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ORIGINAL ARTICLE

Characteristics and management of very elderly patients with heart failure: a retrospective, population cohort study

Mona Olofsson[1,2]*, Krister Lindmark[2], Jan Stålhammar[3], Michael Törnblom[4], Anna Lundberg[5], Gerhard Wikström[6] and Kurt Boman[1,2]

[1]*Research Unit, Medicine-Geriatric, Skellefteå County Hospital, Skellefteå, Sweden;* [2]*Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden;* [3]*Department of Public Health and Caring Sciences, Family Medicine and Preventive Medicine, Uppsala University, Uppsala, Sweden;* [4]*IQVIA, Solna, Sweden;* [5]*Novartis Sweden AB, Stockholm, Sweden; and* [6]*Department of Medical Sciences, Uppsala University, Uppsala, Sweden*

Abstract

Aims Unmet needs exist in the diagnosis and treatment of heart failure (HF) in the elderly population. Our aim was to analyse and compare data of diagnostics and management of very elderly patients (aged ≥85 years) compared with younger patients (aged 18–84 years) with HF in Sweden.

Methods Incidence of ≥2 HF diagnosis (ICD-10) was identified from primary/secondary care in Uppsala and Västerbotten during 2010–2015 via electronic medical records linked to data from national health registers. Analyses investigated the diagnosis, treatment patterns, hospitalizations and outpatient visits, and mortality.

Results Of 8702 patients, 27.7% were ≥85 years old, women (60.2%); most patients (80.7%) had unknown left ventricular ejection fraction; key co-morbidities comprised anaemia, dementia, and cerebrovascular disease. More very elderly patients received cardiovascular disease (CVD)-related management after diagnosis in primary care (13.6% vs. 6.5%; $P < 0.0001$), but fewer patients underwent echocardiography (19.3% vs. 42.9%; $P < 0.0001$). Within 1 year of diagnosis, very elderly patients were less likely to be hospitalized (all-cause admissions per patient: 1.9 vs. 2.3; $P < 0.0001$; CVD-related admissions per patient: 1.8 vs. 2.1; $P = 0.0004$) or prescribed an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) plus a β-blocker (45.2% vs. 56.9%; $P < 0.0001$) or an ACEI/ARB plus a β-blocker plus a mineralocorticoid receptor antagonist (15.4% vs. 31.7%; $P < 0.0001$). One-year mortality was high in patients ≥85 years old, 30.5% (CI: 28.3-32.7%) out of 1797 patients.

Conclusions Despite the large number of very elderly patients with newly diagnosed HF in Sweden, poor diagnostic work-up and subsequent treatment highlight the inequality of care in this vulnerable population.

Keywords Elderly; Heart failure; Hospitalization; Mortality; Sweden; Treatment

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Correspondence to: Mona Olofsson, Department of Public Health and Clinical Medicine, Umeå University, SE-901 87 Umeå, Sweden. Tel.: +46910771569; +46706479430; Fax: +4691010274. Email: mona.olofsson@regionvasterbotten.se

Introduction

It is widely recognized that heart failure (HF) primarily affects the elderly population.[1–3] The elderly HF population is generally considered to include individuals aged 70–80 years,[4,5] with very elderly patients being aged ≥85 years.[6,7] In developed countries, HF is estimated to affect 1–2% of the adult population, increasing to more than 10% in individuals aged 70 years and older.[8,9] This situation is set to worsen in the future owing to our ageing society[4,6]; until 2011, the number of patients with HF aged 80 years and older has almost doubled.[2]

Patients with HF have myriads of co-morbidities, many of which complicate the process of HF diagnosis, including ischaemic heart disease (IHD), hypertension, and chronic obstructive pulmonary disease.[3,10] Because of the ageing pro-

cess, elderly people are particularly prone to depression,[10] cognitive impairment,[11] and frailty[12] and are less likely than younger individuals to tolerate HF medications,[13] partly owing to age-related physiological changes that influence drug pharmacokinetics and pharmacodynamics.[14]

The median survival of patients with HF aged 85 years or greater is approximately 20 months compared with 50 months for those younger than 85 years.[6] Findings from our research in Sweden support a significantly increased risk of all-cause and cardiovascular disease (CVD)-related mortality at 1 year after HF diagnosis with increasing age.[15] Despite the poor prognosis and complexities inherent to the elderly HF population, these patients are mostly referred to primary care physicians (PCPs) or geriatricians rather than cardiologists.[3,16,17] Additionally, because very elderly people have a greater predisposition to HF with preserved ejection fraction (HFpEF) and are under-represented in randomized clinical trials of HF treatments, current guidelines for HF management are less relevant to this population.[3,8,18] Therefore, there is limited guidance on how best to manage HF in these vulnerable patients.

Challenges associated with the diagnosis of HF in elderly patients together with a limited understanding of how best to treat these individuals result in key unmet needs in HF. We therefore aimed to analyse and compare data of the characteristics, management, and outcomes of very elderly patients with HF (85 years and older) with those of patients aged 18–84 years included in a large retrospective study in Sweden.[15]

Methods

Study design and patients

Study design and timelines, enrolled patients, and study variables have been published previously.[15] Briefly, this was a retrospective, non-interventional cohort study that used longitudinal, patient-level data of individuals with HF in Sweden. Data were collected from electronic medical records (EMRs) from five hospitals and 83 primary care centres, as well as from local echocardiography (echo) registries, in the counties of Uppsala and Västerbotten. EMR data, which were linked via unique identifiers issued by the National Board of Health and Welfare to data from national health registers, including the National Patient Register (NPR), the National Dispensed Drug Register (NDR), and the Cause of Death Register, were anonymized before the linked database was released to the research group. Ethical approval from the regional Ethical Review Board in Uppsala, Sweden (2015-045), was obtained before data extraction.

Patients aged ≥18 years with at least two documented HF diagnoses, based on the International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I11.0, I13.0, or I13.2 as primary or secondary diagnoses, during the analysis period from January 2010 to March 2015 were eligible for inclusion in the analysis. The HF phenotype [HFpEF, defined as a left ventricular ejection fraction (LVEF) of at least 50%, and HF with reduced ejection fraction (HFrEF), defined as a LVEF of less than 50%] was determined based on data from local echo registries. The rationale for this cut-off is based on data constraints; LVEF is recorded categorically in the echo registers, with the categories used differing between the county councils such that 50% was the only option that allowed for a common threshold. Ethical approval for the study was granted by the regional Ethical Review Board in Uppsala, Sweden (2015-045), and was performed in accordance with the Declaration of Helsinki. No informed consent was required for this retrospective, anonymized study.

Study timelines

Patient data were obtained from EMRs based on an observed HF diagnosis during 1994–2015 for Uppsala County and 1992–2015 for Västerbotten County. The analysis period was 1 January 2010–31 March 2015, with a 'look-back' period in the EMR data from the date of the first data available until 31 December 2009; for NPR data, the look-back period spanned from 1 January 1997 to 31 December 2009. Patients in whom a diagnosis of HF was made during the look-back period comprised the prevalent HF population, whereas patients in whom a first diagnosis was made during the analysis period made up the incident HF population. The index date was defined as the date of the first HF diagnosis during the analysis period, and follow-up was defined as the period between the index date and study completion, the date of data availability for patients who moved to another region, or the date of death, whichever came first.

Variables analysed and statistical analyses

Data were sourced from EMRs using the Pygargus Customized eXtraction Program (CXP 3.0). Except for mortality investigations, analyses were conducted for patients classified as having incident HF and were stratified according to age group [18–84 years (younger) and 85 years and older (very elderly)] and HF phenotype (HFrEF, HFpEF, and unknown LVEF). For categorical outcomes, the chi-square test was performed, and for a comparison of means, a *t*-test was conducted (unless stated otherwise). All confidence intervals (CIs) were calculated at the 95% level. SAS, Version 9.3 or higher, was used for statistical analysis and data management.

Descriptive statistics were used to assess patient demographics, clinical characteristics, and laboratory measures. Co-morbidities, based on data from primary (EMR) and secondary (EMR and NPR) care and stratified according to HF phenotype, were summarized per a pre-defined list of ICD-10 codes. Co-morbidity data were collected from both the primary and secondary diagnoses in all healthcare visits (including primary care, outpatient visits, and inpatient visits) that occurred 0–5 years before the date of the first HF diagnosis. The Charlson co-morbidity index (CCI; ranging from 0 to >10, where higher scores signify greater co-morbidity) was also calculated using information from 0 to 5 years before the index date. All-cause mortality was modelled by Cox proportional hazards regression with comparison groups stratified by age group (reference group: 18–54 years), Similarly, CVD-related mortality was modelled by Fine and Gray model, which accounts for competing risks from other causes of death. Diagnostic work-up of patients according to the setting in which they were receiving CVD-related care during the first year after their HF diagnosis was stratified by age group, as were diagnostic tests [i.e. N-terminal pro-B-type natriuretic peptide (NT-proBNP) testing and echo] performed during the 6 months before and after the first HF diagnosis. Local echo registries did not include private practices in Uppsala County or the smallest hospital in Västerbotten County.

Combination treatment patterns were based on data for prescribed and pharmacy-dispensed medication as available in the NDR (no hospital-administered treatments were included in the analyses) and were examined 1 year before and after the first HF diagnosis. A patient was considered to be prescribed combination therapy if at any time during a 30-day period they were prescribed a pre-specified combination of therapies [i.e. an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) plus a β-blocker (BB) or an ACEI/ARB plus a BB plus a mineralocorticoid receptor antagonist (MRA)]. For each HF drug class (ACEI, ARB, BB, and MRA), the proportion of patients who were prescribed a median maintenance dose [defined as the amount of drug dispensed (mg)/duration of dispensation (days)] of at least 50% or 100% of the European Society of Cardiology (ESC) 2012-recommended target dose for individual treatments within the class for HFrEF[8] was stratified by HF phenotype and the two age groups. Analysis of dosing patterns was based on data for prescribed and pharmacy-dispensed medications as available in the NDR.

The mean number of hospitalizations and outpatient visits and the mean number of hospital days (excluding patients with zero hospitalizations) for all-cause, CVD-related, and HF-related events were assessed at 1 and 3 years after the first HF diagnosis. Additionally, all-cause and CVD-related mortality in the prevalent HF population, stratified by age group, was examined in the calendar year 2014, with additional analyses investigating the most common causes of death.

Results

Baseline demographics and clinical characteristics

Overall, 33 120 patients with newly diagnosed HF were identified from the Uppsala County and Västerbotten County EMRs, of whom 8702 (8.3%) had at least two HF diagnoses during the analysis period and no HF diagnoses during the look-back period. In the incident HF population, 2409 patients (27.7%) were aged 85 years and older ('very elderly patients'), and 6293 (72.3%) were aged 18–84 years ('younger patients') (*Table 1*). Very elderly patients were more likely to be women, and body mass index (BMI) was generally lower vs. younger patients (*Table 1*). The HF phenotype was known in 3167 patients (36.4%) overall [1120 (35.4%) of these patients had HFpEF, and 2047 (64.6%) had HFrEF]. In total, LVEF was unknown in 5535 patients (63.6%); for very elderly patients, it was 1943/2409 (80.7%) (*Table 1*).

Mean NT-proBNP levels at baseline were higher in very elderly patients than in younger patients, and for NT-proBNP levels above 3000 pg/mL, the percentages were 40.9% and

Table 1 Baseline demographic and clinical characteristics in patients with a diagnosis of HF from the counties of Uppsala and Västerbotten, stratified by age group

Characteristic	Age 18–84 years (*N* = 6293)	Age ≥85 years (*N* = 2409)
Sex, *n* (%)		
Male	3736 (59.4)	959 (39.8)
Female	2557 (40.6)	1450 (60.2)
Body mass index[a] (kg/m^2), *n* (%)		
Underweight (<18.5)	108 (1.7)	73 (3.0)
Normal (18.5–24.9)	1116 (17.7)	590 (24.5)
Overweight (25.0–29.9)	1208 (19.2)	372 (15.4)
Obese (≥30.0)	817 (13.0)	111 (4.6)
HF phenotype, *n* (%)		
HFrEF	1799 (28.6)	248 (10.3)
HFpEF	902 (14.3)	218 (9.0)
Unknown LVEF	3592 (57.1)	1943 (80.7)
CCI 0–5 years before diagnosis[b], mean (SD)	1.9 (2.3)	1.6 (2.0)
Common co-morbidities 0–5 years before diagnosis[c], *n* (%)		
Hypertension	3240 (51.5)	1261 (52.3)
Atrial fibrillation	1852 (29.4)	757 (31.4)
IHD (angina or MI)	1386 (22.0)	487 (20.2)
Diabetes	1302 (20.7)	314 (13.0)
Cancer	885 (14.1)	395 (16.4)
Dyslipidaemia	1011 (16.1)	140 (5.8)
Anaemia	704 (11.2)	369 (15.3)
Cerebrovascular disease	697 (11.1)	346 (14.4)
Dementia	270 (4.3)	253 (10.5)

CCI, Charlson co-morbidity index; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IHD, ischaemic heart disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; SD, standard deviation.

[a]Body mass index data missing for 3044 patients aged 18–84 years and 1263 patients aged ≥85 years.

[b]Includes patients with a CCI of 0 (i.e. no co-morbidities).

[c]Co-morbidities occurring in ≥10% of patients in either group are included.

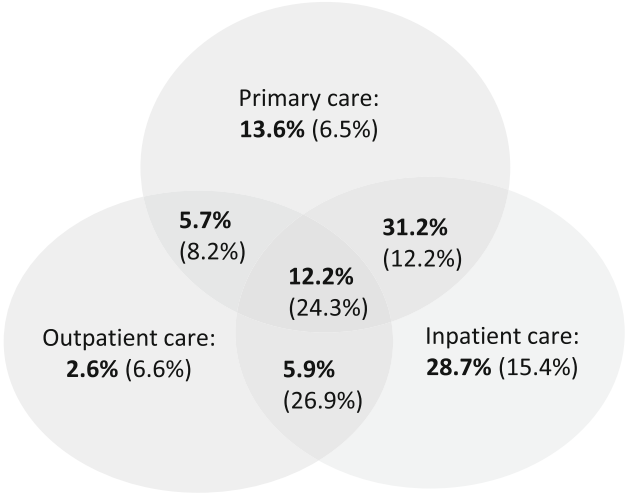
32.8%, respectively. Conversely, estimated glomerular filtration rate, haemoglobin concentration, and ferritin levels were higher in the younger patient group (*Table S1*). Mean CCIs were unexpectedly lower, in very elderly compared with younger patients, 1.6 and 1.9, respectively (*Table 1*). Patients with the highest mean CCI (2.1) were younger patients with an unknown LVEF.

Irrespective of age, the most common underlying CVDs were hypertension, atrial fibrillation, and IHD (*Table 1*). Comorbidities that occurred more frequently in very elderly patients than in younger patients included anaemia, dementia, and cerebrovascular disease (*Table 1*), as well as stroke (9.7% vs. 7.0%, respectively), hypotension (3.1% vs. 1.9%), and Alzheimer's disease (3.8% vs. 1.5%). Although depression was less common in very elderly patients than in younger patients (2.8% vs. 3.8%), the use of anti-depressants in the first year before HF diagnosis was more common among very elderly patients (16.9% vs. 13.4%).

Diagnostic work-up

In the year following the first HF diagnosis, more very elderly patients than younger patients were receiving CVD-related care in primary care alone, as inpatients alone, and in primary care plus inpatient settings (*Figure 1*). Significantly fewer very elderly patients underwent echo at diagnosis (19.3% vs. 42.9%; $P < 0.0001$). NT-proBNP tests were performed in most patients regardless of age, although the proportion of very elderly patients who underwent this test was significantly lower than that of younger patients (82.0% vs. 84.0%; $P = 0.0243$). The proportion of patients undergoing both echo and NT-proBNP testing was also significantly lower for very elderly (18.3% vs. 38.5%; $P < 0.0001$).

Figure 1 Settings of cardiovascular disease-related care received in the first year after the first diagnosis of heart failure in patients aged 18–84 years and ≥85 years. Values in parentheses are data of patients aged <85 years. Total number of patients: 18–84 years, *N* = 4184; ≥85 years, *N* = 1602. Statistically significant differences between the two age groups for each care setting were observed ($P < 0.0001$ for all care settings except primary care plus outpatient care).



Treatment patterns

In the first year following the first HF diagnosis, significantly fewer very elderly patients were prescribed HF treatment combinations as recommended by the ESC for HFrEF [ACEI/ARB plus BB (45.2% vs 56.9%; $P < 0.0001$) or ACEI/ARB plus BB plus MRA (15.4% vs 31.7%; $P < 0.0001$)].

Hospitalizations

The mean numbers of all-cause and CVD-related hospitalizations and outpatient visits per patient were significantly lower in the first year after the first HF diagnosis for very elderly patients (*Table 2*). A significantly lower number of HF-related outpatient visits were also observed between the age groups at this time point ($P < 0.0001$); however, this was not true for HF-related hospitalizations. At 3 years after the first HF diagnosis, the mean numbers of all-cause, CVD-related, and HF-related hospitalizations and outpatient visits per patient and year were lower than those observed in the first year after HF diagnosis (*Table 2*). Statistically significant differences in the number of events at 3 years between age groups were observed for all events except for HF-related hospitalizations (*Table 2*). In the first year after the first HF diagnosis, the mean numbers of hospitalization days (excluding patients with no hospitalizations) for very elderly patients and younger patients were 20.9 and 21.7 days ($P = 0.0017$) for all-cause events, 20.4 and 20.7 days ($P = 0.0004$) for CVD-related events, and 18.6 and 17.1 days ($P < 0.0001$) for HF-related events, respectively. The number of hospital days for all patients declined at 3 years after HF diagnosis, and the differences between the two age groups were no longer statistically significant (*Table 2*).

Mortality

Mortality was high in patients ≥85 years old. One-year mortality was 30.5% (CI: 28.3–32.7%) out of 1797 patients as compared with 5.8% (CI: 3.5–8.1%) among those 18–54 years, 9.6% (CI: 7.3–11.8%) among 55–64 years, 10.7% (CI: 9.1–12.3%) among 65–74 years, and 16.6% (CI: 15.0–18.1%) among 75–84 years. Hazard ratio (HR) was 4.58 (2.98–7.04) for patients ≥85 years old compared with reference patients (18–54 years). For patients 55–64, 65–74, and 75–84 years, corresponding HRs were 1.33 (CI: 0.81–2.18), 1.49 (CI: 0.95–2.34), and 2.46 (CI: 1.60–3.79), respectively.[15]

Table 2 All-cause, CVD-related, and HF-related hospitalizations at 1 and 3 years following the first HF diagnosis, stratified by age group

	1 year after first HF diagnosis			3 years after first HF diagnosis		
Hospitalizations	Age 18–84 years (N = 4184)	Age ≥85 years (N = 1602)	P value	Age 18–84 years (N = 1345)	Age ≥85 years (N = 370)	P value
All-cause						
No. of hospitalizations, mean (SD)	2.3 (2.4)	1.9 (1.8)	<0.0001	1.1 (1.9)	1.0 (1.4)	NS
No. of hospital days[a,b], mean (SD)	21.7 (28.2)	20.9 (20.6)	0.0017	17.1 (20.2)	15.5 (14.9)	NS
No. of outpatient visits, mean (SD)	3.9 (5.8)	1.7 (2.4)	<0.0001	3.0 (5.8)	1.3 (2.0)	<0.0001
CVD related						
No. of hospitalizations, mean (SD)	2.1 (2.3)	1.8 (1.7)	0.0004	1.0 (1.7)	0.9 (1.3)	NS
No. of hospital days[a,c], mean (SD)	20.7 (26.7)	20.4 (20.0)	0.0004	16.9 (19.3)	15.3 (14.5)	NS
No. of outpatient visits, mean (SD)	1.6 (3.9)	0.4 (0.8)	<0.0001	1.1 (4.8)	0.2 (0.6)	<0.0001
HF related						
No. of hospitalizations, mean (SD)	1.5 (1.7)	1.5 (1.5)	NS	0.5 (1.2)	0.6 (1.1)	0.0002
No. of hospital days[a,d], mean (SD)	17.1 (22.4)	18.6 (18.9)	<0.0001	15.7 (18.0)	15.0 (14.1)	NS
No. of outpatient visits, mean (SD)	0.8 (1.2)	0.2 (0.5)	<0.0001	0.3 (0.8)	0.1 (0.3)	<0.0001

CVD, cardiovascular disease; HF, heart failure; NS, not significant; SD, standard deviation.
[a]Excludes patients with zero hospitalizations, for 1 and 3 years after the first HF diagnosis.
[b]18–84 years (N = 3302 and N = 587), ≥85 years (N = 1265 and N = 190).
[c]18–84 years (N = 3238 and N = 543), ≥85 years (N = 1248 and N = 178).
[d]18–84 years (N = 2919 and N = 334), ≥85 years (N = 1159 and N = 135).

One-year CVD mortality was 16.8% (15.1–18.6%) compared with 1.8% (CI: 0.8–3.5%) among those 18–54 years, 3.4% (CI: 2.2–5.0%) among 55–64 years, 4.1% (CI: 3.1–5.2%) among 65–74 years, and 6.9% (CI: 5.9–8.0%) among 75–84 years. With age category 18–54 as referent, corresponding HRs for 55–64, 65–74, 75–84, and ≥85 years were 1.69 (CI: 0.71–4.02), 1.84 (CI: 0.82–4.10), 3.35 (CI: 1.55–7.25), and 8.86 (CI:4.12–19.04), respectively.[15]

Discussion

Our main findings were that very elderly patients, who comprised more than one-quarter of the individuals newly diagnosed with HF, were more likely to be women and had increased NT-proBNP levels. Most important was that LVEF was left unknown in 80% as only 20% of very elderly patients underwent echo around the time of their first HF diagnosis. This is of concern because it indicates a severe shortfall by healthcare providers of a correct diagnosis of HF in those patients. Of great concern, it potentially raises the question of whether these patients actually had HF because echo is required for making a diagnosis and aiding in decision-making regarding appropriate therapy.[8] Consequently, the lack of echo presents a challenge to both patients and healthcare providers. This, together with our finding that significantly more very elderly than younger patients received CVD-related care in the primary setting, suggests an inequality in the management of these patients. In fact, the examination of hospitalization data in the first year after HF diagnosis showed that very elderly patients had a significantly lower number of all-cause and CVD-related hospitalizations and outpatient visits compared with younger patients.

Our results support observations from other studies showing that elderly patients received less specialist cardiology care and were not diagnosed and treated in accordance with recommendations from the latest HF guidelines at that time.[3,16,17,19] For example, in a U.K. study of 938 patients with newly diagnosed HF (738 patients aged <80 years and 200 patients aged ≥80 years), 46.5% of the elderly patients were referred to a specialist and/or hospitalized within 1 month of the first diagnosis compared with 55.9–70.4% of those aged 40–79 years.[17] Similarly, the EuroHeart Failure Survey II found that echo was performed less often in elderly patients than in younger patients with HF.[4] Awareness of HF diagnosis and adherence to treatment guidelines differ significantly between cardiologists and PCPs, with the latter group being less likely to use diagnostic tests such as echo.[3,20] Indeed, in a cross-sectional study conducted in the Netherlands, patients receiving HF care from a PCP were older, less likely to have echo and less often prescribed HF therapies than those receiving care from a cardiologist.[21] This study also demonstrated that more than one-third of patients classified by PCPs as having HF either did not have HF or had

an uncertain diagnosis.[21] Our study showed that echo was conducted in approximately 50% fewer patients with a first diagnosis in primary care vs. secondary care.[15]

Even when elderly patients are hospitalized with acute HF, they are less likely than younger patients to be evaluated by a cardiologist and receive HF management counselling or follow-up after discharge.[3] This disparity in HF care can have detrimental effects on patient outcomes. In the Understanding National Variation and Effects of Interventions at different Levels of Care for Heart Failure (UNVEIL-CHF) study, which restricted analysis to data from patients with HFrEF, referral to a cardiologist for follow-up after discharge from the hospital occurred more often in patients aged 60–80 years or younger than in those older than 80 years.[16] Moreover, this study demonstrated that referral to a cardiologist after discharge was associated with reduced mortality at 30 days [odds ratio (OR), 0.66; 95% CI, 0.61–0.72; $P < 0.001$] and at 1 year (OR, 0.74; 95% CI, 0.70–0.78; $P < 0.001$) compared with that without a cardiologist follow-up.[16] Additionally, in a Canadian study of 7634 patients newly hospitalized for HF, those treated by generalists (internists or family doctors) alone had a higher risk of mortality at 30 days (OR, 1.50; 95% CI, 1.18–1.91) and 1 year (OR, 1.29; 95% CI, 1.10–1.50), as well as a higher risk of a 1-year composite outcome of death and hospital readmission, compared with those treated by cardiologists.[22] This study also found that patients who received specialist cardiology care were more likely to undergo diagnostic procedures such as echo and had higher rates of evidence-based pharmacological therapy use such as BBs than those treated by generalists alone.[22]

As expected in our study, all-cause mortality in very elderly patients was significantly greater than in younger patients in the prevalent population. Our findings were similar to the 28% overall mortality observed at 1 year after discharge in patients older than 80 years in the EuroHeart Failure Survey II (vs. 18.5% for patients <80 years old).[4] In that study, age was a strong independent predictor of 1-year mortality in very elderly patients surviving after discharge (adjusted hazard ratio, 1.51; 95% CI, 1.24–1.84), as were co-morbidities (diabetes and renal dysfunction).[4] Similarly, in the Danish pooled analysis, the hazard ratio (95% CI) for mortality during long-term follow-up in patients aged 85 years and older vs. those aged <85 years was 1.71 (1.52–1.92).[6] Although the setting of HF diagnosis and follow-up care can impact patient outcomes, a combination of co-morbidities, social factors, and treatment patterns may influence mortality in very elderly patients.

Despite evidence demonstrating improved outcomes in patients with HF when physicians prescribe therapies according to HF guideline recommendations,[23–25] most eligible patients in our Swedish HF population did not seem to receive drug regimens as recommended by the ESC. There may be many patient-specific and physician-specific reasons for under-prescription of recommended HF medications in very elderly patients. These reasons include unclear diagnosis of HF, poor tolerability, multiple co-morbidities, polypharmacy, physician inertia (not up-titrate medications for fear of adverse events), and possibly because of a break in the continuum of care as patients move from one care setting to another. In addition, our findings of co-morbidities assessed by Charlson index was somewhat unexpected and might be a consequence of some survival paradox but probably more of a registration bias and/or insufficient diagnostics. In elderly patients treated in primary care or at nursing homes, the focus may rather be on symptom relief rather than diagnostics procedures. For example, depression was less common in the very elderly although they had more of antidepressant treatment. Additionally, little treatment guidance is available that is specific to very elderly patients with HF not only because they are seldom included in randomized clinical trials but also because treatment guidelines are based on studies in younger patients with HFrEF.[3,8,26]

Limitations of this study have been discussed in detail previously.[15,27] In short, the retrospective design of the present study is accompanied with challenges of identifying a cohort with a confirmed and validated diagnosis of HF, accounting for missing values for LVEF due to the absence of echo. Two diagnoses to define HF were expected to increase specificity, which might have excluded of more recent or milder cases of HF. The low number of echoes might partially be due to more than 6 months waiting times for echo validation. The total number of echoes in each patient was thus probably higher, but an echo within 6 months seemed most relevant for the actual diagnosis of HF.

Recording and registration bias might explain the difference in findings regarding depression at baseline (less frequently reported in very elderly), as the use of antidepressants was greater in the very elderly group. This might be due to the fact that psychotropic agents often were dispensed by default in elderly patients.

Nevertheless, this, to the best of our knowledge, is one of very few such studies to focus on a 'very elderly' HF population in a real-world setting, with previous elderly HF clinical studies tending to focus on patients aged 70–80 years and older.[1,4,5,7,18]

Conclusions

Very elderly individuals comprise a substantial proportion of the HF population in Sweden; in our cohort, they represented more than a quarter of all patients. Although these patients were older and sicker than their younger counterparts, being burdened with an array of co-morbidities, it is apparent from our results that very elderly patients do not undergo adequate tests for HF diagnostic work-up, which may result in inappropriate treatment. Indeed, available

guidance in the elderly is limited, and optimal therapy in this population is unclear. As such, further studies are urgently needed to gain a better understanding of how best to manage these very elderly patients and improve their overall quality of life.

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Conflict of interest

Mona Olofsson, Jan Stålhammar, and Kurt Boman received reimbursement from Novartis via IQVIA for conducting the study. Mona Olofsson and Kurt Boman also received lecture grants from Novartis. Krister Lindmark received lecture grants and consultant fees from Novartis. Gerhard Wikström has no conflicts of interest to declare, although Uppsala University received research funding from Novartis for conducting this study. Anna Lundberg is an employee of Novartis Sweden AB. Michael Törnblom was employed by IQVIA, Sweden, at the time of the study. IQVIA was commissioned to conduct the study on behalf of Novartis Pharma AG and has ongoing consulting and research relationships with Novartis Pharma AG.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Key laboratory measures at baseline in patients with newly diagnosed heart failure, stratified by age group

References

1. Vigder C, Ben Israel Y, Meisel SR, Kaykov E, Gottlieb S, Shotan A. Management and 1 year outcome of oldest-old, hospitalized heart failure patients: A subacute geriatric hospital survey. *Isr Med Assoc J*. 2010; **12**: 483–488.
2. Wong CY, Chaudhry SI, Desai MM, Krumholz HM. Trends in comorbidity, disability, and polypharmacy in heart failure. *Am J Med*. 2011; **124**: 136–143.
3. Lazzarini V, Mentz RJ, Fiuzat M, Metra M, O'Connor CM. Heart failure in elderly patients: Distinctive features and unresolved issues. *Eur J Heart Fail*. 2013; **15**: 717–723.
4. Komajda M, Hanon O, Hochadel M, Lopez-Sendon JL, Follath F, Ponikowski P, Harjola VP, Drexler H, Dickstein K, Tavazzi L, Nieminen M. Contemporary management of octogenarians hospitalized for heart failure in Europe: EuroHeart failure survey II. *Eur Heart J*. 2009; **30**: 478–486.
5. Manzano L, Babalis D, Roughton M, Shibata M, Anker SD, Ghio S, van Veldhuisen DJ, Cohen-Solal A, Coats AJ, Poole-Wilson PPA, Flather MD, the SENIORS Investigators. Predictors of clinical outcomes in elderly patients with heart failure. *Eur J Heart Fail*. 2011; **13**: 528–536.
6. Mogensen UM, Ersbøll M, Andersen M, Andersson C, Hassager C, Torp-Pedersen C, Gustafsson F, Køber L. Clinical characteristics and major co-morbidities in heart failure patients more than 85 years of age compared with younger age groups. *Eur J Heart Fail*. 2011; **13**: 1216–1223.
7. Kawai Y, Inoue N, Onishi K. Clinical picture, and social characteristics of super-elderly patients with heart failure in Japan. *Congest Heart Fail*. 2012; **18**: 327–332.
8. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Køber L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Rønnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Trindade PT, Voors AA, Zannad F, Zeiher A, ESC Committee for Practice Guidelines. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The task force for the diagnosis and treatment of acute and chronic heart failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2012; **33**: 1787–1847.
9. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Magid D, Marcus GM, Marelli A, Matchar DB, McGuire D, Mohler ER, Moy CS, Mussolino ME, Nichol G, Paynter NP, Schreiner PJ, Sorlie PD, Stein J, Turan TN, Virani SS, Wong ND, Woo D, Turner MB, American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2013 update: A report from the American Heart Association. *Circulation*. 2013; **127**: e6–e245.
10. Cobretti MR, Page R II, Linnebur SA, Deininger KM, Ambardekar AV, Lindenfeld J, Aquilante C. Medication regimen complexity in ambulatory older adults with heart failure. *Clin Interv Aging*. 2017; **12**: 679–686.
11. Dodson JA, Truong TT, Towle VR, Kerins G, Chaudhry SI. Cognitive impairment in older adults with heart failure: Prevalence, documentation, and impact on outcomes. *Am J Med*. 2013; **126**: 120–126.
12. Vidán MT, Blaya-Novakova V, Sánchez E, Ortiz J, Serra-Rexach JA, Bueno H. Prevalence and prognostic impact of frailty and its components in non-dependent elderly patients with heart failure. *Eur J Heart Fail*. 2016; **18**: 869–875.

13. de Freitas EV, Batlouni M, Gamarsky R. Heart failure in the elderly. *J Geriatr Cardiol*. 2012; **9**: 101–107.
14. Azad N, Lemay G. Management of chronic heart failure in the older population. *J Geriatr Cardiol*. 2014; **11**: 329–337.
15. Lindmark K, Boman K, Olofsson M, Törnblom M, Levine A, Castelo-Branco A, Schlienger R, Bruce Wirta S, Stålhammar J, Wikström G. Epidemiology of heart failure and trends in diagnostic work-up: A retrospective, population-based cohort study in Sweden. *Clin Epidemiol*. 2019; **11**: 231–244.
16. Emdin CA, Hsiao AJ, Kiran A, Conrad N, Salimi-Khorshidi G, Woodward M, Anderson SG, Mohseni H, McMurray JJV, Cleland JGF, Dargie H, Hardman S, McDonagh T, Rahimi K. Referral for specialist follow-up and its association with post-discharge mortality among patients with systolic heart failure (from the National Heart Failure Audit for England and Wales). *Am J Cardiol*. 2017; **119**: 440–444.
17. Johansson S, Wallander MA, Ruigómez A, García Rodríguez LA. Incidence of newly diagnosed heart failure in UK general practice. *Eur J Heart Fail*. 2001; **3**: 225–231.
18. Ozierański K, Balsam P, Tymińska A, Peller M, Kapłon-Cieślicka A, Marchel M, Drożdż J, Filipiak KJ, Opolski G. Heart failure in elderly patients: Differences in clinical characteristics and predictors of 1-year outcome in the Polish ESC-HF long-term registry. *Pol Arch Med Wewn*. 2016; **126**: 502–513.
19. Cvetinovic N, Loncar G, Farkas J. Heart failure management in the elderly – A public health challenge. *Wien Klin Wochenschr*. 2016; **128**: 466–473.
20. Rutten FH, Grobbee DE, Hoes AW. Differences between general practitioners and cardiologists in diagnosis and management of heart failure: A survey in every-day practice. *Eur J Heart Fail*. 2003; **5**: 337–344.
21. Valk MJ, Mosterd A, Broekhuizen BD, Zuithoff NP, Landman MA, Hoes AW, Rutten FH. Overdiagnosis of heart failure in primary care: A cross-sectional study. *Br J Gen Pract*. 2016; **66**: e587–e592.
22. Boom NK, Lee DS, Tu JV. Comparison of processes of care and clinical outcomes for patients newly hospitalized for heart failure attended by different physician specialists. *Am Heart J*. 2012; **163**: 252–259.
23. Komajda M, Cowie MR, Tavazzi L, Ponikowski P, Anker SD, Filippatos GS, QUALIFY Investigators. Physicians' guideline adherence is associated with better prognosis in outpatients with heart failure with reduced ejection fraction: The QUALIFY international registry. *Eur J Heart Fail*. 2017; **19**: 1414–1423.
24. Muiesan ML, Paini A, Agabiti Rosei C, Bertacchini F, Stassaldi D, Salvetti M. Current pharmacological therapies in heart failure patients. *High Blood Press Cardiovasc Prev*. 2017; **24**: 107–114.
25. Chin KL, Skiba M, Tonkin A, Reid CM, Liew D, Krum H, Hopper I. The treatment gap in patients with chronic systolic heart failure: A systematic review of evidence-based prescribing in practice. *Heart Fail Rev*. 2016; **21**: 675–697.
26. Jonsson A, Edner M, Alehagen U, Dahlstrom U. Heart failure registry: A valuable tool for improving the management of patients with heart failure. *Eur J Heart Fail*. 2009; **12**: 25–31.
27. Boman K, Lindmark K, Stålhammar J, Olofsson M, Costa-Scharplatz M, Fonseca AF, Johansson S, Heller V, Törnblom M, Wikström G. Healthcare resource utilization and costs associated with heart failure: A retrospective, population-based cohort study in Sweden. *BMJ Open*. 2021; **11**: e053806. https://bmjopen.bmj.com/content/11/10/e053806 (19 october 2021).