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Chronic heart failure in an internal medicine outpatient setting: a retrospective real-world observational study of 30-day readmission and all-cause mortality

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Contributions: Ettore Napoli: study concept, data collection and analysis, and draft of the manuscript. Laura Schiavon: data interpretation and critical revision of the manuscript. Stefano Cuppini: study supervision, clinical interpretation, and manuscript revision. Alberto Mazza: study supervision, critical revision of the manuscript, and final approval of the version to be submitted. All authors read and approved the final manuscript.

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Ethics approval and consent to participate: this retrospective observational study was conducted in accordance with the principles of the Declaration of Helsinki and local institutional procedures. The study protocol was approved by the local Ethics Committee and conducted according to the “Guide to Good Clinical Practice” established by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH E6(R3)).

Informed consent: the patients expressed their informed consent to the study during the post-discharge visit. In addition, all the data collected have been anonymized in a database with spreadsheet.

Patient consent for publication: all subjects were informed of the study protocol and expressed their informed consent to participate in the same.

Availability of data and materials: the data underlying this article are available from the corresponding author upon reasonable request.

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Abstract

Heart failure (HF) remains a major cause of hospitalization, mortality, and healthcare burden, and its long-term management increasingly relies on structured outpatient care. This retrospective single-center observational study describes the clinical characteristics, treatment patterns, and outcomes of patients with chronic HF referred to an internal medicine outpatient clinic after hospital discharge. A total of 135 consecutive patients who attended the first specialist outpatient visit and had baseline clinical data available were included and classified according to left ventricular ejection fraction as HF with reduced, mildly reduced, or preserved ejection fraction. For this study, baseline assessment and time zero were defined as the first post-discharge outpatient visit rather than hospital discharge. The primary endpoint was readmission within 30 days from outpatient baseline assessment; the secondary endpoint was all-cause mortality during follow-up. The overall 30-day readmission rate, therefore interpreted from outpatient reassessment rather than from discharge, was 9.6%, with no significant differences across ejection fraction categories. During follow-up, 32 deaths occurred (23.7%). Although mortality was numerically higher in patients with reduced ejection fraction, survival did not significantly differ among ejection fraction groups. In adjusted analyses, older age and higher NT-proBNP appeared to carry stronger prognostic information than the ejection fraction category alone. These findings should be interpreted in light of the retrospective observational design, the selected post-discharge outpatient cohort, the limited sample size, and the definition of baseline at the first outpatient visit, which may underestimate very early post-discharge readmission events.

Introduction

Heart failure (HF) is a complex clinical syndrome associated with major morbidity, impaired functional capacity, reduced quality of life, and high healthcare costs.¹⁻³ Its prevalence increases sharply with advancing age, and for this reason HF is encountered very frequently in internal medicine wards and outpatient services. In routine practice, patients are rarely represented by a single disease process: instead, they often combine cardiac dysfunction with chronic kidney disease, diabetes, anemia, hypertension, atrial fibrillation, and frailty, all of which may influence therapeutic choices and prognosis.

Although the evidence base for HF has expanded considerably and guideline-directed medical therapy has improved outcomes, the translation of recommendations into everyday care remains challenging.¹⁻⁴ This is particularly true during the period immediately after discharge, when congestion may recur, renal function and electrolytes may fluctuate, treatment titration may still be incomplete, and the patient is exposed to a high risk of clinical instability. Therefore, outpatient follow-up is not simply an administrative continuation of care, but rather a decisive phase in which diagnosis is refined, pharmacological therapy is optimized, and the overall trajectory of the syndrome can be influenced.

The outpatient internal medicine setting deserves specific attention because it often manages elderly and clinically heterogeneous patients who may not fit the profile of highly selected trial populations.^{2,5-8} In this context, it is important not only to assess outcomes such as readmission and mortality, but also to describe the baseline phenotype of the population and the patterns of treatment actually prescribed in real-world care. This perspective is essential for understanding how guidelines are implemented in daily practice and where the most relevant gaps may persist.

Beyond the distinction between reduced, mildly reduced, and preserved ejection fraction (EF), HF should also be interpreted as a dynamic syndrome in which symptom burden, congestion, renal function, biomarker profile, and therapeutic response evolve over time. For this reason, outpatient care offers a privileged setting to observe the interaction between phenotype, treatment, and prognosis. A descriptive study of this phase may therefore provide clinically useful information even when derived from a single-center real-world cohort.

The present study was therefore designed to describe the baseline characteristics, pharmacological treatment, and outcomes of a real-world cohort of patients with chronic HF followed in an internal medicine outpatient clinic. Particular attention was paid to two clinically relevant outcomes: 30-day readmission, as an indicator of early post-discharge vulnerability, and all-cause mortality, as an indicator of long-term prognosis.

Materials and Methods

This was a retrospective, single-center observational study including 135 consecutive patients with chronic HF who were referred to and attended a dedicated internal medicine outpatient clinic after hospital discharge. Patients were managed according to routine clinical practice rather than a study protocol. Eligibility for inclusion in the present analysis required attendance at the first specialist outpatient visit and availability of core baseline clinical data. Thus, the cohort reflects a selected post-discharge outpatient population rather than all patients hospitalized with chronic HF.

Patients were categorized according to left ventricular EF into heart failure with reduced ejection fraction (HFrEF) ($\leq 40\%$), heart failure with mild reduced ejection fraction (HFmrEF) (41-49%), and heart failure with preserved ejection fraction (HFpEF) ($\geq 50\%$), in line with contemporary clinical classification. Baseline data included age, sex, body mass index, major comorbidities, laboratory variables, echocardiographic measures, and pharmacological treatment. For the purposes of this study, time zero was defined as the first specialist outpatient visit after discharge; this choice was dictated by the retrospective structure of the dataset but differs from the conventional approach used in studies that begin follow-up at hospital discharge.

The primary endpoint was readmission within 30 days after baseline outpatient assessment and treatment initiation or optimization. Readmission was defined as any hospital readmission occurring within 30 days from the first outpatient visit, not within 30 days from discharge. The secondary endpoint was all-cause mortality during follow-up. Because the interval between discharge and baseline outpatient evaluation was not systematically available for all patients in this retrospective dataset, the reported 30-day readmission rate should be interpreted as referring to the outpatient observation window and may underestimate very early post-discharge events.

Continuous variables were summarized according to their distribution and categorical variables as counts and percentages. To preserve model stability, multivariable models were kept parsimonious and limited to clinically relevant variables. Nonetheless, given the modest number of events, especially for subgroup analyses, the comparative results should be interpreted cautiously because of limited statistical power, possible type II error, and a potential risk of overfitting in adjusted Cox models.

Results

The cohort consisted predominantly of patients with HF_rEF (92/135, 68.1%), followed by HF_pEF (31/135, 23.0%) and HF_mrEF (12/135, 8.9%). The study population was elderly across all EF categories, with mean age around 80 years, and showed a broad burden of comorbidity. A large proportion of patients fell within NYHA class II or III, confirming that most subjects were clinically symptomatic but not usually in terminal functional stages. Sex distribution differed across EF phenotypes, with a male predominance in HF_rEF and a greater proportion of women in HF_mrEF and HF_pEF.

Biochemical and clinical findings were consistent with a fragile chronic HF population. NT-proBNP values were markedly elevated across all EF categories, while glucose levels were frequently above the normal range and hemoglobin and iron parameters tended to be lower than ideal, suggesting a clinically relevant burden of metabolic and hematinic abnormalities. The most frequent comorbidities were hypertension, ischemic heart disease, and diabetes mellitus, emphasizing the coexistence of cardiovascular and systemic disease typically encountered in internal medicine practice.

From a therapeutic perspective, beta-blockers and loop diuretics were the most commonly prescribed drug classes, and more than half of the cohort was treated with mineralocorticoid receptor antagonists. By contrast, lower prescription rates were observed for ACE inhibitor/ARNI-based therapy and SGLT2 inhibitors, with relevant differences across EF categories (Table 1). These data reflect the real-world complexity of implementing guideline-directed medical therapy in elderly multimorbid patients, in whom hypotension, renal dysfunction, therapeutic inertia, or evolving indications may influence prescribing patterns.

When the baseline profile is examined as a whole, the cohort appears representative of the patient population usually encountered in everyday internal medicine rather than of a highly selected trial sample. The combined presence of advanced age, multiple comorbidities, abnormal biomarkers, and frequent use of symptomatic therapies such as loop diuretics underscores that these patients required individualized balancing of efficacy, tolerability, and safety. This context is crucial for interpreting outcomes, because it helps explain why mortality may remain relevant even when short-term readmission is contained.

The overall 30-day readmission rate, calculated from the first outpatient visit rather than from hospital discharge, was 9.6%, with very similar proportions across EF categories: 9.8% in HF_rEF, 8.3% in HF_mrEF, and 9.7% in HF_pEF (Table 2). These figures therefore describe early events after outpatient reassessment in patients who had already survived and reached specialist follow-up; they should not be interpreted as conventional post-discharge 30-day readmission rates and may underestimate events occurring immediately after discharge.

In unadjusted Cox analysis, reduced EF showed a significant association with worse prognosis compared with preserved EF (Table 3). However, this association lost statistical significance after adjustment for

age, sex, and NT-proBNP, suggesting that the crude effect of EF was attenuated when markers more directly related to biological risk and overall disease severity were considered. In this cohort, age and NT-proBNP emerged as the most informative prognostic variables in the adjusted models.

Discussion

The present study provides a descriptive real-world picture of chronic HF management in an internal medicine outpatient setting. Two findings are especially relevant. First, the observed readmission rate within 30 days from outpatient reassessment was 9.6%, with no meaningful differences across EF categories. Second, despite this relatively low early event rate within the observed outpatient window, long-term mortality remained substantial (Figure 1). These findings should be interpreted descriptively and should not be construed as evidence that the outpatient pathway itself reduced readmission, because the retrospective observational design and the absence of a control group do not allow causal inference. The interpretation of the readmission finding deserves particular caution. In many HF studies, follow-up begins at hospital discharge. In our cohort, however, baseline corresponded to the first specialist outpatient visit after discharge. This methodological choice creates an inevitable survivor effect and likely excludes some events occurring in the immediate post-discharge phase. Consequently, the 9.6% value is best understood as a 30-day readmission rate from outpatient baseline assessment rather than as a conventional post-discharge metric.

Another important message of this cohort is that prognosis appeared to be influenced more by overall disease severity than by EF category alone. While HFrEF showed a significant adverse association in the unadjusted model, that signal disappeared after multivariable adjustment. In practical terms, this suggests that the crude prognostic effect of EF may have been partly explained by age and biomarker burden, particularly NT-proBNP, which in this cohort captured risk more directly than EF classification alone (Figures 2 and 3). At the same time, because the sample size was modest and the HFmrEF subgroup was very small, the absence of significant differences among EF groups should not be interpreted as proof of clinical equivalence, since a type II error remains possible.

The treatment patterns observed in this study also help explain the gap between guideline recommendations and real-world practice. Beta-blocker use was high, whereas the uptake of more recent therapies such as ARNI and SGLT2 inhibitors was lower in some groups. In an elderly and multimorbid internal medicine population, this discrepancy may reflect several factors acting simultaneously, including the progressive introduction of newer therapies during the study period, renal dysfunction, hypotension, frailty, polypharmacy, and tolerability issues. Because of the retrospective design, it was not possible to systematically distinguish therapeutic inertia from appropriate non-prescription related to contraindications or clinical judgment.

The descriptive signal regarding cause and pattern of death should also be interpreted within this framework. In a multimorbid internal medicine population, death is rarely attributable to a single mechanism in isolation; rather, it is often the result of the interaction between HF progression, renal dysfunction, infection, arrhythmias, metabolic instability, and general frailty. This is one of the reasons why all-cause mortality is a robust endpoint in this setting and why it may be more informative than disease-specific labels alone.

From a practical standpoint, the data support the relevance of a dedicated outpatient pathway for chronic HF within internal medicine as a setting for reassessment, treatment optimization, and continuity of care. However, our findings remain observational and descriptive. They indicate what happened in a selected real-world outpatient cohort; they do not demonstrate that structured follow-up caused the observed readmission pattern or improved outcomes compared with other care models.

A further implication of these results concerns communication between hospital and ambulatory care. The quality of discharge planning, timing of follow-up, and clarity of therapeutic instructions may all influence whether outpatient treatment is effectively continued and intensified. In this sense, the

outpatient clinic represents the operational bridge between the acute phase and long-term chronic care. The better this bridge is organized, the greater the possibility of stabilizing symptoms early and identifying patients at higher risk before they experience major deterioration.

The study has limitations inherent to its retrospective and single-center design. First, no causal inference can be made. Second, the cohort included only patients who were referred to and attended a dedicated outpatient clinic after discharge; therefore, selection bias and survivor bias cannot be excluded, and more unstable, frail, or poorly adherent patients may have been underrepresented. Third, baseline was defined as the first specialist outpatient visit rather than hospital discharge, so the reported 30-day readmission rate refers to the outpatient observation window and may underestimate very early post-discharge events. Fourth, the sample size was modest, particularly in the HFmrEF subgroup, limiting statistical power and increasing the possibility of type II error in subgroup comparisons. Finally, the number of outcome events may have limited the stability of multivariable Cox models, with a potential risk of overfitting. Overall, our findings provide a real-world observational snapshot of chronic HF follow-up in internal medicine. The data suggest that, within a selected post-discharge outpatient cohort, early readmission from the time of outpatient reassessment was relatively infrequent, whereas long-term prognosis remained strongly influenced by age, biomarker burden, and overall disease severity.

Conclusions

In this retrospective real-world cohort of patients with chronic HF managed in an internal medicine outpatient clinic, the rate of readmission within 30 days from the first outpatient visit was relatively low, whereas long-term all-cause mortality remained substantial. Because of the observational design, the selected post-discharge cohort, and the definition of baseline at outpatient reassessment rather than at hospital discharge, these findings should be interpreted as descriptive and hypothesis-generating rather than causal.

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Table 1. Baseline pharmacological therapy by EF category.

| Drug class | HFrEF (n=92) | HFmrEF (n=12) | HFpEF (n=31) |
|--|--------------|---------------|--------------|
| ARNI (sacubitril/valsartan) | 68 (73.9%) | 4 (33.3%) | 5 (16.1%) |
| Beta-blockers | 64 (87.7%) | 7 (77.8%) | 22 (84.6%) |
| Mineralocorticoid receptor antagonists | 41 (55.4%) | 5 (55.6%) | 15 (57.7%) |
| Diuretics | 63 (86.3%) | 7 (77.8%) | 24 (96.0%) |
| SGLT2 inhibitors | 18 (19.6%) | 8 (66.7%) | 22 (71.0%) |
| ARNI dose 24/26 | 53 (57.6%) | 4 (33.3%) | 5 (16.1%) |
| ARNI dose 49/51 | 12 (13.0%) | 0 (0.0%) | 0 (0.0%) |
| ARNI dose 97/103 | 3 (3.3%) | 0 (0.0%) | 0 (0.0%) |

HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mild reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; ARNI, angiotensin receptor-neprilysin inhibitors; SGLT2, sodium-glucose transport protein 2.

Table 2. Outcomes by EF category.

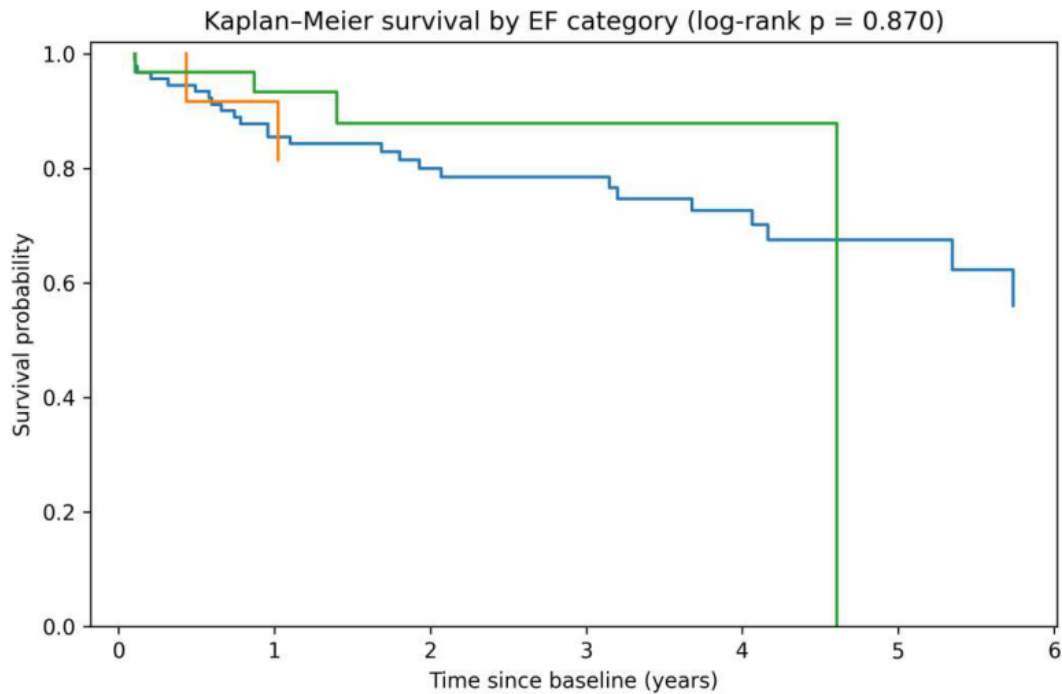
| EF category | 30-day readmission | Deaths, n (%) | Median follow-up, years | Person-years | Death rate per 100 PY |
|-------------|--------------------|---------------|-------------------------|--------------|-----------------------|
| HFrEF | 9.8% | 26 (28.3%) | 2.04 | 246.0 | 10.57 |
| HFmrEF | 8.3% | 2 (16.7%) | 1.27 | 18.3 | 10.94 |
| HFpEF | 9.7% | 4 (12.9%) | 1.63 | 47.5 | 8.41 |
| Overall | 9.6% | 32 (23.7%) | 1.87 | 341.7 | 9.36 |

HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mild reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction.

Table 3. Cox regression models for all-cause mortality (HFpEF reference).

| Model | Variable | HR | 95% CI | p-value |
|---------|------------------|------|-----------|---------|
| Model 0 | HFrEF vs. HFpEF | 1.16 | 1.06-1.26 | <0.001 |
| | HFmrEF vs. HFpEF | 1.14 | 0.25-5.20 | 0.862 |
| Model A | HFrEF vs. HFpEF | 1.11 | 0.37-3.35 | 0.854 |
| | HFmrEF vs. HFpEF | 1.10 | 0.20-6.02 | 0.915 |
| | Age (per year) | 1.04 | 1.03-1.06 | <0.001 |
| | Male sex | 1.85 | 0.79-4.34 | 0.154 |
| Model B | HFrEF vs. HFpEF | 0.31 | 0.07-1.31 | 0.111 |
| | HFmrEF vs. HFpEF | 0.47 | 0.05-4.78 | 0.525 |
| | Age (per year) | 1.04 | 1.00-1.08 | 0.043 |
| | Male sex | 3.02 | 1.08-8.47 | 0.036 |
| | log(NT-proBNP) | 2.11 | 1.43-3.11 | <0.001 |

HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mild reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; CI, confidence interval.



| Group | Mortality 1y (%) [at risk] | Mortality 3y (%) [at risk] | Mortality 5y (%) [at risk] | Note |
|---------|-------------------------------|-------------------------------|-------------------------------|--|
| Overall | 14.6 [83] | 24.0 [39] | 38.5 [18] | |
| HFfrEF | 17.2 [60] | 25.0 [37] | 36.6 [18] | |
| HFmrEF | 8.3 [7] | 21.4 [1] | 21.4 [0] | 3y estimate unstable; 5y estimate unstable |
| HFpEF | 6.7 [16] | 15.8 [1] | 100.0 [0] | 3y estimate unstable; 5y estimate unstable |

Figure 1. Kaplan–Meier survival curves for all-cause mortality stratified by EF category, with summary numbers at risk reported below the figure. Survival probability is plotted from outpatient baseline assessment to death or censoring at last available follow-up. Log-rank $p=0.870$. Number at risk at 1/3/5 years: Overall 83/39/18; HFfrEF 60/37/18; HFmrEF 7/1/0; HFpEF 16/1/0. Late estimates for HFmrEF and HFpEF should be interpreted cautiously because the number at risk becomes very small. Kaplan–Meier mortality estimates by group were as follows: overall 14.6% at 1 year, 24.0% at 3 years, and 38.5% at 5 years; HFfrEF 17.2%, 25.0%, and 36.6%; HFmrEF 8.3%, 21.4%, and unstable at 5 years; HFpEF 6.7%, 15.8%, and unstable at 5 years owing to zero patients remaining at risk.

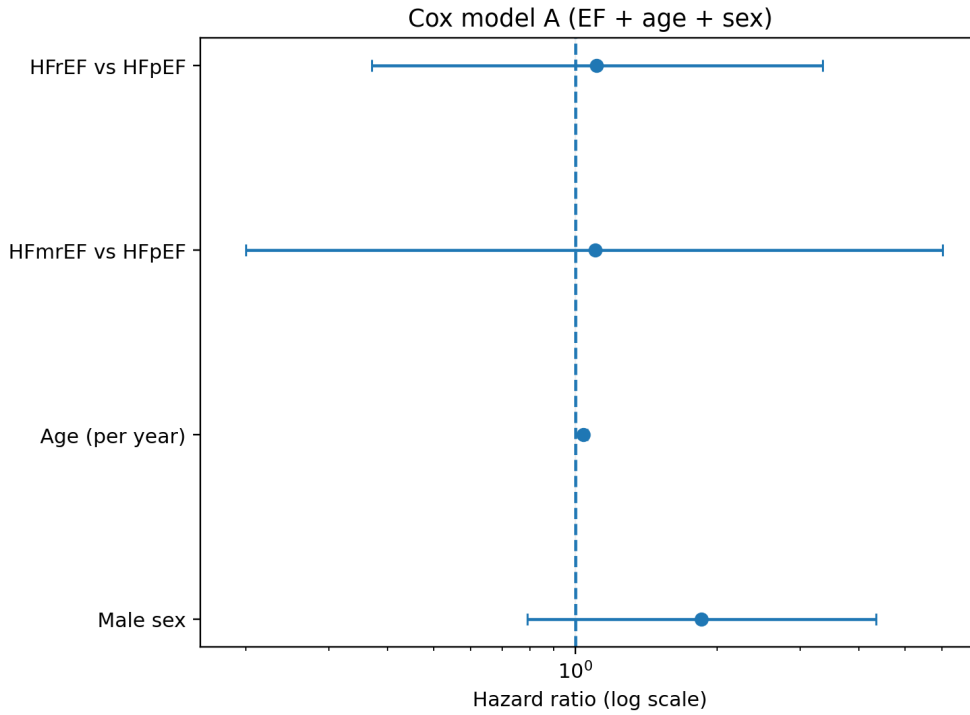


Figure 2. Forest plot for Cox model A (EF + age + sex). Hazard ratios are shown on a logarithmic scale; the dashed vertical line indicates HR=1.

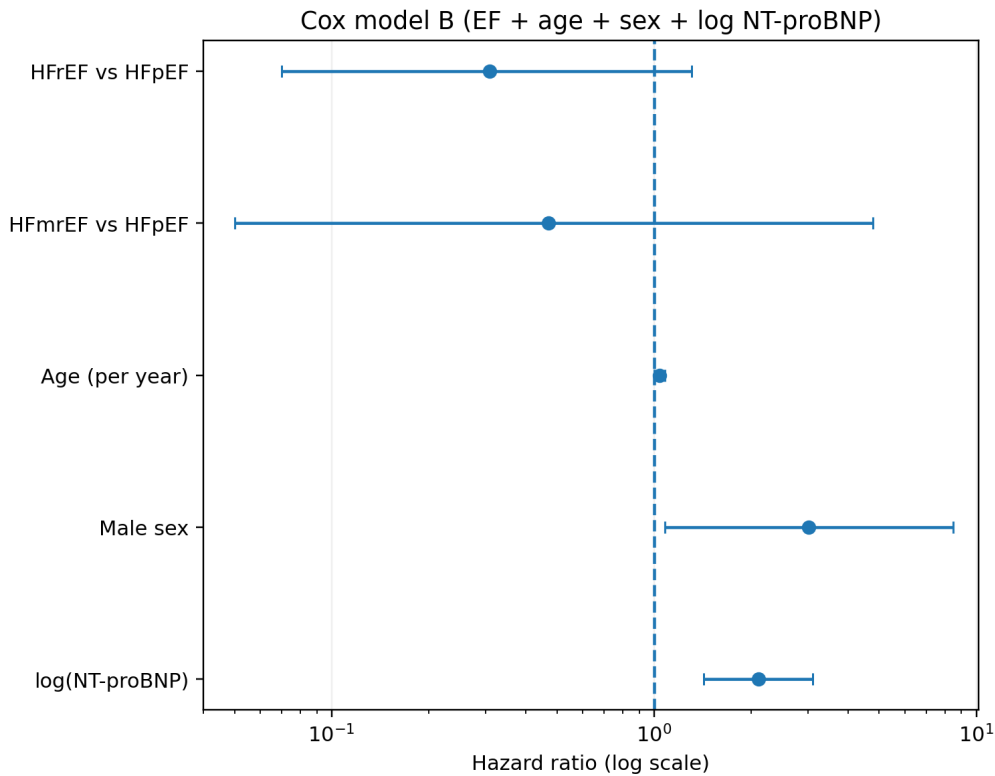


Figure 3. Forest plot for Cox model B (EF + age + sex + log NT-proBNP). Hazard ratios are shown on a logarithmic scale; the dashed vertical line indicates HR=1.