Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i4.5668

EFFECTS OF NOVEL THERAPIES ON HEART FAILURE PATIENTS INVESTIGATE THE EFFICACY AND SAFETY OF EMERGING TREATMENTS OR THERAPIES FOR HEART FAILURE MANAGEMENT

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Abstract

Background: Heart failure (HF) is a serious worldwide health issue that is defined by the heart's incapacity to adequately pump blood to meet the body's needs

Objective: The research main objective was to examine the safety and effectiveness of novel medications or treatments for the management of HF.

Methodology: The purpose of this prospective cohort study was to assess the safety and effectiveness of new heart failure treatments at MTI Lady Reading Hospital Peshawar, Pakistan. A total of 320 adult patients with heart failure (HFpEF or HFrEF) were enrolled between 1st April 2020 and 26th March 2023. Comprehensive data was collected using structured data collecting forms, and treatment outcomes were assessed using follow-up examinations conducted at 3, 6, and 12 months. Subgroup studies based on HF subtype were planned, and descriptive and inferential statistical analyses were used to compare results between innovative and traditional therapy.

Results: The groups' baseline characteristics were comparable. The mean ejection fraction increased by +8.4% (±3.6) in the Novel Therapy group (NTG) and +5.9% (±2.8) in the Standard Therapy group (STG) ($p < 0.001$). Furthermore, improvement in NYHA functional class was observed in a larger proportion of patients in the NTG (76.2% vs. 62.5%, $p = 0.013$). According to the Kansas City Cardiomyopathy Questionnaire, the group receiving novel therapy had a considerably higher quality of life (45.7 ± 6.3) than the group receiving standard therapy (39.5 ± 7.1) ($p < 0.001$). The group receiving Novel Therapy saw fewer hospitalizations (15.6%) for worsening heart failure than the group receiving Standard Therapy (23.8%) ($p = 0.049$). There was no discernible difference in mortality rates across the groups (6.3% vs. 9.4%, $p = 0.214$).

Conclusion: Comparing novel therapy to established treatments, there were notable improvements in heart function, symptom management, and quality of life. These results highlight the necessity for ongoing research and individualized treatment plans, and they promote the inclusion of novel therapies in HF care protocols.

Keywords: Heart failure, Novel therapies, Emerging treatments, Personalized medicine.

Introduction

Heart failure (HF) is a serious worldwide health issue that is defined by the heart's incapacity to adequately pump blood to meet the body's needs [1,2]. Patients suffer from symptoms like exhaustion, dyspnea, and fluid retention as a result, which severely lowers their quality of life [3]. The management of heart failure (HF) is still difficult despite improvements in medical research. Therefore, in order to enhance patient outcomes, new medications must be continuously explored and evaluated [4].

There has been a surge in interest in creating novel treatments for HF outside of traditional pharmaceutical approaches within the last few decades [5]. Gene therapy, stem cell therapy, device-based interventions, and tailored pharmacotherapies are only a few examples of the diverse range of innovative therapies available today. Each strategy seeks to address distinct pathophysiological pathways that underlie HF and has the potential to completely transform the field of HF treatment [6]. For example, gene therapy holds the potential to alter genetic variables that contribute to the development of HF, addressing underlying defects and regaining cardiac function [7, 8]. Conversely, stem cell therapy investigates how injured heart tissue may be repaired by stem cells, promoting myocardial healing [9]. Furthermore, device-based therapies like cardiac resynchronization treatment (CRT) and left ventricular assist devices (LVADs) have shown promise in managing advanced heart failure (HF) by providing mechanical support and enhancing cardiac function [10].

Targeted pharmacotherapies that are customized to each patient's unique profile are being developed in conjunction with these interventions with the goal of achieving improved efficacy and fewer side effects in comparison to conventional drugs [11]. These pharmacological advancements frequently target certain pathways, such as neurohormonal regulation, myocardial energetics, and inflammation, that are implicated in the pathophysiology of HF [12].

Notwithstanding the enthusiasm around these innovative treatments, it is crucial to thoroughly assess their safety and efficacy. In this sense, clinical trials are crucial because they inform evidence-based practice and offer insightful information about how beneficial these therapies are in real-world settings [13].

Objective:

The research main objective was to examine the safety and effectiveness of novel medications or treatments for the management of HF.

Material and Methods

Study Design and Setting:

This study was carried out in the tertiary care MTI Lady Reading Hospital Peshawar, Pakistan, using a prospective cohort design. The time frame for the study was 1st April 2020 to 26th March 2023 The main location for data gathering was the hospital's cardiology department, which is well-known for its cutting-edge infrastructure and proficiency in the treatment of heart failure. The prospective cohort design was selected in order to monitor treatment outcomes and safety profiles related to new HF medicines by following the participants over an extended period of time.

Inclusion and Exclusion Criteria

Adults with HF who are willing to take part in the study, receiving treatment at LRH in Peshawar, Pakistan, between 1st April 2020 and 26th March 2023, and who can undergo follow-up exams at three,

six, and twelve months are eligible to be diagnosed with heart HF. It is necessary to have access to comprehensive data, including demographic information, medical history, baseline clinical features, laboratory results, echocardiography findings, and prescription histories. Patients who did not meet the inclusion criteria or who did not have a HF diagnosis, were unable or unwilling to give informed consent, received treatment outside the hospital during the study period, were enrolled outside of the specified time frame were unable or unwilling to participate in follow-up exams, did not receive either standard or novel therapies for the management of HF, and had incomplete or missing data.

Sample Size:
Based on a 95% confidence level and a 5% margin of error, the sample size was determined. The sample size was determined based on the predicted prevalence of favorable response to new medicines in patients with HF. In order to achieve sufficient statistical power for identifying noteworthy alterations in treatment results between the innovative medicines and traditional treatments, a sample size of 320 individuals was determined to be reasonable.

Data Collection:
Comprehensive data, including demographics, medical history, baseline clinical features, laboratory tests, echocardiography results, prescription schedules, and specifics of new therapies taken, were gathered using an organized data collecting form. Predetermined intervals, such as three, six, and twelve months, were used for follow-up evaluations to examine treatment effectiveness, safety results, illness progression, and patient-reported outcomes.

Statistical Analysis:
The study population's baseline characteristics were compiled using descriptive statistics, such as averages with standard deviations or the medians with interquartile variability for continuous data, and incidences with ratios for categorical variables. To compare results between groups (e.g., NTG vs. conventional therapy group) and evaluate the efficacy and safety of innovative therapies, inferential statistics were employed, such as chi-square tests and t-tests. It was also planned to conduct subgroup analyses based on HF subtype (HFpEF vs. HFrEF) and other pertinent stratifications to investigate treatment effects across a range of patient profiles.

Ethical Approval:
The Institutional Review Board (IRB) of the hospital granted ethical permission for this study, guaranteeing adherence to moral guidelines, patient privacy, and rights protection during the research procedure. Prior to their inclusion in the study, all enrolled subjects or their legal representatives provided informed consent. During the data collection, analysis, and reporting stages, precautions were taken to ensure participant anonymity, data security, and adherence to ethical norms.

Results
The baseline characteristics of the study participants in the Standard Therapy Group (STG) (n=160) and the NTG (n=160) are displayed in Table 1. The groups' mean ages were comparable: the mean age of the STG was 64.8 years (±7.9), while the mean age of the NTG was 65.2 years (±8.3) ($p = 0.632$). There was a modest male predominance in the gender distribution, with 90 men in the STG and 95 males in the NTG ($p = 0.421$). With 80 patients in each HF subgroup for both the novel and STG ($p = 0.287$ and $p = 0.521$, respectively), the distribution of HF subtypes, HFpEF and HFrEF, was similar between the groups. The NYHA Functional Class distribution (I–IV), with p-values ranging from 0.519 to 0.731 across classes, also showed no discernible difference between the groups. Baseline ejection fraction values were similar in both groups, with averages of 30.5% (±5.2) in the NTG and 31.2% (±4.8) in the STG ($p = 0.498$). Comorbidities such hypertension, diabetes mellitus, and coronary artery disease were also comparable. The medical histories of previous myocardial infarctions and HF hospitalizations did not significantly vary from one another ($p = 0.213$ and 0.326,

correspondingly). P-values of 0.289 and 0.176, respectively, indicate that there was no noteworthy difference in the means of 5.8 ± 1.2 and 1.5 ± 0.8 in the NTG and 6.2 ± 1.3 and 1.8 ± 0.9 in the STG for the severity of symptoms. Measures of functional status, such as peak oxygen consumption and the distance covered in a 6-minute walk test, showed similarities between the groups (means of 15.2 ± 2.1 ml/kg/min and 320 ± 45 meters in the NTG and 14.8 ± 2.0 ml/kg/min in the STG, with p-values of 0.412 and 0.348, correspondingly). There were no obvious distinctions between the groups in terms of biomarker levels (BNP and NT-proBNP) or drug histories (ACE inhibitors/ARBs, mineralocorticoid receptor antagonists, and beta-blockers; p-values ranged from 0.287 to 0.632).

Table 1: Patients' baseline characteristics in this research

Variables	**Novel Therapy Group (n=160)**	**Standard Therapy Group (n=160)**	**p-value**
Age (years), mean ± SD	65.2 ± 8.3	64.8 ± 7.9	0.632
Gender			
Male	95	90	0.421
Female	65	70	
HF Subtype (HFpEF/HFrEF)			
HFpEF	80	85	0.287
HFrEF	80	75	
NYHA Functional Class			
I	32	28	0.519
II	72	75	0.648
III	44	47	0.731
IV	12	10	0.642
Comorbidities (%)			
Hypertension	72	68	0.389
Diabetes Mellitus	48	52	0.462
Coronary Artery Disease	38	42	0.521
Others	22	18	0.317
Baseline Ejection Fraction (%)	30.5 ± 5.2	31.2 ± 4.8	0.498
Medical History			
Previous Heart Failure Hospitalizations	15	20	0.213
History of Myocardial Infarction	25	30	0.326
Symptom Severity			
Dyspnea Scale (0-10)	5.8 ± 1.2	6.2 ± 1.3	0.289
Edema Severity (0-3)	1.5 ± 0.8	1.8 ± 0.9	0.176
Functional Status			
6-Minute Walk Test Distance (meters)	320 ± 40	310 ± 45	0.412
Peak Oxygen Consumption (ml/kg/min)	15.2 ± 2.1	14.8 ± 2.0	0.348
Biomarkers			
BNP (pg/mL)	350 ± 120	380 ± 130	0.521
NT-proBNP (pg/mL)	600 ± 200	620 ± 180	0.632
Medication History			
Beta-Blockers (%)	80	75	0.287
ACE Inhibitors/ARBs (%)	85	80	0.348
Mineralocorticoid Receptor Antagonists (%)	45	50	0.421

The treatment efficacy of standard and innovative therapy for individuals with heart failure is compared in Table 2. The change in ejection fraction in the NTG (n=160) was found to be

substantially larger than that of the STG ($p < 0.001$), with a mean increase of +8.4% (±3.6). Furthermore, with a statistically significant p-value of 0.013, more patients in the NTG (76.2%) than in the STG (62.5%) saw improvements in their NYHA functional class. Additionally, the NTG's Kansas City Cardiomyopathy Questionnaire score (45.7 ± 6.3) was considerably higher than that of the STG (39.5 ± 7.1), indicating a superior quality of life ($p < 0.001$). Additionally, the NTG saw a reduced proportion of hospitalization for worsening HF (15.6%) compared to the STG (23.8%), with a significance level of 0.049. However, there was not a statistically significant variance in the mortality rate among the two cohorts (6.3% vs. 9.4%, $p = 0.214$).

Table 2: Comparison of Treatment Efficacy Between Novel Therapies and Standard Treatments

Outcome Measure	**Novel Therapy Group (n=160)**	**Standard Therapy Group (n=160)**	**p-value**
Change in Ejection Fraction (%)	+8.4 ± 3.6	+5.9 ± 2.8	<0.001
NYHA Functional Class Improvement (%)	76.2	62.5	0.013
Kansas City Cardiomyopathy Questionnaire Score	45.7 ± 6.3	39.5 ± 7.1	<0.001
Hospitalizations for Worsening HF (%)	15.6	23.8	0.049
Mortality Rate (%)	6.3	9.4	0.214

The safety profile comparison of innovative medicines and conventional treatments for the management of HF is presented in Table 3. The incidence of adverse events was found to be 22.5% in the NTG ($n = 160$), which was somewhat higher than the 18.8% recorded in the STG ($p = 0.312$). The NTG experienced 6.9% higher hospitalizations for device-related complications than the STG (4.4%), however this difference was not statistically significant ($p = 0.421$). Likewise, a p-value of 0.586 indicated that the incidence of arrhythmias was marginally greater in the NTG (11.3%) as opposed to the STG (9.6%). 8.1% of patients getting new medicines and 6.3% of individuals receiving traditional treatments reported having infections ($p = 0.487$). Although this difference was not statistically significant ($p = 0.214$), the mortality rate in the Novel Therapy Group was lower than that of the STG (9.4%). In general, the safety endpoints demonstrated results that were similar between the two treatment groups.

Table 3: Safety Profile of Novel Therapies vs. Standard Treatments

Safety Endpoint	**Novel Therapy Group (n=160)**	**Standard Therapy Group (n=160)**	**p-value**
Incidence of Adverse Events (%)	22.5	18.8	0.312
Hospitalizations for Device-related Complications	6.9	4.4	0.421
Arrhythmias (%)	11.3	9.6	0.586
Infections (%)	8.1	6.3	0.487
Mortality Rate (%)	6.3	9.4	0.214

Patients with HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF) who received either innovative therapeutics or standard treatments are compared in Table 4 based on HF subtype. In the NTG, patients with HFrEF showed a higher improvement (+10.1 ± 3.2) in their ejection fraction (%) than patients with HFpEF (+6.2 ± 2.5). There was a significant difference between the subgroups ($p < 0.001$ for HFrEF and $p = 0.017$ for HFpEF). Similarly, in the STG, there was a significant difference ($p < 0.001$ for HFrEF, $p = 0.029$ for HFpEF) between the improvement rates of HFrEF patients (+6.8 ± 2.5) and HFpEF patients (+4.8 ± 2.1). In the NTG, the HFpEF subgroup (80.5%) had a larger percentage of NYHA functional class improvement than the HFrEF

subgroup (71.3%) (p = 0.029 for HFpEF, p = 0.091 for HFrEF). The HFrEF subgroup had a higher frequency of hospitalizations for worsening HF than the HFpEF subgroup in both the STG (p = 0.212) and the NTG (p = 0.046). Nevertheless, there were no statistically significant changes in either therapy group's death rates between the two subgroups (p = 0.451 for HFpEF, p = 0.362 for HFrEF).

Table 4: Subgroup Analysis by Heart Failure Subtype (HFpEF vs. HFrEF)

Subgroup Analysis	**Novel Therapy Group (n=160)**	**Standard Therapy Group (n=160)**	**p-value**
Change in Ejection Fraction (%)	HFpEF: +6.2 ± 2.5, HFrEF: +10.1 ± 3.2	HFpEF: +4.8 ± 2.1, HFrEF: +6.8 ± 2.5	HFpEF: 0.017, HFrEF: <0.001
NYHA Functional Class Improvement (%)	HFpEF: 80.5, HFrEF: 71.3	HFpEF: 64.7, HFrEF: 58.9	HFpEF: 0.029, HFrEF: 0.091
Hospitalizations for Worsening HF (%)	HFpEF: 13.8, HFrEF: 17.4	HFpEF: 20.5, HFrEF: 27.6	HFpEF: 0.212, HFrEF: 0.046
Mortality Rate (%)	HFpEF: 5.8, HFrEF: 6.9	HFpEF: 8.4, HFrEF: 10.3	HFpEF: 0.451, HFrEF: 0.362

A longitudinal evaluation of treatment effects throughout a follow-up period is presented in Table 5, which tracks changes over time in the following variables: ejection fraction (%), NYHA functional class improvement (%), hospitalizations for worsening heart failure (%), and death rate (%). The mean ejection fraction was 30.5 ± 5.2% at baseline. The ejection fraction increased to 32.8 ± 5.4% after three months, and it improved even further at six months (35.2 ± 5.7%) and twelve months (38.9 ± 6.1%). Comparably, the NYHA functional class improvement shown consistent growth over time, as evidenced by percentages rising from 55.6% after three months to 78.9% after twelve. Hospitalizations for deteriorating HF dropped from 12.5% at three months to 6.2% at twelve, while the death rate stayed comparatively constant during the follow-up period, varying between 4.4% and 6.3%.

Table 5: Longitudinal Assessment of Treatment Effects Over Follow-Up Period

Time Point (Months)	**Ejection Fraction (%)**	**NYHA Functional Class (Improvement %)**	**Hospitalizations for Worsening HF (%)**	**Mortality Rate (%)**
Baseline	30.5 ± 5.2			
3	32.8 ± 5.4	55.6	12.5	4.4
6	35.2 ± 5.7	68.2	9.3	5.6
12	38.9 ± 6.1	78.9	6.2	6.3

Table 6 displays quality of life metrics and patient-reported outcomes based on two assessment instruments: the EuroQol-5 Dimension Questionnaire and the Minnesota Living with HF Questionnaire. Compared to the conventional therapy group, which had a higher mean score of 32.1 ± 5.6 (p < 0.001), the innovative therapy group's mean score on the Minnesota Living with HF Questionnaire was 28.5 ± 4.8, showing a lower burden of HF-related symptoms and greater quality of life. Furthermore, there was a significant difference in the EuroQol-5 Dimension Questionnaire scores between the groups receiving innovative therapy (0.72 ± 0.06) and standard therapy (0.65 ± 0.08), indicating that patients receiving novel therapies had superior overall health status and quality of life (p < 0.001).

Table 6: Patient-Reported Outcomes and Quality of Life Measures

Assessment Tool	Novel Therapy Group (n=160)	Standard Therapy Group (n=160)	p-value
Minnesota Living with Heart Failure Questionnaire	28.5 ± 4.8	32.1 ± 5.6	<0.001
EuroQol-5 Dimension Questionnaire	0.72 ± 0.06	0.65 ± 0.08	<0.001

The frequency of unfavorable occurrences in HF subtypes, HFpEF (HF with preserved ejection fraction) and HFrEF (HF with reduced ejection fraction), is contrasted in Table 7. The information reveals that the incidence of infections in the HFpEF group (7.8%) and the HFrEF group (8.4%) did not differ significantly (p = 0.752). Arrhythmias also occurred in similar proportions in the two groups: 9.2% in the HFpEF group and 13.6% in the HFrEF group (p = 0.321). Furthermore, there was no significant difference in the percentage of hospitalizations for worsening HF between individuals with HFpEF (16.5%) and HFrEF (18.9%) (p = 0.623).

Table 7: Comparison of Adverse Events Between Heart Failure Subtypes

Adverse Event	HFpEF Group (n=80)	HFrEF Group (n=80)	p-value
Infections (%)	7.8	8.4	0.752
Arrhythmias (%)	9.2	13.6	0.321
Hospitalizations for Worsening HF (%)	16.5	18.9	0.623

The treatment effects on quality of life measures over time for both the conventional therapy group and the NTG are compared in Table 8. The mean EuroQol-5 Dimension Questionnaire score at baseline was comparable in the two groups: 0.65 ± 0.07 in the group receiving new therapy and 0.66 ± 0.08 in the group receiving traditional therapy (p = 0.427). However, the new therapy group continuously outperformed the traditional therapy group at later time points (3, 6, and 12 months), indicating a higher quality of life. The scores at three months were 0.71 ± 0.06 for the STG and 0.68 ± 0.07 for the new therapy group (p = 0.053). The scores at six months were 0.73 ± 0.06 for the STG and 0.70 ± 0.08 for the new therapy group (p = 0.021). With scores of 0.76 ± 0.07 in the NTG and 0.72 ± 0.09 in the STG at 12 months, the difference was more noticeable (p = 0.009), indicating that the novel therapy was associated with a sustained improvement in quality of life.

Table 8: Comparison of Treatment Effects on Quality of Life Measures Over Time

Time Point (Months)	EuroQol-5 Dimension Questionnaire Score (Novel Therapy Group)	EuroQol-5 Dimension Questionnaire Score (Standard Therapy Group)	p-value
Baseline	0.65 ± 0.07	0.66 ± 0.08	0.427
3	0.71 ± 0.06	0.68 ± 0.07	0.053
6	0.73 ± 0.06	0.70 ± 0.08	0.021
12	0.76 ± 0.07	0.72 ± 0.09	0.009

Discussion

HF continues to pose a major worldwide health burden, making it imperative to consistently investigate new treatments in an effort to enhance patient outcomes. The purpose of our study was to look into the safety and effectiveness of new HF management therapies. The results of our study shed important light on the efficacy of these therapies in the real world and their potential to completely transform HF management. The study participants, who were divided into the NTG and the STG, had baseline characteristics that were similar in terms of age, gender distribution, HF subtype distribution

(HFpEF/HFrEF), NYHA functional class, comorbidities, baseline ejection fraction, symptom severity, functional status measures, biomarker levels, and medication history. These parallels guarantee a fair comparison of the two treatment groups and strengthen the reliability of our results.

Our findings show that when compared to standard treatments, new medicines significantly improved a number of important outcome indicators. Patients in the STG showed an increase in ejection fraction of +5.9% ±2.8, $p < 0.001$, whereas patients in the NTG showed a mean increase of +8.4% (±3.6). Additionally, there was a statistically significant difference ($p = 0.013$) in the percentage of patients in the NTG who saw an improvement in their NYHA functional class (76.2%) as opposed to the STG (62.5%). Additionally, the NTG's Kansas City Cardiomyopathy Questionnaire score (45.7 ± 6.3) was considerably higher than that of the STG (39.5 ± 7.1), indicating a superior quality of life ($p < 0.001$). Furthermore, with a p-value of 0.049, the NTG had a lower percentage of hospitalizations for worsening HF (15.6%) than the STG (23.8%). The death rate between the two groups, however, did not differ statistically significantly (6.3% vs. 9.4%, $p = 0.214$). The results of the study are consistent with previous investigations, showing similar improvements in ejection fraction and NYHA functional class comparing new and traditional therapy for the management of HF [14,15]. Furthermore, our study's findings are consistent with earlier investigations [16, 17], which found that new treatments reduced the number of hospital admissions for HF that worsened. The similar results obtained from these studies provide more proof that new therapies are beneficial in enhancing heart function and patient satisfaction.

Regarding safety, there was a marginally higher frequency of adverse events in the NTG when compared to the STG; nevertheless, there was no statistically significant difference between the two groups ($p = 0.312$; 22.5% vs. 18.8%). Hospitalization rates for arrhythmias (11.3% vs. 9.6%, $p = 0.586$), infections (8.1% vs. 6.3%, $p = 0.487$), device-related complications (6.9% vs. 4.4%, $p = 0.421$), and death (6.3% vs. 9.4%, $p = 0.214$) were similar in both groups. These results imply that new therapeutics have a good safety profile that is on par with existing therapies. These safety results are consistent with earlier investigations assessing the safety profiles of cutting-edge treatments for the treatment of HF [18, 19]. The general safety of new HF therapies is further supported by the rates of device-related problems and arrhythmias that our study observed, which are in line with earlier studies [20].

Patients with HFpEF and HFrEF saw varied treatment outcomes, according to a subgroup analysis based on HF subtype. With innovative therapy, both categories showed improvements in their functional class and ejection fraction; however, patients with HFrEF showed higher improvements in their ejection fraction than patients with HFpEF ($p = 0.017$ for HFpEF, $p < 0.001$ for HFrEF). In the NTG, the percentage of improvement in NYHA functional class was also higher in the HFpEF subgroup (80.5%) than in the HFrEF subgroup (71.3%) ($p = 0.029$ for HFpEF, $p = 0.091$ for HFrEF). The HFrEF subgroup had a higher frequency of hospitalizations for worsening HF than the HFpEF subgroup in both the STG ($p = 0.212$) and the NTG ($p = 0.046$). Nevertheless, there were no statistically significant changes in either therapy group's mortality rates between the two subgroups ($p = 0.451$ for HFpEF, $p = 0.362$). The subgroup analysis aligns with previous studies that show different treatment outcomes depending on the type of HF, since patients with HFrEF showed greater improvements in ejection fraction after receiving new treatments than their HFpEF counterparts [21, 22]. Furthermore, the HFrEF subgroup's higher hospitalization rates for worsening HF are consistent with the findings of a retrospective cohort research, highlighting the need for individualized treatment plans based on the type of HF [23].

Conclusion

Our research emphasizes how innovative medicines have the potential to significantly improve HF patient’s outcomes. We have shown that, in comparison to traditional treatments, new approaches offer significant benefits in terms of heart function, symptom management, and quality of life through a thorough evaluation of therapy efficacy and safety. The results highlight how crucial it is to carry out further research and development in the field of HF management in order to meet patients' unmet

requirements and improve clinical practice. Moreover, subgroup studies based on HF subtype provide significant new information on how different treatments work, highlighting the necessity of individualized therapeutic strategies based on patient characteristics. All things considered, our research adds significant evidence in favor of the addition of cutting-edge treatments to the toolkit for managing heart failure. These treatments have the potential to completely transform patient outcomes and care in the future.

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