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Original article

Effectiveness of guideline-consistent heart failure drug prescriptions at hospital discharge on 1-year mortality: Results from the EPICAL2 cohort study

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ABSTRACT

Background: We aimed to assess the effectiveness of recommended drug prescriptions at hospital discharge on 1-year mortality in patients with heart failure (HF) and reduced ejection fraction (HFREF).

Materials and methods: We used data from the EPICAL2 cohort study. HF patients ≥ 18 years old with left ventricular ejection fraction (LVEF) < 40% and alive at discharge were included and followed up for mortality. Socio-demographic, clinical and therapeutic data were collected at admission. Therapeutic data were collected at discharge and at 6 month. Prescription of an angiotensin-converting enzyme (ACE) inhibitor (or an angiotensin II receptor blocker [ARB] in case of ACE inhibitor intolerance) and a β-blocker at discharge were considered "guideline-consistent discharge prescription" (GCDP). A frailty Cox model after propensity score (PS) matching was used to assess the association of GCDP with survival.

Results: Among 624 patients included, the mean (SD) age was 73.6 (12.8) years; 65% were male. A total of 412 (65.6%) patients received GCDP, and 82.8% still had guideline consistent prescription at 6 months. A total of 166 patients died during the follow-up, 78 in the GCDP group and 88 in the other group. Before PS matching, patients with GCDP were younger (|StDiff| = 48.32%) and had higher body mass index (BMI) (|StDiff| = 11.71%), lower LVEF (|StDiff| = 23.13%) and lower Charlson index (|StDiff| = 55.27%) than patients without GCDP. After PS matching, all characteristics were balanced between the two treatment groups, and GCDP was associated with reduced mortality (pooled HR = 0.51, 95% CI [0.35–0.73]).

Conclusion: Prescription of ACE (or ARB) inhibitors and β-blockers for patients with HFREF may be low despite the evidence for morbidity and mortality improvement with these medications but remains associated with reduced 1-year mortality in unselected HFREF patients.

1. Introduction

From results of randomized controlled trials [1–3], the European Society of Cardiology (ESC) recommended the prescription of angiotensin-converting enzyme (ACE) inhibitors (or angiotensin II receptor antagonists [ARBs] in case of ACE inhibitor intolerance) and β-blockers for all patients with HF and reduced ejection fraction (HFREF) [4–6] to prevent HF hospitalisations and death. These drugs have shown efficacy under experimental conditions of clinical trials in highly selected patients. However, HF patients participating in trials are usually younger, have fewer comorbidities and more recent HF onset than HF patients in current medical practice [7]. In addition, the former patients undergo optimal regimens under close monitoring. These ideal experimental conditions, essential to establish causality, do not correspond to real-life patients and practices in HF. HF patients are usually older than trial patients, and they tend to have several comorbidities [8]. The syndrome is more severe, on average, in real-life HF patients than in trial HF patients [9]. In addition, real-life HF patients are less compliant with drug prescriptions and dietary habits than trial HF patients [10]. Whether recommended HF drugs are efficient in a real world setting

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(i.e., in a population-based sample of HFREF patients) remains unknown. We hypothesised that they do. We used data from the *Epidemiologie et Pronostic de l'Insuffisance Cardiaque Aiguë en Lorraine* (EPICAL2) cohort to assess the effectiveness of recommended HF drug prescriptions at hospital discharge on 1-year mortality in HFREF patients in a real-world setting.

2. Materials and methods

2.1. Setting, design and sampling

EPICAL2 (NCT 02880358) was an observational, prospective, population-based, and multicentre cohort study involving 21 volunteer hospitals spread over the Lorraine region of Northeast France (population of 2,350,000, according to the 2012 census). The cohort enrolled 2254 consecutive adult HF patients hospitalised between October 2011 and October 2012 in cardiology intensive care units, cardiology departments or emergency departments. Patients living in Lorraine and hospitalised for acute heart failure (AHF) were included, as were those in whom AHF developed during hospitalisation. Eligible patients were identified by physicians from the participating departments or by trained clinical research assistants who regularly visited the departments. Included patients were then followed up at 6 months, 1 year, 2 years, and 3 years after discharge from the index hospitalisation or until death, for therapeutic characteristics, by interviewing patients' general practitioner, and for vital status, by request to national civil registries. The main objectives of this cohort study were to 1) describe morbidity and mortality in the short term (0 to 6 months) and midterm (up to 3 years) and identify the main prognostic factors and 2) assess the effectiveness of various aspects and interventions of care, in or out of hospital. For the present investigation, we focused on the 624 HFREF patients defined by left ventricular ejection fraction (LVEF) < 40% at admission who were alive at discharge. Patients with missing prescription at discharge, patients lost to follow-up just after discharge, and patients dead during the follow-up with missing date of death, were excluded (Fig. 1).

2.2. Data collection

Socio-demographic, medical history and clinical characteristics were collected at hospital admission. Therapeutic characteristics were collected at admission, at hospital discharge and 6 months after discharge. Except for therapeutic characteristics collected by patients' general practitioners by standardised interviews 6 months after discharge, all data were collected from medical records by using a standardised form. Unless otherwise specified, all variables were collected and treated as categorical variables.

2.2.1. Socio-demographic characteristics

Socio-demographic data collected were sex, age, area of residence, type of residence (living in a retirement or nursing home or not), and body mass index (BMI). Age and BMI were collected as continuous variables and then classified in 3 categories (age: ≤ 65, 66–80, and > 80 years, and BMI: underweight or normal [< 25 kg/m^2], overweight [25–30 kg/m^2], and obese [> 30 kg/m^2]).

2.2.2. Medical history

We collected ischemic factors precipitating the actual HF decompensation, defined as coronary syndrome with or without ST elevation identified as precipitating HF by a cardiologist; cardiovascular risk factors such as dyslipidaemia, hypertension, smoking, alcohol abuse, and family history of cardiovascular disease; history of HF, acute coronary syndrome with or without ST elevation, stroke or transient ischemic attack, peripheral arterial disease, or other cardiovascular conditions (valvular heart disease, pulmonary embolism and arrhythmia); previous cardiovascular interventions such cardiac resynchronisation therapy or cardiac stimulation; and comorbidities such as diabetes mellitus, asthma or chronic obstructive pulmonary disease, severe chronic respiratory insufficiency, chronic kidney disease, depressive disorder, haematological malignancy, cancer, cirrhosis, peptic ulcer, and AIDS. To summarise some of the comorbidities, the Charlson index was calculated by using age, history of HF hospitalisation(s), and all the aforementioned comorbidities except severe chronic respiratory insufficiency [11]. The Charlson index was classified into 3 categories (≤ 5; 6–8; ≥ 9).

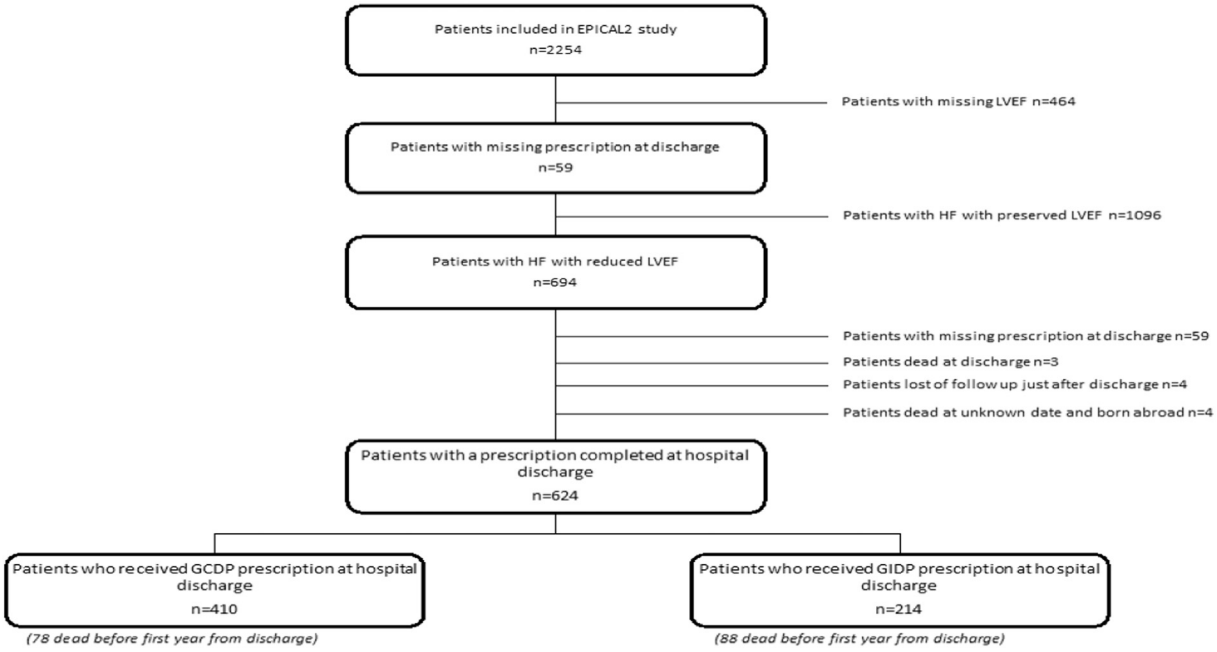

Fig. 1. Flow of patients with heart failure and reduced ejection fraction from the EPICAL2 cohort for evaluating guideline adherence association with survival
Notes: HF, heart failure; LVEF, left ventricular ejection fraction; GCDP, guideline-consistent discharge prescription; GIDP, guideline-inconsistent discharge prescription.