

Unrecognized Chronic Kidney Disease and the Therapeutic Gap in Outpatients with Heart Failure and Reduced Ejection Fraction

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Abstract

Background: Chronic kidney disease (CKD) is common in heart failure with reduced ejection fraction (HFrEF), but its true prevalence may substantially exceed formal diagnosis, contributing to undertreatment with guideline-directed medical therapy (GDMT).

Objectives: To determine the prevalence of unrecognized CKD in an HFrEF outpatient clinic, compare optimized medical therapy (OMT) according to renal status and KDIGO stages, and identify independent predictors of OMT.

Methods: Analytical cross-sectional study including 469 patients with HFrEF (LVEF $\leq 40\%$) followed between 2019–2022 with calculable eGFR (CKD-EPI 2021). Classification: no CKD (eGFR ≥ 60 ; n = 307), hidden CKD (eGFR < 60 without documentation; n = 104), and recognized CKD (formal documentation; n = 58). OMT was defined as RAAS blockade + beta-blocker + MRA at $\geq 50\%$ of target doses.

Results: CKD affected 34.5% by eGFR, but only 15.1% had documentation – 64% were hidden, predominantly G3a (82%) and G3b (64%). OMT followed a monotonic gradient across KDIGO stages: G1 56.5%, G2 48.1%, G3a 38.4%, G3b 24.1%, G4 18.5% (Cochran–Armitage $p < 0.001$). Spironolactone was the most affected therapy (84.7% vs. 60.3%; $p < 0.001$). In multivariable analysis, recognized CKD was associated with lower OMT (OR 0.47; 95% CI 0.23–0.92; $p = 0.03$), along with age (OR 0.95/year; $p < 0.001$), while diabetes was paradoxically associated with higher OMT (OR 1.90; $p = 0.003$).

Conclusion: Nearly two-thirds of CKD cases in HFrEF are unrecognized, concentrated in moderate stages where therapeutic benefit is greatest. Routine calculation of eGFR is a simple intervention to reduce this gap.

Keywords: Heart Failure; Chronic Renal Insufficiency; Glomerular Filtration Rate; Therapeutics; Mineralocorticoid Receptor Antagonists.

Introduction

Heart failure with reduced ejection fraction (HFrEF) is one of the leading causes of cardiovascular morbidity and mortality. Optimized medical therapy (OMT), consisting of renin–angiotensin–aldosterone system (RAAS) blockade, beta-blockers, and mineralocorticoid receptor antagonists (MRAs), reduces mortality by up to 73% when target doses are achieved.^{1,2} The addition of sodium–glucose cotransporter-2 inhibitors (SGLT2i) has further expanded this therapeutic arsenal, providing additional benefit.^{3,4}

Despite this evidence, real-world data show that only 20–50% of patients receive OMT. The CHAMP-HF and CHECK-HF registries documented this gap on a large scale,^{5,6} and Brazilian data from the BREATHE registry confirm a similar scenario.⁷ Among the multiple barriers—hypotension, hyperkalemia, intolerance – chronic kidney disease (CKD) plays a central role as a factor leading to dose reduction or non-prescription of MRAs.^{8,9}

Cardiorenal syndrome type 2 makes CKD highly prevalent in HFrEF.¹⁰ Paradoxically, patients with overlapping HF and CKD are precisely those who benefit most from optimized therapy, as demonstrated in the DAPA-CKD, EMPEROR-Reduced, and FIDELIO-DKD trials.^{3,4,11} The tendency toward undertreatment in this subgroup characterizes the “risk–treatment paradox,” described by Savarese et al. in the Swedish HF registry¹² and by Edner et al. in patients with CKD and HF.¹³

An underexplored aspect is the discrepancy between the true prevalence of CKD—defined as an eGFR < 60 mL/min/1.73 m²—and its formal recognition in medical records. In primary care populations, 40–70% of CKD cases

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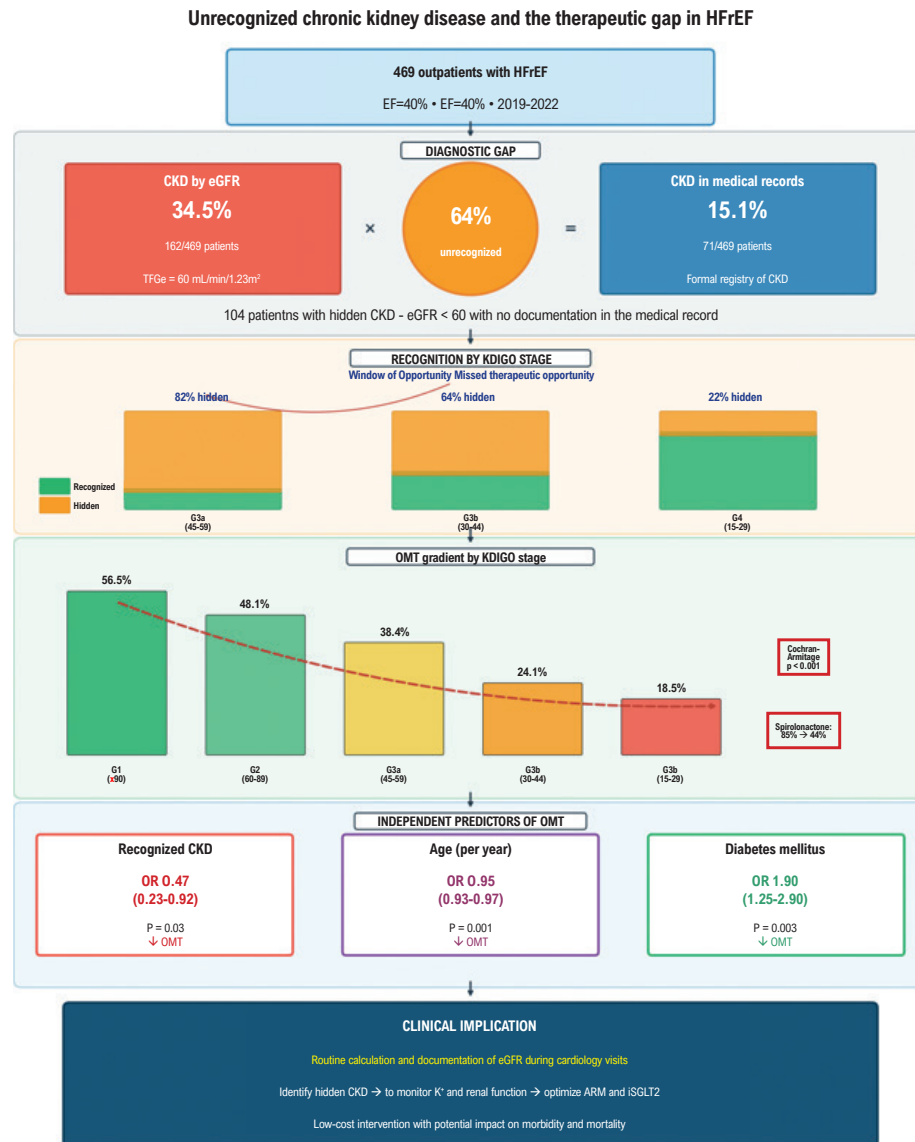
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Central Illustration: Unrecognized Chronic Kidney Disease and the Therapeutic Gap in Outpatients with Heart Failure and Reduced Ejection Fraction

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Unrecognized chronic kidney disease and therapeutic gap in HFrEF. CKD: chronic kidney disease; HFrEF: heart failure with reduced ejection fraction; eGFR: estimated glomerular filtration rate; OMT: optimal medical therapy; MRA: mineralocorticoid receptor antagonist; KDIGO: Kidney Disease: Improving Global Outcomes.

go unrecognized,^{14,15} but data from specialized HFrEF clinics are scarce. When CKD is not identified, a generic concern about “renal function” may limit medication titration without an objective basis.

In Brazil, no studies have evaluated this “hidden CKD” in HFrEF. The present study aimed to: (1) quantify the diagnostic gap; (2) compare OMT according to renal status and KDIGO stages; and (3) identify independent predictors of OMT.

Methods

Design, setting, and population

This was a single-center analytical cross-sectional study conducted in the heart failure (HF) outpatient clinic of a tertiary hospital in Curitiba, Paraná, Brazil. All consecutive patients with HFrEF (EF ≤ 40%) followed between January

2019 and December 2022 who had available serum creatinine measurements were included. Individuals under 18 years of age, those seen only at an initial visit without follow-up, patients with a history of heart transplantation, those receiving exclusive palliative care, and those with insufficient data for renal classification were excluded. The study was approved by the institution's research ethics committee (CAAE: 52796521.3.0000.0020), with a waiver of informed consent.

Exposure variable: renal status

No CKD: estimated glomerular filtration rate (eGFR) $\geq$ 60 mL/min/1.73 m²; Hidden CKD: eGFR < 60 without documentation in the medical record; Recognized CKD: formal documentation of CKD with eGFR < 60.

eGFR was calculated using the 2021 CKD-EPI equation (without race correction).¹⁶ KDIGO stages were classified according to current recommendations (G1–G5).¹⁷ The decision to use documentation in the medical record as the criterion for recognition was intentional: formal documentation is what structures clinical alerts, checklists, and multiprofessional communication – its absence reflects a process gap rather than a lack of knowledge.

Patients with CKD documented in the medical record but with eGFR $\geq$ 60 mL/min/1.73 m² (n = 13) were classified as “no CKD” in the primary analysis, as their renal function was preserved at the time of evaluation. This decision ensured that classification reflected the patient's current objective renal status rather than a potentially outdated diagnosis.

Outcomes

Primary: OMT, defined as RAAS blockade (ACEI, ARB, or sacubitril/valsartan) + beta-blocker + MRA at $\geq$ 50% of target doses.^{1,2} SGLT2 inhibitors were excluded from the primary definition due to their limited availability in the Brazilian public health system (SUS) during 2019–2022 (overall use 13%) and were evaluated in a sensitivity analysis.

Secondary: prescription and target dose by drug class; barriers to optimization according to renal status and KDIGO stage; mortality in the subgroup with EF $\leq$ 25% (exploratory analysis).

Statistical analysis

Categorical variables were analyzed using the chi-square test or Fisher's exact test. Continuous variables were analyzed using the Kruskal–Wallis test (normality rejected by the Shapiro–Wilk test). For post-hoc comparisons, Bonferroni and Dunn adjustments were applied. Trend analysis was performed using the Cochran–Armitage test. Correlations were assessed using Spearman's coefficient.

Multivariable logistic regression was conducted in two steps: (1) bivariate analysis with selection of variables with $p < 0.10$; and (2) an adjusted model with Renal Status as the exposure variable. Continuous eGFR was evaluated separately due to collinearity. Model quality was assessed using the Hosmer–Lemeshow test, AUC-ROC, VIF, and Nagelkerke's pseudo-R². A two-tailed significance level of 5% was adopted. Analyses were performed using R

v.4.4 (packages: gtsummary, rstatix, pROC, DescTools, ResourceSelection).

To assess potential selection bias, the characteristics of included and excluded patients (due to missing creatinine values) were formally compared.

As a sensitivity analysis for the limitation of having only a single creatinine measurement, we compared the prevalence of congestion signs (dyspnea, jugular venous distension, edema, crackles) across renal status groups and repeated the primary analysis restricted to patients without any signs of congestion. Additionally, we evaluated whether hyperkalemia (potassium > 5.0 mEq/L) mediated the association between CKD and lower prescription of spironolactone using a dedicated logistic regression model.

Results

Sample and prevalence of hidden CKD

Of the 608 patients with HFrEF, 469 (77.1%) had creatinine available. The comparison between included (n = 469) and excluded (n = 139) patients showed no significant differences in age (62.6 vs. 61.2 years; $p = 0.42$), OMT (44.2% vs. 41.0%; $p = 0.50$), or beta-blocker use (98.3% vs. 97.8%; $p = 0.73$), although LVEF was marginally lower among excluded patients (28.7% vs. 30.0%; $p = 0.03$). Use of sacubitril/valsartan was paradoxically higher among excluded patients (68.0% vs. 53.9%; $p = 0.004$), possibly reflecting individuals referred with a prior prescription but without laboratory tests performed at the center; this difference did not translate into higher overall OMT ($p = 0.50$). (Supplementary Material, Table S2).

The sample was classified as: no CKD (n = 307; 65.5%), hidden CKD (n = 104; 22.2%), and recognized CKD (n = 58; 12.4%). CKD prevalence based on eGFR was 34.5% (162/469), whereas only 15.1% (71/469) had formal documentation. Therefore, 64% (104/162) of patients with eGFR < 60 had no documented CKD (Central Figure; Figure 1).

The diagnostic gap varied according to KDIGO stage: in G3a (eGFR 45–59), 82% of CKD cases were hidden; in G3b (30–44), 64%; and in G4 (15–29), only 22% (Figure 2). Patients with CKD were older (~69 vs. ~59 years; $p < 0.001$) and had a higher prevalence of atrial fibrillation and hypertension (Table 1).

Overall OMT was 44.2%, with a significant gradient: 51.5% (no CKD), 33.0% (hidden CKD), and 25.9% (recognized CKD; $p < 0.001$) (Table 2). The Cochran–Armitage test confirmed a linear trend across KDIGO stages: G1 56.5%, G2 48.1%, G3a 38.4%, G3b 24.1%, G4 18.5% ($p < 0.001$) (Figure 3).

Spironolactone was the most affected therapy: 84.7% → 81.7% → 60.3% ($p < 0.001$). By KDIGO stage, its use remained stable at ~85% up to G3a, with an abrupt decline to 75% in G3b and 44% in G4 (Figure 4). Betablocker use was nearly universal (~98%). SGLT2 inhibitors showed low and homogeneous use (12–16%; $p = 0.69$).

Notably, the reduction in spironolactone use associated with CKD was not explained by actual hyperkalemia: within each renal-status group, spironolactone prescription was similar between patients with potassium > 5.0 and $\leq$ 5.0 mEq/L. In the

adjusted regression model with spironolactone as the outcome, hyperkalemia was not a significant predictor (OR 1.04; $p = 0.90$), whereas recognized CKD remained independently associated (OR 0.35; 95% CI 0.18–0.68; $p = 0.002$). This finding suggests that the decision not to prescribe spironolactone is driven by the perceived risk associated with a CKD diagnosis rather than by the actual serum potassium level.

Barriers to optimization

Among patients with suboptimal RAAS dosing, “renal dysfunction” was cited in 0% (no CKD), 15% (hidden CKD), and 43% (recognized CKD; $p < 0.001$). Across KDIGO stages, the gradient persisted: 0% (G1–G2), 8% (G3a), 29% (G3b), 55% (G4), and 67% (G5) (Supplementary Material, Figure S1). Cost was the main barrier to SGLT2 inhibitor use.

Independent predictors of OMT

The multivariable model (Table 3; Figure 5) included renal status adjusted for age, atrial fibrillation, diabetes mellitus, and chronic obstructive pulmonary disease (selected by $p < 0.10$ in the bivariate analysis). Recognized CKD was independently associated with lower OMT use (OR 0.47; 95% CI 0.23–0.92; $p = 0.03$). Hidden CKD showed a non-significant trend (OR 0.73; 95% CI 0.43–1.23; $p = 0.23$). Age was the strongest predictor (OR 0.95 per year; $p < 0.001$). Diabetes mellitus was paradoxically associated with higher OMT use (OR 1.90; 95% CI 1.25–2.90; $p = 0.003$). AUC 0.717; Hosmer–Lemeshow $p = 0.71$; VIF < 1.5 .

In the sensitivity analysis using continuous eGFR, each 10 mL/min increase was associated with an OR of 1.09 (95% CI 0.99–1.20; $p = 0.07$), confirming the direction of the effect.

Mortality (subgroup LVEF $\leq 25\%$ — exploratory analysis)

Among the 109 patients with follow-up, a gradient was observed: 11.1% (no CKD), 14.3% (hidden), and 31.2% (recognized; Fisher $p = 0.128$) — an exploratory result, without statistical significance and with insufficient power (Supplementary Material, Figure S3).

Discussion

The present study demonstrated that nearly two-thirds of outpatients with HFrEF who have renal dysfunction do not have documented CKD, and that this gap is concentrated in the moderate stages G3a–G3b — precisely the range in which MRAs and SGLT2 inhibitors provide the greatest benefit with manageable risk.^{11,18,19} OMT decreased progressively and monotonically across KDIGO stages, with a significant linear gradient.

Diagnostic gap and its location

The discrepancy between actual CKD (34.5%) and recognized CKD (15.1%) is consistent with international data,^{14,15} but its magnitude in a specialized outpatient setting is concerning. Recognition was proportional to

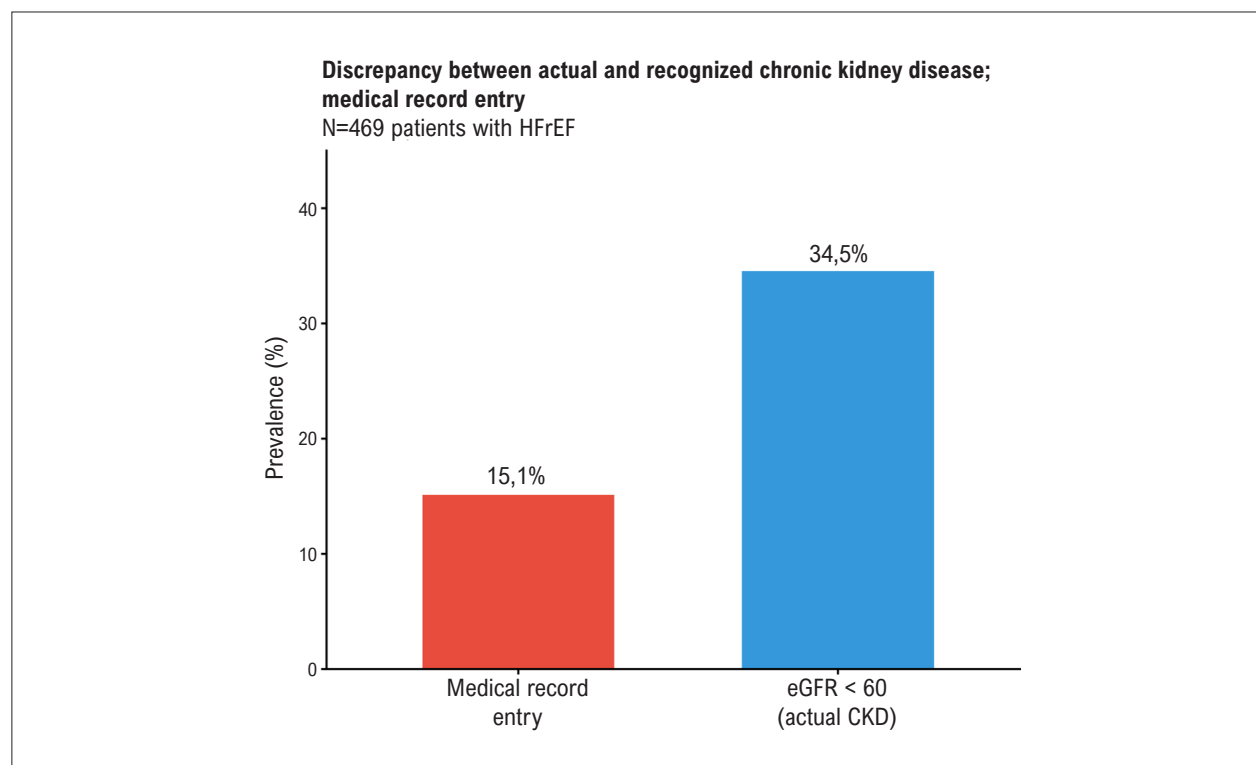


Figure 1 – Discrepancy between the prevalence of chronic kidney disease based on estimated glomerular filtration rate (eGFR < 60 mL/min/1.73 m²) and formal documentation in the medical record.

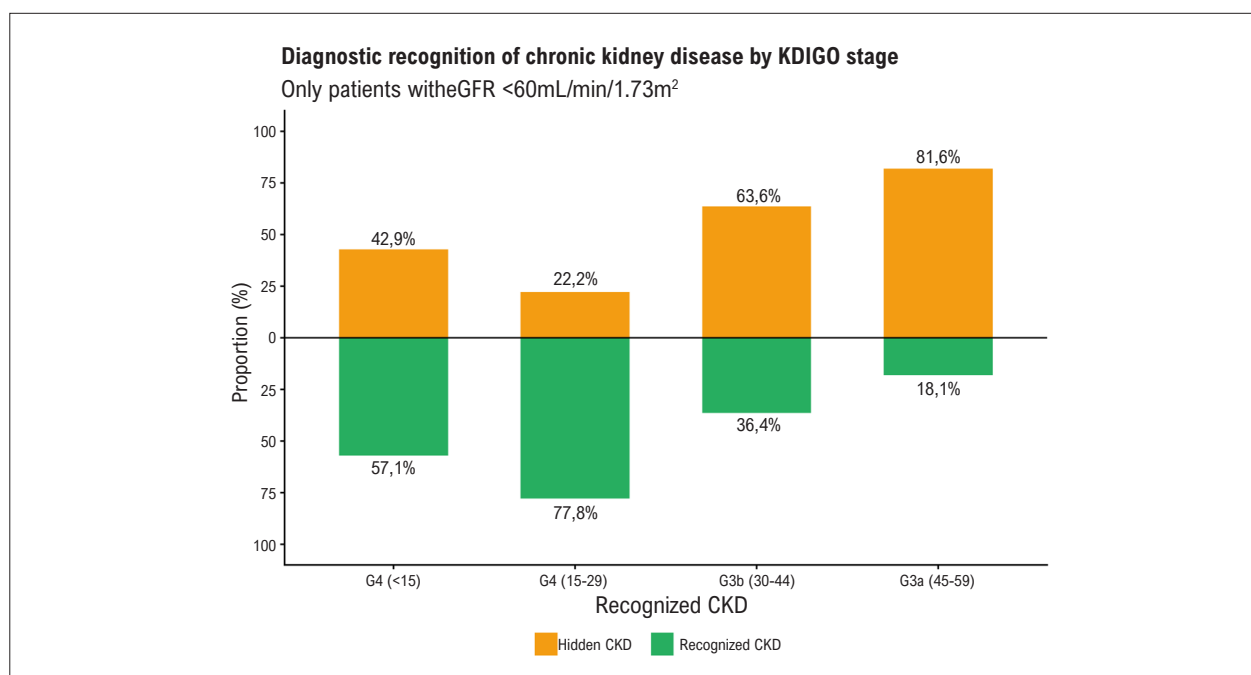


Figure 2 – Proportion of recognized versus hidden chronic kidney disease by KDIGO stage among patients with estimated glomerular filtration rate (GFR) < 60 mL/min/1.73 m².

Table 1 – Clinical and demographic characteristics of patients with heart failure with reduced ejection fraction stratified by renal status (n = 469)

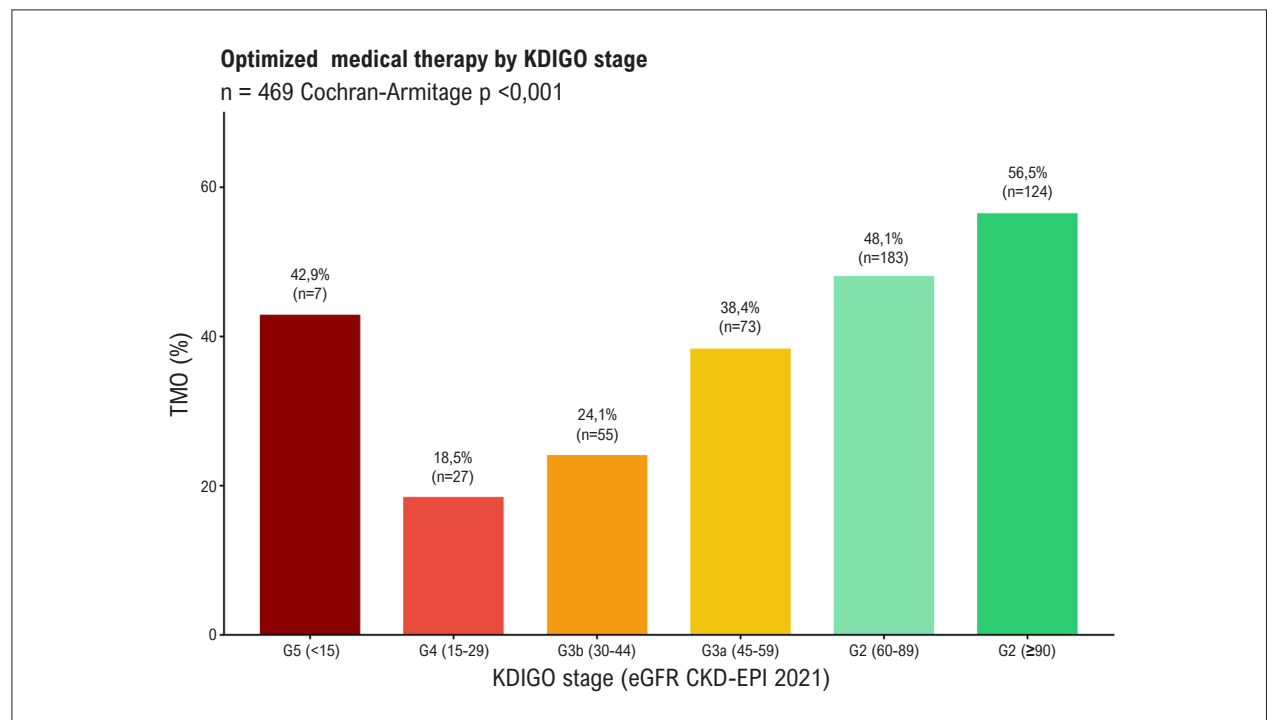
Variable	Total (n=469)	Without CKD (n=307)	Hidden CKD (n=104)	Recognized CKD (n=58)	p
Age (years)	62.6 ± 12.6	59.0 ± 11.9	69.4 ± 10.8	69.3 ± 11.3	<0.001
Male, n (%)	316 (67.4)	215 (70.0)	63 (60.6)	38 (65.5)	0.191
Ischemic etiology, n (%)	199 (42.4)	121 (39.4)	48 (46.2)	30 (51.7)	0.142
NYHA III–IV, n (%)	111 (23.7)	63 (20.5)	28 (26.9)	20 (34.5)	0.049
SBP (mmHg)	107.6 ± 18.9	107.3 ± 17.8	109.5 ± 19.6	105.6 ± 23.1	0.614
DBP (mmHg)	67.6 ± 13.3	67.8 ± 12.9	67.6 ± 13.5	66.2 ± 15.7	0.730
HR (bpm)	71.7 ± 13.1	72.4 ± 12.7	72.1 ± 14.5	68.2 ± 13.4	0.078
LVEF (%)	30.0 ± 6.3	30.1 ± 6.3	30.6 ± 6.2	28.5 ± 6.5	0.096
Potassium (mEq/L)	4.65 ± 0.55	4.56 ± 0.51	4.80 ± 0.60	4.89 ± 0.61	<0.001
Urea (mg/dL)	55.1 ± 27.8	43.5 ± 16.5	71.0 ± 29.6	92.6 ± 39.4	<0.001
Creatinine (mg/dL)	1.27 ± 0.72	0.95 ± 0.21	1.67 ± 0.83	2.25 ± 1.21	<0.001
eGFR CKD-EPI (mL/min/1.73m ²)	70.1 ± 26.3	85.6 ± 16.4	44.2 ± 11.4	34.0 ± 13.2	<0.001
HTN, n (%)	287 (61.2)	174 (56.9)	69 (66.3)	44 (75.9)	0.013
Diabetes mellitus, n (%)	157 (33.5)	97 (31.7)	34 (32.7)	26 (44.8)	0.133
AF/Flutter, n (%)	122 (26.0)	60 (19.6)	38 (36.5)	24 (41.4)	<0.001
COPD, n (%)	32 (6.8)	22 (7.2)	5 (4.8)	5 (8.6)	0.565
Hospitalization for HF, n (%)	190 (40.5)	120 (39.1)	42 (40.4)	28 (48.3)	0.421

Continuous variables: mean ± SD (Kruskal–Wallis). Categorical variables: n (%) (chi-square). *p* < 0.05 in bold. CKD: chronic kidney disease; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; HTN: hypertension; HF: heart failure; NYHA: New York Heart Association; SBP/DBP: systolic/diastolic blood pressure; eGFR: estimated glomerular filtration rate; COPD: chronic obstructive pulmonary disease.

Table 2 – Pharmacological prescription profile and optimized medical therapy by renal status (n=469)

Variable	Total (n=469)	Without CKD (n=307)	Hidden CKD (n=104)	Recognized CKD (n=58)	p
OMT, n (%)	207 (44.2)	158 (51.5)	34 (33.0)	15 (25.9)	<0.001
Any RAAS blockade, n (%), n (%)	445 (94.9)	298 (97.1)	97 (93.3)	50 (86.2)	0.002
Sacubitril/Valsartan, n (%)	249 (53.6)	163 (54.2)	56 (54.4)	30 (51.7)	0.937
% of target dose - Sacubitril/Valsartan	75.9 ± 30.0	79.1 ± 28.9	75.0 ± 29.9	59.2 ± 36.5	0.007
Betablocker, n (%)	461 (98.3)	303 (98.7)	101 (97.1)	57 (98.3)	0.571
% of target dose betablocker	79.6 ± 28.9	82.0 ± 27.8	75.2 ± 30.2	74.6 ± 31.4	0.054
Espironolactone, n (%)	380 (81.0)	260 (84.7)	85 (81.7)	35 (60.3)	<0.001
iSGLT2, n (%)	61 (13.0)	37 (12.1)	15 (14.4)	9 (15.5)	0.691

OMT: optimized medical therapy; RAAS: renin–angiotensin–aldosterone system; BB: beta-blocker; MRA: mineralocorticoid receptor antagonist. % of target dose calculated among users of each drug class. $p < 0.05$ in bold.

**Figure 3 – Optimized medical therapy by KDIGO stage (G1 to G5) in patients with heart failure and reduced ejection fraction.**

severity: 18% in G3a, 36% in G3b, and 78% in G4. This indicates that clinicians tend to recognize CKD only when it is severe—thus missing the therapeutic window in moderate CKD.

The most likely explanation is that serum creatinine alone does not raise concern when it appears “high-normal” (1.0–1.5 mg/dL), even though eGFR is already below 60 in older patients with lower muscle mass.¹⁶ Only the formal calculation of eGFR converts the raw laboratory value into actionable clinical information.

Monotonic gradient of OMT

The gradient of OMT across KDIGO stages (56.5% → 18.5%; $p < 0.001$), spanning six points, is consistent with a progressive relationship between the severity of renal dysfunction and undertreatment. Although the cross-sectional design does not allow formal causal inference, the presence of a monotonic gradient reinforces the plausibility of the association and reduces the likelihood that the finding is entirely explained by confounding.²⁰

Spironolactone was the sentinel class: it remained at a plateau of ~85% up to stage G3a, with a drop to 44% in

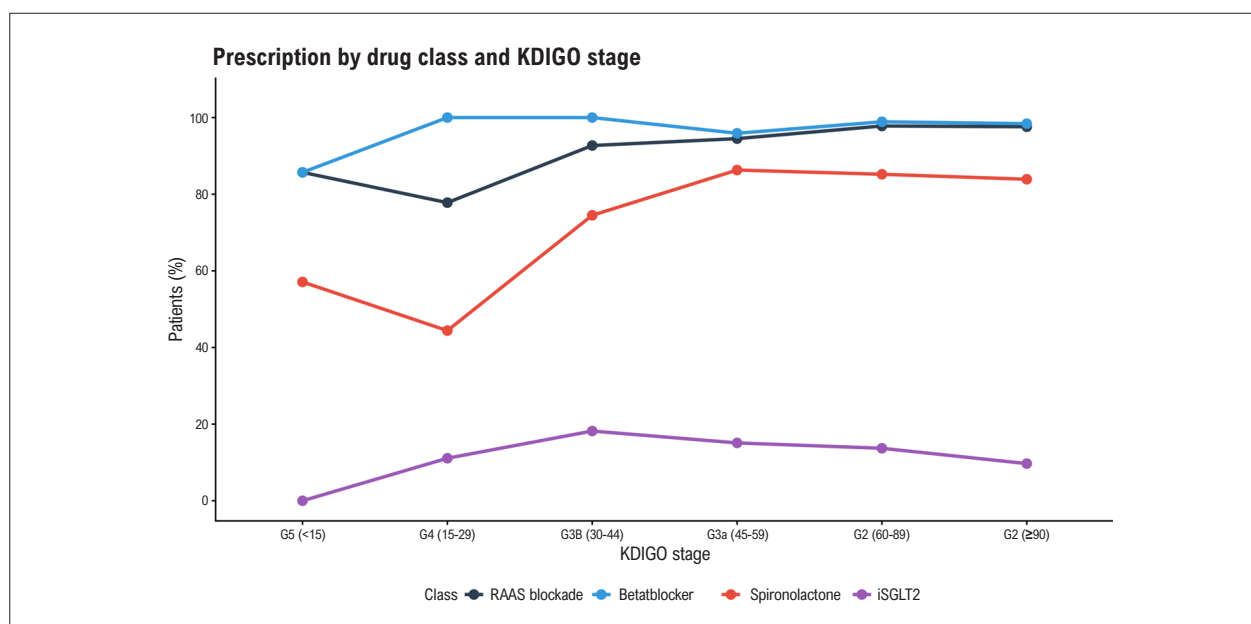


Figure 4 – Prescription of each drug class – renin-angiotensin-aldosterone system (RAAS) blockade, beta-blocker, spironolactone, and SGLT2 inhibitors – by KDIGO stage in patients with heart failure and reduced ejection fraction.

Table 3 – Independent predictors of optimized medical therapy: multivariate logistic regression (n=469)

Predictor	OR	95% CI	p	p global
Renal status				0.071
Without CKD	ref	—		
Hidden CKD	0.73	0.43 – 1.23	0.234	
Recognized CKD	0.47	0.23 – 0.92	0.028	
Age (by year)	0.95	0.93 – 0.97	<0.001	<0.001
Atrial flutter/fibrillation	0.95	0.59 – 1.52	0.817	0.817
Diabetes mellitus	1.90	1.25 – 2.90	0.003	0.003
COPD	0.60	0.24 – 1.40	0.244	0.244

OR: odds ratio; CI: confidence interval; COPD: chronic obstructive pulmonary disease; ref: reference. AUC-ROC: 0.717 (95% CI 0.670–0.763). Hosmer–Lemeshow p: 0.71. Pseudo- R^2 (Nagelkerke): 0.15. $p < 0.05$ in bold; CKD: chronic kidney disease.

G4. The barrier data help clarify the mechanism: “renal dysfunction” as a reason for underdosing followed a gradient from 0% (G1–G2) to 67% (G5). This pattern reflects fear of hyperkalemia, often disproportionate to the actual risk when eGFR is > 30 and potassium is monitored.^{18,19} Data from the CHECK-HF registry confirm that MRAs are the drug class most vulnerable to the inhibitory effect of CKD.⁶

Indeed, in our sample, true hyperkalemia (potassium > 5.0 mEq/L) was not associated with spironolactone prescription (OR 1.04; $p = 0.90$), whereas recognized CKD independently reduced its use (OR 0.35; 95% CI 0.18–0.68; $p = 0.002$). This suggests that the decision not to prescribe spironolactone is driven by the perceived risk associated with a CKD diagnosis, rather than by the actual serum potassium level.

The role of age as a cofounder

Hidden CKD lost statistical significance after adjustment for age (OR 0.73; $p = 0.23$), whereas recognized CKD remained significant (OR 0.47; $p = 0.03$). Age was the strongest predictor (OR 0.95 per year), meaning 40% lower odds of OMT for each additional decade.

Patients with hidden CKD are approximately 10 years older than those without CKD. Advanced age is associated with lower titration due to hypotension, reduced hemodynamic tolerance, and possible prescriber bias toward older adults.^{8,21} Therefore, part of the undertreatment in hidden CKD is mediated by age. However, whether age acts as a mediator (in the causal pathway: CKD $\rightarrow$ aging $\rightarrow$ undertreatment) or as a confounder (a common cause of both CKD and undertreatment) has important implications for interpretation.

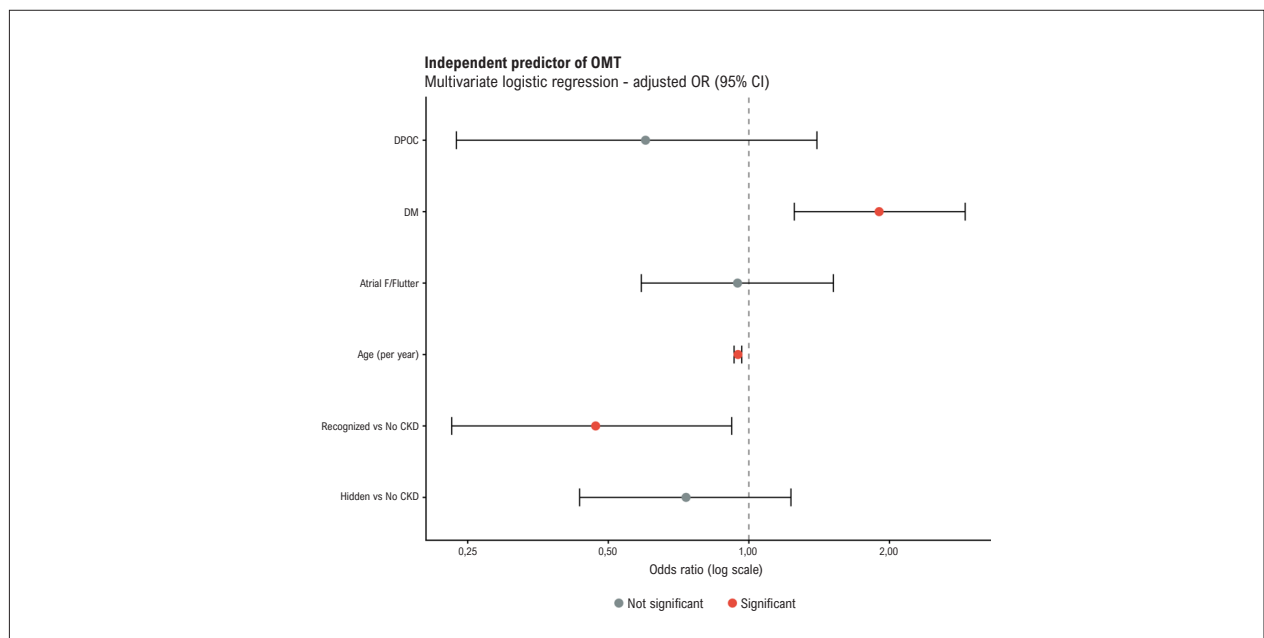


Figure 5 – Forest plot of multivariate logistic regression for optimized medical therapy predictors.

If age is a mediator, adjustment artificially attenuates the true effect of CKD. This ambiguity, inherent to the cross-sectional design, prevents a definitive conclusion and suggests that the adjusted OR of 0.73 may underestimate the true relationship between hidden CKD and undertreatment.

The diabetes paradox

The association between diabetes and higher OMT use (OR 1.90; $p = 0.003$) has precedents in the CHAMP-HF and IMPROVE-HF registries,^{5,8} and was also described in the Swedish registry by Savarese et al.¹² Diabetic patients attend more clinic visits, undergo more testing, and receive greater pharmacologic attention — the so-called “structured care effect.” This finding reinforces that the intensity of follow-up is an underestimated determinant of OMT.

Biases: identification, direction, and impact

Selection bias: 22.9% were excluded due to missing creatinine values. Formal comparison showed no differences in age, OMT, or beta-blocker use. LVEF was marginally lower among excluded patients (28.7% vs. 30.0%; $p = 0.03$), which, if relevant, suggests that sicker patients were excluded — a conservative bias that may underestimate both the prevalence of hidden CKD and the magnitude of undertreatment.

Classification bias: Defining recognized CKD based on documentation may underestimate the clinician’s implicit knowledge. However, missing documentation compromises alerts, longitudinal monitoring, and multidisciplinary communication — a process failure with practical consequences independent of individual knowledge. This bias would tend to shift results toward

the null hypothesis (diluting differences between hidden and recognized CKD), making our findings conservative.

Single creatinine measurement: KDIGO classification requires an eGFR < 60 sustained for ≥ 3 months. Our dataset contains only a single creatinine measurement, which may include cases of transient acute kidney injury, reversible congestion, or pseudo-CKD due to sarcopenia. However, in stable outpatients with chronic HFrEF, the likelihood of transient variation is substantially lower than in hospitalized patients. To assess this possibility, we compared congestion signs (dyspnea, jugular venous distension, edema, crackles) across the three groups and found no significant differences (composite score: 0.68 vs. 0.88 vs. 0.74; $p = 0.127$), suggesting that eGFR < 60 does not reflect transient congestion. Additionally, when restricting the analysis to the 247 patients without any congestion signs, the OMT gradient remained unchanged (52.9% vs. 40.4% vs. 21.4%; $p = 0.005$). If present, this bias would tend to overestimate the prevalence of hidden CKD, inflating the magnitude of the gap — but not its existence.

Residual confounding: The pseudo- R^2 of 0.15 indicates that ~85% of the variance in OMT is not explained by the model. Unmeasured factors — physician preference, access, socioeconomic status, adherence — contribute to undertreatment. The AUC of 0.717 confirms moderate discrimination, consistent with the multifactorial nature of therapeutic decision-making.

Temporal bias: The 2019-2022 period preceded the widespread availability of SGLT2 inhibitors in the public health system. Excluding SGLT2 inhibitors from the primary OMT definition mitigates this bias.

Clinical implications

The data suggest that incorporating automatic eGFR calculation into electronic medical records – a low-cost intervention – could reduce the identified gap. Alert systems that flag eGFR < 60 during the visit would allow clinicians to recognize CKD, stratify risk, monitor potassium, and make therapeutic decisions based on objective data rather than subjective impressions of “the patient’s creatinine.”²²

Limitations

In addition to the biases already detailed: (1) cross-sectional design, preventing causal inference; (2) single tertiary-care center – the gap may be even larger in primary care; (3) absence of albuminuria in the database (information unavailable for retrospective collection), preventing full KDIGO classification and making our estimate potentially conservative; (4) mortality limited to a small subgroup (n = 109), with insufficient statistical power; (5) OMT defined as ≥ 50% of target dose – a lenient threshold that may inflate OMT rates but makes the observed gradient more conservative; (6) lack of data on duration of outpatient follow-up, which likely influences the probability of optimization.

Conclusion

In a specialized outpatient setting, 64% of patients with HFrEF and eGFR < 60 did not have documented CKD, with cases concentrated in stages G3a–G3b. OMT followed a monotonic gradient across KDIGO stages, with spironolactone being the most affected class. Recognized CKD and advanced age were independent predictors of undertreatment. Routine calculation and documentation of eGFR represent a simple intervention with the potential to identify this population and support therapeutic optimization.

Author Contributions

Conception and design of the research and Critical revision of the manuscript for intellectual content: Grillo

FL, Bruscatto JR, Lira RCP, Moura LAZ; Acquisition of data and Writing of the manuscript: Grillo FL, Bruscatto JR, Ross FS, Bergamaschi EZ, Marinho GDT, Nunes JB; Analysis and interpretation of the data: Grillo FL, Ross FS, Bergamaschi EZ, Marinho GDT, Nunes JB; Statistical analysis: Grillo FL.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This article is part of the thesis of master submitted by Rosane Carolina Paes de Lira, from Pontifícia Universidade Católica do Paraná.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Pontifícia Universidade Católica do Paraná under the protocol number 5.338.882 / CAAE: 52796521.3.0000.0020. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

All datasets supporting the results of this study are available upon request from the corresponding author.

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*Supplemental Materials

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