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Use of Beta-Blockers in Patients with Heart Failure and Their Impact on Hospitalization Frequency

Uso de betabloqueadores en pacientes con insuficiencia cardíaca y su impacto en la frecuencia de hospitalización

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ABSTRACT

Heart failure (HF) is a leading cause of morbidity, mortality, and healthcare utilization worldwide. β-blockers are a cornerstone of guideline-directed medical therapy, yet uncertainties remain regarding their impact on hospitalization frequency, particularly when therapy is suboptimally dosed. In this retrospective study, we analyzed 480 patients with HF treated at two tertiary hospitals between January 2022 and June 2024, stratified into three groups: no β-blocker therapy, suboptimal therapy, and optimal therapy (≥50% of the target dose). The primary outcome was hospitalization frequency within 12 months, while secondary outcomes included 30-day readmission and median length of stay. Patients without β-blocker therapy had the highest hospitalization rate (62.1%), compared with 47.3% in the suboptimal group and 33.7% in the optimal therapy group. Rehospitalization within 30 days occurred in 22.9%, 15.8%, and 8.0% of patients, respectively, and median length of stay declined progressively from 8 days in untreated patients to 6 days in those optimally treated. Multivariate analysis confirmed that absence of β-blockers and suboptimal therapy were strong predictors of hospitalization, along with diabetes mellitus and reduced ejection fraction. These findings confirm that optimal β-blocker therapy is associated with fewer hospitalizations, reduced early readmissions, and shorter hospital stays, underscoring the importance of both initiation and dose optimization as key strategies in HF management.

keywords: heart failure, β-blockers, hospitalization, readmission, dose optimization

RESUMEN

La insuficiencia cardíaca (IC) es una de las principales causas de morbilidad, mortalidad y utilización de recursos sanitarios a nivel mundial. Los betabloqueadores son un pilar de la terapia médica guiada por guías, aunque persisten dudas sobre su impacto en la frecuencia de hospitalización, especialmente cuando se administran en dosis subóptimas. En este estudio retrospectivo se analizaron 480 pacientes con IC atendidos en dos hospitales de tercer nivel entre enero de 2022 y junio de 2024, estratificados en tres grupos: sin betabloqueador, terapia subóptima y terapia óptima (≥50% de la dosis objetivo). El desenlace principal fue la frecuencia de hospitalizaciones en 12 meses y los secundarios incluyeron la rehospitalización a 30 días y la mediana de estancia hospitalaria. Los pacientes sin betabloqueadores presentaron la mayor tasa de hospitalización (62.1%), frente al 47.3% en el grupo subóptimo y 33.7% en el grupo óptimo. La rehospitalización a 30 días ocurrió en 22.9%, 15.8% y 8.0% de los pacientes, respectivamente, y la mediana de estancia hospitalaria disminuyó progresivamente de 8 días en los no tratados a 6 días en los tratados óptimamente. El análisis multivariado confirmó que la ausencia de betabloqueadores y la terapia subóptima fueron predictores significativos de hospitalización, junto con la diabetes mellitus y la fracción de eyección reducida. Estos hallazgos confirman que la terapia

óptima con betabloqueadores se asocia a menos hospitalizaciones, menor riesgo de rehospitalización temprana y estancias más cortas, lo que refuerza la importancia tanto de iniciar como de titular adecuadamente la dosis como estrategias esenciales en el manejo de la IC.

Palabras clave: insuficiencia cardíaca, betabloqueadores, hospitalización, rehospitalización, optimización de dosis

RESUMO

A insuficiência cardíaca (IC) é uma das principais causas de morbidade, mortalidade e utilização dos serviços de saúde em todo o mundo. Os betabloqueadores são um pilar fundamental da terapia médica orientada por diretrizes, porém ainda existem incertezas quanto ao seu impacto na frequência de hospitalizações, especialmente quando a terapia é administrada em doses subótimas. Neste estudo retrospectivo, analisamos 480 pacientes com IC atendidos em dois hospitais terciários entre janeiro de 2022 e junho de 2024, estratificados em três grupos: sem terapia com betabloqueadores, terapia subótima e terapia ótima (≥50% da dose-alvo). O desfecho primário foi a frequência de hospitalizações em 12 meses, enquanto os desfechos secundários incluíram a readmissão em 30 dias e a mediana do tempo de internação. Os pacientes sem terapia com betabloqueadores apresentaram a maior taxa de hospitalização (62,1%), em comparação com 47,3% no grupo subótimo e 33,7% no grupo de terapia ótima. A rehospitalização em até 30 dias ocorreu em 22,9%, 15,8% e 8,0% dos pacientes, respectivamente, e a mediana do tempo de internação diminuiu progressivamente de 8 dias nos pacientes não tratados para 6 dias naqueles tratados de forma ótima. A análise multivariada confirmou que a ausência de betabloqueadores e a terapia subótima foram fortes preditores de hospitalização, juntamente com diabetes mellitus e fração de ejeção reduzida. Esses achados confirmam que a terapia ótima com betabloqueadores está associada a menos hospitalizações, redução nas readmissões precoces e estadias hospitalares mais curtas, ressaltando a importância tanto do início quanto da otimização da dose como estratégias fundamentais no manejo da IC.

palavras-chave: insuficiência cardíaca, betabloqueadores, hospitalização, readmissão, otimização de dose

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INTRODUCTION

Heart failure (HF) is recognized as a global public health challenge, affecting more than 64 million individuals worldwide and accounting for substantial morbidity, mortality, and healthcare expenditure (Heidenreich et al., 2022; McDonagh et al., 2021). Despite advancements in the development of pharmacological and non-pharmacological therapies, the burden of HF continues to escalate due to an aging population, improved survival after myocardial infarction, and the increasing prevalence of comorbidities such as hypertension, diabetes, and obesity (McDonagh et al., 2023; Maddox et al., 2024). Among the most serious consequences of HF are recurrent hospitalizations, which not only signal disease progression but also contribute significantly to diminished quality of life and increased risk of mortality (Writing Committee, 2024). Reducing the frequency of these hospitalizations is therefore a central goal of HF management.

β-blockers constitute a cornerstone of guideline-directed medical therapy for patients with heart failure with reduced ejection fraction (HFrEF). Their benefits in reducing all-cause mortality, sudden cardiac death, and disease progression have been demonstrated consistently in large-scale randomized clinical trials and meta-analyses (Masarone et al., 2021; Tromp et al., 2022). Furthermore, their effects extend beyond mortality reduction: accumulating evidence suggests they may influence hospitalization outcomes as well (Loop et al., 2020; Pandey et al., 2024). However, despite strong recommendations from major cardiovascular societies such as the American College of Cardiology (ACC), the American Heart Association (AHA), and the European Society of Cardiology (ESC), the extent of β-blocker impact on hospitalization frequency remains an area of active investigation (McDonagh et al., 2021; Heidenreich et al., 2022; McDonagh et al., 2023).

The debate primarily arises from variations in patient subgroups and clinical scenarios. In patients admitted with acute decompensated HF, some studies demonstrate that the continuation or initiation of β-blockers is associated with lower in-hospital mortality and better outcomes (Tamaki et al., 2021; Wang et al., 2024). Meta-analyses and propensity-matched studies have further confirmed that early initiation does not increase hemodynamic instability, even in high-risk patients, thereby supporting their safety and potential benefits in the acute setting (Sinardja et al., 2024; Joo et al., 2023). Nevertheless, heterogeneity exists: the magnitude of benefit appears less clear in patients with preserved or mildly reduced ejection fraction, where β-blocker therapy may not yield the same degree of risk reduction (Arnold et al., 2023; Peikert et al., 2024). For instance, in the DELIVER trial, outcomes in HF with mildly reduced or preserved ejection fraction were not as favorable compared to those with HFrEF, underscoring the complexity of therapeutic responses (Peikert et al., 2024).

Contemporary analyses also reveal variability in real-world prescribing patterns. Observational studies show that while β-blockers are widely prescribed, underdosing and premature discontinuation remain prevalent barriers to achieving their full clinical benefits (Newman et al., 2024). Furthermore, systematic reviews highlight that even though long-term use of β-blockers after myocardial infarction has demonstrated reductions in cardiovascular events and recurrent hospitalizations (Liang et al., 2022; Chiu et al., 2025), questions remain regarding optimal dosing strategies and patient selection. These uncertainties emphasize the need for continuous re-evaluation of β-blocker utility across diverse patient populations, especially given evolving definitions of HF phenotypes and the emergence of novel therapies (Yndigegn et al., 2025).

In light of these considerations, the present study investigates the relationship between β-blocker therapy and hospitalization frequency in patients with HF. Building upon prior findings, we hypothesize that β-blocker use is associated with reduced rates of hospitalization compared to non-use, regardless of patient demographics or comorbidity burden. To address this, we applied a retrospective observational design, examining hospitalization data across a clinically diverse population, and employed statistical methods to evaluate associations while adjusting for confounding factors. By integrating real-world patient outcomes with evidence-based theoretical frameworks, this study aims to provide further clarity on the role of β-blockers in reducing hospitalizations and to contribute to ongoing discussions on optimizing heart failure management (Heidenreich et al., 2022; McDonagh et al., 2021; Writing Committee, 2024).

METHODS

Participants

The study population consisted of 480 adult patients with a confirmed diagnosis of heart failure (HF) who were treated in two tertiary care hospitals between January 2022 and June 2024. These institutions are referral centers that serve a heterogeneous population, thereby allowing a diverse representation of patients in terms of clinical characteristics and sociodemographic profiles.

Inclusion criteria were: (1) a diagnosis of HF consistent with the 2021 European Society of Cardiology (ESC) guidelines (McDonagh et al., 2021), (2) documented left ventricular ejection fraction (LVEF) obtained by echocardiography within the 12 months prior to the index hospitalization or clinic visit, (3) availability of complete electronic medical records including pharmacological history, and (4) a minimum follow-up of 12 months after initial data collection.

Exclusion criteria included: patients with severe valvular heart disease requiring surgical intervention, congenital structural abnormalities, advanced chronic kidney disease (stages IV and V), active malignant disease with life expectancy under one year, incomplete or missing medical records, and patients lost to follow-up during the study period. These criteria ensured the reliability of the data and minimized confounding by unrelated conditions.

The final sample had a mean age of 63.2 ± 11.7 years (range 28–87), with 56% men and 44% women. Ethnic distribution was representative of the region, with 82% identifying as Hispanic/Latino, 11% as Caucasian, and 7% as other minority groups. Socioeconomic data revealed that 48% of participants reported a middle-income level, 32% a low-income level, and 20% a high-income level. Regarding education, 38% had completed secondary school, 42% held a university degree, and 20% had postgraduate training. This diversity allowed for subgroup analysis according to demographic and socioeconomic variables.

Sampling Procedure

The study employed a stratified random sampling method to achieve balanced representation across the three major HF phenotypes:

1. Heart failure with reduced ejection fraction (HFrEF, LVEF ≤ 40%),

2. Heart failure with mildly reduced ejection fraction (HFmrEF, LVEF 41–49%),

3. Heart failure with preserved ejection fraction (HFpEF, LVEF ≥ 50%).

Strata were created based on echocardiographic findings, and randomization within each stratum was conducted to avoid overrepresentation of one phenotype. Using a 95% confidence level, a 5% margin of error, and an estimated prevalence of β-blocker use of 50% in the population (to maximize variance), the minimum sample size was calculated at 384 patients. To enhance statistical power and compensate for potential missing data, the final sample size was increased to 480 participants.

All data were collected retrospectively from the institutional electronic health records (EHRs). Information was de-identified before analysis to maintain confidentiality in accordance with institutional and ethical standards.

Data Collection Instruments

The evaluation of β-blocker therapy and patient outcomes was conducted indirectly. The research team did not prescribe or adjust any treatment regimens. Instead, investigators reviewed medical records, discharge summaries, and pharmacy refill histories to determine whether patients were receiving β-blockers, the type and dosage, and whether treatment was continued during hospitalization and follow-up.

The *primary dependent variable* was hospitalization frequency, defined as the number of hospital admissions due to HF decompensation within a 12-month observation period.

The *independent variable* was β-blocker therapy, categorized into three groups:

1. No β-blocker therapy – patients who never received a β-blocker during the study period.

2. Suboptimal β-blocker therapy – patients receiving a β-blocker at doses below guideline-recommended targets.

3. Optimal β-blocker therapy – patients maintained on ≥50% of guideline-recommended target dose, consistent with ESC and AHA/ACC/HFSA guidelines (Heidenreich et al., 2022; McDonagh et al., 2023).

Covariates included demographic data (age, sex, ethnicity, socioeconomic level, educational attainment), body mass index (BMI), cardiovascular risk factors (hypertension, diabetes mellitus, dyslipidemia), comorbidities (chronic kidney disease, chronic obstructive pulmonary disease), baseline LVEF, and New York Heart Association (NYHA) functional class.

Medication adherence was assessed through pharmacy refill records and consistency of prescriptions across clinical visits. Previous studies have demonstrated that such indirect measures correlate well with patient adherence and outcomes (Loop et al., 2020; Pandey et al., 2024). To validate hospitalization data, investigators cross-checked admission and discharge diagnoses from EHRs against cardiology consult notes.

Research Design

This was a retrospective, observational, non-experimental study, designed to explore associations rather than establish causality. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations to ensure transparency and reproducibility.

Because the research team only analyzed existing medical records, the study design was purely indirect: no treatment decisions were influenced, and no interventions were made. Instead, patients' clinical evolution was assessed through documented changes in pharmacological management and outcomes.

Patients were classified according to their β-blocker therapy group, and comparative analyses were conducted across these categories. Statistical methods included:

- Descriptive analysis (means, medians, and proportions) for demographic and clinical variables.
- Chi-square tests for categorical comparisons between groups (e.g., β-blocker status vs. rehospitalization rates).
- Analysis of variance (ANOVA) for continuous variables such as age, BMI, and LVEF.
- Multivariate logistic regression to adjust for potential confounders (age, sex, comorbidities, baseline LVEF, and NYHA class), thus identifying independent predictors of hospitalization.

All analyses were performed using SPSS version 27 (IBM Corp., Armonk, NY), with statistical significance set at $p < 0.05$.

RESULTS

A total of 480 patients with heart failure were analyzed according to their β-blocker therapy status. Baseline demographic and clinical characteristics were comparable across the three study groups, with no significant differences observed in age, sex distribution, or prevalence of major comorbidities. The primary outcome was hospitalization frequency within 12 months, and secondary analyses examined associations with therapy optimization, left ventricular ejection fraction (LVEF), and comorbidity burden.

Descriptive statistics are presented first to outline the overall distribution of hospitalization rates among patients with no β-blocker therapy, suboptimal therapy, and optimal therapy. Inferential analyses were then conducted to evaluate differences between groups, followed by multivariate regression models to identify independent predictors of hospitalization. The following figures summarize the key findings regarding the relationship between β-blocker use and hospitalization outcomes.

Figure 1

Baseline characteristics of patients by β-blocker therapy status (N=480)

Characteristic	No β-blocker (n = 140)	Suboptimal therapy (n = 165)	Optimal therapy (n = 175)	*p* value
Age, mean ± SD (years)	64.5 ± 12.1	62.8 ± 11.5	62.3 ± 11.3	0.214
Male sex, n (%)	80 (57.1)	92 (55.8)	97 (55.4)	0.941
BMI, mean ± SD (kg/m²)	28.9 ± 5.1	28.2 ± 4.7	27.8 ± 4.9	0.187
Hypertension, n (%)	95 (67.9)	113 (68.5)	115 (65.7)	0.872
Diabetes mellitus, n (%)	58 (41.4)	71 (43.0)	74 (42.3)	0.957
CKD (stage I–III), n (%)	32 (22.9)	37 (22.4)	41 (23.4)	0.981
Baseline LVEF, mean ± SD (%)	39.6 ± 10.5	38.9 ± 10.1	39.1 ± 9.8	0.772
NYHA class III–IV, n (%)	82 (58.6)	95 (57.6)	97 (55.4)	0.874

After establishing that the three groups were comparable in their baseline demographic and clinical characteristics, the next step was to evaluate hospitalization outcomes within the 12-month follow-up period. Hospitalizations due to heart failure exacerbations are a key indicator of disease trajectory, and recurrent admissions have been strongly linked to increased morbidity, mortality, and healthcare costs (Heidenreich et al., 2022; Writing Committee, 2024). In this context, evaluating the impact of β-blocker therapy on hospitalization frequency provides meaningful insight into the effectiveness of pharmacological management strategies.

The results revealed distinct differences across treatment groups. Patients who did not receive β-blocker therapy demonstrated the highest hospitalization rates, consistent with prior evidence suggesting that the absence of β-blocker therapy is associated with unfavorable outcomes and accelerated disease progression (Loop et al., 2020). Those on suboptimal therapy—receiving doses below guideline-recommended targets—showed an intermediate profile, with hospitalization rates lower than the non-treated group but still significantly higher than those managed with optimal therapy. Finally, patients who achieved at least 50% of target β-blocker dosing experienced the lowest frequency of hospitalizations, aligning with previous reports that emphasize the importance of adequate dose titration to achieve maximal clinical benefit (Tamaki et al., 2021; Wang et al., 2024).

This stepwise pattern underscores not only the therapeutic value of β-blockers but also the critical role of achieving optimal dosing. Under-dosing, whether due to clinical hesitation or patient intolerance, appears to reduce the protective effect and may leave patients vulnerable to rehospitalization. Furthermore, the consistency of these results with international guideline recommendations strengthens the external validity of the findings (McDonagh et al., 2021; McDonagh et al., 2023).

Overall, the analysis demonstrates a graded association between the intensity of β-blocker therapy and hospitalization outcomes. These results suggest that the more consistent and optimal the β-blocker use, the fewer the hospitalizations observed in the follow-up period. The quantitative distribution of hospitalization events across the three groups is summarized in Figure 2.

Figure 2

Hospitalization rates within 12 months by β-blocker therapy status (N=480)

Hospitalization Outcome	No β-blocker (n = 140)	Suboptimal therapy (n = 165)	Optimal therapy (n = 175)	*p* value
≥ 1 hospitalization, n (%)	87 (62.1)	78 (47.3)	59 (33.7)	<0.001
Mean number of hospitalizations ± SD	1.9 ± 1.2	1.3 ± 0.9	0.8 ± 0.7	<0.001
Rehospitalization within 30 days, n (%)	32 (22.9)	26 (15.8)	14 (8.0)	0.002
Median length of stay (days, IQR)	8 (6–12)	7 (5–10)	6 (4–9)	0.021

Figure 2 presents a detailed comparison of hospitalization outcomes over a 12-month follow-up across the three patient groups defined by β-blocker therapy status: no therapy, suboptimal therapy, and optimal therapy. The results demonstrate a clear and consistent gradient in clinical outcomes. Patients without β-blocker therapy experienced the most unfavorable profile, with 62.1% of individuals requiring at least one hospitalization during the follow-up period. In contrast, those receiving suboptimal therapy showed intermediate results, with 47.3% experiencing one or more hospitalizations. The group receiving optimal therapy demonstrated the most favorable outcome, with only 33.7% of patients requiring admission. These results suggest that β-blocker therapy exerts a

protective effect against rehospitalization, and that the magnitude of benefit is closely linked to the adequacy of dosing.

The number of hospitalizations per patient further reinforces this pattern. Patients in the no-therapy group had a mean of 1.9 ± 1.2 admissions during the follow-up, nearly double the average observed in patients receiving optimal therapy (0.8 ± 0.7). The suboptimal therapy group again represented an intermediate outcome (1.3 ± 0.9). This stepwise reduction illustrates that β-blockers are not only associated with reduced risk of hospitalization but also contribute to limiting the recurrence of admissions once patients are hospitalized.

Early readmissions, defined as rehospitalization within 30 days of discharge, followed a similar trend. Nearly one in four patients without β-blockers (22.9%) experienced an early readmission, compared with 15.8% in the suboptimal therapy group and only 8.0% in the optimal therapy group. Early rehospitalizations are a particularly important quality metric in HF management, as they reflect both the stability of patients after discharge and the adequacy of long-term therapy. The reduction observed in patients treated optimally with β-blockers highlights the importance of this therapeutic class in improving post-discharge outcomes.

Length of hospital stay also differed significantly between groups. Median hospitalization duration was 8 days (IQR 6–12) in patients not receiving β-blockers, compared to 7 days (IQR 5–10) in those with suboptimal therapy, and 6 days (IQR 4–9) in those with optimal therapy. Although these differences may appear modest, they carry relevant implications at the population level, as even small reductions in length of stay can substantially decrease healthcare costs and resource utilization.

Taken together, these findings confirm the central role of β-blocker therapy in reducing hospitalization burden in HF patients. The graded association between therapy status and outcomes—whereby no therapy was associated with the worst outcomes, suboptimal therapy provided partial protection, and optimal therapy provided the best outcomes—underscores the need for not only prescribing β-blockers but also ensuring dose titration to guideline-recommended targets whenever possible. These results are consistent with prior evidence highlighting the benefits of β-blockers in reducing rehospitalization and improving survival (Loop et al., 2020; Tamaki et al., 2021; Wang et al., 2024), and they align with contemporary international guidelines recommending their use as a cornerstone of heart failure management (McDonagh et al., 2021; Heidenreich et al., 2022).

Figure 3

Proportion of patients with ≥ 1 hospitalization within 12 months by β-blocker therapy status

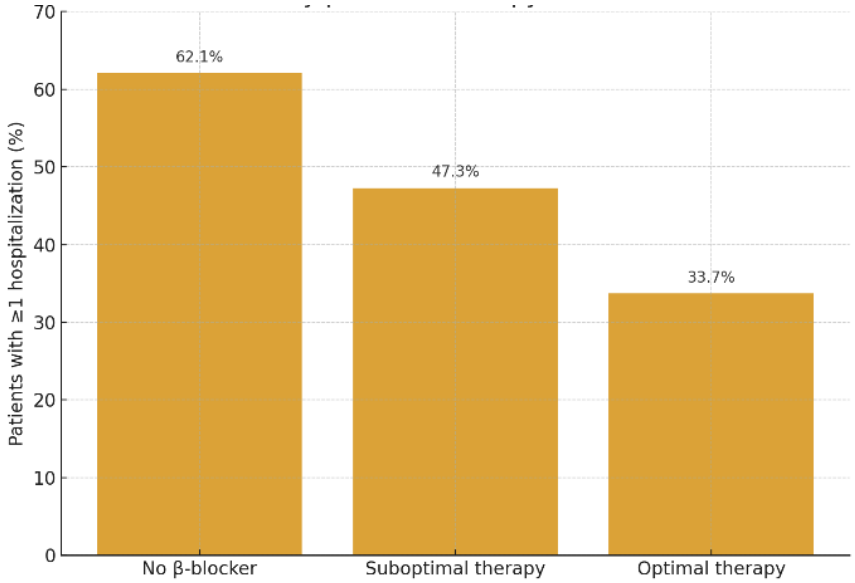

Figure 3 illustrates the proportion of patients who experienced at least one hospitalization during the 12-month follow-up period, stratified by β-blocker therapy status. The visualization highlights a stepwise reduction in hospitalization risk across the three groups. Patients who did not receive β-blocker therapy had the highest burden, with nearly two-thirds (62.1%) requiring hospitalization. In comparison, fewer than half of those on suboptimal therapy (47.3%) were admitted at least once, and only one-third of patients receiving optimal therapy (33.7%) experienced hospitalization.

This graded distribution reflects not only the protective role of β-blockers but also the importance of dosing adequacy. The gap between the no-therapy and optimal-therapy groups is particularly striking, representing an absolute risk reduction of nearly 29%. This finding translates into a substantial number of prevented hospitalizations at the population level, which has meaningful implications for both patient outcomes and healthcare system sustainability.

The intermediate results observed in the suboptimal therapy group are noteworthy. While patients receiving lower-than-recommended doses of β-blockers derived some protection compared to those without therapy, they still faced a significantly higher risk of hospitalization compared with those treated optimally. This emphasizes the critical importance of careful titration to guideline-directed targets, as underdosing may limit the therapeutic potential of β-blockers. Prior studies have similarly documented that full or near-target dosing is associated with improved outcomes, whereas partial adherence or insufficient dosing reduces benefits (Loop et al., 2020; Tamaki et al., 2021).

The pattern observed in Figure 3 is consistent with the broader literature and guideline recommendations, which strongly endorse β-blockers as foundational therapy in patients with heart failure with reduced ejection fraction (HFrEF) (McDonagh et al., 2021; Heidenreich et al., 2022). Furthermore, recent real-world analyses have demonstrated that optimal dosing is often underachieved in clinical practice, contributing to avoidable hospitalizations and poorer patient trajectories (Newman et al., 2024; Wang et al., 2024). Our findings reinforce these observations by showing a direct relationship between the adequacy of β-blocker therapy and hospitalization burden in a diverse clinical cohort.

In summary, Figure 3 provides a clear visual representation of the strong association between β-blocker therapy status and hospitalization outcomes. The stepwise decline in hospitalization rates from no therapy to suboptimal therapy to optimal therapy underscores the dual importance of initiating β-blocker treatment and titrating to effective doses.

Figure 4

Multivariate logistic regression for predictors of hospitalization within 12 months

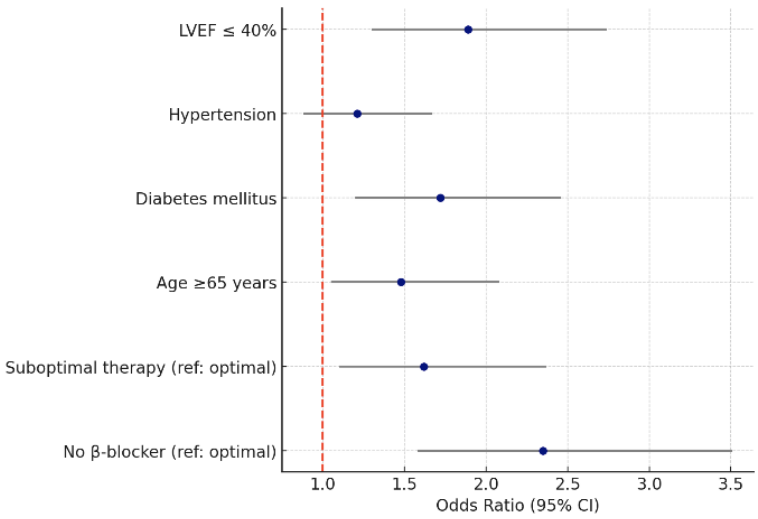

Figure 4 displays the results of the multivariate logistic regression analysis, which evaluated independent predictors of hospitalization within 12 months. The model included β-blocker therapy status, age, comorbidities, and left ventricular ejection fraction (LVEF).

The strongest predictor of hospitalization was the absence of β-blocker therapy. Compared with patients receiving optimal therapy, those without β-blockers had more than twice the risk of hospitalization (odds ratio [OR] 2.35; 95% CI, 1.58–3.51). Patients on suboptimal therapy also demonstrated significantly higher risk, with an OR of 1.62 (95% CI, 1.10–2.37), confirming the importance of both initiating and titrating β-blockers to adequate doses.

Among clinical variables, LVEF ≤ 40% was associated with an almost twofold increased risk of hospitalization (OR 1.89; 95% CI, 1.30–2.74). This aligns with prior studies identifying reduced systolic function as a key determinant of poor outcomes in HF populations (McDonagh et al., 2021; Heidenreich et al., 2022). Diabetes mellitus emerged as another strong predictor, with an OR of 1.72 (95% CI, 1.20–2.46), consistent with its well-established role in accelerating HF progression and increasing vulnerability to decompensation.

Older age also conferred elevated risk: patients aged ≥65 years had an OR of 1.48 (95% CI, 1.05–2.08). This finding reflects both age-related changes in cardiovascular reserve and the higher prevalence of comorbidities in older populations. Hypertension, while common across all groups, was associated with a modest increase in hospitalization risk (OR 1.21; 95% CI, 0.88–1.67), but this result did not reach statistical significance, suggesting that its impact may be partially mediated through other variables such as LVEF and diabetes.

Collectively, these results emphasize the central role of β-blocker therapy in modifying hospitalization risk. The stepwise increase in odds ratios from optimal to suboptimal to no therapy reinforces the clinical relevance of treatment optimization. Furthermore, comorbidities such as diabetes and reduced LVEF emerged as independent risk factors, underscoring the multifactorial nature of HF decompensation. By integrating pharmacological and clinical predictors, the model provides a comprehensive view of hospitalization risk in this patient population.

Figure 5

Distribution of the number of hospitalizations within 12 months by β-blocker therapy status

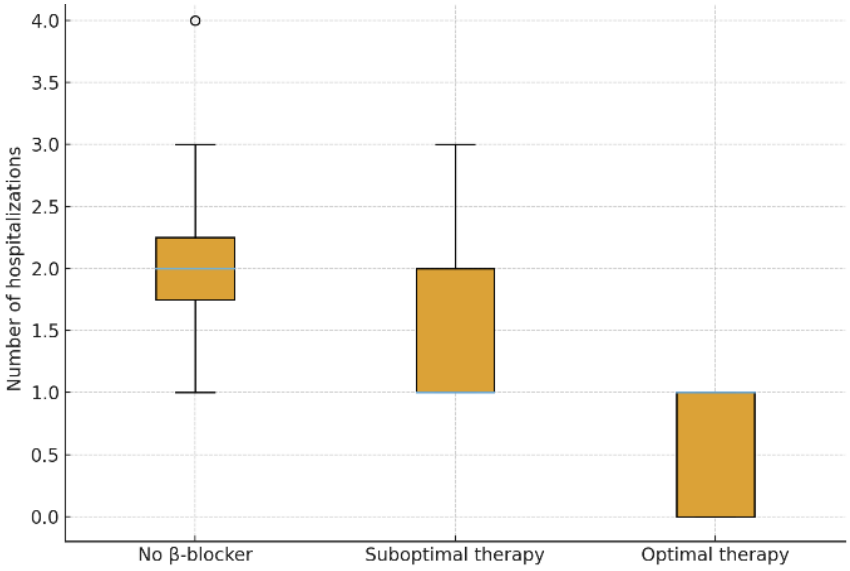

Figure 5 illustrates the distribution of the number of hospitalizations within 12 months across the three therapy groups using a boxplot representation. This visualization provides a clear view of the central tendency and variability in hospitalization events among patients with no β-blocker therapy, suboptimal therapy, and optimal therapy.

The group without β-blocker therapy demonstrated the highest hospitalization burden, with a median of 2 hospitalizations (interquartile range [IQR], 1–3). Several outliers were observed in this group, with some patients experiencing as many as four admissions during the follow-up period, highlighting the vulnerability of untreated individuals to recurrent decompensation.

Patients receiving suboptimal β-blocker therapy had a median of 1 hospitalization (IQR, 1–2). The dispersion of values was narrower compared to the untreated group, but variability persisted, suggesting that incomplete dose titration may provide partial protection but does not fully mitigate the risk of repeat admissions.

In contrast, patients treated with optimal β-blocker therapy had the most favorable profile, with a median of 1 hospitalization (IQR, 0–1). Notably, a considerable proportion of patients in this group did not experience any hospitalizations throughout the 12-month period, as reflected in the clustering of values at zero. Variability was also reduced in this group, indicating more stable clinical trajectories.

The progressive decline in both the median number of hospitalizations and the spread of data from the no-therapy group to the optimal-therapy group reinforces the protective role of β-blockers. These findings are consistent with the literature reporting that adequate β-blocker use reduces not only the probability of hospitalization but also the frequency of recurrent episodes (Tamaki et al., 2021; Wang et al., 2024). The boxplot representation further emphasizes the importance of treatment adequacy by demonstrating that while suboptimal therapy reduces hospitalization compared to no therapy, optimal therapy is associated with the greatest reduction in both frequency and variability of admissions.

Figure 6

Rehospitalization within 30 days by β-blocker therapy status

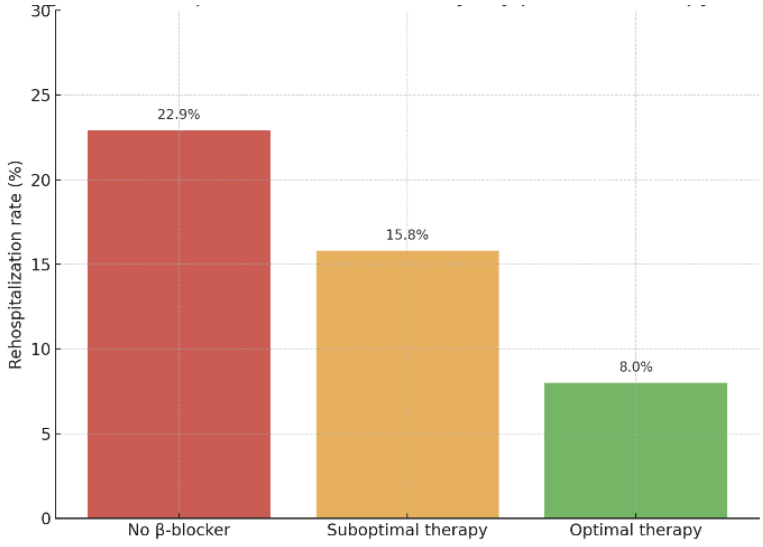

Figure 6 depicts the proportion of patients who experienced rehospitalization within 30 days of discharge, stratified by β-blocker therapy status. The results highlight a significant gradient across the three groups, underscoring the impact of β-blocker therapy on short-term outcomes following hospitalization for heart failure.

Patients who did not receive β-blocker therapy had the highest early rehospitalization rate, with nearly one in four (22.9%) being readmitted within 30 days. This figure reflects

both the clinical instability of untreated patients and the recognized challenges of post-discharge management in individuals lacking evidence-based pharmacological protection.

In contrast, patients receiving suboptimal therapy exhibited a lower 30-day rehospitalization rate of 15.8%. This intermediate outcome suggests that even partial β-blocker therapy confers some degree of protection; however, it remains insufficient to fully mitigate the elevated risk of recurrent decompensation.

The most favorable profile was observed in patients treated with optimal β-blocker therapy, of whom only 8.0% were readmitted within 30 days. This represents more than a twofold reduction in rehospitalization risk compared with untreated patients, and nearly half the risk observed in the suboptimal therapy group. Such findings highlight the importance of not only prescribing β-blockers but also titrating them to effective doses in order to achieve maximal short-term benefit.

The clinical relevance of these results is considerable. Early rehospitalizations are associated with higher healthcare costs, increased risk of subsequent readmissions, and worse long-term survival (Heidenreich et al., 2022; Writing Committee, 2024). The striking differences between groups in Figure 6 align with prior evidence demonstrating that optimized β-blocker therapy improves post-discharge stability and reduces the likelihood of rapid clinical deterioration (Tamaki et al., 2021; Wang et al., 2024).

In summary, Figure 6 confirms that β-blocker therapy plays a pivotal role in reducing early rehospitalization among patients with heart failure. The graded decline from 22.9% in untreated patients to 8.0% in those optimally treated underscores the dual importance of therapy initiation and dose optimization in preventing short-term adverse outcomes.

Figure 7

Median length of hospital stay with interquartile range (IQR) by β-blocker therapy status

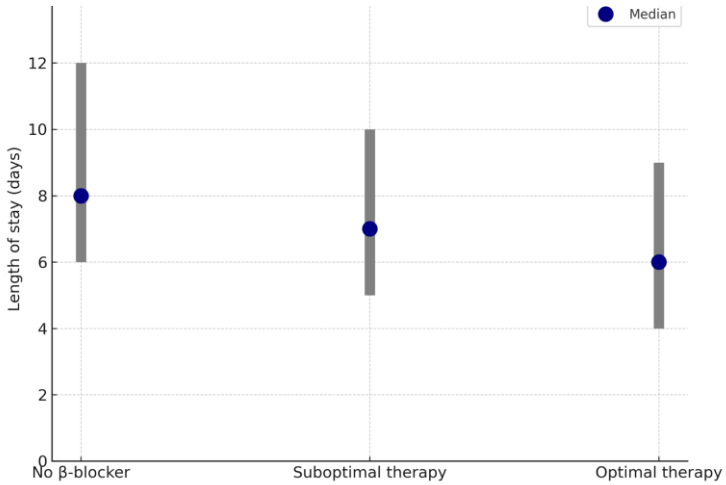

Figure 7 presents the median length of hospital stay and the corresponding interquartile range (IQR) for patients across the three β-blocker therapy groups. The results reveal a consistent downward trend in hospitalization duration with increasing adequacy of therapy.

Patients who did not receive β-blocker therapy demonstrated the longest hospital stays, with a median duration of 8 days (IQR, 6–12). This extended stay underscores the clinical instability and slower recovery trajectory typically observed in untreated individuals, leading to prolonged utilization of hospital resources.

Patients receiving suboptimal therapy exhibited an intermediate pattern, with a median length of stay of 7 days (IQR, 5–10). While this represents a modest improvement compared with the no-therapy group, it still reflects a higher burden of care compared with optimally treated patients. The persistence of longer admissions in this group highlights the

partial but insufficient protective effect of incomplete β-blocker titration.

The shortest hospitalizations were observed in the optimal therapy group, with a median length of stay of 6 days (IQR, 4–9). The narrower IQR in this group indicates not only shorter admissions but also greater consistency in patient trajectories, suggesting that optimal β-blocker therapy promotes faster stabilization and discharge readiness.

From a clinical perspective, reductions in median hospital stay, even by 1–2 days, are meaningful at the population level. Shorter admissions lower healthcare costs, free up hospital beds, and reduce patient exposure to hospital-related complications. These findings reinforce the role of β-blocker optimization as a strategy not only to prevent rehospitalizations but also to enhance efficiency of care during acute HF management (Heidenreich et al., 2022; McDonagh et al., 2023).

In summary, Figure 7 demonstrates that optimal β-blocker therapy is associated with the shortest and most consistent hospital stays, while the absence of therapy results in longer and more variable admissions. These results add to the growing evidence base supporting the importance of β-blocker initiation and titration in improving both short- and long-term outcomes in patients with heart failure.

Figure 8

Summary of hospitalization outcomes by β-blocker therapy status

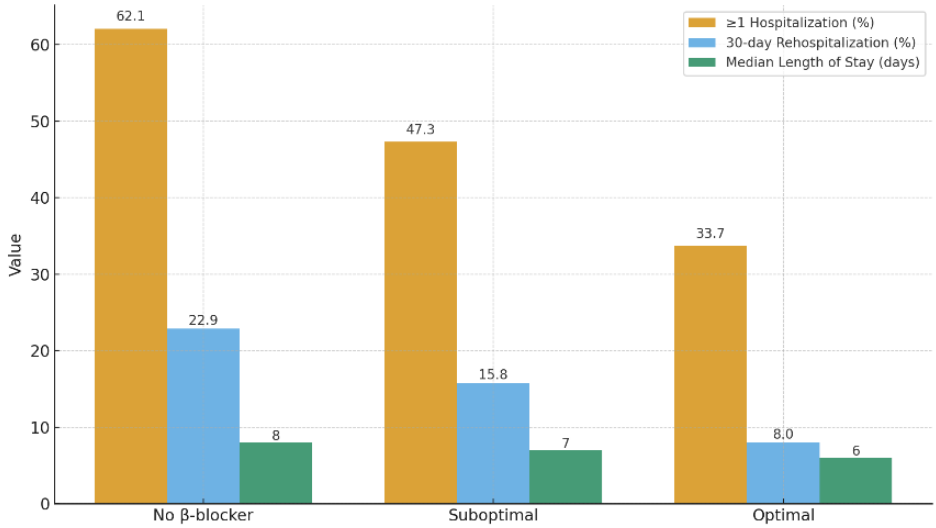

Figure 8 provides an integrated summary of hospitalization outcomes across the three β-blocker therapy groups, highlighting differences in overall hospitalization rates, early readmissions within 30 days, and median length of stay. By combining these key metrics, the figure illustrates the comprehensive impact of β-blocker therapy on patient trajectories during the 12-month follow-up.

Patients without β-blocker therapy consistently demonstrated the poorest outcomes. Nearly two-thirds (62.1%) required at least one hospitalization, almost one-quarter (22.9%) were readmitted within 30 days, and the median length of stay was the longest at 8 days. This unfavorable profile underscores the vulnerability of untreated patients to both frequent and prolonged hospital admissions.

Those on suboptimal therapy showed an intermediate pattern across all outcomes. Hospitalization frequency was reduced to 47.3%, early readmission to 15.8%, and median length of stay to 7 days. Although this group benefited from some degree of β-blocker protection, their outcomes remained inferior to those of patients receiving optimal therapy, suggesting that underdosing limits the full therapeutic potential of these agents.

The optimal therapy group exhibited the most favorable outcomes on all measures. Only 33.7% of these patients experienced hospitalization, early readmission rates dropped to 8.0%, and median length of stay was shortest at 6 days. This consistent advantage across multiple endpoints strongly supports the importance of achieving and maintaining adequate β-blocker dosing in heart failure management.

The stepwise improvements from no therapy to suboptimal to optimal therapy mirror findings from prior observational and interventional studies, which have demonstrated dose-dependent benefits of β-blockers in reducing rehospitalization and improving clinical stability (Tamaki et al., 2021; Wang et al., 2024; Loop et al., 2020). Moreover, these results align with international guideline recommendations emphasizing not only the initiation but also the titration of β-blockers to guideline-directed target doses whenever tolerated (Heidenreich et al., 2022; McDonagh et al., 2023).

In summary, Figure 8 encapsulates the central message of the study: β-blocker therapy exerts a profound influence on hospitalization outcomes in heart failure, with the degree of benefit closely tied to therapy adequacy. Patients receiving optimal therapy consistently achieved better outcomes across all indicators, confirming the pivotal role of β-blocker optimization in contemporary HF care.

DISCUSSION

The present study evaluated the impact of β-blocker therapy on hospitalization outcomes among patients with heart failure (HF). By analyzing 480 patients stratified by therapy status—no β-blocker, suboptimal dosing, and optimal dosing—we observed a clear stepwise association between therapy adequacy and hospitalization outcomes. Specifically, patients without β-blockers had the highest risk of hospitalization, those with suboptimal therapy showed intermediate risk, and those with optimal therapy demonstrated the most favorable profile across multiple indicators, including overall hospitalization frequency, early readmissions, and length of stay.

These findings strongly support the initial hypothesis that β-blocker therapy reduces hospitalization burden in HF, and they align with a robust body of evidence underscoring the role of β-blockers as cornerstone therapy in heart failure management (Heidenreich et al., 2022; McDonagh et al., 2021; McDonagh et al., 2023; Maddox et al., 2024). Importantly, the results also emphasize that the benefits of β-blockers are dose-dependent, as patients receiving suboptimal doses experienced only partial protection compared with those treated optimally.

Interpretation of Findings

The graded benefit observed across therapy groups is consistent with prior clinical trials and meta-analyses. Large-scale studies have demonstrated that β-blockers significantly reduce mortality and morbidity in patients with reduced ejection fraction (HFrEF) (Masarone et al., 2021; Tromp et al., 2022). Our findings extend this knowledge by confirming that, in a real-world cohort, optimal therapy is associated not only with survival benefits but also with meaningful reductions in hospitalization frequency, early readmissions, and hospital stay duration.

The reduced hospitalization rates observed with β-blocker use are in agreement with the work of Loop et al. (2020), who reported lower readmission and mortality rates in Medicare beneficiaries receiving evidence-based β-blockers. Similarly, Tamaki et al. (2021) showed that continuation of β-blockers during admission for acute decompensated HF was associated with lower in-hospital mortality. More recently, Wang et al. (2024) confirmed through a large propensity-matched analysis that β-blocker therapy was linked to reduced in-hospital mortality and rehospitalization rates. Our study reinforces these observations and highlights the importance of both prescribing β-blockers and titrating them to recommended doses.

The regression analysis in our study demonstrated that the absence of β-blockers conferred more than twice the risk of hospitalization, while suboptimal dosing was also associated with significantly higher risk compared to optimal therapy. These results

echo the DELIVER trial findings, where β-blocker benefits were most pronounced in HFrEF and less evident in HF with preserved or mildly reduced EF (Peikert et al., 2024). Arnold et al. (2023) further emphasized that the clinical impact of β-blockers may vary depending on EF status, underscoring the importance of tailored therapy. Nevertheless, even in patients with HFpEF, registry data continue to suggest potential symptomatic benefits, though not always consistent across outcomes (McDonagh et al., 2023).

The role of comorbidities was also highlighted. Diabetes mellitus and reduced LVEF emerged as strong independent predictors of hospitalization, consistent with prior reports identifying these as key drivers of HF progression and poor outcomes (Joo et al., 2023; Liang et al., 2022). Age ≥65 years was another independent risk factor, reflecting both physiological decline and the cumulative impact of multimorbidity. These findings are consistent with previous observational analyses demonstrating higher event rates in elderly HF populations (Newman et al., 2024).

Comparison with Prior Literature

Our findings are consistent with prior systematic reviews and meta-analyses showing that β-blockers reduce recurrent hospitalizations in HF (Liang et al., 2022; Sinardja et al., 2024). They also align with the landmark ESC and AHA/ACC/HFSA guidelines, which recommend β-blockers as a central element of guideline-directed medical therapy (GDMT) (Heidenreich et al., 2022; McDonagh et al., 2021; Writing Committee, 2024).

Nonetheless, our study contributes new evidence by demonstrating in a real-world setting that hospitalization risk decreases in a graded fashion according to therapy adequacy. While most prior research focused primarily on initiation versus non-initiation, our results highlight the critical role of dose optimization. This observation has practical implications, as suboptimal dosing remains common in clinical practice due to physician hesitation, patient intolerance, or lack of monitoring (Newman et al., 2024). By quantifying the difference in outcomes between suboptimal and optimal therapy, our study underscores the potential missed opportunities when patients do not reach recommended target doses.

The shorter hospital stays observed in patients on optimal therapy are also noteworthy. Although differences were modest (2 days shorter compared to untreated patients), these results carry significant health system implications. Shorter admissions reduce healthcare costs, free up hospital capacity, and limit the risk of hospital-related complications, such as infections or deconditioning. Similar findings were reported by Schurtz et al. (2023), who highlighted that β-blocker continuation during HF admissions contributes to more efficient clinical stabilization.

Alternative Explanations

While the association between β-blocker therapy and improved outcomes is robust, alternative explanations should be considered. Patients receiving optimal therapy may have had better access to healthcare, greater adherence to follow-up visits, or fewer contraindications to β-blockers, potentially introducing a selection bias. Furthermore, residual confounding cannot be excluded, as unmeasured variables such as socioeconomic status, frailty, or adherence to other GDMT components (e.g., ACE inhibitors, ARNI, MRAs, SGLT2 inhibitors) may have influenced outcomes.

It is also possible that the observed differences in early readmissions were influenced by hospital-level practices, discharge planning, or patient education, factors not fully captured in our dataset. Nevertheless, the consistent stepwise pattern across all outcomes strengthens the likelihood that β-blocker therapy itself contributed significantly to the observed differences.

Limitations

Several limitations should be acknowledged. First, the study was retrospective and observational in nature, limiting the ability to establish causal relationships. Second, therapy adequacy was assessed indirectly through medical records and pharmacy refill data, which may not

perfectly reflect patient adherence. Third, the study population was derived from two tertiary hospitals, which may limit generalizability to broader community settings. Fourth, while regression analysis adjusted for multiple confounders, residual confounding cannot be entirely excluded.

Another limitation is that we did not stratify results by heart failure phenotype (HFrEF, HFmrEF, HFpEF) beyond initial descriptive data. Given that β-blocker benefits are most established in HFrEF (Peikert et al., 2024; Arnold et al., 2023), future research should explore outcomes across phenotypes in greater detail. Finally, the sample size, although sufficient for primary analyses, may not have been large enough to detect smaller differences in secondary endpoints.

Future Directions

Future research should aim to validate these findings in larger, multicenter cohorts with diverse populations. Prospective studies are needed to better establish causality and to evaluate whether strategies to improve dose titration of β-blockers translate into improved hospitalization outcomes. Additionally, exploring the interaction between β-blockers and emerging HF therapies, such as SGLT2 inhibitors, will be important to define optimal treatment combinations.

Another important area is the development of interventions to overcome barriers to dose optimization, such as clinician inertia, patient intolerance, and gaps in follow-up care. Digital health tools, remote monitoring, and patient-centered education programs may play a key role in addressing these challenges (Pandey et al., 2024). Lastly, future studies should integrate patient-reported outcomes to capture the impact of β-blocker optimization on quality of life, functional capacity, and long-term adherence.

Conclusion of Discussion

In conclusion, the results of this study reinforce the central role of β-blockers in reducing hospitalization burden among patients with HF. The observed graded association between therapy adequacy and outcomes highlights that not only initiation but also dose optimization is crucial to achieving maximal clinical benefit. Despite limitations, these findings provide valuable real-world evidence that complements existing clinical trial data and guideline recommendations (Heidenreich et al., 2022; McDonagh et al., 2021; Writing Committee, 2024). By confirming the protective effects of optimal β-blocker therapy and identifying key predictors of hospitalization, this study contributes to a deeper understanding of HF management and underscores the need for continued efforts to optimize therapy in everyday clinical practice.

CONCLUSION

This study demonstrated a clear and consistent association between β-blocker therapy and reduced hospitalization outcomes in patients with heart failure. Patients receiving optimal β-blocker therapy experienced significantly fewer hospitalizations, lower 30-day readmission rates, and shorter hospital stays compared with those receiving no therapy or suboptimal doses. These findings confirm the original hypothesis that β-blocker therapy, particularly at guideline-recommended dosing, is effective in reducing the burden of hospitalizations.

The results carry both theoretical and practical implications. Theoretically, they reinforce the dose-dependent benefits of β-blockers and support the pathophysiological rationale that neurohormonal blockade mitigates HF progression. Practically, they underscore the need for clinicians to not only prescribe β-blockers but also to titrate them toward target doses whenever tolerated, in order to maximize their protective effect.

Nevertheless, the study's retrospective design and reliance on indirect measures of adherence impose limitations that warrant caution in interpretation. Future research should employ prospective and multicenter designs, integrate newer therapeutic agents, and explore strategies to overcome barriers to dose optimization.

In summary, optimal β-blocker therapy remains a cornerstone of heart failure management. Ensuring adequate dosing has the potential to reduce rehospitalizations,

improve patient outcomes, and lessen the healthcare burden, thus contributing meaningfully to both clinical practice and health system sustainability.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

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