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ORIGINAL ARTICLE

Evidence-Based Process Performance Measures and Clinical Outcomes in Patients With Incident Heart Failure With Reduced Ejection Fraction: A Danish Nationwide Cohort Study

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BACKGROUND: Data on the association between quality of heart failure (HF) care and outcomes among patients with incident HF are sparse. We examined the association between process performance measures and clinical outcomes in patients with incident HF with reduced ejection fraction.

METHODS: Patients with incident HF with reduced ejection fraction (n=10 966) between January 2008 and October 2015 were identified from the Danish HF Registry. Data from public registries were linked. Multivariable regression analyses were used to assess the association between 6 guideline-recommended HF care processes (New York Heart Association assessment, use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, beta-blockers, and mineralocorticoid receptor antagonists, exercise training, and patient education) and all-cause and HF readmission, all-cause and HF hospital days, and mortality within 3 to 12 months after HF diagnosis. The associations were analyzed according to the percentages of all relevant performance measures fulfilled for the individual patient (0%–50% [reference group], >50%–75%, and >75%–100%) and for the individual performance measures.

RESULTS: Fulfilling >75% to 100% of the performance measures (n=5341 [48.7%]) was associated with lower risk of all-cause readmission (adjusted hazard ratio, 0.78 [95% CI, 0.68–0.89]) and HF readmission (adjusted hazard ratio, 0.71 [95% CI, 0.54–0.92]), lower use of all-cause hospital days (adjusted mean ratio, 0.73 [95% CI, 0.70–0.76]) and HF hospital days (adjusted mean ratio, 0.79 [95% CI, 0.70–0.89]), and lower mortality (adjusted hazard ratio, 0.42 [95% CI, 0.32–0.53]). A dose-response relationship was observed between fulfilling more performance measures and mortality (adjusted hazard ratio, 0.62 [95% CI, 0.49–0.77] fulfilling >50%–75% of the measures). Fulfilling individual performance measures, except mineralocorticoid receptor antagonist therapy, was associated with lower adjusted all-cause readmission, lower adjusted use of all-cause and HF hospital days, and lower adjusted mortality.

CONCLUSIONS: Fulfilling more process performance measures was associated with better clinical outcomes in patients with incident HF with reduced ejection fraction.

Key Words: exercise ■ health care ■ heart failure ■ mortality ■ patient readmission ■ process assessment ■ registries

Heart failure (HF) is a serious condition associated with frequent hospitalizations, high mortality, and reduced quality of life.[1] Over the last 3 decades, several landmark studies have provided robust evidence on improved clinical and patient-reported outcomes of medical treatment, devices, and care organizations.[2,3]

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For Sources of Funding and Disclosures, see page 292.

WHAT IS KNOWN

- Nonadherence to evidence-based guideline-recommended heart failure (HF) care contributes to increased morbidity and mortality
- Decreased fulfillment of process performance measures has a decremental impact on mortality in patients with HF

WHAT THE STUDY ADDS

- This study adds to the understanding of the relationship between performance measures and outcomes among patients with incident HF with reduced ejection fraction and important clinical outcomes other than mortality
- Patients fulfilling increased numbers of process performance measures experienced a lower risk of all-cause and HF readmission, lower use of all-cause and HF hospital days, and decreased mortality within 3 to 12 months after HF diagnosis

Nonstandard Abbreviations and Acronyms

ACEI	angiotensin-converting enzyme inhibitor
ARB	angiotensin II receptor blocker
DHFR	Danish Heart Failure Registry
HF	heart failure
HFrEF	heart failure with reduced ejection fraction
LVEF	left ventricular ejection fraction
MRA	mineralocorticoid receptor antagonist

Nonadherence with evidence-based guideline-recommended HF care may have a substantially negative impact on patient outcomes.[2] Therefore, monitoring and reporting on the quality of care are used in many European countries and the United States to facilitate improvements in HF care quality. Adherence to clinical guideline recommendations is assessed using performance measures reflecting whether specific care processes are delivered, for example, initiation of pharmacological therapy, exercise training, or patient education.[4,5] Previous studies that have addressed the associations between process performance measures and clinical outcomes have primarily focused on patients with chronic HF and mortality.[6–14] The relationship between the use of ACE (angiotensin-converting enzyme) inhibitor (ACEI)/angiotensin II receptor blocker (ARB) therapy, beta-blocker therapy, and patient education with subsequent lower mortality seems consistent.[7,9,14,15] However, there is currently limited evidence of a direct link between the fulfillment of HF performance measures and a broader range of clinical outcomes, including hospital readmission and hospital bed days in real-world clinical settings among patients with incident HF with reduced ejection fraction (HFrEF). Therefore, we conducted a nationwide population-based cohort study of patients with a confirmed first-time primary diagnosis of HFrEF. This study investigated the association between the performance measures for initial HF care and hospital readmission, hospital bed days, and mortality within 3 to 12 months after incident HFrEF diagnosis.

METHODS

Data cannot be shared publicly because of Danish legislation. Data can be accessed through the Danish Health Data Authority and Statistics Denmark for researchers at authorized institutions. Information on data access is available online (http://sundhedsdatastyrelsen.dk/da/forskerservice). Access to data requires approval from the Danish Data Protection Agency (https://www.datatilsynet.dk/english/legislation). The authors did not have special access privileges to these data.

Study Context

Denmark has a public-provision and public insurance-funded health care system that provides equal access to in-hospital care, hospital outpatient visits and general practitioners free of charge, and partial reimbursement of prescription medication costs. Moreover, Denmark is a relatively homogenous society with only minor geographic variations in demographic characteristics and health care utilization.[16] In Denmark, patients diagnosed with HF are referred to follow-up in a hospital-based HF clinic as part of a multidisciplinary HF management program.

Design and Data Sources

This study was based on a cohort of patients with incident HFrEF in the Danish HF Registry (DHFR).[17] Data from the DHFR were linked with other Danish public registries. All residents have a unique personal civil registration number, enabling linkage of individual-level information across registries.[18]

The details of the DHFR have been described previously.[17] Briefly, this nationwide clinical quality database covers adult patients with a first-time primary diagnosis of HF diagnosed in hospital inpatient and outpatient settings. The inclusion and exclusion criteria used in the DHFR are presented in Table S1. A cardiologist verifies the HF diagnosis before registry inclusion. Reporting to DHFR is mandatory for all Danish hospitals responsible for HF care. The DHFR contains prospectively collected data on HF care and sociodemographic, clinical, and lifestyle data.[17]

Study Population

We identified all inpatients (discharged alive) and outpatients with a first-time primary diagnosis of HFrEF with left ventricular ejection fraction (LVEF) ≤40% registered in the DHFR from January 1, 2008 to October 31, 2015. Patients diagnosed with HF in the outpatient setting were also required to have an inpatient secondary diagnosis of HF within 30 days. We were able to identify inpatients directly from the DHFR. Outpatients were identified by linking data from DHFR with data in the Danish National Patient Registry.[19] We identified 17 214 patients eligible for inclusion (Figure 1). Patients with missing data on cohabitation status and family income were excluded (n=92), and patients without documentation for echocardiography performed within 6 months before or 7 days after hospital admission date or the outpatient visit date (n=946). Furthermore, we excluded patients with missing data on a process performance measure (n=886) and patients who were readmitted or died within 90 days (n=4324) after hospital discharge or first outpatient visit. The 90-day time interval was chosen to ensure that all patients had the same opportunity to achieve the care processes (Table 1). Our final cohort study included 10 966 patients (Figure 1).

Performance Measures

The quality of care was assessed using 6 evidence-based process performance measures (Table 1) for incident HFrEF monitored in the DHFR.[17] Mineralocorticoid receptor antagonist (MRA) treatment was only monitored in patients with HFrEF and LVEF ≤35% as dictated by the guidelines.[2,3] The DHFR board had defined these process performance measures, including the timeframe for each process.[17] We obtained information on individual performance measures from the DHFR. The overall quality of HF care in each patient was summarized using an opportunity-based score. The numerator was defined as the number of performance measures fulfilled. The denominator was defined as the number of relevant performance measures (6 for LVEF ≤35% and 5 for LVEF >35%). The opportunity-based score was calculated and divided into 3 categories (0%–50%, >50%–75%, and >75%–100% fulfillment).

Clinical Outcomes

Clinical outcomes were all-cause and HF readmission, all-cause and HF hospital bed days, and all-cause mortality within 3 to 12 months after HF diagnosis. Information about hospitalization within 1 year after hospital discharge for inpatients and after the first appointment for outpatients was obtained from the Danish National Patient Registry. Readmission was defined as acute, unplanned hospitalization, including at least 2 calendar dates. HF readmission was identified as a primary discharge diagnosis of HF (*International Classification of Diseases [ICD], Tenth Revision [ICD-10]* codes: I50.0, I50.1, I50.9, I09.9A, I11.0, I13.0, I13.2). All-cause and HF hospital bed days were calculated as the total number of hospital overnight stays during follow-up. Information on vital status during follow-up was ascertained from the Danish Civil Registration System.[20]

Patient Characteristics

Information for age, sex, LVEF, New York Heart Association (NYHA) class, hypertension, chronic obstructive pulmonary

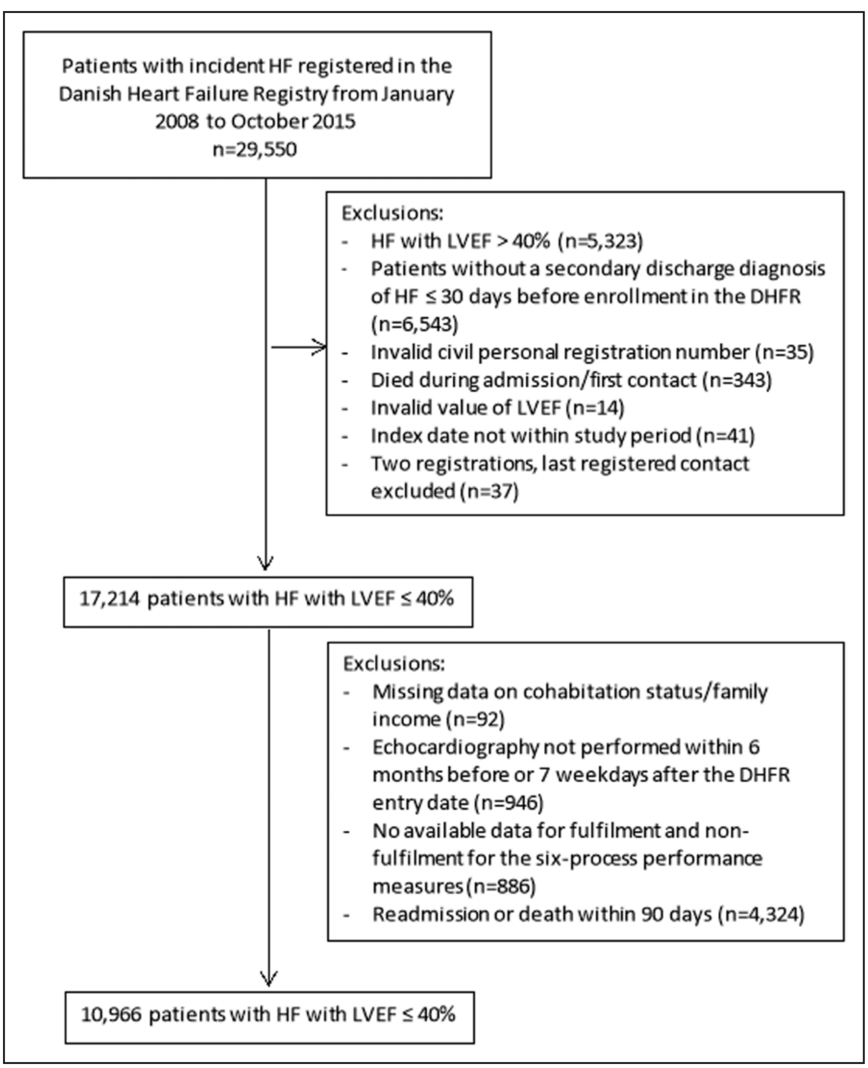

Figure 1. Flowchart of study population selection.
DHFR indicates Danish Heart Failure Registry; HF, heart failure; and LVEF, left ventricular ejection fraction.

Table 1. Process Performance Measures Monitored in Patients With HFrEF in the Danish Heart Failure Registry

Process performance measure	Definition	Measurement period*	Number, %
NYHA classification	Percentages of patients undergo NYHA classification	Within 12 wk†	10 047 (91.6)
ACEI/ARB	Percentages of patients treated with ACEI/ARB	Within 8 wk	10 248 (93.5)
Beta-blockers	Percentages of patients treated with beta-blocker	Within 12 wk	9748 (88.9)
MRA	Percentages of patients with HFrEF with LVEF ≤35% treated with MRA	Within 12 wk	3453 (38.7)
Exercise training	Percentages of patients started individual exercise training in a hospital or referred for exercise training in the municipality‡	Within 12 wk	3147 (28.7)
Patient education	Percentages of patients started a structured patient education (eg, nutrition, exercise training, understanding medical treatment, risk factors, and HF symptoms)	Within 12 wk	9233 (84.2)

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; and wk, weeks.
*Defined from admission to either hospital or outpatient clinic.
†The timeframe was in 2011 extended from discharge/first outpatient contact to 12 wks.
‡Defined from 2008 to 2010 as the percentages of patients who started exercise training in the hospital/municipality.

disease, myocardial infarction, stroke, diabetes, atrial fibrillation, S-creatinine level ≥150 µmol/L, smoking, and alcohol consumption were obtained from the DHFR. Data on primary and secondary diagnoses for all hospital contacts preceding the HF diagnosis were collected from the Danish National Patient Registry. These data were used to identify patients with previous myocardial infarction, stroke, and diabetes, calculate a modified Charlson comorbidity index score,[21] excluding points for HF (Data on International Classification of Disease codes and Charlson comorbidity index weights are shown in Table S2), and calculate the number of inpatient contacts during the preceding 1 and 10 years. We retrieved information on redeemed drug prescriptions for antipsychotic and antidepressant drugs 12 months before HF diagnosis from the National Prescription Register.[22] A redeemed prescription was considered a proxy for mental illness or vulnerability. Information on migration and household composition was retrieved from The Central Population Register, and highest attained educational level from the educational Attainment Register,[23] annual family income from the Family Income Register,[24] and employment status from The Labor Force Statistics,[25] all registers located at the Statistics Denmark.[18]

A list of variables is presented in Table S3.

Statistical Methods

The hospital admission date for inpatients and the first appointment date for outpatients defined the performance measurement period's index date. The follow-up period for the clinical outcomes started at day 91 to allow timely fulfillment of the process performance measures to avoid immortal time bias.[26] Patients were followed from day 91 after discharge date (inpatients)/first appointment date (outpatients) until death, migration, or 365 days.

We used Cox proportional hazards regression analysis to assess the association between the opportunity-based score and the fulfillment of each performance measure and all-cause readmission, HF readmission, and mortality. We computed crude and adjusted cause-specific hazard ratios with 95% CIs.

We used Poisson regression to determine the relationship between the opportunity-based score and each performance measure, respectively, and the use of all-cause and HF hospital bed days. To take the competing risk of death into account in the analysis, we added an offset variable for the different follow-up times to the models. The effect measure of the Poisson regression was interpreted as cause-specific ratios between the mean number of hospital bed days in each exposure group and the respective reference groups presented with 95% CIs.

We performed 3 statistical models; an unadjusted model and 2 adjusted models. First, we adjusted for the a priori identified potential confounders (Figure 2). Next, in models with the individual performance measure as exposure, we mutually adjusted for other performance measures. Moreover, the adjusted analyses were stratified by age group, sex, HF diagnosis setting, years 2008 to 2010 versus 2011 to 2015, cohabitation status, education, and income to examine whether these covariates modified the associations. Furthermore, to take the implementation of the care processes at the hospital site into account, we conducted adjusted/mutually adjusted multilevel Cox regression analyses with shared frailty for each hospital and case-mix adjusted by patient characteristics represented by inverse probability of treatment weights conditioned on the individual hospitals to take the clustered nature of the data into account. Two hospitals were excluded in the multilevel models because of a low number of patients (n=17). Finally, for comparison, complete case analyses were performed. In the analyses, all variables were handled as categorical variables.

We used multiple imputation by chained equations[27] to account for missing covariates (Table 2) based on the assumption that data were missing at random. Analyses were performed using 20 imputed datasets. The imputation models included all variables with missing data (Table 2), all variables used in the subsequent analytical models performed, as well as auxiliary variables (migration status, antidepressant or antipsychotic medication, previous hospitalizations [12 months]), predictive of missing values. An event and censoring indicator and the Nelson–Aalen estimator were included in Cox regression imputation models.

We performed all statistical analyses using Stata 16.1 (StataCorp, 2017, College Station, TX).

Ethics

This study was approved by the Danish Data Protection Agency (Reference number 1-16-02-324-16) and the Danish Clinical Registries and followed the Helsinki Declaration's principles, revised in 2013. Registry-based studies do not require informed participant consent or research ethics committee approval in Denmark.

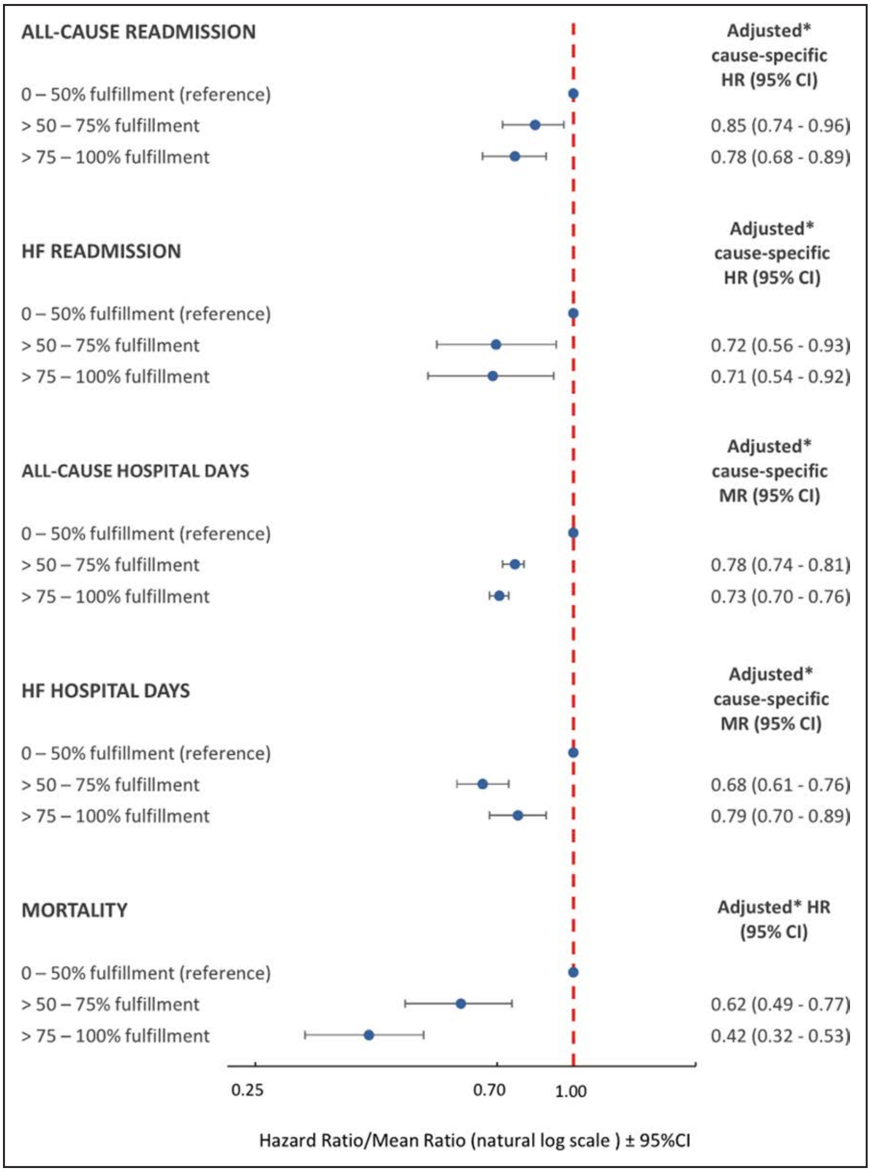

Figure 2. Associations between opportunity-based performance score (0%–50%, >50%–75%, and >75%–100% fulfillment) and clinical outcomes.
Adjusted hazard/mean ratio for all-cause and heart failure (HF) readmission, all-cause and HF hospital bed days, and mortality within 3 to 12 mo after HF with reduced ejection fraction diagnosis according to the performance score intervals. *Adjusted for age group, sex, HF diagnosis setting, left ventricular ejection fraction, New York Heart Association class, Charlson comorbidity index score, acute myocardial infarction, hypertension, stroke, diabetes, atrial fibrillation, creatinine level, previous hospitalizations (10 y), alcohol intake, smoking habits, region, calendar year, cohabitation status, education, and income. HR indicates hazard ratio; and MR, mean ratio.

RESULTS

Patient characteristics stratified by the opportunity-based score are listed in Table 2. Within the 3 to 12 months follow-up, 3252 patients (29.5%) were readmitted at least once, 669 patients (6.1%) had at least one HF-readmission, and 656 patients (6.0%) died. The mean number of all-cause and HF hospital bed days was 10.3 and 6.8 days, respectively, among those who had been readmitted once or more during follow-up.

The proportion of patients receiving >75% of the relevant performance measures was more likely male, younger, and had a lower comorbidity burden than patients who met 50% or less of the relevant performance measures. They were also more likely outpatients, cohabitating, employed, with higher family income, and had less likely redeemed a prescription for an antidepressant or antipsychotic drug within 12 months before HFrEF diagnosis (Table 2).

Associations Between Performance Measures and Clinical Outcomes

Figure 3 summarizes the main findings of the associations between quality performance measures and clinical outcomes in patients with incident HFrEF. Table S4 shows the number of outcome events according to individual performance measures, and Tables S5 and S6 offer all regression analyses of readmission, hospital bed days, and mortality according to the opportunity-based score and individual performance measures, respectively.

Performance Measures, Readmission, and Hospital Bed Days

Using patients fulfilling 0% to 50% of the relevant process performance measures as the reference, patients who fulfilled >50% to 75% or >75% to

Table 2. Baseline Characteristics of Patients With Incident HFrEF, LVEF ≤40%, According to the Percentages of Performance Measures Fulfilled

		The percentages of fulfilled process measures		
	Total	0%–50%	>50%–75%	>75%–100%
	(n=10 966)	(n=784)	(n=4841)	(n=5341)
Male	7658 (69.8)	474 (60.5)	3777 (69.8)	3807 (71.3)
Age group, y				
≤65	3823 (34.9)	180 (23.0)	1420 (29.3)	2223 (41.6)
65–80	4840 (44.1)	278 (35.4)	2204 (45.5)	2358 (44.2)
>80	2303 (21.0)	326 (41.6)	1217 (25.2)	760 (14.2)
Region				
Capital Region	2888 (26.4)	272 (34.7)	1462 (30.2)	1154 (21.6)
Zealand Region	2214 (20.2)	117 (14.9)	961 (19.8)	1136 (21.3)
Southern Denmark	2765 (25.2)	143 (18.3)	1142 (23.6)	1480 (27.7)
Central Denmark	2218 (20.2)	142 (18.1)	866 (17.9)	1210 (22.6)
North Denmark	881 (8.0)	110 (14.0)	410 (8.5)	361 (6.8)
Country of origin				
Danish	10 397 (94.8)	736 (93.9)	4475 (94.5)	5086 (95.2)
EU/OECD countries	362 (3.3)	29 (3.7)	165 (3.4)	168 (3.2)
Other countries	207 (1.9)	19 (2.4)	101 (2.1)	87 (1.6)
LVEF, %				
<25	3415 (31.1)	211 (26.9)	1605 (33.2)	1599 (29.9)
25–35	5514 (50.3)	369 (47.1)	2849 (58.8)	2296 (43.0)
>35–40	2037 (18.6)	204 (26.0)	387 (8.00)	1446 (27.1)
NYHA class				
Class I	1306 (11.9)	35 (4.4)	573 (11.8)	698 (13.1)
Class II	6200 (56.5)	144 (18.4)	2694 (55.7)	3363 (62.9)
Class III	2375 (21.7)	104 (13.3)	1085 (22.4)	1186 (22.2)
Class IV	170 (1.6)	19 (2.4)	84 (1.7)	67 (1.3)
Missing	915 (8.3)	482 (61.5)	405 (8.4)	28 (0.5)
CCI-score				
0	1422 (13.0)	91 (11.6)	598 (12.4)	733 (13.7)
1–2	5760 (52.5)	373 (57.6)	2493 (51.5)	2894 (54.2)
3–4	3032 (27.6)	254 (32.4)	1381 (28.5)	1397 (26.2)
≥5	752 (6.9)	66 (8.4)	369 (7.6)	317 (5.9)
Comorbidities				
Myocardial infarction	3639 (33.2)	203 (25.9)	1485 (30.7)	1951 (36.5)
Stroke	1226 (11.2)	119 (15.2)	615 (12.7)	492 (9.2)
COPD	1563 (14.3)	122 (15.6)	729 (15.1)	712 (13.3)
Missing	162 (1.5)	22 (2.8)	78 (1.6)	62 (1.2)
Hypertension	4126 (37.6)	269 (34.3)	1814 (37.5)	2043 (38.3)
Missing	78 (0.7)	12 (1.5)	34 (0.7)	32 (0.6)
Diabetes	2366 (21.6)	188 (24.0)	1040 (21.5)	1138 (21.3)
Atrial fibrillation	3162 (28.8)	242 (30.9)	1521 (31.4)	1399 (26.2)
Missing	13 (0.1)			
S-creatinine ≥150 µmol/L (yes)	1001 (9.1)	131 (16.7)	549 (11.3)	321 (6.0)
Missing	7 (0.1)			
Smoking habits				
Smoker	3050 (27.8)	211 (26.9)	1359 (28.1)	1480 (27.7)
Missing	974 (8.9)	182 (23.2)	464 (9.6)	328 (6.1)

(*Continued*)

Table 2. Continued

		The percentages of fulfilled process measures		
	Total	0%–50%	>50%–75%	>75%–100%
	(n=10 966)	(n=784)	(n=4841)	(n=5341)
Alcohol intake, drinks/wk				
>14/21 female/male	939 (8.6)	54 (6.9)	436 (9.0)	449 (8.4)
Missing	1441 (12.9)	214 (27.3)	436 (14.5)	449 (9.3)
Setting for HF diagnosis				
Inpatient	6240 (56.9)	614 (78.3)	2826 (58.4)	2800 (52.4)
Outpatient	4726 (43.1)	170 (21.7)	2015 (41.6)	2541 (47.6)
Cohabitation status				
Living alone	4064 (37.1)	378 (48.2)	1892 (39.1)	1794 (33.6)
Cohabiting	6902 (62.9)	406 (52.8)	2949 (60.9)	3547 (66.4)
Educational level, levels				
Primary and lower secondary	4613 (42.1)	354 (45.2)	2095 (43.3)	2164 (40.5)
Upper secondary	4222 (38.5)	218 (27.8)	1802 (37.2)	2202 (41.2)
≥Short cycle tertiary	1649 (15.0)	97 (12.4)	715 (14.8)	837 (15.7)
Missing	482 (4.4)	115 (14.7)	229 (4.7)	138 (2.6)
Family income,* US dollars/y				
≤39 447	3656 (33.4)	389 (49.6)	1776 (36.7)	1491 (27.9)
39 454–66 028	3655 (33.3)	233 (29.7)	1656 (34.2)	1766 (33.1)
≥66 049	3655 (33.3)	162 (20.6)	1409 (29.1)	2084 (39. 0)
Employment status				
Employed	2,190 (20.0)	84 (10.7)	823 (17.0)	1283 (24.0)
Pensioners	7063 (64.4)	609 (77.7)	3370 (69.6)	3084 (57.8)
Other/missing	1711 (15.6)	11.6 (11.6)	13.4 (13.4)	18.2 (18.2)
Previous hospitalizations, 10 y				
0	2330 (21.2)	153 (19.5)	1023 (21.1)	1154 (21.6)
1–2	3978 (36.3)	222 (28.3)	1698 (35.1)	2058 (38.5)
3–9	3992 (36.4)	352 (44.9)	1765 (36.5)	1875 (35.1)
≥10	666 (6.1)	57 (7.3)	355 (7.3)	254 (4.8)
Previous hospitalizations, 12 mo (yes)	5705 (52.2)	362 (46.2)	2440 (50.4)	2903 (54.4)
Antidepressant or psychotic medication use	1774 (16.2)	165 (21.1)	793 (16.4)	816 (15.3)

CCI indicates Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; EU, the European Union; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and OECD, the Organization for Economic Co-operation and Development.

*Average annual family income in 5 y before HF diagnosis.

100% of the relevant process performance measures had a lower risk of all-cause and HF readmission and a lower number of all-cause and HF hospital bed days (Figure 2).

The mutually adjusted analyses showed that fulfilling the performance measures for New York Heart Association classification, ACEI/ARB therapy, beta-blocker therapy, exercise training, and patient education were associated with a lower risk of all-cause and HF readmission (Figure 4) and lower use of all-cause and HF hospital bed days (Figure 5). However, not all associations were statistically significant. In patients with HFrEF, LVEF ≤35%, the mutually adjusted analyses showed that fulfilling the performance measure for MRA therapy was associated with a higher number of all-cause and HF hospital bed days (Figure 5) but not with all-cause and HF readmission (Figure 4).

Performance Measures and Mortality

We observed a dose-response relationship between the proportion of the relevant performance measures fulfilled and time to mortality in the follow-up period. The adjusted HRs for mortality were 0.62 (95% CI, 0.49–0.77) for patients meeting >50% to 75% of the relevant performance measures and 0.42 (95% CI, 0.32–0.53) for patients meeting >75% to 100% of the performance measures (Figure 2). After mutual adjustment fulfilling

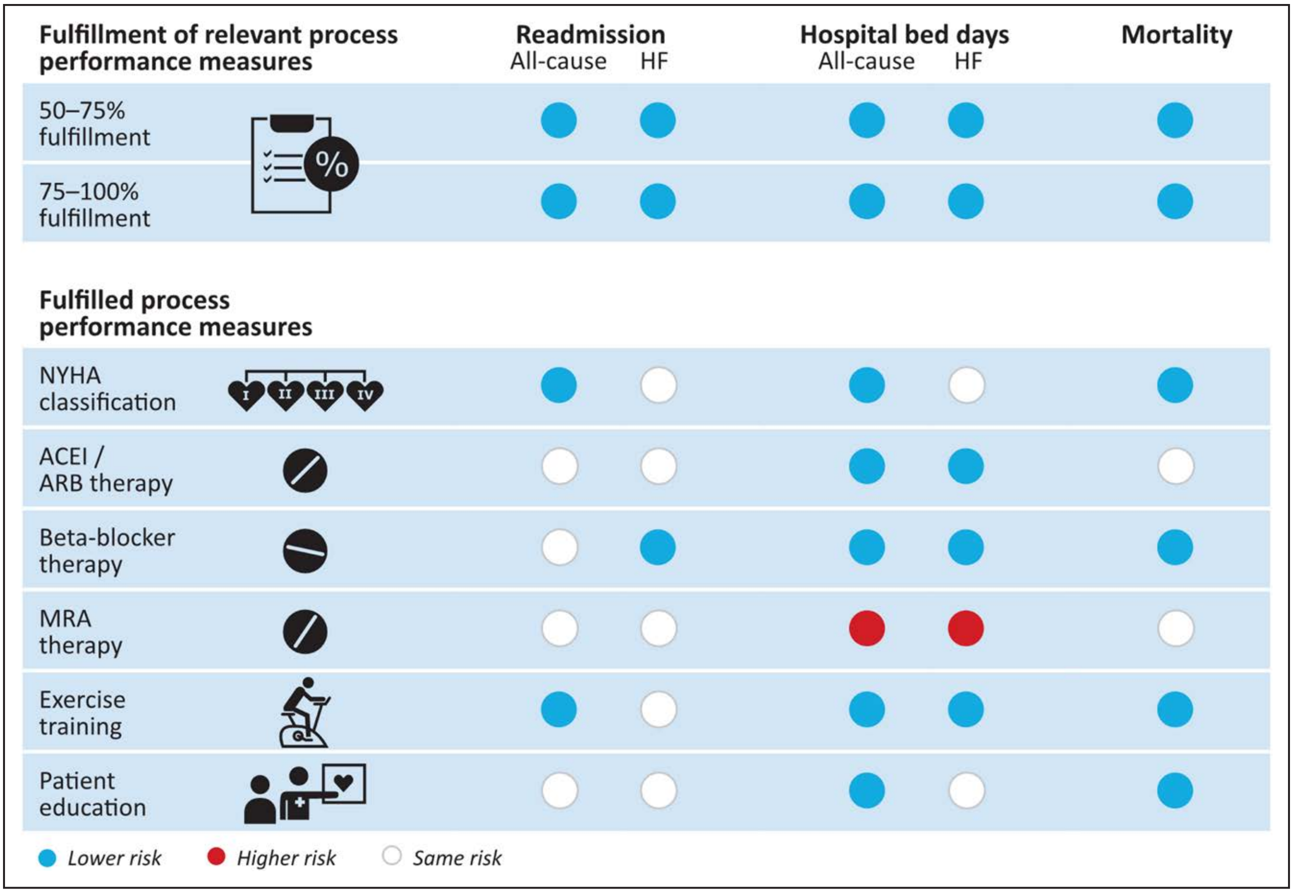

Figure 3. Associations between heart failure (HF) care quality and clinical outcomes within 3 to 12 mo after HF with reduced ejection fraction diagnosis.
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; MRA, mineralocorticoid receptor antagonist; and NYHA, New York Heart Association.

the individual performance measures was associated with lower mortality (Figure 6), except for the ACEI/ARB and MRA performance measures.

Stratified adjusted analyses indicated possible interaction between the MRA performance measure and age and socioeconomic factors (Table S7). Fulfillment of the MRA performance measure was associated with lower mortality (hazard ratio, 0.60 [95% CI, 0.45–0.82]) among patients aged 80 years or older, whereas this was not the case among patients aged 18 to 65 years (hazard ratio, 1.43 [95% CI, 0.89–2.30]) and 65 to 80 years (hazard ratio, 1.15 [95% CI, 0.87–1.53]). The same was true for living alone compared with cohabitating, low-level education compared with mid-level education, and low-level income compared with high-level income.

Apart from the above differences in stratified analysis for MRA therapy and mortality, no systematic differences were observed across the examined subgroups. (Tables S7 and S8). The results based on the adjusted and mutually adjusted multilevel analyses were broadly comparable with the adjusted analyses for the opportunity-based score and the mutually adjusted analyses for the individual performance measures (Tables S5 and S6). Finally, complete case analyses were broadly comparable with imputation analyses.

DISCUSSION

There is widespread use of measurement and public reporting of HF process-of-care performance measures as an important quality improvement tool. The underlying assumption is that there is a direct link between each process performance measure and patient outcomes.[4] Our novel findings demonstrated that patients with incident HFrEF fulfilling more performance measures experienced better clinical outcomes (readmission, hospital bed days, and mortality).

Performance Measures and Clinical Outcomes

The potential synergistic effect of fulfilled HFrEF performance measures is of particular interest, as the opportunity-based score reflects the overall care quality provided. Although other studies also have elaborated on the relationship between a composite score and clinical outcomes, these studies had primarily centered

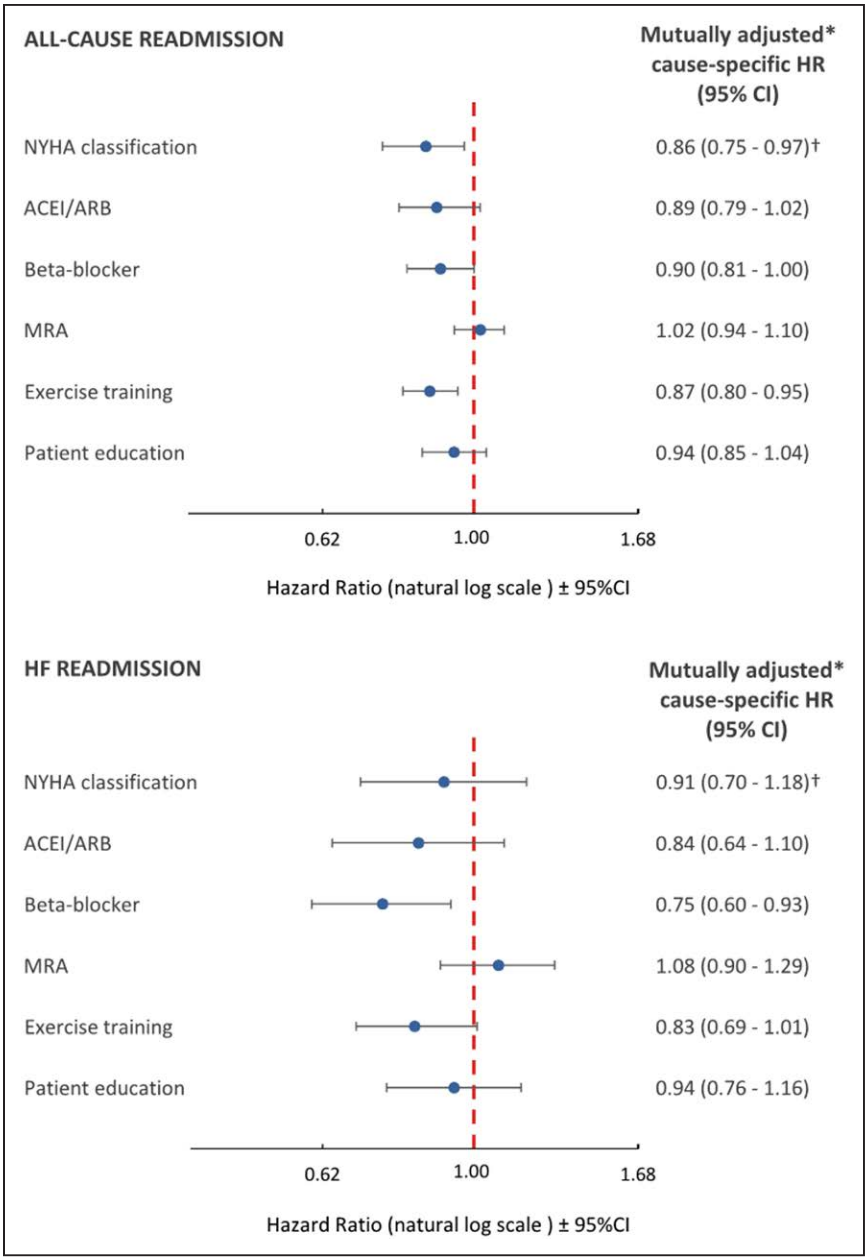

Figure 4. Associations between individual performance measures and readmission.
Mutually adjusted cause-specific hazard ratio (HR) for all-cause and heart failure (HF) readmission within 3 to 12 mo after diagnosis of HF with reduced ejection fraction according to individual performance measures. *Adjustment as in Figure 2 and other performance measures. † No adjustment for New York Heart Association (NYHA) class. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; and MRA, mineralocorticoid receptor antagonist.

on patients with chronic HF,[8,9,11] mortality,[8,9,14] or other process performance measures.[8,10,11] In contrast, our study focused on patients with incident HFrEF. We are unaware that other studies have examined the associations between readmission, hospital bed days, and mortality, respectively, and the opportunity-based score of the performance measures used in our research, reflecting essential components of modern HFrEF treatment.[2,3]

Using the opportunity-based score, we observed the strongest association for mortality. Our finding of an association between the opportunity-based score and mortality within 3 to 12 months after HF diagnosis corroborates with a previous Danish study.[14] Other studies have also reported improved survival for patients meeting multiple performance measures.[8,9,11] Like some previous studies,[8,9] we also found a dose-response association between the number of HF processes provided and mortality. A possible explanation for these findings may be that if a patient meets more of the national process measures, it reflects a well-functioning care pathway and adherent individuals.

Using individual performance measures, we examined associations between care processes and all-cause and HF hospital bed days, which, to the best of our knowledge, have not been addressed in previous studies. We demonstrated that meeting the individual performance measures for initial HFrEF care, besides MRA therapy, was associated with lower all-cause and HF hospital days in the follow-up period. Our findings extend current knowledge on the relationship between performance measures and readmission(s). Adherence to performance measures impacts readmission risk among

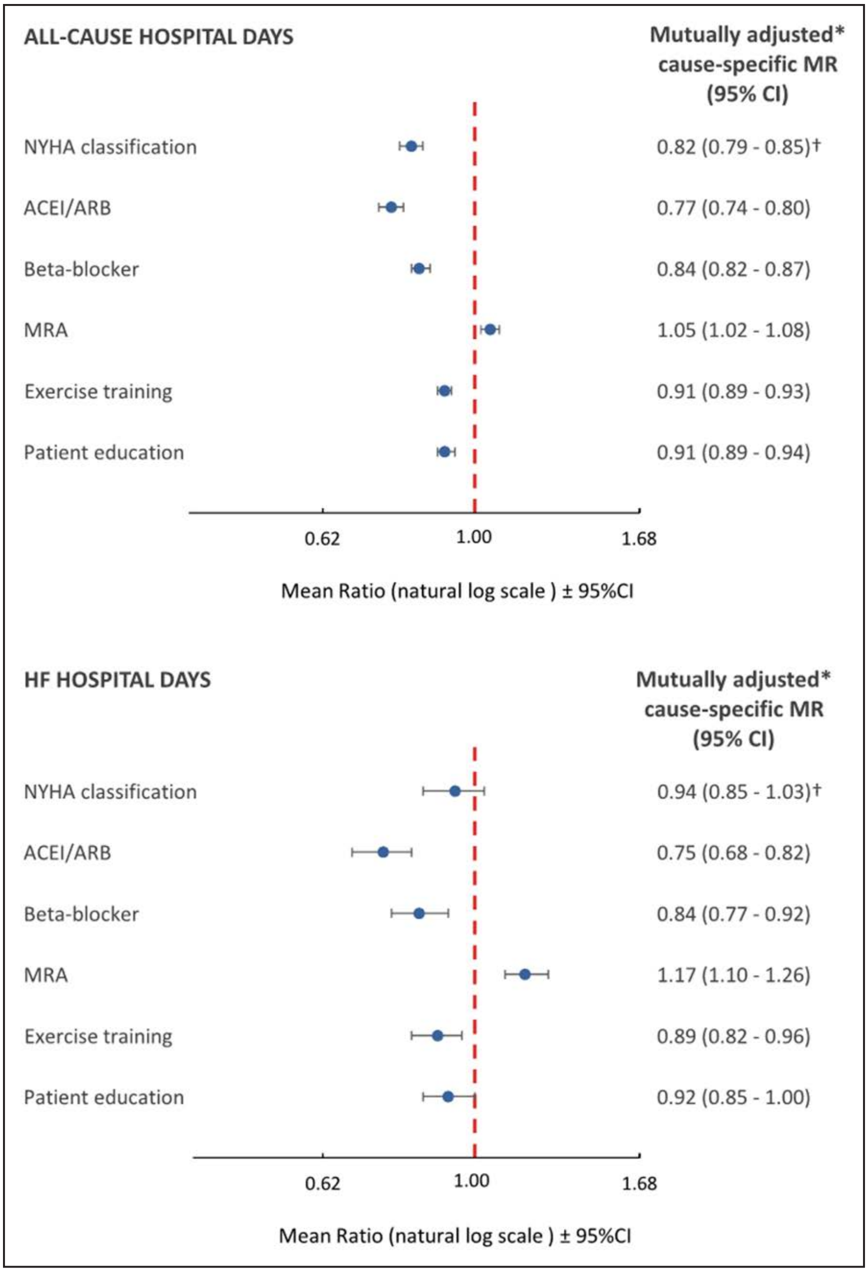

Figure 5. Associations between individual performance measures and hospital days.
Mutually adjusted cause-specific mean ratio (MR) for all-cause and heart failure (HF) hospital within 3 to 12 mo after HF with reduced ejection fraction diagnosis according to individual performance measures. *Adjustment as in Figure 2 and other performance measures. † No adjustment for New York Heart Association (NYHA) class. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; and MRA, mineralocorticoid receptor antagonist.

patients with incident HFrEF and the total number of hospital bed days, both of which are of significant importance from a patient and societal perspective.

MRA therapy has been shown to reduce HF readmission in randomized clinical trials. Therefore, it is recommended for symptomatic HFrEF patients in international HF guidelines.[2,3] We found that MRA therapy was associated with significantly higher use of all-cause and HF hospital days. Furthermore, we demonstrated a nonsignificantly higher risk of all-cause and HF readmission, which corroborates previous studies that have addressed MRA treatment performance measures and 1-year HF/cardiovascular readmission among patients admitted with acute decompensated HF.[12,13] In contrast, MRA treatment at hospital discharge have been reported associated with lower 3-year HF readmission risk among patients with HFrEF.[28] However, patients included in randomized controlled MRA trials may differ from those in cohort registries, so the relationship between MRA treatment and readmission may also be different.[12] Initiating MRA therapy may cause complications and needs regular monitoring of renal function and potassium levels and follow-up.[2,3] Because of these factors, not only an MRA process performance measurement has been included in the American College of Cardiology/American Heart Association Clinical Performance and Quality Measures for Adults With HF, 2020, but also a safety performance measure on laboratory monitoring after MRA prescription in patients with HFrEF.[5] Implementation and monitoring of these 2 performance measures in clinical practice may probably improve MRA therapy quality.

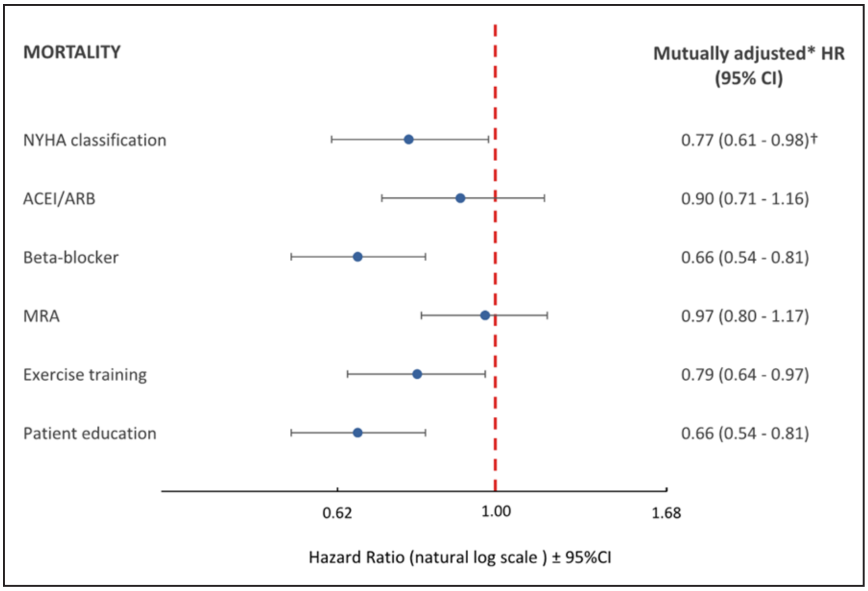

Figure 6. Associations between individual performance measures and mortality.
Adjusted hazard ratio (HR) for mortality within 3 to 12 mo after heart failure with reduced ejection fraction diagnosis according to individual performance measures. *Adjustments as in Figure 2 and other performance measures. † No adjustment for New York Heart Association (NYHA) class. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; and MRA, mineralocorticoid receptor antagonist.

In our study, fulfilling the New York Heart Association assessment and exercise training measure was significantly associated with lower all-cause readmission risk. Beta-blocker therapy was associated with lower HF readmission risk. ACEI/ARB use and patient education were associated with a nonsignificantly lower risk of all-cause and HF readmission. Some previous cohort studies, who have addressed the association between treatment performance measures for ACEI/ARB and beta-blockers and readmission, found that ACEI/ARB prescribed at hospital discharge was significantly associated with a lower risk of readmission.[7,11] Other studies have reported a positive—but nonsignificant—direction of the associations between the prescription of these 2 drugs and readmission.[6,7,12,13] Overall, meeting the performance measures for ACEI/ARB and beta-blockers seems to be associated with lower readmission rates in both patients with chronic and incident HFrEF.

Overall, the results in our study on mortality are supported by a range of randomized clinical trials,[2,3] and cohort studies.[8,9,11–14] However, in our study, no differences in mortality related to MRA treatment were found. This result is in line with previous cohort studies among inpatients and outpatients with HFrEF.[9,10,12,13,28] Though, we found significant differences in the association between MRA use and mortality according to age groups and socioeconomic factors. In contrast, a meta-analysis study showed that MRA therapy had an equal benefit in older and younger patients with HFrEF.[29] MRA therapy was only initiated in 38.7% of the patients in our cohort. Thus, our findings related to the MRA performance measure may be confounded by indication.

Exercise training is recommended for patients with HFrEF in international guidelines.[2,3] Studies have shown that exercise training reduces HF hospitalizations and mortality.[2,3] Our finding of improved survival with the exercise training process measure for patients with incident HFrEF is in line with a previous Danish study.[14] Thus, our study provides evidence to support the implementation of performance measures for exercise training referral to improve HF care quality among patients with HFrEF.[5]

Patient education is a crucial component in HF management programs to promote self-care.[2,3,30] Our study showed that patients who began individual patient education had a significantly lower mortality risk. This finding is in line with previous studies among patients with HFrEF.[8,9,14] Literature has suggested that patient education reduces hospital admissions in patients with HF.[31] In our study, patient education was associated with lower hospital bed day use but not with readmission risk. The patient's self-care ability may promote earlier identification of worsening status and earlier discharge resulting in lower hospital bed day use.[32] Our findings provide additional evidence supporting the process-outcome link between exercise training and patient education, respectively, and clinical outcomes in real-world HFrEF care settings.

Our results may reflect the total effect of all appropriate care provided in clinical practice, also care processes that are not directly measured. Hence, if a hospital fulfills the official performance measures, it will likely provide a high quality of care for other care processes that are not monitored. Moreover, our study demonstrates that adherence to clinical guidelines in real-world clinical practice has consequences for patients with incident HFrEF. This supports and extends the hypothesis that benefits can be translated from randomized controlled studies into routine clinical practice.

Thus, our findings may have important clinical and public health implications. They provide additional evidence to support the link between current guideline-recommended initial HF care processes and readmission, hospital bed days, and mortality in patients with incident HFrEF in real-world clinical practice. Moreover, sustained efforts to improve adherence to HF process performance measures may impact clinical outcomes positively. Development and implementation of quality reporting and quality improvement HF registries may improve HF care, self-care ability, and clinical outcomes in patients with HFrEF. However, other care dimensions may also be worth examining to improve HF care and outcomes, for example, structural measures (organization evaluation), patient satisfaction, and patient-reported outcome measures (eg, quality of life).[33]

Strengths and Limitations

The strengths of our study are a contemporary, sizeable real-world cohort of patients with a first-time primary validated HFrEF diagnosis and a complete follow-up. We assessed the associations between process performance measures within different HF care domains and readmission, hospital days, and mortality. These associations do not imply causality. Although they may reflect the quality of HF care provided in clinical practice, they could instead reflect confounding by indication, incline to favor these associations. The Danish hospitals treating patients with HFrEF are quite homogeneous in their quality performance. Therefore, we focused on performance measures at the patient level and not at the hospital level in this study. However, to take hospital sites into account, multilevel regression analyses were performed, showing only slight changes in results.

Extensive adjustment for potential confounding factors was performed, including individual-level socioeconomic factors, which only had a minor impact on the analyses. We, therefore, found solid adjusted associations with a high degree of precision between the fulfillment of performance measures and clinical outcomes. However, we could not adjust for patient adherence and medical care changes during follow-up. Furthermore, we could not investigate whether the impact of MRA therapy on HF outcomes was modified by compliance with the new American College of Cardiology/American Heart Association performance measure on laboratory monitoring.[5]

We used stratification, multiple imputations, and complete case analyses to account for potential confounding in addition to multivariable analyses. However, unknown confounders and lack of information, for example, contraindications for medical, doses of drugs prescribed, beta-blocker prescribed, how much exercise and education were done, and patient preferences, may have affected our results. Moreover, our findings are only applicable to a selected HFrEF population with incident HFrEF who survive for >90 days without an acute admission after diagnosis.

The DHFR data were collected during routine clinical practice, which may affect data accuracy. However, comprehensive efforts have been accomplished to ensure data validity (eg, detailed written instructions, data definitions, a standardized registration scheme, and annual clinical audits).[17] Finally, we only examined the performance measures monitored in the DHFR. We did not evaluate other care processes, such as hydralazine and isosorbide therapy and defibrillator with cardiac resynchronization, which should also be considered in some patients with HFrEF.

CONCLUSIONS

In conclusion, fulfilling more process performance measures for initial HF care was associated with improved clinical outcomes in real-life inpatients and outpatients with incident HFrEF. Continued efforts are warranted to ensure guideline-recommended HF care processes are delivered to patients with incident HFrEF.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S8

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