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Impact of Pharmacotherapy Optimization on Health-related Quality of Life in a Long-term Follow-up Program for Patients with Heart Failure

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Abstract:

Background: Heart failure (HF) is a complex clinical syndrome that impacts a patient's health and quality of life (QoL). Pharmacological management, especially therapy that adheres to established clinical guidelines on patients' health status and QoL, reduces mortality and hospitalization of HF patients and ejection fraction (HFrEF).

Objective: This study aimed to evaluate changing health-related quality of life (HRQoL) and medication prescription in patients with HF during a long-term monitoring program.

Methods: This observational analysis included 118 HF patients who were discharged from the Department of Cardiology after an episode of decompensated HF (ICD-10 code I50). HRQoL was observed using the Minnesota Living with Heart Failure Questionnaire (MLHFQ). Patients were divided into two groups. Group I (N=71, 60.2%) had a decrease in MLHFQ scores of more than 10 points, and group II (N=47, 39.8%) had stable or less than 10-point increases in MLHFQ scores.

Results: In group I, there was a statistically significant decrease in the use of angiotensin-converting enzyme inhibitors (ACEI), an increase in the administration of angiotensin receptor-neprilysin inhibitors (ARNI), and the optimal use of renin-angiotensin-aldosterone system (RAAS) inhibitors. This group demonstrated substantial improvements in HRQoL across emotional, physical, and social domains. In contrast, group II exhibited suboptimal usage of RAAS inhibitors and modest improvements in HRQoL.

Conclusion: The optimization of medication therapy, including the transition to ARNIs and comprehensive RAAS inhibition, in group I (lower mean LVEF, higher proportion of NYHA class III-IV) contributed to substantial improvements in HRQOL. In contrast, the suboptimal usage of RAAS inhibitors in group II (higher mean LVEF, lower proportion of NYHA class III-IV) may have contributed to the modest HRQOL improvements observed in this group.

Keywords: Heart failure, Health-related quality of life, Long-term monitoring program, Management, Treatment, RAAS.

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1. INTRODUCTION

HF is a severe global health condition that significantly affects many aspects of patients' lives, significantly decreasing their HRQoL [1, 2]. HRQOL serves as a crucial patient-reported metric that incorporates patients' viewpoints regarding the impact of HF on their daily lives and overall well-being [2, 3]. An essential objective in the management of patients dealing with HF and reduced

ejection fraction (REF) is to enhance their overall well-being, encompassing the alleviation of symptoms, enhancement of functional capabilities, and the improvement of their QoL [4-6]. Ensuring medication adherence according to the HF management guidelines and introducing all primary groups of medications, such as renin-angiotensin-aldosterone system (RAAS) blockers, aldosterone receptor antagonists (MRAs), beta-blockers (BB), and sodium-glucose cotransporter-2 inhibitors (SGLT2is) [7], as fast as possible are vital for HF patients to attain improved health outcomes [5, 6, 8]. Consequently, medication adherence is presumed to be linked to an enhanced HRQoL [9, 10]. Global efforts are underway to develop and implement monitoring programs to reduce HF-related hospitalizations and improve patients' functional status and HRQoL [11, 12].

Hobbs *et al*. showed that HF patients experience statistically significant impairments in QoL in all aspects of life. Research has revealed a relationship between the emotional aspects of QoL and medication use [13, 14]. Despite the established efficacy of recommended medicament treatment for HF patients, optimal treatment recommendations are not followed, resulting in decreased overall treatment efficacy. It is estimated that at least one in four patients with HF do not adhere to their prescribed medication [15-17].

Although increased survival is undoubtedly of the most significant clinical importance, it is also necessary to prioritize the well-being of individuals with HF, especially compared to other common chronic diseases, as HF patients experience a significantly more significant impact on their physical health [13, 18, 19].

The study aimed to investigate the effect of medication administration in HF patients in a long-term monitoring program.

2. MATERIALS AND METHODS

Between March 2019 and December 2020, a study was conducted by the Department of Cardiology at the Hospital of Lithuanian University of Health Sciences Kaunas Clinics. This observational study analyzed a prospective cohort of 118 HF patients released from the Cardiology department after experiencing HF decompensation. These patients were diagnosed under the ICD-10 code I50, which includes both chronic decompensated and new onset cases. According to the Health Minister's directive No. V-1330 from November 24, 2015, regarding the stipulations for cardiac consultations and patient education, each patient underwent four sequential educational consultations over a year. Data collection occurred during these sessions.

The study included 118 patients who participated in four consultations with a cardiologist and an HF nurse over 12 months. All HF patients were treated and discharged from the Cardiology department because of HFrEF with the recommendation of medical treatment. All study participants provided written informed consent, allowing them to utilize their information for scientific investigation and sharing findings while preserving privacy and anonymity.

Exclusion criteria involved HF patients who did not participate in all four consultations, those with a life expectancy of less than one year, or those who died within a year of hospitalization for HF. Additionally, patients who were severely cognitively impaired, bedridden, or otherwise unable to participate effectively in assessments were also excluded.

For detailed analysis, the study participants were segregated into two groups. Group I (N=71, 60.2%) had decreased MLHFQ scores by more than 10 points, indicating improved HRQoL aligning with the standards of November 2015 Ministerial Order No. V-1330. Group II (N=47, 39.8%) had stable or less than 10-point increases in MLHFQ scores, suggesting inadequate HRQOL improvement. The group in which the MLHFQ scores decreased by 10 points or more was identified as the group with improved QoL. This improvement was indicated by the inverse relationship between MLHFQ scores and QoL; a lower MLHFQ score corresponded to a higher QoL. Both patient groups were treated according to established clinical guidelines with pharmacological and non-pharmacological measures. Cardiology and laboratory tests were performed at each clinical visit following a standardized consultation protocol.

2.1. Clinical Data Collection

At the initial consultation, detailed demographic profiles and clinical characteristics of patients were collected, encompassing gender, age, physical activity level as assessed by the New York Heart Association (NYHA) classification, and the presence of comorbidities, such as cardiomyopathies (CMP), arterial hypertension (AH), history of myocardial infarction (MI), significant coronary artery disease (CAD), history of cerebrovascular stroke (CS), and type 2 diabetes mellitus (T2DM).

Obesity, ankle edema, and symptoms of dyspnea were evaluated and recorded. The degree of obesity was determined based on a body mass index (BMI) of ≥30 kg/m^2. The severity of ankle edema was evaluated using a graded scale, ranging from 1+, indicating mild edema, to 4+, representing severe edema. Symptoms of dyspnea were evaluated using the 6-minute walk test (6MWT), a standardized assessment tool for measuring functional exercise capacity [20].

Laboratory assessments performed during each visit included measurements of electrolytes (potassium, sodium), renal function tests [evaluating levels of urea, creatinine, and estimating the glomerular filtration rate (GFR)], measurement of uric acid levels, and liver enzyme tests (assessing aspartate aminotransferase (AST), alanine transaminase (ALT), and gamma-glutamyl transferase (GGT) activities) and bilirubin levels (total and direct), along with alkaline phosphatase and N-terminal pro-B-type natriuretic peptide (NT-proBNP).

At the initial consultation and the fourth follow-up visit, an echocardiographic examination was performed to evaluate the systolic function of the left and right ventricles and assess cardiac status.

2.2. Assessment of QoL

MLHFQ was used to assess the impact of HF symptoms on participants' QoL during regular appointments. The 21-item MLHFQ, a disease-specific instrument, was initially employed to gauge participants' perceptions of the impact of HF on their physical and emotional states [3, 21, 22]. The responses to each question on the questionnaire were rated using a Likert scale ranging from 0 (representing 'No') to 5 (representing 'Very much'), and the aggregate score from all 21 items was computed. A higher MLHFQ score suggested a diminished HRQoL. Extensive research has been conducted on the MLHFQ's validity and reliability across different HF groups, verifying its effectiveness in evaluating HRQoL [3, 21]. In this investigation, the Cronbach's alpha coefficient for the MLHFQ was determined to be 0.943, indicating its high reliability and consistency as an evaluative tool.

2.3. Medication Adherence Data

The information on patient's medication usage, including ACEIs, BBs, ARBs, ARNIs, MRAs, SGLT2is (in the study population, SGLT2 inhibitors were not part of the prescribed treatments), and loop diuretics, was retrieved and recorded from the respective medical records. According to the ESC Heart Failure Management 2021 Guidelines, four conventional groups of medications for managing HFrEF must be prescribed, which include ACEIs or ARNI, beta-blockers, MRAs, and SGLT2is [5, 6, 23]. Loop diuretics are a choice for patients with congestion until the symptoms are present [8].

2.4. Statistical Analysis

Data analysis was performed using SPSS 27 (Statistical Package for the Social Sciences) [24]. The continuous variables were expressed as the mean value accompanied by the standard deviation (SD). The McNemar's test, a non-parametric method, was applied to dependent samples. The categorical variables were analyzed using the chi-square ($\chi 2$) test. The Wilcoxon test was employed to assess the normality of the data. A *p*-value of less than 0.05 was considered to indicate statistical significance.

2.5. Ethical Consideration

Every participant was provided with written details outlining the study objectives and significance, which were accompanied by the guarantee of maintaining the confidentiality of their data and the assurance that they could withdraw their participation at any point. Informed consent was obtained in writing from all participants. To maintain anonymity, all data gathered from the participants were assigned unique, anonymized identifiers. The study was evaluated and approved by the Kaunas Regional Biomedical Research Ethics Committee (date of approval: October 11, 2022; reference no.: P1-BE-2-5/2018).

3. RESULTS

3.1. Baseline Clinical Parameters of the Study Population

The previously described division of participants into two groups (group I, N=71, and group II, N=47) exhibited a comparable gender distribution. An analysis revealed a comparable male predominance across group I (85.9%) and group II (85.1%), with a *p*-value of 0.902, indicating a lack of statistical dissimilarity (Table **1**).

When evaluating data, group I had a higher percentage of patients in the III-IV NYHA functional class (27.3%), compared to group II (16.3%), and a significantly lower LVEF (24.72% *vs*. 29.01%, $p=0.043$). Also, right ventricular dysfunction was more prominent in group I patients ($p=0.031$).

Group II patients had a higher prevalence of severe comorbidities, such as prior MI (66% *vs*. 46.5%, $p=0.038$) and significant CAD (74.5% *vs*. 49.3%, $p=0.006$). The prevalence of T2DM and AH was comparable between the study groups ($p=0.984$ and $p=0.771$, respectively).

Table 1. Baseline demographic data, clinicopathological parameters, and laboratory values in a heart failure study population participating in a prospective longitudinal observation program.

Demographic and Clinical Parameters of Participants	Participants		Observed Significance Level
	Group I (N=71)	Group II (N=47)	
Males, n (%)	61 (85.9)	40 (85.1)	$p=0.902$
Age, mean ± SD (years)	63.6 (±11.8)	59.06 (±13.9)	$p=0.05$
NYHA functional status distribution			
Class I-II, n (%)	48 (72.7)	36 (83.7)	$p=0.182$
Class III-IV, n (%)	18 (27.3)	7 (16.3)	
Comorbidity profile			
History of MI, n (%)	33 (46.5)	31 (66.0)	$p=0.038$
Significant CAD, n (%)	35 (49.3)	35 (74.5)	$p=0.006$
AH, n (%)	59 (83.1)	40 (85.1)	$p= 0.771$
Other CMP	19 (26.8)	17 (36.2)	$p=0.277$
History of CS, n (%)	8 (11.3)	2 (4.3)	$p= 0.181$
T2DM, n (%)	15 (21.1)	10 (21.3)	$p= 0.984$

(Table 1) contd.....

Demographic and Clinical Parameters of Participants	Participants		Observed Significance Level
	Group I (N=71)	Group II (N=47)	
Clinical parameters			
Existing ankle edema, n (%)	21 (29.5%)	16 (34.0%)	p=0.05
Obesity, n (%)	32 (42.1%)	22 (52.4%)	p=0.283
6-MWT, m (±SD)	365.90 (±115.06)	400 (±96.73)	p=0.122
Biochemical and hematological parameters			
NT-proBNP level, pg/mL (median, IQR)	614.0 (60.5-1577,3)	103,0 (146,0-1277,0)	p=0.062
Urea, mmol/l (±SD)	8.0 (±3.7)	8.3 (±3.5)	p=0.779
K+, mmol/l (±SD)	4.5 (±0.5)	4.5 (±0.6)	p=0.839
Na+, mmol/l (±SD)	134.4(±3.2)	136.4 (±3.6)	p=0.105
UA, mg/dL (±SD)	459.3(±153.1)	435.5 (±113.8)	p=0.406
sCr, µmol/l (±SD)	107.7 (±30.9)	111.1 (±26.8)	p=0.584
eGFR, mL/min/1.73m2 (mean ± SD)	66.23(±20.8)	64.1 (±24.6)	p=0.677
TBil, µmol/l (±SD)	17.8 (±9.3)	19.3 (±9.6)	p=0.380
DBil, µmol/l (±SD)	3.5 (±3.3)	2.8 (±1.9)	p=0.306
AST, U/l (±SD)	23.1 (±9.2)	27.1 (±14.3)	p=0.05
ALT, IU/L (±SD)	25.2 (±13.6)	42.2 (±53.5)	p=0.010
GGT, U/L (±SD)	42.9 (±43.2)	70.6 (±84.2)	p=0.031
ALP, U/l (±SD)	74.8 (±19.9)	78.6 (±19.0)	p=0.439
Hb concentration, g/l (±SD)	134.45 (±16.4)	129.8 (±37.6)	p=0.565
Echocardiographic characteristics			
LVEDD: mm (mean ± SD)	61.47 (±9.0)	61.38 (±8.9)	p=0.963
LVEF: % (mean ± SD)	24.72 (±10.7)	29.01 (±11.7)	p=0.043
Left atrial dimension: mm (mean ± SD)	53.57 (±17.0)	54.65 (±14.2)	p=0.767
TAPSE: mm (mean ± SD)	13.06 (±3.5)	15.70 (±5.3)	p=0.031

Abbreviations: AH - arterial hypertension; ALT - alanine aminotransferase; AST - aspartate aminotransferase; ALP - alkaline phosphatase; CAD - coronary artery disease; CMP - cardiomyopathy; CS - cerebrovascular stroke; DBil - direct bilirubin; eGFR - estimated glomerular filtration rate; GGT - gamma-glutamyl transpeptidase; HB - hemoglobin; LVEDD - left ventricular end-diastolic diameter; LVEF - left ventricular ejection fraction; MI - myocardial infarction; 6-MWT - 6-minute walk test; NYHA - New York Heart Association; NT-proBNP -N terminal pro-B-type natriuretic peptide; SCr - serum creatinine; TAPSE - tricuspid annular plane systolic excursion; TBil - total bilirubin; T2DM - type 2 diabetes mellitus; UA - uric acid.

Ankle edema, a common clinical sign of worsening HF, tended to occur more often in group II, with a p-value bordering significance (p=0.05). The prevalence of obesity and the 6-MWT performance did not exhibit statistically significant differences between the study groups (p=0.283 and p=0.122, respectively).

Regarding laboratory parameters, NT-proBNP levels were higher in group II (median: 1030 pg/mL) compared to group I (median: 614.0 pg/mL); however, the difference between the groups did not reach the level of significance (p=0.062). Liver function tests, including ALT, AST, and GGT, were significantly elevated in group II (p=0.010, p=0.05, and p=0.031, respectively). Additional biochemical and hematological parameters, including hemoglobin concentration, markers of renal function, and serum electrolyte levels, did not demonstrate statistically significant intergroup variations.

Statistical differences in the groups were revealed in both the comprehensive score change of the MLHFQ (p<0.001) and all its subscales, encompassing emotional, physical, and social domains (p<0.001) (Table **2**) during the long-term monitoring program. The intergroup differences in health-related QoL exhibited statistically significant variations across all domains (p<0.001), with the intervention cohort (group I) demonstrating substantially superior improvements in QoL measures compared to the control group (group II). These findings suggest that despite the two groups' distinct clinical profiles and comorbidity burdens, group I benefited more from the interventions and treatments applied during the long-term monitoring program, significantly enhancing their emotional, physical, and social well-being and overall QoL. In contrast, group II showed only a tiny improvement in QoL, which may have been affected by a higher prevalence of comorbidities and less pronounced changes in the treatment regimen.

The study evaluated changes in medication usage patterns between the initial (visit 1) and follow-up (visit 4) visits among HF patients undergoing a long-term monitoring program (Table **3**).

ACEI usage demonstrated a notable decline, with the proportion of patients receiving ACEIs decreasing from 58.5% at visit 1 to 46.6% at visit 4 (p=0.003). The reduction was likely attributed to a transition toward the newer ARNI class, whose utilization increased significantly from 7.6% at visit 1 to 21.2% at visit 4 (p=0.010). These observations suggest a strategic shift from ACEIs to ARNIs, which may offer improved therapeutic profiles and better tolerance in the management of HF.

Table 2. Longitudinal evaluation of quality of life in a chronic heart failure cohort utilizing the Minnesota living with heart failure questionnaire.

Domains of QoL	Group I (N=71)	Group II (N=47)	*p*-value
	Mean (SD)	Mean (SD)	
Emotional well-being	6.38 (±5.2)	-1.4 (±5.9)	$p<0.001$
Physical functioning	12.88 (±8.1)	-3.21 (±8.3)	$p<0.001$
Social engagement	8.52 (±7.2)	-3.4 (±9.7)	$p<0.001$
Overall QoL	28.82 (±16.1)	-6.91 (±19.4)	$p<0.001$

Table 3. Usage of medications during a long-term monitoring program for heart failure patients.

Medications Used	Visit 1	Visit 4	*p*-value
RAAS blockers, n (%)	83 (70.3)	85 (72.0)	$p=0.850$
ACEI, n (%)	69 (58.5)	55 (46.6)	$p=0.003$
ARB, n (%)	6 (5.1)	5 (4.2)	$p=1.000$
ARNI, n (%)	9 (7.6)	25 (21.2)	$p=0.010$
BB, n (%)	101 (85.6)	95 (80.5)	$p=0.286$
MRA, n (%)	81 (68.6)	77 (65.3)	$p=0.617$
SGTL2is, n (%)	2 (1.7)	3 (2.5)	$p=1.000$
Diuretics, n (%)	99 (83.9)	92 (78.0)	$p=0.189$

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor/neprilysin inhibitors; BB, beta-blockers; MRA, aldosterone receptor antagonists; RAAS, renin-angiotensin-aldosterone system blockers.

Table 4. Heart failure medication prescription and usage at visit I and visit II between the study groups of patients.

Use of Medications	Group I (N=71)			Group II (N=47)		
	Visit 1	Visit 4	*p*-value	Visit 1	Visit 4	*p*-value
RAAS blockers, n (%)	45 (63.4)	52 (73.2)	$p = 0.0156$	39 (82.9)	33 (70.2)	$p = 0.031$
ACEI, n (%)	39 (54.9)	29 (40.8)	$p=0.0019$	30 (63.8)	26 (55.3)	$p=0.283$
ARB, n (%)	2 (2.8)	4 (5.6)	$p=0.500$	4 (8.5)	1 (2.1)	$p=0.375$
ARNI, n (%)	4 (5.6)	19 (26.8)	$p=0.000061$	5 (10.6)	6 (12.8)	$p=1.00$
BB, n (%)	61 (85.9)	60 (84.5)	$p=1.000$	40 (85.1)	35 (74.5)	$p=0.359$
MRA, n (%)	45 (63.4)	47 (66.2)	$p= 0.888$	36 (76.6)	30 (63.8)	$p=0.345$
Diuretics, n (%)	59 (83.1)	54 (76.1)	$p=0.458$	40 (85.1)	38 (80.9)	$p=0.803$

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor/neprilysin inhibitors; BB, beta-blockers; MRA, aldosterone receptor antagonists; RAAS, renin-angiotensin-aldosterone system blockers.

Group I demonstrated notable changes in medication use: a significant reduction in ACEI use (from 54.9% to 40.8%, $p=0.0019$) and a substantial increase in ARNI prescription (from 5.6% to 26.8%, $p=0.000061$). Consequently, this group's overall RAAS inhibitor usage increased from 63.4% to 73.2% ($p=0.0156$). The proportion of patients receiving diuretic therapy decreased from 83.1% at visit 1 to 76.1% at visit 4, although this change was not statistically significant ($p=0.458$). The use of MRAs remained relatively stable, with 63.4% receiving MRAs at visit 1 and 66.2% at visit 4 ($p=0.888$).

In contrast, group II showed different medication-use trends: no significant changes in ACEI or ARNI use between visits. This group's overall RAAS inhibitor usage decreased from 82.9% to 70.2% ($p=0.031$). The proportion of patients receiving diuretics remained relatively stable, with 85.1% receiving diuretics at visit 1 and 80.9% at visit 4 ($p=0.803$). MRAs decreased from 76.6% at visit 1 to 63.8% at visit 4, although this change was not statistically significant ($p=0.345$) (Table 4).

4. DISCUSSION

The study population consisted of patients who were allocated to two distinct study groups. The first group (group I) comprised 71 study participants, representing 60.2% of the cohort, whose MLHFQ scores decreased by more than 10 points between the first and fourth consultations. In the second group (group II), 47 patients, representing 39.8% of the cohort, whose MLHFQ scores did not change or increase by less than 10 points between the first and fourth consultations, were included.

Group I had a higher proportion of patients in NYHA

functional class III-IV (27.3% *versus* 16.3% in group II) and a significantly lower LVEF (24.72% *versus* 29.01%, p=0.043). Conversely, group II had a higher prevalence of severe comorbidities, including prior MI (66% *versus* 46.5%, p=0.038) and significant CAD (74.5% *versus* 49.3%, p=0.006). These findings indicate that group I presented with more severe HF symptoms and worse baseline cardiac function.

These clinical differences may have influenced the observed changes in HRQOL. Previous studies have shown a higher NYHA functional class as associated with poorer HR due to increased symptom burden and reduced physical functioning [25, 26]. Similarly, lower LVEF often correlates with poorer HR [27], indicating more severe cardiac dysfunction and more significant limitations in daily activities [28, 29].

A key finding was the significant reduction in ACEI usage from 54.9% to 40.8% (p=0.0019) in group I, accompanied by a substantial increase in ARNI prescriptions from 5.6% to 26.8% (p=0.000061). This shift aligns with the latest 2024 guidelines from the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) [30-32], which prioritize ARNI therapy for managing HFrEF [4, 5, 7, 33]. Studies, such as the PARADIGM-HF trial, have demonstrated ARNIs, such as sacubitril/valsartan, to be superior to ACEIs in reducing mortality and hospitalization rates and improving HRQOL in HFrEF patients [34-37].

In addition, total RAAS inhibitor use in group I increased from 63.4% to 73.2% (p=0.0156), indicating more complete RAAS inhibition. This comprehensive approach is critical to managing HFrEF as it helps reduce the severity of symptoms, slow disease progression, and improve survival [5, 38, 39].

In contrast, group II exhibited decreased RAAS inhibitor usage from 82.9% to 70.2% (p=0.031), potentially contributing to the modest HRQOL improvements observed. Despite having a higher mean LVEF, group II patients had severe clinical conditions, evidenced by the pronounced predisposition towards previous MI and the substantial burden of significant CAD. The suboptimal RAAS inhibition in this group could have hindered more substantial improvements in HRQOL.

The study revealed that only 70% of patients received RAAS inhibitors, and similar adherence levels were observed for BB and MRA. This indicates suboptimal adherence to guideline-directed medical therapy [40], which could negatively impact patient outcomes. Optimal adherence is crucial for achieving the best possible clinical outcomes in HFrEF management [4-6, 30].

It is important to note that HRQOL assessments can be influenced by various factors, such as age, gender, socioeconomic status, and comorbidities [41, 42]. For instance, elevated liver enzyme levels, such as AST (p=0.050), ALT (p=0.010), and GGT (p=0.031) in group II, could be associated with chronic HF and may have contributed to poorer HRQOL assessments [43-45]. Additionally, higher NT-proBNP levels in group II (median: 1030 pg/mL) compared to group I (median: 614.0 pg/mL), although not statistically significant (p=0.062), may have typically been associated with more severe HF progression and negatively impact HRQOL [34, 46-48].

The findings of this study have been found to be consistent with those of other significant clinical trials. The DAPA-HF trial showed that the SGLT2 inhibitor dapagliflozin and standard therapy significantly reduced the risk [49] of HF mortality and hospitalization and improved HRQOL [50]. Although this study did not directly evaluate the effects of ARNIs or RAAS inhibitors, it highlighted the importance of optimizing drug therapy to improve outcomes, including quality of life.

The BIOSTAT-CHF prospective observational study evaluated the utility of biomarkers, such as NT-proBNP, in predicting outcomes and optimizing drug therapy in HF patients. The study found that monitoring biomarkers and tailoring drug therapy based on them can improve outcomes, including QoL [48, 51, 52]. This aligned with the present study's findings, which showed higher NT-proBNP levels to be associated with poorer QoL.

Finally, the QUALIFY prospective observational study evaluated the impact of various factors, including drug therapy, on QoL in patients with HF. The results showed an optimal combination of drugs, including ARNIs, beta-blockers, and MRAs, to be associated with better QoL scores [53, 54]. This further corroborates the conclusions of the present study regarding the importance of RAAS inhibitors and optimized drug therapy in improving the QoL in HF patients.

In summary, these additional clinical trials provide important evidence supporting the importance of optimized drug therapy, particularly ARNIs, RAAS inhibitors, and biomarker monitoring, in improving the QoL in patients with HF.

4.1. Limitation

Although this study provides valuable insights into the relationship between medication use and quality of life in heart failure patients, several limitations should be considered. First, selection bias may have resulted from focusing on patients with a full 12-month follow-up, potentially excluding individuals with different experiences in the final sample. Second, although the study used a widely accepted and reliable measure of health-related quality of life (Cronbach's alpha = 0.943), the inherent bias in patient interpretation and response to such measures should be acknowledged. Finally, the single-center design of the Kaunas Clinics Hospital of the Lithuanian University of Health Sciences, the main tertiary referral center in Lithuania, may influence the generalizability of the findings to other populations and healthcare facilities.

CONCLUSION

The optimization of medication therapy, including the transition to ARNIs and comprehensive RAAS inhibition, in group I (lower mean LVEF, higher proportion of NYHA

class III-IV) was observed to contribute to substantial improvements in HRQOL. In contrast, the suboptimal usage of RAAS inhibitors in group II (higher mean LVEF, lower proportion of NYHA class III-IV) may have contributed to the modest HRQOL improvements observed in this group.

AUTHORS' CONTRIBUTION

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

LIST OF ABBREVIATIONS

HF	=	Heart failure
QoL	=	Quality of life
MLHFQ	=	Minnesota Living with Heart Failure Questionnaire
ACEI	=	Angiotensin-converting enzyme inhibitors
RAAS	=	Renin-angiotensin-aldosterone system
ARNI	=	Angiotensin receptor-neprilysin inhibitors
NYHA	=	New York Heart Association
CMP	=	Cardiomyopathies
AH	=	Arterial hypertension
CAD	=	Coronary artery disease
MI	=	Myocardial infarction
T2DM	=	Type 2 diabetes mellitus
6MWT	=	6-minute walk test
GGT	=	Gamma-glutamyl transferase
AST	=	Assessing aspartate aminotransferase
SD	=	Standard deviation

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Kaunas Regional Biomedical Research Ethics Committee, Lithuania (date of approval: October 11, 2022; reference no.: P1-BE-2-5/2018).

HUMAN AND ANIMAL RIGHTS

All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

All study participants were informed about the study objectives and provided written informed consent to participate. The privacy and anonymity of all participants were ensured.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this published article.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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