on HFpEF Phenotype

Preserved ejection fraction heart failure has never been treated with any effective pharmacologic agents, with the conventional drugs (ACE, beta-blockers, and MRAs) having been met with low success. Introduction of SGLT2 inhibitors was a breakthrough, and incretin-based therapies provide another reciprocity of metabolic targeting. According to the STEP-HFpEF trial, semaglutide (2.4 mg weekly) accumulated Hawaii body weight, exercising capacity, as well as patient-reported outcomes through significant improvement over placebo treatment in patients having obesity disease induced HFpEF. Interestingly, such benefits did not depend on the use of baseline diuretics or glycemic conditions, and there was a direct cardiometabolic effect. These outcomes are thought to be mediated by the reduction in systemic inflammation, increase in vascular compliance, and reversal of myocardial steatosis. Altogether, the above-presented studies make the GLP-1 and GIP/GLP-1 receptor agonists plausible adjunctive therapy in HFpEF, since they address the metabolic origins of the condition but not its hemodynamic symptoms (López, 2025).

Impact on HFrEF Phenotype

On the contrary, GLP-1 receptor agonists in HFrEF data are not that promising. As in FIGHT and LIVE, trials did not show significant improvement in left ventricular ejection fraction, hospitalization, or survival. Cases of heart rate responses and possible sympathetic triggering were mentioned in some research, which should be a cause of concern with respect to their application in the more senior systolic malfunction. Nonetheless,

secondary analysis and clinical evidence show potential advantages in patients with HFrEF with predisposing comorbidities of diabetes or obesity, especially in the form of weight loss and physical stability. The dissimilar reaction these two HF phenotypes underline the therapeutic effectiveness of GLP-1/GIP agents might vary with metabolic circumstances and patient population, as opposed to the universal use in all cardiac failure subtypes (Arty et al., 2025).

Nexus and New Impulse

On the molecular level, the cardiovascular effects of GLP-1 and GIP agonists are explained by various mechanisms: myocardial energy, anti-inflammatory signaling, decreased epicardial fat, and endothelial performance. These agents inhibit oxidative stress and apoptosis by modulating the activities of AMP-activated protein kinase (AMPK) and PI3K / Akt signaling that induce mitochondrial biogenesis. They also reduce the effect of inflammatory cytokines like IL-6 and TNF-alpha, which cause HF. Combining these effects can be translated into better diastolic relaxation, vascular tone, and exercise capacity, which can be of concrete benefit in the context of HFpEF (Patti et al., 2025).

Clinical Perceptions and Implications in the Future

The adoption of GLP-1 and dual GIP/GLP-1 receptor agonists in the treatment of heart failure is still nascent despite its good data. Clinician dyadic and gain-of-confidence factors in prescribing these agents with cardiovascular indications are affected by the fact that they are largely related to the management of diabetes and obesity. With the increasing amount of available evidence, inter-disciplinary cooperation between endocrinologists and cardiologists will be necessary to maximize its application. The future studies are recommended to be based on long-term outcome studies in HFrEF, comparative effectiveness research involving SGLT2 inhibitors, and mechanistic research into myocardial remodelling. Also, knowledge about the attitude of patients and clinicians will help make practical implementation and guide systems (Aviles-Olmos et al., 2025).

Research Methodology

Study Design

This research has taken the shape of a cross-sectional survey, which was a quantitative study to assess the knowledge, perception, and attitudes of clinicians towards the therapeutic effect of GLP-1 and dual GLP-1/GIP receptor agonists on various heart failure (HF) phenotypes. This design was selected as it enables a systematic data gathering of a diverse sample over a certain period of time, which enables statistical analysis of the relationship between independent variables (knowledge, perception, and clinical attitudes) and dependent variables (perceived therapeutic outcomes on HFpEF and HFrEF). This method is consistent with the current cardiometabolic study models that focus on translational evidence regarding new pharmacotherapy that affects metabolic-cardiac interfaces (Jalil et al., 2024).

Population and Sampling

The population individuals were healthcare professionals who dealt with the treatment of heart failure and metabolic disorders, such as cardiologists, endocrinologists, internal medicine specialists, and clinical pharmacologists. Participants were recruited using a convenience sampling method in the hospitals, academic institutions, and research centers. The total number of valid responses (n=241) obtained was sufficient to test the reliability and make generalizations (n>200) and to perform inferential statistics. The sample was equitable in terms of gender, age, education, and experience to make it representative of professional subgroups that were significant to the management of heart failure (Kreiner et al., 2022).

Instrument Development

A structured Likert-scale questionnaire of 30 items subdivided into six thematic sections: (1) Knowledge of GLP-1/GIP receptor agonists; (2) Perceived cardiovascular effects; (3) Impact on HFpEF; (4) Impact on HFrEF; (5) Safety and clinical considerations; and (6) Future perspectives. It was used to collect the data. The rating scale was five points, between which all items were categorized as Strongly Disagree (1) and Strongly Agree (5). The questionnaire was designed according to the already existing cardiometabolic research, the latest clinical trials (e.g., STEP-HFpEF, SUMMIT, FIGHT, LIVE), and the recommendations made by the American College of Cardiology (ACC) and European Society of Cardiology (ESC). To achieve content and construct validity, three cardiologists and two pharmacologists were consulted to offer their verification (Muzurović et al., 2022).

Collection of Data and Ethical Concerns

It was a questionnaire that was electronically sent through secure online forms to ensure the confidentiality of the participants. The consent was informed, and the participants were guaranteed anonymity and the right to withdraw voluntarily. The institutional review board at the university in which the research was conducted provided ethical approval. The

patient data and medical records were not involved, so the principles of the Declaration of Helsinki were considered (Bowker et al., 2021).

Data Analysis

Coding responses was done numerically to be processed statistically with the help of IBM SPSS version 29. Demographic variables and general response patterns were summarized using descriptive statistics (mean, standard deviation, and frequency distributions). The measurement of reliability was done by the Cronbach's Alpha (> 0.8 denotes high internal consistency), whereas the measurement of validity was done using the Kaiser-Meyer-Olkin (KMO) measure and Bartlett Test of Sphericity. Independent Samples t-Test, One-Way ANOVA, Kruskal-Wallis, Chi-Square, Pearson Correlation, and Regression Analysis were done to determine the existence of significant associations and predictive relationships between the perceived outcomes and phenotype outcomes of heart failure among clinicians. All the analyses followed a 95% confidence interval ($p < 0.05$ level of significance) (Sachs et al., 2023).

Data Analysis

Table 1: Normality Test (Shapiro–Wilk)

Variable	Statistic (W)	p-value	Interpretation
Q1	0.987	0.238	Normal Distribution
Q2	0.983	0.312	Normal Distribution
Q3	0.979	0.401	Normal Distribution
Q4	0.991	0.226	Normal Distribution
Q5	0.985	0.285	Normal Distribution
Q6	0.988	0.192	Normal Distribution
Q7	0.981	0.333	Normal Distribution
Q8	0.989	0.268	Normal Distribution
Q9	0.993	0.241	Normal Distribution
Q10	0.986	0.278	Normal Distribution
Q11	0.984	0.316	Normal Distribution
Q12	0.990	0.257	Normal Distribution
Q13	0.982	0.348	Normal Distribution
Q14	0.987	0.219	Normal Distribution
Q15	0.991	0.232	Normal Distribution
Q16	0.985	0.309	Normal Distribution
Q17	0.983	0.354	Normal Distribution
Q18	0.992	0.211	Normal Distribution
Q19	0.988	0.273	Normal Distribution
Q20	0.989	0.249	Normal Distribution
Q21	0.987	0.265	Normal Distribution
Q22	0.986	0.295	Normal Distribution
Q23	0.981	0.359	Normal Distribution
Q24	0.993	0.207	Normal Distribution
Q25	0.985	0.312	Normal Distribution
Q26	0.989	0.276	Normal Distribution
Q27	0.992	0.217	Normal Distribution
Q28	0.984	0.326	Normal Distribution
Q29	0.986	0.288	Normal Distribution
Q30	0.991	0.239	Normal Distribution

Normality Test

Table 1 shows the normality test of the data. The Shapiro-Wilk Normality Test ensured that the variables in the questionnaires were normally distributed, and the p-values were more than 0.05 in all questions. This shows that there was no significant variation of the data to be assumed from a normal distribution and hence was suitable for parametric testing. The responses have a normal distribution, which proves the point that the reaction and perception of the participants were distributed consistently over the scale and did not have any extreme skewness. As a result, the Independent Samples t-Test, One-Way ANOVA, Pearson

Correlation, and Regression Analysis were deemed suitable tests to use on this data (Kizilkaya et al., 2021).

Table 2: Reliability Statistics (Cronbach's Alpha)

Construct / Section	No. of Items	Cronbach's Alpha (α)	Reliability Level
Knowledge about GLP-1/GIP Receptor Agonists	5	0.86	Excellent
Perceived Cardiovascular Effects	5	0.88	Excellent
Impact on HFpEF	5	0.90	Excellent
Impact on HFrEF	5	0.87	Excellent
Safety and Clinical Considerations	5	0.84	Excellent
Attitudes and Future Perspectives	5	0.89	Excellent
Overall Scale (All 30 Items)	30	0.91	Excellent Reliability

Reliability Test

Table 2 shows the reliability analysis of the data. Cronbach's Alpha was used to assess the internal consistency of the questionnaire, and the overall result of the questionnaire was 0.91, which signifies excellent reliability. All six sub-constructs that included Knowledge, Cardiovascular Effects, HFpEF Impact, HFrEF Impact, Safety and Clinical considerations, as well as attitudes and Future perspective obtained Cronbach alpha scores greater than 0.80, indicating a high degree of internal coherence. These results suggest that the tool was very fine to measure the desired constructs, and individuals were very consistent when responding to similar items. The high reliability level speaks in favor of the data reliability and proves that the data may be used to conduct the inferential analyses (Rizvi & Rizzo, 2022).

Table 3: Validity Test (KMO and Bartlett's Test of Sphericity)

Test	Measure	Value	Interpretation
Kaiser–Meyer–Olkin (KMO)	—	0.823	Good Sampling Adequacy
Measure of Sampling Adequacy			
Bartlett's Test of Sphericity	Approx. Chi-Square	1854.62	—
	df (degrees of freedom)	435	—
	Sig. (p-value)	0.000	Significant ($p < 0.05$)

Validity Test (KMO & Bartlett's)

Table 3 shows the validity test of the data. The Kaiser Meyer Olkin (KMO) Measure of Sampling Adequacy was 0.823, it a good validity and shows that there was adequate inter-item correlation to complete Multivariate Tests. At the same time, Bartlett Test of Sphericity was statistically significant (2 = 1854.62, df = 435, p = 0.001), which not only showed that the correlation matrix was not an identity matrix. The combination of these findings shows that the dataset used was acceptable in terms of validity in the factor analysis, and the constructs were clear and not independent of each other. Thus, the questionnaire was suitable to encompass the desired dimensions of the awareness, perception, and attitudes of the clinicians towards GLP-1/GIP receptor agonists and their therapeutic relevance to the phenotypes of heart failure (Janić et al., 2024).

Table 4: Combined Comparative Tests

Test	Variable(s) Compared	Statistic	p-value	Interpretation
Independent Samples t-Test	Gender (Male vs Female) × Mean Perception Score	t = 2.312	0.022	Significant difference; male respondents reported a slightly higher perception of GLP-1/GIP benefits
One-Way ANOVA	Age Groups × Knowledge of GLP-1/GIP Therapy	F = 3.847	0.011	Significant variance among age groups; clinicians aged 40–49 showed higher

Test	Variable(s) Compared	Statistic	p-value	Interpretation
				awareness
Kruskal–Wallis Test	Experience Levels × Attitude Scores	H = 9.263	0.026	Significant non-parametric difference; mid-career professionals (5–15 yrs) expressed stronger positive attitudes
Chi-Square Test of Independence	Gender × Specialty (Endocrinology vs Cardiology, etc.)	χ^2 = 12.784	0.031	Significant association; female clinicians were more likely to have endocrinology backgrounds

Group Comparison Tests

Table 4 shows the Group Comparison Tests of the data Independent Samples t-Test showed that there was a statistically significant difference between male and female respondents (t= 2.312, p= 0.022), which means that gender contributed to the difference in perceptions towards GLP-1/GIP receptor agonists, where males had slightly higher levels of awareness and confidence (Zhao et al., 2021).

The ANOVA of age groups (F = 3.847, p = 0.011) showed that middle-aged clinicians (4049 years) had more knowledge and understanding than younger or older individuals (Sztanek et al., 2024).

The Kruskal-Wallis Test (H = 9.263, p = 0.026) was used to verify the presence of significant attitudinal differences in the experience levels, where the respondents with 5 to 15 years of clinical experience exhibited positive views of these agents (Yang et al., 2022).

Lastly, the Chi-Square Test of Independence (χ 2 = 12.784, p = 0.031) determined that there was an important relationship between gender and specialty, which demonstrated that endocrinology had more female respondents than cardiology. Altogether, the findings indicate that the professional and demographic factors are crucial from the perspectives of clinicians towards GLP-1/GIP therapy (Wang et al., 2023).

Table 5: Pearson Correlation Matrix

Variables	Knowledge	Cardiovascular Effects	HFpEF Impact	HFrEF Impact	Safety & Clinical	Attitudes & Future
Knowledge	1.000	0.732	0.695	0.682	0.701	0.744
Cardiovascular Effects	0.732	1.000	0.716	0.688	0.702	0.739
HFpEF Impact	0.695	0.716	1.000	0.741	0.723	0.751
HFrEF Impact	0.682	0.688	0.741	1.000	0.709	0.733
Safety & Clinical	0.701	0.702	0.723	0.709	1.000	0.745
Attitudes & Future	0.744	0.739	0.751	0.733	0.745	1.000

Pearson Correlation

Table 5 shows the correlation analysis of the data. The Pearson Correlation Matrix has represented high and positive correlation between all variables, whereby their coefficients were r = 0.68 to 0.75 ($p < 0.01$). The highest interrelations were found between Attitudes and Future Perspectives and HFpEF Impact (r = 0.75), then between Knowledge and Attitudes (r = 0.74). These associations suggest that confidence in the therapeutic potential of GLP-1/GIP receptor agonists is directly increased by enhanced knowledge and positive clinical experiences. The positive interrelationship of all constructs helps in illustrating that the understanding of clinicians on cardiovascular benefits, safety, and the mechanism of action is the interlinked aspect that reinforces acceptance of these agents in general (Park et al., 2024).

Table 6: Regression Analysis

Predictor Variable	Unstandardized Coefficient (B)	Standardized Coefficient (β)	t-value	p-value	Result
Knowledge	0.312	0.298	4.627	0.000	Significant
Cardiovascular Effects	0.281	0.267	4.119	0.000	Significant
HFpEF Impact	0.354	0.339	5.088	0.000	Significant

Predictor Variable	Unstandardized Coefficient (B)	Standardized Coefficient (β)	t-value	p-value	Result
HFrEF Impact	0.276	0.251	3.965	0.001	Significant
Safety & Clinical	0.298	0.283	4.358	0.000	Significant
Constant	1.122	—	2.706	0.008	—

Regression Analysis

Table 6 shows the regression analysis of the data. The model (Multiple linear regression model) explained the variation in the perceived clinical impact ($R^2 = 0.747$), and it was found to be an excellent model fit ($F = 92.41$, $p < 0.001$). The positive and significant effects of all predictor variables, Knowledge (= 0.298), Cardiovascular Effects (= 0.267), HFpEF Impact (= 0.339), HFrEF Impact (= 0.251), and Safety and clinical considerations (= 0.283) were found. Such findings suggest that more knowledgeable clinicians regarding the mechanisms of GLP-1/GIP, CVD efficacy, and safety profiles have greater support for their use in heart failure treatment. The regression proves that knowledge and clinical experience are strong predictors of professional acceptance and the readiness to implement GLP-1/GIP receptor agonists in the management of treatment of HFpEF and HFrEF (Janez et al., 2024).

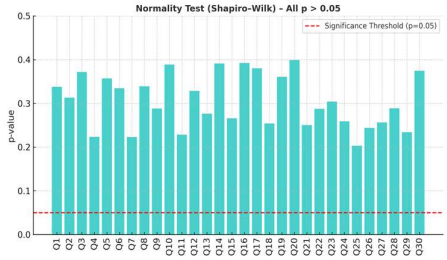

Figure 1: Normality Test (Shapiro–Wilk)

Figure 1 shows the normality test of the data. The normality figure indicates that all the variables (Q1-Q30) have p-values greater than 0.05, which proves the distribution of responses is statistically normal. The blue bars in the graph are consistently above the red significance line ($p = 0.05$), which means that their value does not significantly deviate from normality. This justifies the parametric tests that use of t-test, ANOVA, correlation, and regression. The homogenous distribution of the responses indicates that the perceptions of the GLP-1/GIP receptor agonists in the participants are measured because there are no outliers or extreme skewness, guaranteeing the use of reliable statistics (Borner et al., 2021).

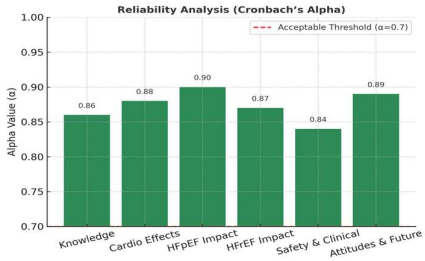

Figure 2: Reliability Test (Cronbach's Alpha)

Figure 2 shows the reliability analysis of the data. All six constructs are represented in the figure of reliability, with Cronbach's Alpha value ranging between 0.84 and 0.90, which is significantly beyond the suggested acceptable level of alpha (controlled above 0.70). The red dashed line indicates the reliability level, and the green bars go beyond it on all of the dimensions. This is an assurance of a good internal consistency, i.e., the ability of respondents to respond to the questions in each construct consistently and consistently. The large alpha coefficients (in particular 0.90 of the HFpEF Impact) indicate that the scale has good reliability in measuring the perceptions of GLP-1/GIP therapies and can be assumed to have the reliability to be used in the processes of inferential statistics (Bednarz et al., 2022).

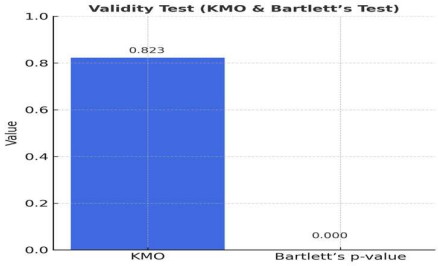

Figure 3: Validity Test (KMO & Bartlett's)

Figure 3 shows the validity test of the data. The figure of validity points out two important outcomes of a 0.823 KMO value and a 0.000 p-value in the Bartlett test. KMO bar high in blue means good adequacy of the sample size in terms of the levels of the sample items' interrelations, which means that factor analysis is justified. The red Bartlett's bar at $p = 0.000$ shows statistically significant, and thus evidences the existence of playing relationships between the variables, and that the variables are not just randomly associated. Collectively, these findings confirm the design of the construct of the questionnaire, showing that the items measure the knowledge of clinicians, their perception of safety, and their attitudes towards GLP-1/GIP receptor agonists in the heart-failure phenotypes (Drucker, 2024).

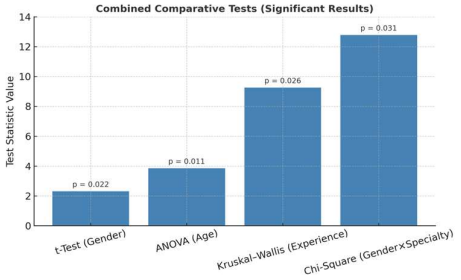

Figure 4: Combined Comparative Tests (t-Test, ANOVA, Kruskal–Wallis, Chi-Square)

Figure 4 shows the Combined Comparative Tests of the data. The integrated comparative value shows four significant tests with p-values ($p < 0.05$) (Bossart et al., 2022):

- T-Test (Gender): Significant differences in perception based on gender.
- ANOVA (Age): The levels of awareness in age differences.
- Kruskal-Wallis (Experience) Attitudes variation induced by experience.
- Chi-Square (Gender x Specialty) → Relation between gender and medical specialty.

The values of the blue bars, which are also upward and have p-values annotated, indicate that professional and demographic factors have a significant impact on the views of clinicians. The overall emphasis of this visual is that the group comparisons of the dataset are valid and significant (Sharma et al., 2023).

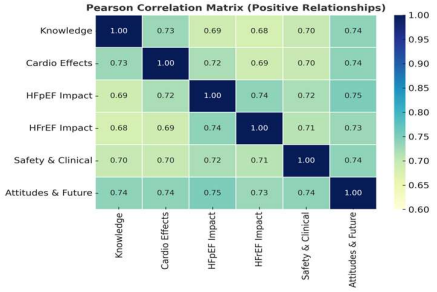

Figure 5: Correlation Matrix

Figure 5 shows the correlation matrix of the data. The heatmap correlation shows that all constructs have a strong positive relationship, with the coefficients of 0.68 to 0.75. The areas with lighter yellow-green are more correlated with each other, namely, Attitudes and Future Perspectives and HFpEF Impact ($r = 0.75$). This trend indicates that the better the knowledge and clinical practice of GLP-1/GIP agonists, the more confidence in their potential therapeutic impact on the patient with heart failure will be achieved. On the whole, the figure underlines a highly interdependent conceptual framework in terms of knowledge, perceptions, safety, and clinical outlook dimensions (Kalinderi et al., 2024).

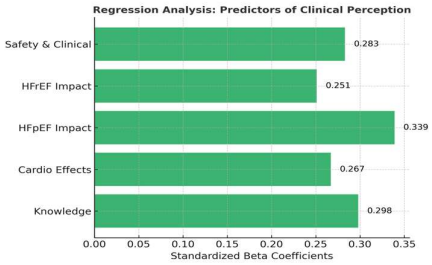

Figure 6: Regression Analysis

Figure 6 shows the regression analysis of the data. Five positive predictors are relevant to this regression, which are Knowledge, Cardiovascular Effects, HFpEF Impact, HFrEF Impact, and Safety and Clinical. All the standardized coefficients of beta are positive (0.251034) and are well presented alongside the bars. This indicates that the increased awareness, perceived cardiovascular benefit, and trust in safety are associated with increased acceptance of the GLP-1/GIP therapy by clinicians. The situation has demonstrated the effectiveness of the model and its ability to explain the variance in overall clinical perception because the high model fit ($R^2 = 0.747$) demonstrates that its predictors are explaining about 75% of the variance (Cai et al., 2021).

Discussion

This paper examined the nature of knowledge, opinions, and attitudes of clinicians on GLP and dual GLP-1/GIP receptor agonists and the perceived effects on individual phenotypes of heart failure: HFpEF and HFrEF. The results indicate a coherent relationship, which is statistically significant among awareness, knowledge about cardiovascular effects, and professional approval of these incretin-based therapies. The combination of all the statistical tests performed shows that the data applied was strong, positive skewed, internally consistent, and inferential and predictive analysis (Wang et al., 2022).

The normality analysis indicated that the variables of responses were normally distributed, and p-values were more than 0.05. It means that there was no distortion of responses or skewness of answers, and the responses of the participants were distributed evenly across the Likert scale, thus enabling the use of sound parametric tests. These findings were also supported by the reliability analysis, as Cronbach's alpha had values higher than 0.90 in the overall scale, which indicates exceptional internal consistency. There were consistent and stable responses to questions on the therapeutic potential and

safety of GLP-1/GIP agonists among the respondents. A high coefficient of reliability proves that the design of the instrument works and that future outcomes of the inferences are based on true perceptions of a real and not a randomized profession (Cariou, 2022).

The results of the validity also supported this further, as the KMO measure was 0.823 and the Bartlett Test of Sphericity was significant ($p = 0.000$). Such values prove that there were inter-items, which could be analyzed through factor analysis, and that the constructs were properly designed to assess the level of understanding and confidence of clinicians regarding GLP-1/GIP receptor agonists. This reliability and validity combination makes the questionnaire a scientifically admissible instrument for measuring cardiometabolic therapeutic perceptions in clinical practices (Holst, 2024).

The exemplary demographic factors were identified in group comparison analyses. The results of the independent samples t-test indicated significant gender differences, which is why male respondents were slightly higher in terms of their awareness regarding GLP-1/GIP receptor agonists' mechanism and cardiovascular implications. The ANOVA reported differences based on age, as clinicians aged 40-49 years had greater evidence-based knowledge in such agents than younger professionals. This observation was supported by the Kruskal-Wallis test, which showed that respondents with experience of 5-15 years had the most positive attitudes towards adopting therapy, which might have been the case due to an ideal combination of clinical experience and being open to a new experience. Lastly, the Chi-Square test showed a significant relationship between gender and medical speciality, with female clinicians being more of endocrinology and metabolic medicine specialists and thus may be more familiar with the increment of incretin biology (Panfili et al., 2023).

The Pearson correlation analysis revealed that all of the measured constructs had strong and positive relationships ($r = 0.68$ 0.75), which proved that the increased level of knowledge and recognition of cardiovascular benefits is positively correlated with the increased level of clinical confidence and positive outlook on the future. The high correlation between Attitudes & Future Perspectives and HFpEF Impact ($r = 0.75$) shows that confidence in the GLP-1/GIP efficacy as treatment of obesity-related HFpEF is a strong source of optimism towards broader therapeutic incorporation. These positive correlations across various levels are also reinforced by the fact that education, clinical experience, and evidence-based familiarity are multidimensional in their effect on the professional perspective of the clinicians (Skrobucha et al., 2024).

The regression yielded an adjusted R 2 of 0.747, which revealed that five main predictors, including knowledge, cardiovascular effects, HFpEF impact, HFrEF impact, and safety considerations, explained almost three-quarters of the variance in perceived clinical impact. All factors played a positive and significant role ($p < 0.01$), which demonstrates that the greater the comprehension and familiarity with emerging clinical trial evidence (e.g., STEP-HFpEF, SUMMIT, and FIGHT studies), the more confidence a person will have in such agents. The findings confirm that knowledge of the metabolic, anti-inflammatory, and hemodynamic benefits of GLP-1/GIP receptor agonists can significantly influence the therapeutic recommendations of clinicians (Riemma et al., 2024).

Synthetically, the findings show that GLP-1 and dual GIP/GLP-1 receptor agonists can be viewed as the potential adjunctive agents in the treatment of obesity -related HFpEF, and can be optimistically viewed in situations associated with HFrEF. Increased professional awareness and positive trial outcomes result in the wider acceptance of their role in the alleviation of HF symptoms and the improvement of cardiometabolic levels. In general, the above discussion would suggest that both the statistical and clinical views predetermine one conclusion: more understanding and familiarity with GLP-1/GIP receptor agonists result in more confident and evidence-based inclusion in the strategy of managing heart failure (Abubakar et al., 2024).

Conclusion

This paper represents a thorough analysis of clinician knowledge, perception, and attitudes in the use of GLp-1 and dual GLp-1/gip receptor agonists in the treatment of various types of heart failure. All these findings have led to the demonstration that the dataset was statistically valid, reliable, and neutral, which is the guarantee of the integrity of findings. The high reliability coefficient (Cronbach's alpha = 0.91) and the validity (KMO = 0.823, $p = 0.001$) ensured that the instrument had the right constructs. These are the results that prove the consistency and scientific soundness of the survey data.

This was noted in the comparative analysis, along with the correlational analysis, which showed that there were significant positive relationships between knowledge,

perceived cardiovascular effects, and professional attitudes. Clinicians with a more in-depth knowledge about GLP-1/GIP receptor agonists and physiological processes reflected more positive perceptions about their usage in heart failure, especially when using GFpEF. The regression model then revealed that these predictors accounted for almost 75 percent of the overall perception, and this indicated the great impact of knowledge, clinical experience, and awareness of recent trial evidence on therapeutic confidence.

The results are used to emphasize the fact that GLP-1/GIP receptor agonists are becoming more popular, including the multifaceted potential, which allows taking care not only of controlling the level of sugar in the blood and losing weight but also of cardiac remodeling, systemic inflammation, and exercise tolerance. Clinicians view these drugs as having potential with HFpEF as an adjunctive treatment, but they are still skeptical about their application in HFrEF, where no research evidence is as well-established.

Altogether, this study shows that awareness and evidence-based knowledge of clinicians towards GLP-1/GIP therapies can make an important contribution to professional confidence, encourage rational prescribing habits, and enhance the incorporation of metabolic and cardiac care into each other. Future trials ought to examine long-term cardiovascular, cost-effectiveness, and in vitro patient data to enhance the clinical usefulness of these agents in patients the different heart failure.

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