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PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Heart failure prognosis and management in over-80-year-old patients: data from a French national observational retrospective cohort

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Abstract
Purpose The aim of the study was to assess the impact of clinical characteristics and management on the mid- to long-term follow-up prognosis of unselected over-80-year-old patients hospitalized for a first heart failure (HF) episode in a real-life setting. Despite the increasing proportion of HF patients over 80 years of age, the latter remain a poorly studied population.
Methods Analysis was based on the EGB ("*Echantillon Généraliste des Bénéficiaires*") database. A cohort comprising 1825 adult patients with a first admission for HF between 2009 and 2011 was created and followed until June 2013 for survival analysis.
Results Over-80-year-old patients represented 53 % of this cohort, with a median follow-up of 18.6 (3.3–29.5) months. Only 5 % of patients over 80 years received an optimal treatment at discharge [combination of angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB), beta-blockers (BB), and mineralocorticoid receptor antagonists (MRA)]. During the follow-up period, only BB prescription levels (p=0.02) increased. In over-80-year-olds, in-hospital mortality was 12 % (range, 10–14) and survival was 62.8 % (59.6–65.7) and 48.7 % (45.4–51.9) at 12 and 24 months, respectively. On multivariate analysis, dyslipidemia [0.74 (0.58–0.94), p=0.02], vitamin K antagonists [0.55 (0.44–0.69), p<0.001], ACEi/ARB+BB+MRA [0.56 (0.32–0.96), p=0.04], and ACEi/ARB+BB [0.57 (0.45–0.72), p<0.001] were associated with improved survival, conversely to cardiogenic shock [3.37 (1.90–5.98), p<0.001], denutrition [1.61 (1.24–2.09), p<0.001], and age over 90 [1.35 (1.09–1.67), p=0.01].
Conclusions These real-life HF data provide insight into prognostic factors and demonstrate that over-80-year-old HF patients displaying several comorbidities are poorly managed, despite the confirmed clinical benefit of HF drugs.

Keywords Heart failure · Elderly · Management · Epidemiology · Prognosis

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Introduction

In Western countries, chronic heart failure (HF) is a major public health issue due to its poor prognosis and high incidence especially in the elderly. An improved management of cardiovascular diseases (ischemic cardiomyopathies, hypertension) and other comorbidities [1] together with improved

prognosis of HF [2] and the aging of the population may explain the high prevalence of HF [3].

Over the last 25 years, advances in treatment have led to recent guidelines recommending the combined use of renin–angiotensin–aldosterone system blockers and beta-blockers (BB) [4, 5]. Furthermore, it is now well established that adherence of physicians in recommending HF treatment is a strong predictor of fewer cardiovascular hospitalizations [6]. Unfortunately, over-80-year-old HF patients are often underrepresented in clinical trials [7, 8]. Comorbidities and iatrogenic risk are likely explanations for the underuse of recommended HF treatments in the elderly [9]. Only a few studies [10, 11] or sub-group analyses [12, 13] have attempted to assess the benefit of such drugs or management in elderly HF patients. Moreover, clinical characteristics, management, and prognosis have been generally evaluated in carefully selected and followed over-80-year-old patients but never in a "real-life" population [14–16]. As a result, there is a clear gap between patients enrolled in clinical trials and those treated in daily clinical practice.

The aim of the present study was to assess the impact of clinical characteristics and acute and chronic management (according to international guidelines) on the mid- to long-term follow-up prognosis of unselected over-80-year-old patients hospitalized for a first HF episode in a real-life setting.

Material and methods

Study design and data source

This cohort study used data extracted from the EGB (*Échantillon Généraliste des Bénéficiaires*) database, a representative 1/97th random sample of the population covered by the French national health insurance system (approximately 80 % of the French population) [17, 18]. At the time of the study, the EGB included over 600,000 individuals and has been widely used for public health and pharmacoepidemiological purposes for more than 5 years [19–24].

Since 2005, the EGB database includes basic demographic data and prospectively collects all claims for visits to physicians and exhaustive claims for all reimbursed drugs dispensed in retail pharmacies (including dates of prescription, dispensing, and quantities delivered). Medications are identified by their Anatomical Therapeutic Chemical class (ATC) codes, which are included in the EGB database. The EGB database also contains data collected by the *Programme de Médicalisation des Systèmes d'Information* (PMSI, national hospital discharge database) in healthcare institutions (medical and surgical departments); during the patient's stay, principal diagnoses (PDs) and associated diagnoses (ADs) are available and coded according to the International Classification of Diseases (ICD 10). Associated diagnoses represent a proxy for comorbidity assessment and identification of triggering factors. All medical procedures performed during each stay are identified with their specific codes from the Common Classification of Medical Procedures. The EGB database also includes registration of the date of death, recorded automatically from the National Institute for Statistics and Economic Studies (INSEE), independently of the use or not of healthcare resources.

No clinical data (e.g., blood pressure, creatinine concentration, left ventricular ejection fraction, etc.) were available.

Study population

A cohort of adult HF episodes was generated, divided into two subgroups: <80 vs. ≥80 years of age. All adult patients (≥18 years) who had a first admission for HF (HF as principal diagnosis identified according to the following ICD10 codes—I500, congestive HF; I501, left ventricular HF; R570, cardiogenic shock; I110, hypertensive cardiomyopathy and HF symptoms; J81, acute pulmonary edema) between January 1, 2009 and December 31, 2011, defined by the absence of HF admission during the four preceding years, were considered. The date of this first admission represented the index date. Dates of death were available until 30 June 2013, allowing at least 18 months of follow-up for all patients included. The following clinical characteristics at initial presentation were analyzed: clinical presentation, etiology, cardiovascular risk factors, and comorbidities (ascertained from ADs); cardiac decompensation triggers (inferred from the ADs); in-hospital procedures; diagnostic and therapeutic acts (administration of vasoactive amines, coronarography, cardiac resynchronization therapy, electrocardiogram, transthoracic echocardiography, endotracheal intubation, close monitoring in a cardiac intensive care unit, non-invasive ventilation) as well as previous and post first discharge treatments. Drug treatments were identified by the dispensation of at least one specific medication during the month preceding the hospitalization for HF or during the 60 days following discharge. Loop diuretics were identified as the C03C ATC class, beta-blockers (BB) as C07A class, angiotensin converting enzyme inhibitors (ACEi) as C09A or C09B, angiotensin receptor blockers (ARB) as C09C or C09D, anti-platelet agents as B01AC, vitamin K antagonists (VKA) as B01AA, mineralocorticoid receptor antagonists (MRAs) as C03DA, class 3 anti-arrhythmic drugs (AA3) as C01BD, and digoxin as C01AA05. Drug combinations were classified into each specific class. Thus, the numbers presented for a single drug group (e.g., ACEi) represents the total use of each group: combination (e.g., ACEi+BB) and isolated use. Readmission rates (at 3, 6, 9, and 12 months after the index date) and survival (48-month maximal) were determined and potential predictive factors associated with mortality were examined. In

order to improve the exhaustiveness of comorbidity data, all diagnoses and conditions recorded during possible previous hospitalizations were considered, irrespective of the cause of admission.

Statistical analysis

Statistics were computed with STATA V12 (Stata Corp, College Station, Texas, USA). Data were expressed as frequencies and associated percentages for categorical data and as mean±standard deviation and as median and [interquartile range] for quantitative parameters. The evolution of drug prescription after the first HF admission was tested by the χ^2 trend test. The evolution of drug prescription before and after hospitalization was tested by the McNemar test.

For survival analysis, patients were selected at first admission with HF as PD on the ICD-10 classification.

Date of admission was considered as the starting date and date of death (or of last information) as the ending (or censoring) date for survival analysis.

Analysis of admission-free survival was based on the above same method, but with first readmission or death considered as the event.

Survival was estimated using the Kaplan-Meier method. Survival at different time points (6, 12, 18, 24, 36, and 48 months) are given with 95 % confidence intervals.

Survival according to age group was also analyzed using the same approach, with differences compared by means of a log-rank test.

Factors were analyzed after adjusting for age (taking 85–89-year-old patients as reference to plot survival curves). Associated p values were computed with a Cox model (proportional-hazard hypothesis verified using Schoenfeld's test and plotting residuals vs. time [25]) adjusted for age, for which corresponding hazard ratios (HR) are shown with their 95 % confidence intervals.

Multivariate analysis was developed with a Cox proportional hazard model by stepwise analysis (backward and forward) of the factors considered significant in univariate analysis (entered into the model if $p<0.15$) and according to clinically relevant parameters (e.g., hypertension and type 2 diabetes) [26, 27]. In the multivariate model, several variables were tested: first year of HF hospitalization, acute coronary syndrome, obesity, initial presentation, age, sex, drugs, diabetes mellitus, arterial hypertension, denutrition, dyslipidemia, infection, cardiopathy etiologies (ischemic, dilated, …), atrial fibrillation, pulmonary embolism, chronic obstructive pulmonary disease, chronic and terminal kidney disease, alcohol consumption, pacemaker, acute kidney disease, and acute infectious pneumonia.

Results

Clinical characteristics

Table 1 presents the characteristics for the 1825 patients admitted for the first time for HF between 2009 and 2011. The median follow-up period after discharge from first HF admission was 18.6 (3.3–29.5)months. Over-80-year-old patients represented 53 % (n=969) of the cohort. The annual incidence of first hospitalization for HF was 1297 (1217–1378) per 100,000 in patients over 80 years old and 77.4 (72.2–82.6) per 100,000 in patients between 20 and 80 years old. Compared to the "<80 group", over-80-year-olds were more frequently female [615 (63 %) vs. 341 (40 %), $p<0.001$]. The main etiologies of underlying cardiopathies were comparable in both age subgroups except for a higher prevalence of dilated cardiomyopathy in the "<80 group" ($p<0.001$). Over-80-year-olds displayed more frequently hypertension ($p<0.001$) and less frequently diabetes mellitus ($p=0.001$), dyslipidemia ($p<0.001$), and obesity ($p<0.001$). Several factors known to trigger acute decompensated HF were identified (acute renal failure, anemia, infection, and acute coronary syndrome), which were more frequently implicated in over-80-year-olds compared to "<80 group". The most frequent comorbidities differed in over-80-year-olds compared to "<80 group", with a higher prevalence of atrial fibrillation ($p=0.002$), chronic kidney disease ($p=0.007$), and denutrition ($p<0.001$), along with a lower frequency of chronic obstructive pulmonary disease ($p=0.05$) and alcohol consumption ($p<0.001$).

Initial pharmacological and in-hospital management

In 2011, e.g., prior to first admission for HF, 46 % of over-80-year-old patients received loop diuretics, 27 % BB, 18 % ACEi, 5 % MRA, 16 % ACEi/ARB+BB, and only 1 % ACEi/ARB+BB+MRA (Table 2). Overall prescriptions (except for ARB, $p=0.15$) increased significantly between admission and discharge over the 3-year study period. At discharge in 2011, 76 % of over-80-year-olds received loop diuretics, 49 % BB, 33 % ACEi, 11 % MRA, 32 % ACEi/ARB+BB, and only 5 % ACEi/ARB+BB+MRA. Only BB prescriptions increased significantly at discharge between 2009 and 2011 ($p=0.02$), unlike ACEi, loop diuretics, VKA, ACEi/ARB+BB bitherapy, and ACEi/ARB+BB+MRA tritherapy ($p=0.48$, $p=0.77$, $p=0.08$, $p=0.12$, and $p=0.87$, respectively). All HF recommended drug classes were less prescribed at discharge (except for loop diuretics, ARB, and digoxin) in over-80-year-old patients compared to the "<80 group" ($p<0.05$) (Fig. 1).

Furthermore, less invasive management and/or cardiac exploration (coronaroangiography, amine support, transthoracic echocardiography, and intensive care unit admission;

Table 1 Population characteristics according to age subgroup

Patient characteristics	<80	≥80	*p* value
N	856	969	
Gender (F)—Nb (%)	341 (40)	615 (63)	<0.001
Age (years)—mean (±SD)	66.7 (11.6)	86.6 (4.5)	<0.001
Min–max	1–79	80–106	
Length of stay			
Mean±SD	8.4±7.2	10±7.5	<0.001
Median (interquartile range)	7 (4–11)	8 (5–13)	
Initial presentation—Nb (%)			
Congestive HF	344 (40)	402 (41)	0.57
Left-sided HF	343 (40)	411 (42)	0.31
Cardiogenic shock	45 (5)	16 (2)	<0.001
Hypertensive cardiomyopathy and HF symptoms	14 (2)	24 (2)	0.21
Acute pulmonary edema	29 (3)	24 (2)	0.25
Unspecified HF	81 (9)	92 (9)	0.98
Etiologies—Nb (%)			
Ischemic cardiopathy	301 (35)	336 (35)	0.83
Dilated cardiomyopathy	147 (17)	60 (6)	<0.001
Hypertensive cardiomyopathy and congestive HF	72 (8)	86 (9)	0.73
Cardiovascular risk factors—Nb (%)			
Hypertension	510 (60)	656 (68)	<0.001
Diabetes mellitus	272 (32)	241 (25)	0.001
Dyslipidemia	228 (27)	189 (20)	<0.001
Obesity (BMI >30 kg/m^2)	175 (20)	85 (9)	<0.001
Precipitating factors (Nb (%))			
Infection	107 (13)	214 (22)	<0.001
Anemia	65 (8)	87 (9)	0.29
Acute coronary syndrome	37 (4)	64 (7)	0.03
Acute kidney injury	41 (5)	58 (6)	0.26
Comorbidities—Nb (%)			
Atrial fibrillation	305 (36)	413 (43)	0.002
Chronic kidney disease	129 (15)	193 (20)	0.007
Chronic obstructive pulmonary disease	123 (14)	109 (11)	0.05
Chronic VKA treatment	30 (4)	32 (3)	0.81
Denutrition	46 (5)	99 (10)	<0.001
Alcohol consumption	101 (12)	17 (2)	<0.001
Acute and chronic management—Nb (%)			
Amine	47 (6)	12 (1)	<0.001
Coronarography	167 (20)	34 (4)	<0.001
Cardiac resynchronization therapy	13 (1.6)	2 (0.2)	0.002
Electrocardiogram	500 (60)	594 (65)	0.05
Transthoracic echocardiography	475 (57)	475 (52)	0.02
Endotracheal intubation	3 (0.4)	0 (0)	0.07
Intensive care unit	161 (19)	110 (12)	<0.001
Non-invasive ventilation	25 (3)	19 (2)	0.21
VO_2 max	3 (0.4)	0 (0)	0.07
Mode of discharge—Nb (%)			
Transfer to another hospital or intra-hospital department	163 (19)	205 (21)	0.26
Home	649 (76)	652 (67)	<0.001
Death	44 (5)	112 (12)	<0.001

BMI body mass index, *CV* cardiovascular, *F* female, *HF* heart failure, *Nb* number, *SD* standard deviation, *VKA* vitamin K antagonists

Table 2 Evolution of HF drug prescriptions in over-80-year-old patients

Therapeutic agents—Nb (%)	2009		2010		2011		*p* value 1	*p* value 2
	BA	AD	BA	AD	BA	AD		
N	339	293	327	290	303	274		
Loop diuretics	145 (43)	218 (74)	162 (50)	215 (74)	139 (46)	207 (76)	0.77	<0.001
BB	81 (24)	116 (40)	101 (31)	128 (44)	81 (27)	135 (49)	0.02	<0.001
ACEi	61 (18)	106 (36)	57 (17)	105 (36)	55 (18)	91 (33)	0.48	<0.001
ARB	51 (15)	49 (17)	60 (18)	50 (17)	62 (20)	57 (21)	0.23	0.15
Anti-platelet	91 (27)	116 (40)	107 (33)	123 (42)	95 (31)	113 (41)	0.69	<0.001
VKA	44 (13)	86 (29)	39 (12)	94 (32)	47 (16)	100 (36)	0.08	<0.001
MRA	9 (3)	30 (10)	17 (5)	25 (9)	16 (5)	29 (11)	0.91	<0.001
AA3	35 (10)	53 (18)	33 (10)	65 (22)	27 (9)	59 (22)	0.32	<0.001
Digoxin	18 (5)	33 (11)	16 (5)	25 (9)	17 (6)	25 (9)	0.39	0.001
(ACEi/ARB)+BB+MRA	1 (0)	15 (5)	2 (1)	6 (2)	3 (1)	15 (5)	0.87	<0.001
(ACEi/ARB)+BB	41 (12)	76 (26)	52 (16)	79 (27)	48 (16)	88 (32)	0.12	<0.001

BA before admission, *AD* at discharge, *BB* beta-blockers, *ACEi* angiotensin converting enzyme inhibitors, *ARB* angiotensin receptor blockers, *VKA* vitamin K antagonists, *MRA* mineralocorticoid receptor antagonists, *AA3* class 3 anti-arrhythmic drugs, *p value 1* comparison for each treatment at discharge between 2009 and 2011, *p value 2* comparison for each treatment between BA and AD for the 3 years

$p<0.001$, $p<0.001$, $p=0.02$, and $p<0.001$, respectively) were performed in over-80-year-olds.

Prognosis

Nineteen percent of over-80-year-old patients vs. 18 % of <80-year-old patients ($p=0.85$) were readmitted at least once after initial discharge: 9.5 % (7.7–11.7) vs. 9 % (7.2–11.1) at 3 months, 13.8 % (11.6–16.5) vs. 11.9 % (9.8–14.4) at 6 months, and 20.4 % (17.7–23.6) vs. 15.7 % (13.3–18.4) at 12 months. However, when taking into account censoring in survival analysis, over-80-year-old patients were more readmitted compared to the "<80 group" ($p=0.049$). In-hospital mortality from all causes in the over-80-year-old group was higher compared to the "<80 group" (12 % vs. 5 %, $p<0.001$).

Survival after the index date was significantly lower in over-80-year-old patients than in "<80 group" [HR=2.46

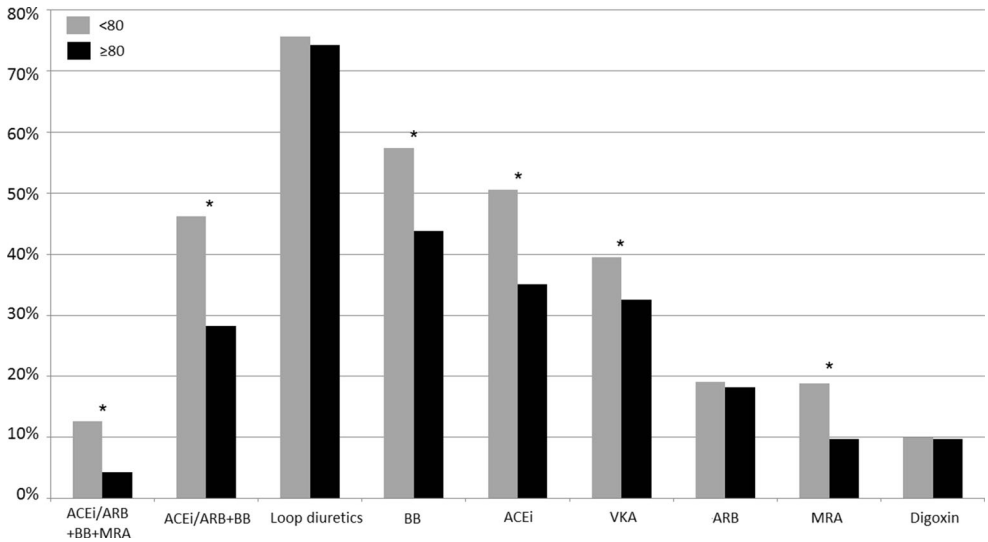

Fig. 1 Comparison of HF medications at discharge between in over-80-year-old patients vs. patients <80. Heart failure drug prescriptions at discharge according to age subgroup (*black columns*—≥80 years old; *white columns bars*—<80 years old) over a period of 3 years (2009 to 2011). All HF recommended drug classes were less prescribed at discharge (except for loop diuretics, ARB, and digoxin) in over-80-year-olds compared to the "<80 group" ($p<0.05$). *ACEi* angiotensin converting enzyme inhibitors, *ARB* angiotensin receptor blockers, *BB* beta-blockers, *MRA* mineralocorticoid receptor antagonists, *VKA* vitamin K antagonists. *$p<0.05$

(2.12–2.85), $p<0.001$], with a median survival of 23.2 months (19.7–25.2) (Fig. 2).

When comparing over-80-year-old HF patients, survival was higher in women ($p=0.01$) (Fig. 3a), lower in patients with terminal kidney disease (KD) compared to patients without chronic KD (CKD) ($p=0.02$), and with no difference between patients with CKD and without CKD ($p=0.10$) (Fig. 3b). Survival was higher in patients receiving ACEi/ARB+BB+MRA or ACEi/ARB+BB compared to neither of these two combinations ($p=0.04$ and $p<0.001$, respectively) (Fig. 3c). There was no difference between bitherapy and tritherapy [0.87 (0.49–1.53), $p=0.63$]. Finally, survival was higher in patients with atrial fibrillation (AFib) compared to those without AFib ($p=0.001$) (Fig. 3d). Interestingly, we observed that VKA were less prescribed in no AFib groups whatever the age class, i.e., in the over-80-year-old group [86 (18 %) in no AFib group vs. 194 (51 %) in AFib group, $p<0.001$].

In multivariate analysis, factors significantly associated with better survival were dyslipidemia [0.74 (0.58–0.94), $p=0.02$], vitamin K antagonists [0.55 (0.44–0.69), $p<0.001$], associated ACEi/ARB+BB+MRA [0.56 (0.32–0.96), $p=0.04$], and ACEi/ARB+BB [0.57 (0.45–0.72), $p<0.001$], in contrast to in-hospital cardiogenic shock [...], denutrition [...] and age over 90 [1.35 (1.09–1.67), $p=0.01$] (Fig. 4).

Discussion

The present study provides "real-life" data, including morbidity/mortality and survival factors, for the first time in unselected over-80-year-old HF patients with a mid- to long-term follow-up (48 months maximum) after a first hospitalization for HF.

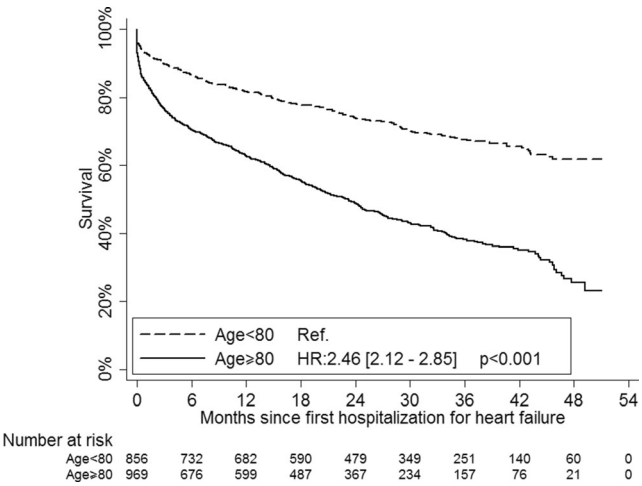

Fig. 2 Kaplan-Meier survival curves after first hospital admission for HF according to age. Kaplan-Meier survival curves according to age: ≥80 years old vs. <80 years old. Survival after the index date was significantly lower in over-80-year-old patients than in "<80 group" ($p<0.001$)

Likewise to recent registry data showing the increase in the prevalence of HF in elderly subjects [16], our study showed that more than 50 % of patients admitted for a first hospitalization for HF were aged over 80 years. This proportion was higher in our database (53 %) than in another French study (38 %) [15], which may be due to the selective inclusion in the latter study of patients recruited only from cardiological departments which usually manage younger patients. Indeed, the EGB database exhibits a more representative feature by systematically recording all hospitalizations regardless of the department involved (geriatrics, cardiology, general medicine, internal medicine, etc.).

Compared to the EGB database, over-80-year-old HF patients are less represented in European registries (Euro Heart Failure Survey (EHFS) 1 [14], EHFS 2 [16], and Danish registry [28] with 26, 21, and 20 % of over-80-year-old patients, respectively). One explanation for this discrepancy may lie in a selection bias of patients included in registries or studies performed by national or international cardiological societies (cardiological departments where elderly patients are less hospitalized). Finally, another database from the French insurance system confirmed the considerable proportion of elderly patients (66 % of HF patients were older than 75 years) [29]. In the present study, we observed an important incidence of HF in over-80-year-olds, which was more than 16 times higher than in the <80 group, consistent with recent registry data [15].

Clinical characteristics of over-80-year-old patients in our study were similar to those already described in international registries [14–16]. Indeed, we confirmed that over-80-year-old HF patients were more frequently female [30], hypertensive [31], and presented more frequently chronic atrial fibrillation [28, 32]. These patients also displayed several other comorbidities including chronic kidney disease and denutrition. Furthermore, ischemic cardiomyopathies were more frequent in over-80-year-olds than dilated cardiomyopathy, possibly in line with the increasing prevalence of coronary artery disease with age. Elderly patients were less well managed than younger patients, with fewer admissions in an intensive care unit, fewer cardiac explorations, and less vasopressive amine support.

More importantly, we observed and confirmed an underuse of HF drugs in over-80-year-olds compared to younger patients as suggested in other registries [14–16, 28–32]. However, this database also allowed to highlight the benefit of recommended HF treatments (ACEi/ARB, BB, MRA or ACEi/ARB, BB) in over-80-year-olds (Fig. 3c). Interestingly, regardless of left ventricular ejection fraction status, we observed an efficacy of bi- or tritherapy (ACEi/ARB, BB, MRA or ACEi/ARB, BB) on survival in over-80-year-old HF

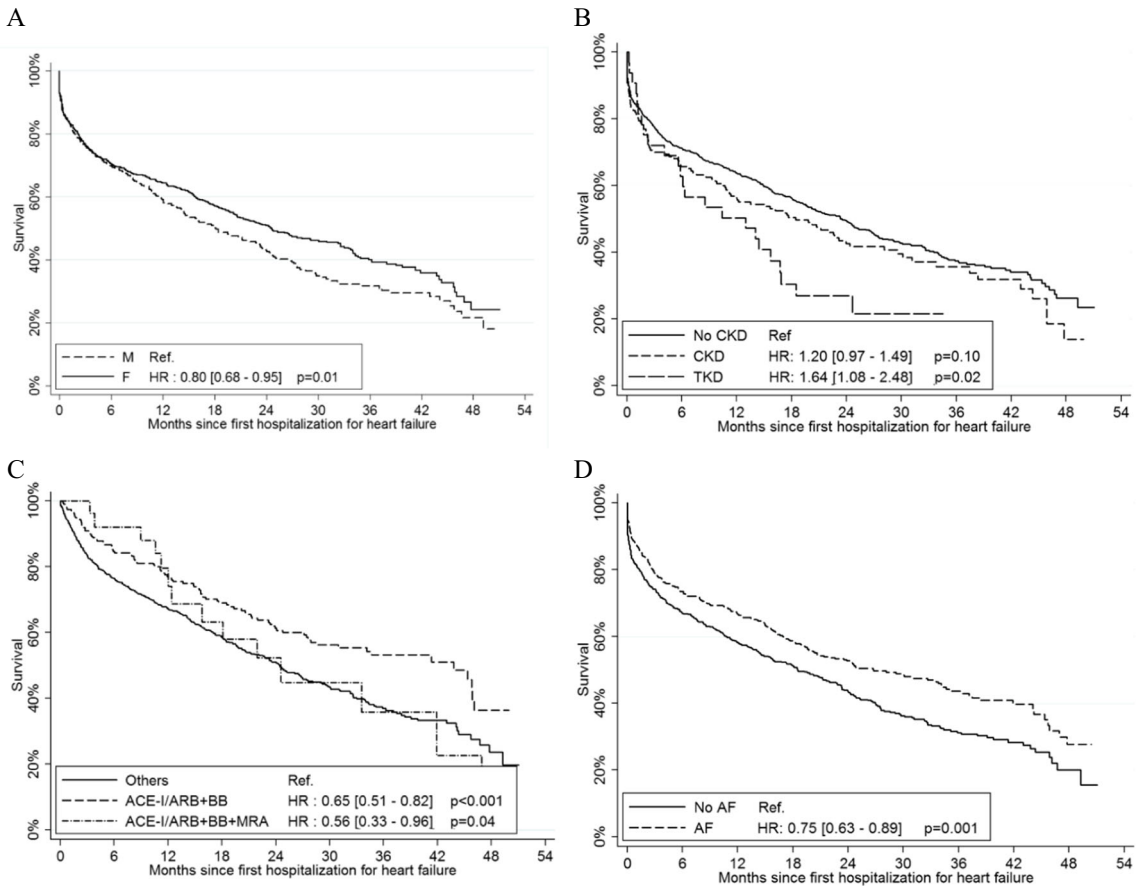

Fig. 3 Kaplan-Meier survival curves in four subgroups among 80-year-old HF patients. When comparing over-80-year-old HF patients, survival was higher in women, lower in patients with terminal kidney disease (KD) compared to patients without chronic KD (CKD), and with no difference between patients with CKD and without CKD. Survival was higher in patients receiving ACEi/ARB+BB+MRA or ACEi/ARB+BB compared to neither of these two combinations. Finally, survival was higher in patients with atrial fibrillation (AFib) compared to those without AFib. *HR* hazard ratio, *ACEi* angiotensin conversing enzyme inhibitors, *ARB* angiotensin receptor blockers, *MRA* mineralocorticoid receptor antagonists, *BB* beta-blockers

patients. However, patients receiving these bi or tritherapy may be under more qualified care. Since our study is based on the analysis of a retrospective administrative database, we could not have a definitive conclusion on the specific role of drug treatment, but anyway, this observation reveals an interesting benefit to use ACEi/ARB, BB, and MRA. Of particular note, elderly patients more often display HF with preserved ejection fraction (HFPEF) whose treatment is poorly defined and possibly based on classes of drugs other than those used in HFREF (HF with reduced EF). The present study constitutes an analysis in "real-life" conditions, which may explain the lower but more representative rate of drug prescriptions in comparison to international registries [11, 13] such as EHFS 1 and EHFS 2.

During our analysis period (2009 to 2011), there was only an increase in BB use, possibly as a result of the SENIORS study [10] which confirmed the benefit of nebivolol in HF patients aged over 70 years. In contrast, there was no increase in prescription of ACEi and MRAs despite guidelines [4, 5] and the EPHESUS [33] and EMPHASIS-HF [7] studies. There are probably many explanations for these low prescriptions rates in the elderly, including numerous comorbidities, increased risk of adverse drug effects, and drug-drug interactions (risk of orthostatic hypotension, hyperkalemia, and acute renal failure). Interestingly, recent post hoc analysis confirmed the safety and efficacy of drugs such as MRAs in the elderly [12], although further studies are nonetheless needed [11].

As previously described, in-hospital mortality was higher in over-80-year-old patients [16]. We also confirm the poor prognosis of elderly HF patients as reported by Mahjoub et al. [15] and EHFS 2 [16]. Of note, the survival of HF over-80-year-old patients was quite similar to 90-year-old patients without HF.

The present study also highlights some factors associated, after adjustment, with improved survival: dyslipidemia and vitamin K antagonists (VKA). Thus, we confirmed in this unselected cohort the results of the prospective AFFIRM study, i.e., the benefit of warfarin in AFib patients [34], which

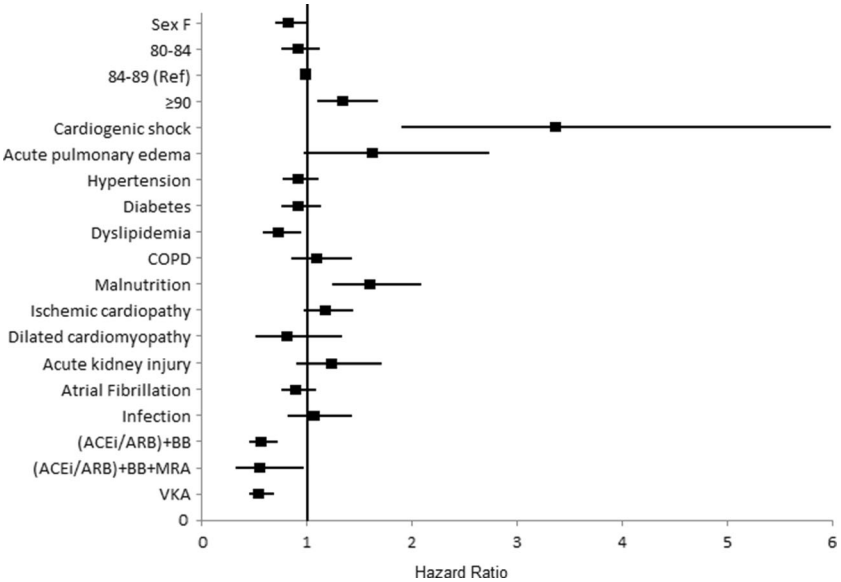

Fig. 4 Multivariate analysis for predictive factors for death in over-80-year-old HF patients. In multivariate analysis, factors significantly associated with better survival were dyslipidemia [0.74 (0.58–0.94), p=0.02], vitamin K antagonists [0.55 (0.44–0.69), p<0.001], associated ACEi/ARB+BB+MRA [0.56 (0.32–0.96), p=0.04], and ACEi/ARB+BB [0.57 (0.45–0.72), p<0.001], in contrast to in-hospital cardiogenic shock [...], denutrition [...] and age over 90 [1.35 (1.09–1.67), p=0.01]. *F* female, *COPD* chronic obstructive pulmonary disease, *ACEi* angiotensin converting enzyme inhibitors, *ARB* angiotensin receptor blockers, *BB* beta-blockers, *MRA* mineralocorticoid receptor antagonists. Reference class for age: ≥80

could explain the higher survival in these patients. The benefit due to dyslipidemia appears to be artificial and could be explained by a large prescription of statins in developed countries and known to reduce acute decompensation of ischemic cardiopathy [35]. This study also revealed pejorative factors other than cardiac status (cardiogenic shock, acute pulmonary edema, dilated cardiomyopathy), including denutrition, acute renal failure, and advanced age (over 90 years), all of which have previously been reported as factors of poor prognosis [36].

Study limitations

Study limitations include those common to most healthcare databases (only administrative data in the present study), namely the limited detailed clinical information regarding comorbidities and paraclinical examination results. Particularly, echocardiographic parameters of left ventricle ejection fraction or blood test results were not available which did not allow us to distinguish between HFPEF and HFREF or to assess the prognostic impact of natremia, hemoglobin, or natriuretic peptides. HF patients are often misdiagnosed, especially the elderly. Since we use an administrative database, this study displays the classical limitations concerning the validity of data coding, such as coding of diagnoses. Despite these limitations, our results are in line with published data and it is also worth noting that more and more studies are performed from the EGB database, some of them specifically at the request of the French health authorities, emphasizing the significance of the results produced.

Conclusion

Chronic heart failure management in the elderly represents the next challenge for cardiologists, general practitioners, geriatricians, and scientists because of its increasing prevalence and incidence. The present study puts into focus the high proportion of over-80-year-old HF patients. The real-life pharmacological management of over-80-year-old HF patients in France needs to be improved. Furthermore, ACEi/ARB+BB±MRAs is associated with a benefit for patient survival in this unselected HF cohort suggesting that the elderly may be treated as any other patient, taking into account their comorbidities and the risk of adverse effects.

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Conflict of interest None

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