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USE OF SGLT2 INHIBITORS IN PATIENTS WITH HEART FAILURE TREATED AT A SPECIALIZED SUS CLINIC: A RETROSPECTIVE OBSERVATIONAL ANALYSIS AT QUALICIS IN GUARAPUAVA, PARANÁ

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Abstract: Introduction: Sodium-glucose cotransporter-2 (SGLT2) inhibitors have come to occupy a central role in the treatment of heart failure (HF), with demonstrated benefits across different ejection fraction ranges, regardless of the presence of diabetes mellitus. Objective: To evaluate, in a retrospective cohort of patients with heart failure followed in a specialized SUS service, echocardiographic, clinical, and renal outcomes observed after the use of SGLT2Is, with an emphasis on changes in left ventricular ejection fraction (LVEF), the occurrence of cardiovascular events, and serum creatinine trends. Methods: An observational, analytical, and retrospective study based on electronic medical records of 200 patients with HF followed at QUALICIS in Guarapuava, Paraná. Sociodemographic, clinical, echocardiographic, and laboratory variables were analyzed according to their availability in the records. Subanalyses of LVEF and creatinine were restricted to patients with documented paired measurements. For clinical outcomes, a descriptive analysis of events after initiation of therapy and an estimate of event-free survival using the Kaplan-Meier method were performed. Results: Among the 59 patients with paired LVEF, the mean change was +2.54 percentage points (SD $\pm$ 8.37), with a median of +5.0. Super-response, defined as an increase in LVEF of $\geq$ 10 percentage points, was observed in 27.1% (n = 16). Among the 22 patients with a baseline LVEF < 40%, 54.5% (n = 12) met the criteria for heart failure with a recovered ejection fraction. In the exploratory analysis of predictors, obesity showed a tendency toward a association with super-response (41.7% versus 17.1%; OR 3.45; p = 0.07). Among 198 patients evaluated for events, 22 (11.1%) experienced a cardiovascular or hospitalization outcome after initiating iS-

GLT2. In the creatinine-matched subsample (n = 69), the mean change was +0.16 mg/dL (SD $\pm$ 0.55). Conclusion: In this real-world retrospective cohort, the use of iSGLT2 was associated with an overall favorable profile of clinical stability, a low frequency of recorded events, and echocardiographic and renal behavior consistent with the applicability of this class in a specialized outpatient setting within the Brazilian Unified Health System (SUS). The findings should be interpreted with caution due to the observational design, the absence of a control group, and the significant incompleteness of data.

Keywords: heart failure; SGLT2 inhibitors; dapagliflozin; empagliflozin; ejection fraction; observational study.

Introduction

Heart failure (HF) is a complex clinical syndrome with high morbidity and mortality, characterized by symptoms and signs resulting from cardiac structural and/or functional abnormalities, with hemodynamic and neurohormonal repercussions. Its contemporary classification includes, among other phenotypes, heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction, and preserved ejection fraction—a distinction relevant for therapeutic, prognostic, and research purposes. (2)

In recent decades, the treatment of HF has evolved from a predominantly symptomatic strategy to an approach guided by prognosis-modifying therapy. In this context, SGLT2 inhibitors have taken on a prominent role. Initially developed for the treatment of type 2 diabetes mellitus, these drugs have demonstrated consistent cardiovascular benefits in patients with HF, inclu-

ding those without diabetes, with reduced hospitalization for heart failure and benefits in composite cardiovascular outcomes across different ejection fraction ranges. (6–8)

This evidence has led to their progressive incorporation into international guidelines. The 2022 AHA/ACC/HFSA guidelines now include iSGLT2s among the four therapeutic pillars of heart failure with preserved ejection fraction (HFpEF), and also recognize benefits in patients with mildly reduced ejection fraction. In the 2023 ESC focused update, iSGLT2s received a Class I recommendation, Level of Evidence A, also for patients with HF with mildly reduced and preserved ejection fraction, reflecting the consolidation of their role across the broad spectrum of the syndrome. (3,5)

Despite the robustness of clinical trials, the evaluation of real-world data remains important. Clinical cohorts can provide insights into applicability, behavior in , more heterogeneous populations, renal profiles in daily practice, and local patterns of therapeutic response. In regional SUS services, this type of observation is particularly relevant, as it reflects the implementation of evidence in a less controlled environment with greater clinical and documentation variability.

Given this, the present study aimed to evaluate, in patients with heart failure followed at QUALICIS in Guarapuava, Paraná, the echocardiographic, clinical, and renal outcomes observed after the use of iSGLT2, with an emphasis on changes in LVEF, the frequency of cardiovascular events, and serum creatinine trends during outpatient follow-up.

Objectives

Primary Objective

To evaluate the clinical, echocardiographic, and renal outcomes observed after the use of iSGLT2 in patients with heart failure followed at QUALICIS in Guarapuava, Paraná.

Specific Objectives

To evaluate changes in left ventricular ejection fraction in patients with paired echocardiographic measurements; to identify exploratory clinical factors associated with echocardiographic super-response; to describe the occurrence of cardiovascular events and hospitalizations after treatment initiation; and to analyze serum creatinine trends, especially in the elderly and patients with chronic kidney disease.

Methodology

This is an observational, analytical, and retrospective study with a quantitative approach, conducted through a review of electronic medical records of patients followed at the QUALICIS specialty center in Guarapuava, Paraná. The initial sample comprised 200 patients diagnosed with heart failure, followed in a specialized outpatient setting. Data were retrospectively extracted from the IDS Saúde electronic system.

Depending on availability in the records, sociodemographic, clinical, and laboratory variables were collected, including age, sex, comorbidities, New York Heart Association (NYHA) functional class, left ventricular ejection fraction (LVEF), and serum creatinine. Given the nature of the

service and the retrospective data extraction, analyses were conducted based on the completeness of the documentation. Thus, the echocardiographic and renal subanalyses were restricted to subsets with available paired measurements.

For the analysis of ventricular remodeling, 59 patients with quantitative LVEF measurements at two time points—before and after the introduction of iSGLT2—were included. The super-response was operationally defined as an absolute increase in LVEF of 10 percentage points or more. In patients with a baseline LVEF of less than 40%, the phenotype of heart failure with recovered ejection fraction was considered when the following were present: initial LVEF of less than 40%, an absolute increase of 10 percentage points or more, and final LVEF greater than 40%, in accordance with contemporary classification literature. (2)

The analysis of clinical predictors of super-response was exploratory and univariate, including type 2 diabetes mellitus, hypertension, coronary artery disease, and obesity. For the analysis of clinical outcomes, an event was defined as the first occurrence, after initiation of iSGLT2, of hospitalization for heart failure, a major cardiovascular event, or severe clinical instability. Event-free survival was estimated using the Kaplan-Meier method. As in the original database, missing records or events occurring prior to prescription were treated as the absence of an event during the analyzed period, a methodological choice that increases the risk of information bias and overestimation of event-free survival and should be interpreted with caution.

Renal safety was assessed in 69 patients with matched serum creatinine levels before and after the start of therapy. The interpreta-

tion of the observed increases took into account the knowledge that iSGLT2s may be associated with initial hemodynamic changes in glomerular filtration. To contextualize creatinine behavior, the KDIGO criterion of an increase greater than or equal to 0.3 mg/dL was used as a reference as a warning marker for acute kidney injury. (4)

Data processing, collection, and statistical analyses were performed in January and February 2026, after the study received approval from the Research Ethics Committee; approval number 7,948,106 was issued on November 4, 2025. Sociodemographic (age, sex), clinical (comorbidities, functional status according to NYHA class), echocardiographic (left ventricular ejection fraction—LVEF), and laboratory (serum creatinine) variables were analyzed. Due to the nature of the healthcare service and the retrospective data collection, the data were analyzed based on their availability in the electronic records. Consequently, for variables with a higher rate of missing records (e.g., creatinine and LVEF), the analysis was restricted to subgroups of patients with complete documented data. For the analysis, information collected from electronic medical records was tabulated and values were calculated. Python was used in a Google Colab environment for graphical representations, with continuous variables presented as mean and standard deviation and categorical variables as absolute and relative frequencies. The significance level adopted was 5% ($p \leq 0.05$).

Results

Variation in Ejection Fraction and Reverse Remodeling

Among the 200 patients in the cohort, 59 had quantitative echocardiographic records at two time points, allowing for a paired analysis of LVEF. In this subsample, the mean absolute change in LVEF was +2.54 percentage points (SD $\pm$ 8.37), with a median of +5.0. These values suggest an overall trend toward ventricular functional improvement in some of the evaluated patients, although with significant heterogeneity in response.

When patients were stratified according to the magnitude of change in FEVE, a super-response—defined as an increase of 10 percentage points or more—was observed in 27.1% ($n = 16$). An intermediate response or stabilization, corresponding to a change between 0 and 9 points, was identified in 25.4% ($n = 15$), while 47.5% ($n = 28$) showed no improvement in ventricular function during the analyzed period.

In the subgroup with a baseline LVEF below 40% ($n = 22$), 54.5% ($n = 12$) met operational criteria for heart failure with recovered ejection fraction, considering a baseline LVEF below 40%, an absolute increase of 10 percentage points or more, and a final LVEF above 40%. Although this finding is clinically interesting, it should be interpreted as a descriptive subgroup observation, without the possibility of inferring an isolated causal effect of iSGLT2.

Exploratory clinical predictors of super-response

In the exploratory univariate analysis, obesity was the variable with the greatest apparent difference between groups. Obese patients had a super-response rate of 41.7% (10/24), compared with 17.1% (6/35) among non-obese patients, corresponding to an OR of 3.45 and $p = 0.07$. The result suggests tendency toward an association, but does not reach conventional statistical significance and should be treated as an exploratory finding generating a hypothesis.

The presence of type 2 diabetes mellitus was not associated with a higher probability of over-response, with similar rates among diabetics and non-diabetics. Similarly, the presence of coronary artery disease did not appear to limit the echocardiographic response. These findings, however, stem from univariate analysis in a small sample, without adjustment for potential confounders.

Response by heart failure category

When comparing the three classic phenotypes of the syndrome, a statistically significant difference was observed in the variation of FEVE ($p = 0.0018$). The group with preserved ejection fraction showed the greatest mean gain ($+10.9\% \pm 14.8\%$), while the groups with systolic dysfunction exhibited, on average, stability or a slight decline in LVEF. This finding should be understood as descriptive, and not as evidence of greater relative efficacy of the class in this phenotype.

Clinical Events and Event-Free Survival

The clinical analysis included 198 patients. Of these, 22 (11.1%) had a record of

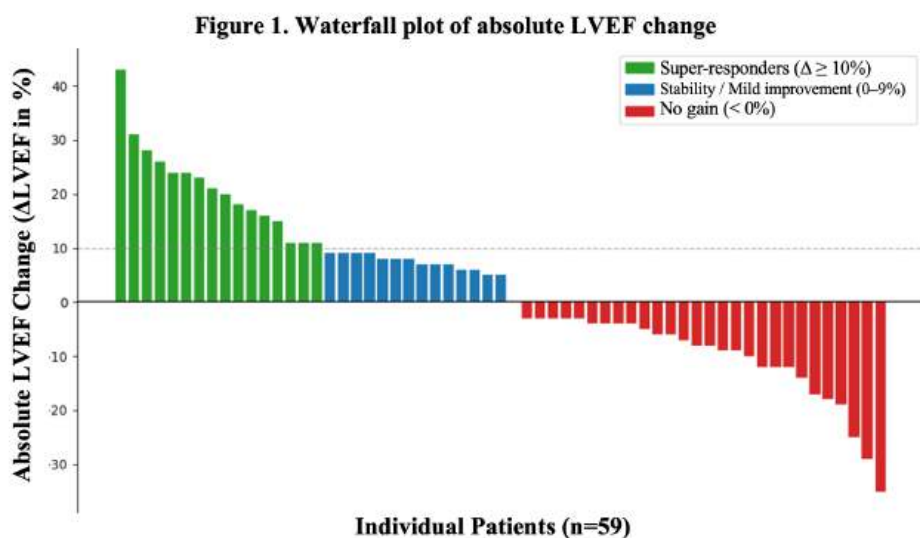


Figure 1 Caption: Figure 1. Waterfall plot of individual absolute left ventricular ejection fraction (Δ LVEF) change. Green bars indicate super-responders ($\Delta \geq 10\%$); blue bars indicate stability or mild improvement (0–9%); red bars indicate no functional gain ($< 0\%$).

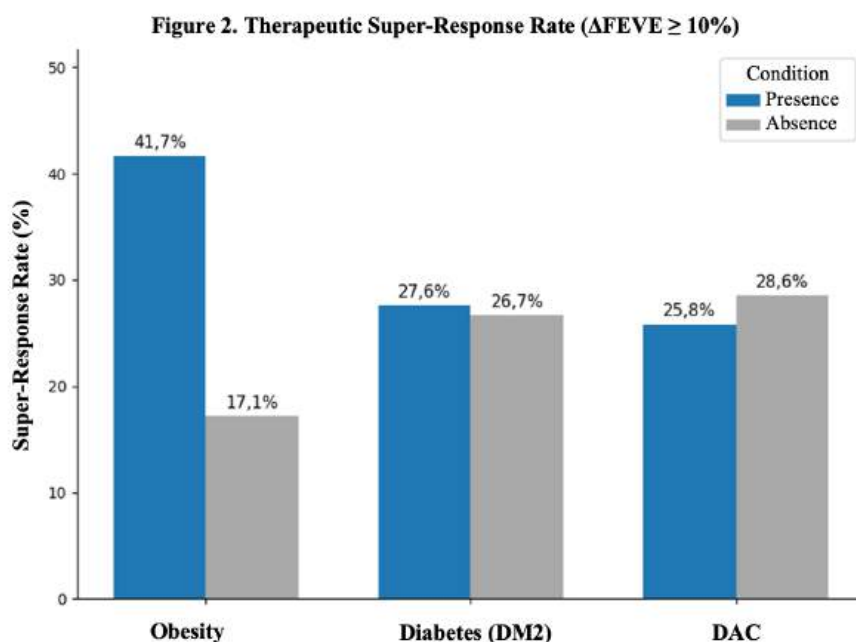


Figure 2 Caption: Figure 2. Therapeutic Super-Response Rate (Δ FEVE $\geq 10\%$) stratified by the presence (Blue) or absence (Gray) of major comorbidities. Obesity stands out as a factor associated with a higher response rate (41.7%), while Diabetes and CAD showed a neutral pattern.

a cardiovascular event or hospitalization after initiation of iSGLT2 therapy. The reported median follow-up was 518 days, with cases exceeding three years. The Kaplan-Meier curve showed sustained high probability of event-free survival throughout the follow-up period.

Although this result is descriptively favorable, it should not be directly compared to rates from randomized trials, because the present cohort included a more heterogeneous population, lacked a control arm, used local operational definitions of events, and had missing data that potentially inflated estimates of non-occurrence of outcomes.

Duration of Use and Echocardiographic Response

In 57 patients, the relationship between duration of iSGLT2 exposure and changes in LVEF was evaluated. Pearson's linear correlation did not demonstrate a statistically significant association between duration of use and magnitude of the echocardiographic response ($r = 0.065$; $p = 0.63$). Stratification by time intervals suggested a nonlinear pattern, but this behavior should be interpreted strictly as exploratory.

Renal Profile

Among 69 patients with matched serum creatinine levels, the overall mean change was $+0.16$ mg/dL (SD ± 0.55), with a median of $+0.12$ mg/dL. Patients with chronic kidney disease had a greater mean increase than those without known nephropathy ($+0.26$ versus $+0.08$ mg/dL). Among the elderly, a greater mean creatinine fluctuation was observed than among non-elderly patients ($+0.19$ versus $+0.04$ mg/dL). These

results are consistent with the need for closer laboratory monitoring in patients with greater renal fragility, but do not suggest, on average across the analyzed cohort, abrupt renal deterioration or a uniformly impeding effect on the use of this class of drugs.

Data completeness

Analysis of data integrity revealed substantial heterogeneity in the availability of longitudinal information. The baseline eEFV record was relatively robust; however, there were significant gaps in echocardiographic and laboratory follow-up, as well as a high percentage of missing NYHA functional classifications. Data incompleteness constitutes a central limitation of the study and restricts the inferential power of secondary and subgroup analyses.

Discussion

The findings of this retrospective cohort suggest that the use of iSGLT2 in patients followed in a specialized SUS service was associated with an overall favorable profile across three observational domains: echocardiographic response in a subsample with matched LVEF, low frequency of recorded clinical events after initiation of therapy, and renal function generally compatible with continued treatment in most of the evaluated patients. These results are consistent with the contemporary literature, which recognizes iSGLT2s as a fundamental therapy for HF across a broad spectrum of ejection fractions. (3,5)

However, the main contribution of this study is not in replicating clinical trials, but in providing a real-world description in a regional setting. Trials such as DAPA-HF, EMPEROR-Reduced, EMPEROR-Preser

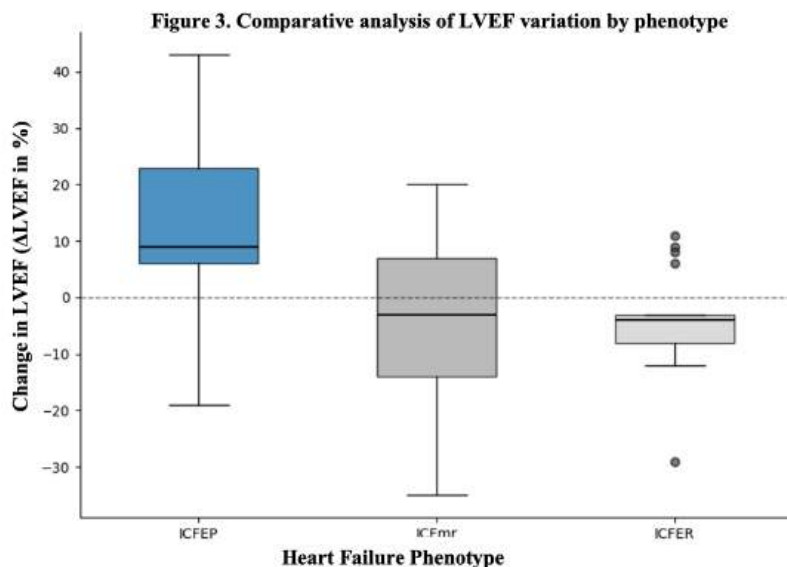


Figure 3 Caption: Figure 3. Comparative analysis of ejection fraction variation (Δ LVEF) among heart failure phenotypes: Preserved (HFpEF), Mildly Reduced (HFmr), and Reduced (HFrEF). Greater functional improvement is observed in the ICFEP group, while groups with systolic dysfunction tend toward stability or moderate decline, despite isolated cases of recovery (positive *outliers*).

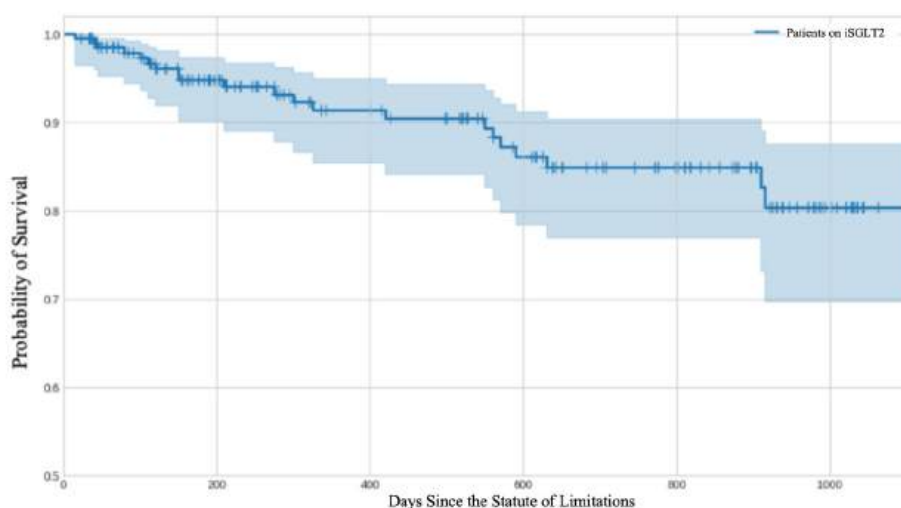


Figure 4 Caption: Figure 4. Kaplan-Meier curve estimating the probability of survival free of cardiovascular events (hospitalization or intervention) over the duration of iSGLT2 use. The blue line represents the probability of not experiencing an event; the stability of the curve (slow decline) indicates a high rate of protection, with more than 97% of patients event-free at the end of the 2-year follow-up.

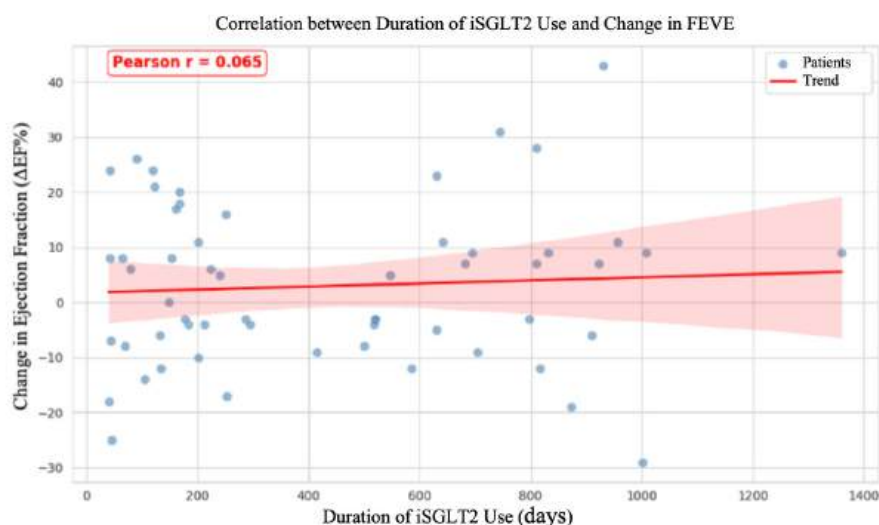


Figure 5 Caption: Figure 5. Scatter plot correlating duration of iSGLT2 use (in days) with change in ejection fraction (Δ FEVE). The red trend line and Pearson's correlation coefficient ($r=0.065$) indicate the absence of a direct linear correlation, suggesting that the therapeutic response is complex and possibly not linearly cumulative

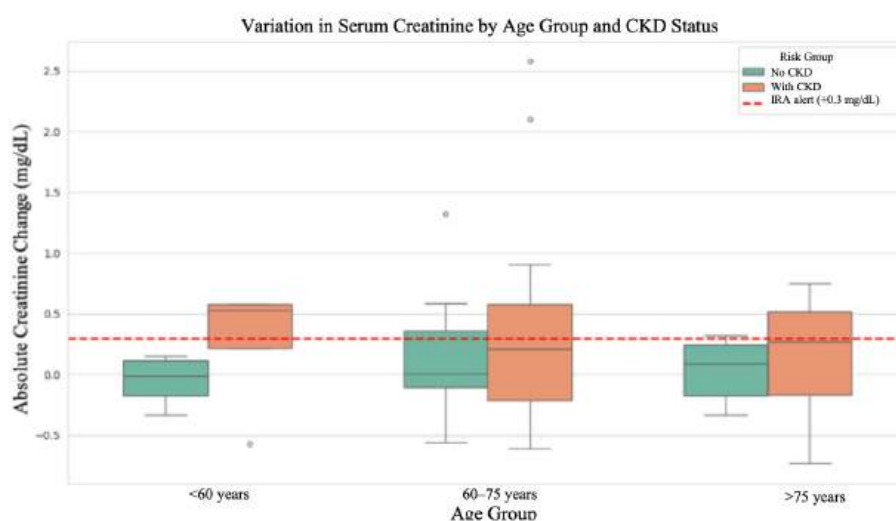


Figure 6 Legend: Figure 6. Box plot showing the absolute change in serum creatinine (mg/dL) after initiation of iSGLT2 treatment. Data are stratified by the presence of Chronic Kidney Disease (CKD) and age group. The red dotted line indicates the variation threshold of +0.3 mg/dL, frequently used as a warning marker for acute kidney injury..

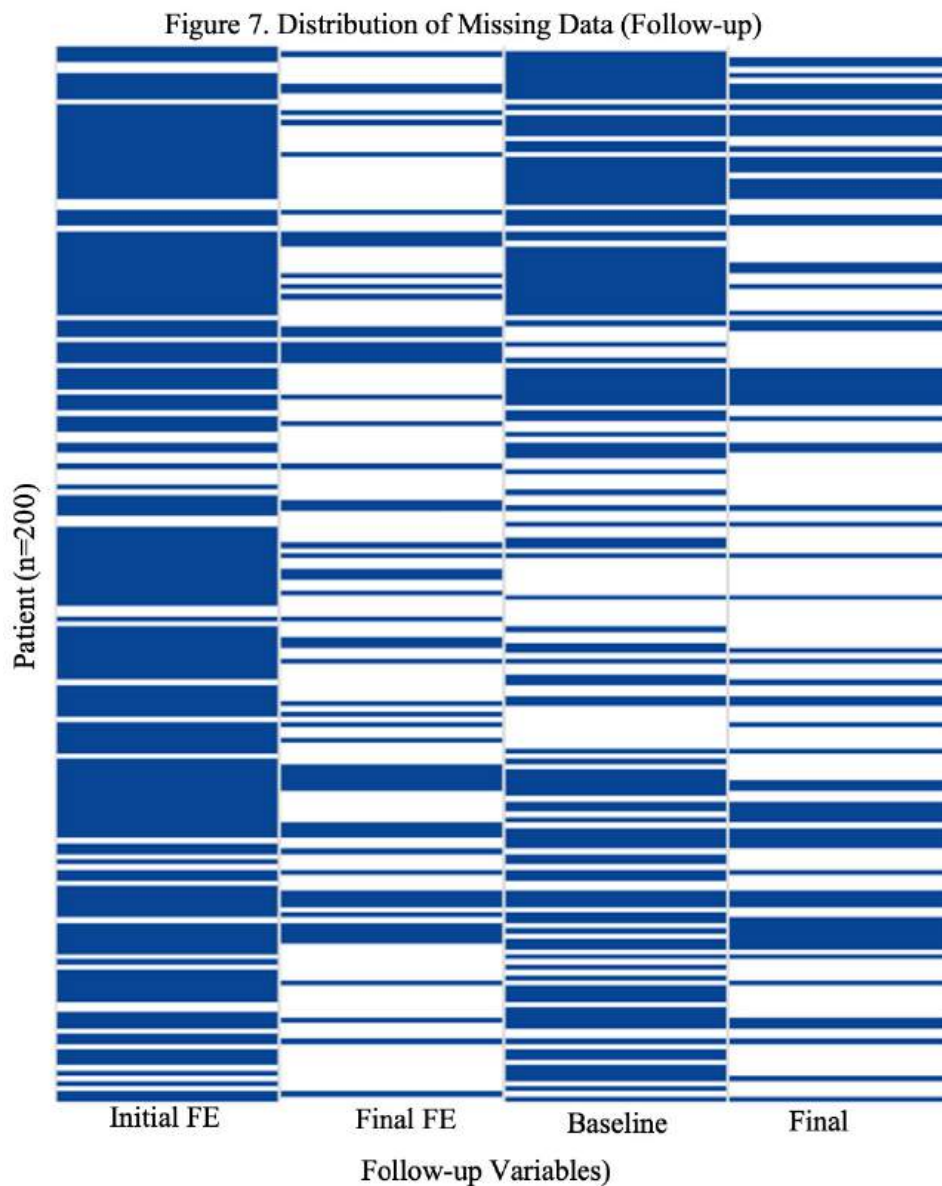


Figure 7 Caption: Figure 7. Invisibility matrix showing the distribution of missing data (blank spaces) in patient follow-up (n=200).

Figure 8. Invisibility Ranking by Clinical Variable

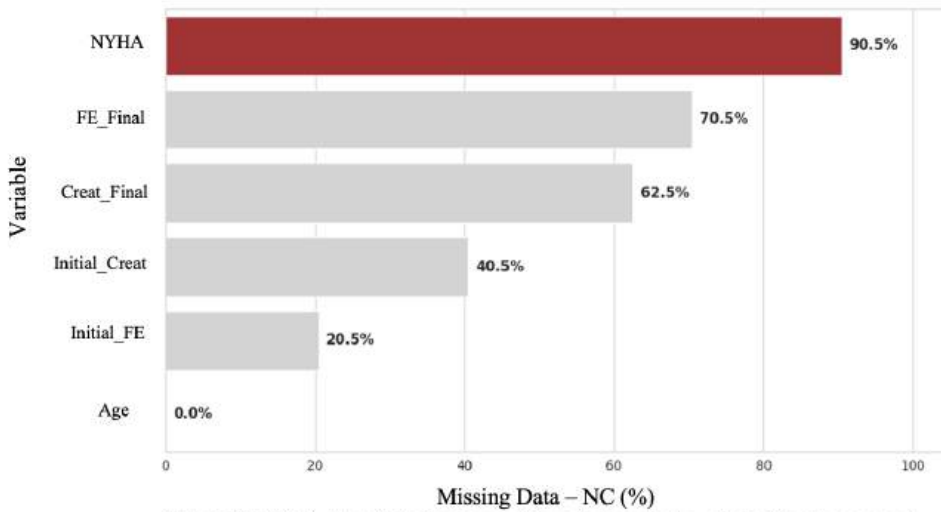


Figure 8 Caption: Figure 8. Bar chart showing the percentage ranking of clinical variables with the highest rate of missing data (NC) in the IDS Saúde system.

ved, and DELIVER demonstrated a reduction in the risk of worsening heart failure and/or cardiovascular death in carefully selected populations, with rigorous standardization of outcomes and follow-up. In this cohort, by contrast, there is greater clinical heterogeneity, an absence of randomization, likely differences in concomitant therapies, and significant data incompleteness. Therefore, the local findings should be viewed as complementary and contextualizing, rather than as a direct comparison of efficacy. (1,6–8)

The median change of +5 points in LVEF and the identification of a 27.1% super-response warrant attention. Clinically, this pattern suggests that, in a subset of patients with available paired measurements, there was significant ventricular functional improvement after the start of therapy. Even s , since nearly half of the patients did not show an increase in LVEF during the analy-

zed window, the echocardiographic response was clearly heterogeneous.

The proportion of patients with a baseline LVEF below 40% who met the criteria for recovered ejection fraction is also relevant from a descriptive standpoint. However, this phenomenon cannot be attributed solely to iSGLT2. Patients with HFrEF frequently receive multiple therapies with the potential for reverse remodeling, such as beta-blockers, renin-angiotensin system inhibitors, mineralocorticoid receptor antagonists, and, eventually, ARNI. (3,5)

The trend toward an association between obesity and super-response, although not statistically significant, is interesting as a generative hypothesis. It is plausible that phenotypes with a greater metabolic, inflammatory, and congestive component exhibit a differential response profile to therapies with systemic hemodynamic and metabolic effects. Nevertheless, the small sample size and the absence of multivariate

adjustment prevent this finding from being presented as a confirmed predictor.

In the clinical setting, the 11.1% event rate after initiation of therapy appears favorable, but should be interpreted with particular caution. The Kaplan-Meier analysis method itself classified cases with missing records and situations where the event had occurred prior to prescription as “no event,” a decision that tends to artificially reduce the observed incidence. Thus, although the curve suggests overall clinical stability in a large portion of the cohort, the exact magnitude of event-free survival is likely subject to overestimation.

Regarding the renal profile, the small mean elevation in creatinine is consistent with the expected physiology of this class. The literature has already described that iSGLT2 inhibitors can produce an initial hemodynamic change in glomerular filtration rate without this necessarily implying clinical nephrotoxicity. Ideally, future studies in the same department should incorporate estimated glomerular filtration rate, albuminuria, episodes of medication discontinuation, the need for therapeutic adjustment, and clinically relevant renal outcomes. (4)

The study has significant limitations. It is a retrospective, single-center study based on electronic medical records, lacking a control group, and exhibiting significant loss of completeness in critical variables, particularly follow-up eGFR, paired creatinine levels, and NYHA functional class. The absence of multivariate modeling and reliance on subsamples reduce the robustness of inferences. Despite this, the study has merit for documenting the implementation of guideline-based therapy in a regional population served by the SUS and for suggesting that the benefits observed in large

studies may, to some extent, also be observed in daily clinical practice.

Conclusion

In this retrospective cohort of patients with heart failure followed in a specialized SUS service, the use of iSGLT2 was associated with an overall favorable profile of clinical progression and e, with a low frequency of events recorded after initiation of therapy, echocardiographic improvement in some patients with paired LVEF, and renal function consistent with the monitored use of this class in an outpatient setting.

Among patients with complete echocardiographic data, a median change of +5 percentage points in LVEF was observed, with an over-response in 27.1% of cases and a recovery in ejection fraction in a significant proportion of cases with a baseline LVEF below 40%. Among patients with matched creatinine levels, the observed fluctuations were, on average, modest, although more pronounced in the elderly and in patients with chronic kidney disease.

The results should be interpreted with caution due to the observational design, the absence of a comparator group, the clinical heterogeneity of the cohort, and the significant incompleteness of the data. Nevertheless, the findings reinforce the applicability of iSGLT2s in a real-world regional setting and support the need for prospective studies, with standardized outcomes and improved data completeness, to further evaluate the efficacy and safety of this class in this context.

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