ORIGINAL RESEARCH ARTICLE

Managing older patients with heart failure calls for a holistic approach

Julia H.I. Wiersinga[1]*, Hanneke F.M. Rhodius-Meester[1,2], Emma E.F. Kleipool[1], Louis Handoko[3], Albert C. van Rossum[3], Su-San Liem[4], Marijke C. Trappenburg[1,5], Mike J.L. Peters[1] and Majon Muller[1]

[1]*Department of Internal Medicine, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Cardiovascular Sciences, De Boelelaan 1117, Amsterdam, 1081HV, The Netherlands;* [2]*Alzheimer Center Amsterdam, Department of Neurology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Neuroscience, Amsterdam, The Netherlands;* [3]*Department of Cardiology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Cardiovascular Sciences, Amsterdam, The Netherlands;* [4]*Department of Cardiology, Amstelland Hospital, Amstelveen, The Netherlands; and* [5]*Department of Internal Medicine, Amstelland Hospital, Amstelveen, The Netherlands*

Abstract

Aims This study aims to assess the presence of geriatric domain impairments in an older heart failure (HF) outpatient population and to relate these domain impairments with 1 year mortality risk in comparison with a geriatric outpatient population without HF.

Methods and results Data were used from two different prospective cohort studies: 241 outpatients with HF (mean age 78 ± 9 years, 48% female) and 686 geriatric outpatients (mean age 80 ± 7 years, 55% female). We similarly assessed the following geriatric domains in both cohorts: physical function, nutritional status, polypharmacy, cognitive function, and activities in daily living. Cox proportional hazards analyses were used to relate individual domains to 1 year mortality risk in both populations and to compare 1 year mortality risk between both populations. Of the patients with HF, 34% had impairments in ≥3 domains, compared with 38% in geriatric patients. One-year mortality rates were 13% and 8%, respectively, in the HF and geriatric populations; age-adjusted and sex-adjusted hazard ratio (95% confidence interval) for patients with HF compared with geriatric patients was 1.7 (1.3–2.6). The individual geriatric domains were similarly associated with 1 year mortality risk in both populations. Compared with zero to two impaired domains, age-adjusted and sex-adjusted mortality risk (hazard ratio, 95% confidence interval) for three, four, or five impaired domains ranged from 1.6 (0.6–4.2) to 6.5 (2.1–20.1) in the HF population and from 1.4 (0.7–2.9) to 7.9 (2.9–21.3) in the geriatric population.

Conclusions In parallel with geriatric patients, patients with HF often have multiple geriatric domain impairments that adversely affect their prognosis. This similarity together with the findings that patients with HF have a higher 1 year mortality risk than a general geriatric population supports the integration of a multi-domain geriatric assessment in outpatient HF care.

Introduction

Heart failure (HF) is a major public health problem as its prevalence and incidence increase with age.[1] In addition, HF is associated with accelerated biological ageing resulting in an increased risk for other health issues.[2–6]

The co-occurrence of HF with other health issues and their association with an increased risk of adverse health outcomes, such as functional decline, institutionalization, and mortality, calls for a holistic approach. The European Society of Cardiology (ESC) 2016 HF guideline states that a more holistic approach, by monitoring frailty and cognitive impairment, should be a key component in managing older patients with HF.[7] A multi-domain geriatric assessment can be helpful to identify impairments in geriatric domains to develop a co-ordinated and integrated plan for improving health outcomes for older adults with HF.[4]

In the majority of HF clinics, a multi-domain geriatric assessment has not yet been incorporated in daily assessment routine, and existing assessments are mainly focused on

co-morbidities rather than impairments in geriatric domains. We recently demonstrated the potential added value of a multi-domain geriatric assessment in the evaluation and treatment of patients with HF, as the number of geriatric domain impairments appeared more strongly associated with short-term (3 months) adverse health outcomes than severity of HF or co-morbidities.[8] However, the prevalence of geriatric domain impairments in older patients with HF in comparison with geriatric patients, in which geriatric domain impairments are routinely assessed,[9] is not precisely known. This study was set up to assess the presence of geriatric domain impairments and to relate geriatric domain impairments with 1 year mortality risk in an outpatient older HF population as compared with a geriatric outpatient population without HF.

Methods

Design and population

This prospective cohort study included 241 consecutive patients aged ≥60 years previously diagnosed with HF (not specified to any underlying cardiac cause) attending outpatient HF clinics between January 2018 and March 2019 in two Dutch hospitals, namely, the Amsterdam University Medical Center, location VUmc, Amsterdam (tertiary hospital) and Amstelland Hospital, Amstelveen (community hospital).

For comparison with a geriatric population, data of 686 geriatric outpatients of the Amsterdam Ageing Cohort were used.[10] The Amsterdam Ageing Cohort is an ongoing longitudinal cohort study of patients visiting the outpatient geriatric clinic at the Amsterdam University Medical Center, location VUmc. Patients are referred to the outpatient clinic for medical care. Patients from the Amsterdam Ageing Cohort were excluded if they did not have a full year of follow-up or if they had been diagnosed with HF according to their electronic medical records.

The local medical ethics committees approved both research protocols, and all patients gave written informed consent before study entry.

Demographics and general assessment

Demographics (age and gender) of both cohorts were assessed at baseline. The general assessment included blood pressure and heart rate measurement (measured with Dinamap® automated blood pressure monitor), and presence of diabetes mellitus was assessed according to the medical history. The standard cardiac assessment in the HF population included N-terminal pro-hormone brain natriuretic peptide, the New York Heart Association classification, and the left ventricular ejection fraction as measured with an echocardiogram. Additionally, patients with HF were categorized

as HF with reduced ejection fraction (HFrEF), HF with mid-range ejection fraction (HFmrEF), and HF with preserved ejection fraction (HFpEF) if their ejection fraction was <40%, 40–49%, or >50%, respectively.[7]

Multi-domain geriatric assessment

A multi-domain geriatric assessment was performed at baseline by a trained nurse (either an HF nurse or geriatric nurse, according to the study population) and covered physical function, nutritional status, cognitive function, co-morbidities/polypharmacy, and dependency in activities of daily living (ADL). We scored the different domains impaired as yes/no according to pre-defined cut-off values and calculated the total sum of impaired domains (zero to five).

Co-morbidities/polypharmacy domain
As proxy of presence of co-morbidities, number of prescribed medication was scored according to the prescribed medication in the electronic health record. Polypharmacy was assessed as a continuous value and dichotomized as 0–9 and ≥10 prescribed drugs. Use of ≥10 drugs was used to define polypharmacy instead of use of ≥5 drugs in this study, because chronic use of more than five drugs is almost universal in the HF population due to treatment guidelines and does therefore not discriminate enough as proxy for co-morbidities.[11]

Physical domain
Physical function was assessed using hand grip strength (kg) and gait speed (m/s). Hand grip strength (kg) was measured using an isometric hand dynamometer (Jamar® hand dynamometer, Sammons Preston) in upright standing position, while holding the dynamometer in one hand. Patients were actively encouraged to squeeze with maximal strength. Two trials were performed alternately for each hand. The best performance out of four measurements was used. Gait speed (m/s) was assessed using a timed 4 m walking test at normal pace from a standing position using a stopwatch. The fastest time of two trials was used for analyses.

The physical domain was considered impaired when a patient had either low hand grip strength or low gait speed. Low handgrip strength was defined as <20 kg for women and <30 kg for men.[12] Low gait speed was defined as a walking speed <0.8 m/s.[13]

Nutritional domain
The Mini Nutritional Assessment-Short Form (MNA-SF) was used to assess the nutritional status.[14] The MNA-SF score ranges from 1 to 14 and assesses six items, including weight loss, body mass index, psychological stress or acute disease, mobility, neuropsychological problems, and food intake. The nutritional domain was considered impaired when the MNA-SF score was below 12.[15]

Cognitive domain

Cognitive function was assessed with the Mini Mental State Examination (MMSE).[16] This widely used screening tool has a maximum of 30 points. The cognitive domain was considered impaired when the MMSE score was below 26.[17]

Dependency domain

The Katz ADL questionnaire was used to evaluate whether a patient needed assistance during one of the following six daily activities: bathing, getting dressed, toileting, transferring from bed to chair, eating/feeding, and continence.[18] The total number of daily activities with need for assistance was assessed. The dependency domain was considered impaired if the patient needed assistance in one or more daily activities.

One-year mortality

For the HF population, mortality data and date of death were derived from the patient's electronic health records 1 year after inclusion as part of the study protocol (i.e. end of follow-up). Furthermore, patients were called at 1 year follow-up, and if they or their first contact could not be reached, their general practitioner was contacted to determine their health status (e.g. death or alive).

For the geriatric population of the Amsterdam Ageing Cohort, mortality data and date of death were obtained from the Dutch municipal population register on the 22nd of January 2020. The cause of death could not be obtained via this register. If patients in the Amsterdam Ageing Cohort died more than 365 days after inclusion, they were scored as alive at 1 year follow-up.

For both cohorts, the difference between inclusion date and date of death was calculated based on the mortality data.

Statistical analysis

Statistical analyses were performed using SPSS Version 26 (IBM, Armonk, NY, USA). A P-value < 0.05 was considered statistically significant.

Baseline characteristics were assessed for the HF population and the geriatric population separately. Continuous variables were presented as mean [standard deviation (SD)] or median (interquartile range), depending on the distribution of the variable. Dichotomous variables were presented as frequencies and percentage. Independent sample t-tests, Mann–Whitney U-tests, and χ^2 tests were used to assess the differences between population groups in mean, median, and frequencies. Additional analyses were performed to compare baseline characteristics between patients with HFmrEF or HFrEF and patients with HFpEF.

Cox proportional hazards analysis was used in three different ways to assess the 1 year mortality risk [hazard ratios (HRs) and 95% confidence interval (95% CI)].

First, we compared the 1 year mortality risk in the older HF population with the 1 year mortality risk in the geriatric population, taken the latter as reference. All analyses were adjusted for age and gender.

Second, we assessed the relation between impairments in geriatric domains (and its individual items) and 1 year mortality within both populations. We assessed the 1 year mortality risk of the geriatric domain impairments per population, using pre-defined cut-off values. Furthermore, we investigated the association of one SD increase in the individual items of the geriatric assessment on mortality risk. For this, to allow comparison of the individual geriatric assessment items, the different variables were converted into Z-scores and inverted when needed, so that one SD increase in the analysis correlated with a worse performance on the measurement. All these analyses were adjusted for age and sex.

Third, we assessed the influence of the accumulation (i. e. sum) of domains impaired on mortality risk per population, using the presence of zero to two domains impaired as the reference category. These analyses were also adjusted for age and sex.

Results

Table 1 presents the baseline characteristics of the HF population (n = 241) and the geriatric population (n = 686) separately. Patients with HF were younger and less often female and had a lower systolic and diastolic blood pressure. Within patients with HF, the number of patients with HFpEF was lower than patients with either HFmrEF or HFrEF: 18% vs. 82%. Patients with HFpEF were older and more often female, but no significant differences in number of medications, renal function, or number of geriatric domains deficits were found between both groups (Supporting Information, *Table S1*).

Presence of geriatric domains

Figure 1A shows the prevalence of impairment in different geriatric domain in the HF and geriatric populations. The prevalence of impairment of the physical and ADL domains was similar for both populations. Polypharmacy was more often present in the HF population, while impairments in the cognitive and nutritional domains were more often present in the geriatric population. A total of 34% in the HF population and 38% in the geriatric population had impairments in three or more domains. The distribution of number of impaired domains did not differ between the HF and geriatric populations (*Figure 1B*).

Table 1 Baseline patient characteristics of the outpatient heart failure population (*n* = 241) and the outpatient geriatric population (*n* = 686)

	N	Outpatient heart failure population (N = 241)	Outpatient geriatric population (N = 686)	*P*-value
Age (mean ± SD)	927	78 ± 9	80 ± 7	0.01
Female (*n*, %)	927	115 (48%)	377 (55%)	0.05
General assessment				
Diabetes mellitus (*n*, %)	927	57 (24%)	138 (20%)	0.25
Systolic BP, mmHG (mean ± SD)	912	124 (19)	145 (20)	<0.01
Diastolic BP, mmHG (mean ± SD)	912	70 (11)	80 (11)	<0.01
Heart rate, per minute	905	72 (11)	71 (14)	0.14
Cardiac assessment				
Ejection fraction (mean ± SD)	207	38 (13)	n.a.	
Type of heart failure	207			
HFrEF (*n*, %)		112 (54%)		
HFmrEF (*n*, %)		56 (27%)		
HFpEF (*n*, %)		39 (19%)		
NT-proBNP (median, IQR)	231	1939 (881–3425)	n.a.	
NYHA class (*n*, %)	235		n.a.	
Class I		57 (24%)		
Class II		110 (47%)		
Class III/IV		68 (29%)		
Geriatric assessment				
Prescribed medication, number (mean ± SD)	925	10 ± 4	7 ± 4	<0.01
Hand grip strength, kg (mean ± SD)	837			
Male		31 ± 10	30 ± 10	0.23
Female		17 ± 7	18 ± 7	0.14
Gait speed, m/s (mean ± SD)	927	0.91 ± 0.54	0.86 ± 0.35	0.08
MNA-SF score (median, IQR)	857	12 (11–14)	12 (10–13)	<0.01
MMSE score (median, IQR)	904	28 (26–29)	25 (22–28)	<0.01
Katz ADL score (median, IQR)	855	0 (0–1)	0 (0–1)	0.48

ADL, activities of daily living; BP, blood pressure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IQR, interquartile range; MMSE, Mini Mental State Examination; MNA-SF, Mini Nutritional Assessment-Short Form; n.a., not applicable; NT-proBNP, N-terminal pro-hormone brain natriuretic peptide; NYHA, New York Heart Association; SD, standard deviation.

Mortality risk in heart failure versus geriatric outpatients

Of the patients with HF, 13% had died within a year, compared with 8% in the geriatric population. *Figure 2* shows the Kaplan–Meier survival curve, stratified per population. The survival curve of older patients with HF is significantly steeper than the curve of the geriatric population (log rank test *P* = 0.027). Cox proportional hazards analyses showed that older patients with HF had a 1.7-fold (95% CI 1.1–2.6) age-adjusted and sex-adjusted 1 year mortality risk compared with the geriatric patients.

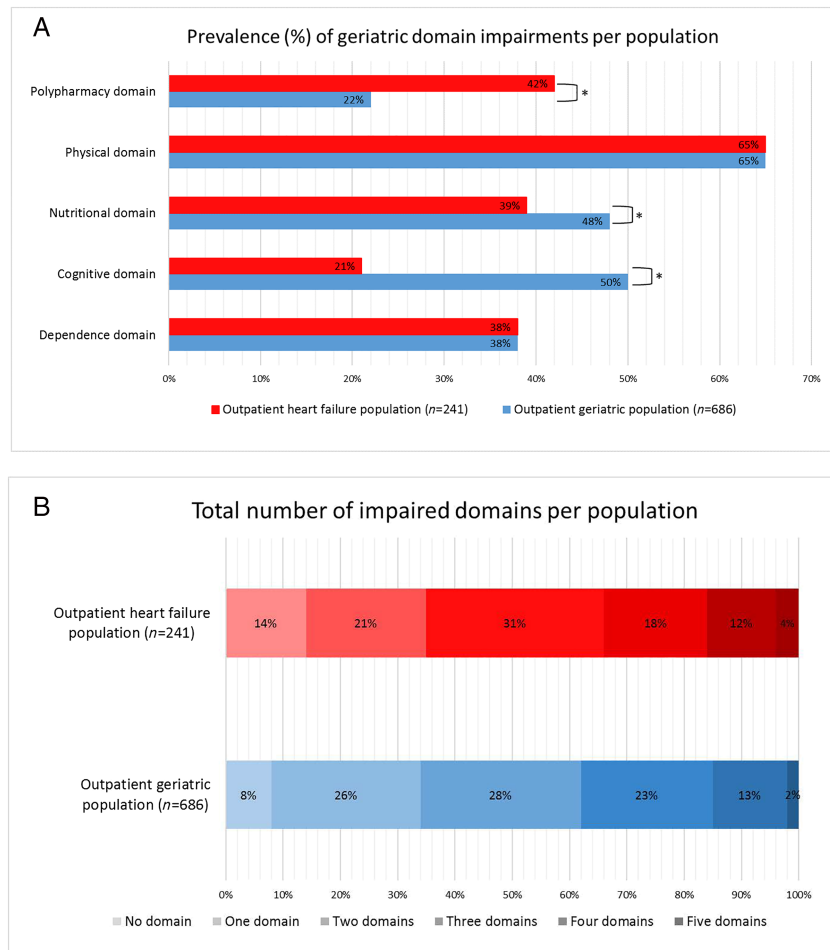## Geriatric domain impairments and mortality risk

In the HF population, impairments in the nutritional and cognitive domain were significantly associated with a higher 1 year mortality risk (*Figure 3*). In the geriatric population, impairments in the polypharmacy, physical, nutritional, and ADL dependency domains were significantly associated with 1 year mortality risk (*Figure 3*). In both populations, similar effect estimates were found for the relation between impairments of the different domains and 1 year mortality risk, except for the polypharmacy domain (HR, 95% CI was 1.3, 0.6–2.6 in the HF population and 2.9, 1.7–4.7 in the geriatric population) and the cognitive domain (HR, 95% CI was 3.1, 1.5–6.3 in the HF population and 1.6, 0.9–2.7 in the geriatric population) (*Figure 3*).

The age-adjusted and sex-adjusted HRs (95% CI) for one SD increase on the individual geriatric assessment items are shown in the supporting information. In the HF population, one SD increase in handgrip strength, MNA-SF score, MMSE score, number of prescribed drugs, and Katz score showed a 1.3 to 1.8 increased 1 year mortality risk. This was comparable with the results in the geriatric population, where these HRs ranged from 1.5 to 2.2 (Supporting Information, *Figure S1*).

An increasing number of impaired geriatric domains were associated with an increased 1 year mortality risk in both populations (*Table 2*); compared with zero to two impaired domains, age-adjusted and sex-adjusted mortality risk (HR, 95% CI) for three, four, or five impaired domains ranged from 1.6 (0.6–4.2) to 6.5 (2.1–20.1) in the HF population and from 1.4 (0.7–2.9) to 7.9 (2.9–21.3) in the geriatric population.

Figure 1 (A) Prevalence of geriatric domain impairments (%) for the outpatient heart failure population (*n* = 241) and the outpatient geriatric population (*n* = 686). (B) Total number of geriatric domain impairments (%) for the outpatient heart failure population (*n* = 241) and the outpatient geriatric population (*n* = 686). Definition of domains: dependence domain, Katz activities of daily living score > 1; cognitive domain, Mini Mental State Examination score < 24; nutritional domain, Mini Nutritional Assessment-Short Form score < 12; physical domain, low gait speed (<0.8 m/s) or low hand-grip strength (<20 kg for women and <30 kg for men); and polypharmacy domain, ≥10 prescribed drugs. *P-value < 0.05.


Discussion

This study illustrates that, in parallel with geriatric outpatients, outpatients with HF often have multiple geriatric domain impairments that adversely affect their prognosis. This together with the finding that outpatients with HF are even more likely to die within 1 year than geriatric outpatients supports the call for a more holistic approach in HF care, as recommended by 2016 ESC HF guidelines.[7] Although a multi-domain geriatric assessment may help to identify impairments across different geriatric domains, the impact of targeted interventions on patient-related outcomes should be subject for future research.

Studies including a multi-domain geriatric assessment in older patients with HF are limited.[4,8] Most studies included

hospitalized patients with HF,[19,20] only focused on physical frailty,[5,21,22] and used age-matched community-dwelling older adults as a comparator group.[23–25] When comparing our results with studies in hospitalized settings, prevalence of geriatric domains seems to be less prevalent and less severe in the outpatient HF population.[19,20] This is in line with our expectations that an outpatient population is in better health than those hospitalized. However, performing a multi-domain geriatric assessment at the outpatient clinic has some major advantages. The environment suits better, and identification of vulnerable patients with HF in an earlier phase (before hospitalization) provides more opportunities for setting up individualized care programmes and advance care planning.

In this study, we used widely accessible and easy to use clinical tools to define the different geriatric domains.[26]

Figure 2 Kaplan–Meier survival curve per population (log rank 0.027) and age-adjusted and sex-adjusted 1 year mortality risk (HR, 95% CI). Observed survival is analysed by Kaplan–Meier whereas the association between heart failure and mortality is analysed with Cox regression analysis, adjusted for age and sex. *P-value < 0.05. CI, confidence interval; HR, hazard ratio.
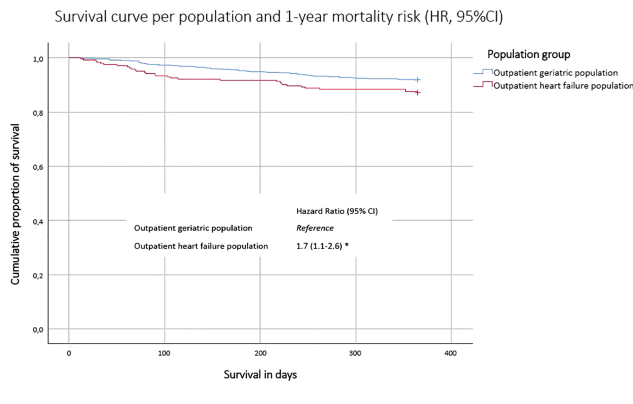
The total multi-domain geriatric assessment used in this study needs minimal training, takes approximately 25 min, could be easily performed by an HF nurse, and is therefore highly feasible in outpatient HF clinics. Similar to the geriatric approach, this assessment should not only function as an inventory for different health problems for which targeted interventions can be applied but also guide physicians to shift focus from a 'problem-based, disease-orientated' approach to 'goal-orientated, integrated' approach, with attention for personalized treatment goals and advance care planning.[27,28] Earlier research has shown that this holistic approach improves outcomes in older hospitalized patients and patients with hip fractures[29–31] and delays progression to frailty in pre-frail outpatients.[9] In another outpatient setting, this multidisciplinary approach is currently implemented in regular care for patients with aortic valve stenosis, where a multidisciplinary 'heart team' makes treatment decisions in terms of undergoing a transcatheter

Figure 3 Association impairment geriatric domains with 1 year mortality in different patient populations, HR (95% CI). Model 1: adjusted for age and sex. Definition of domains: polypharmacy domain, ≥10 prescribed medications; physical domain, low gait speed (<0.8 m/s) or low handgrip strength (<20 kg for women and <30 kg for men); nutritional domain, score < 12 on Mini Nutritional Assessment-Short Form; cognitive domain, score < 24 on Mini Mental State Examination; and ADL, dependence in >1 on Katz ADL score. ADL, activities of daily living; CI, confidence interval; HR, hazard ratio.
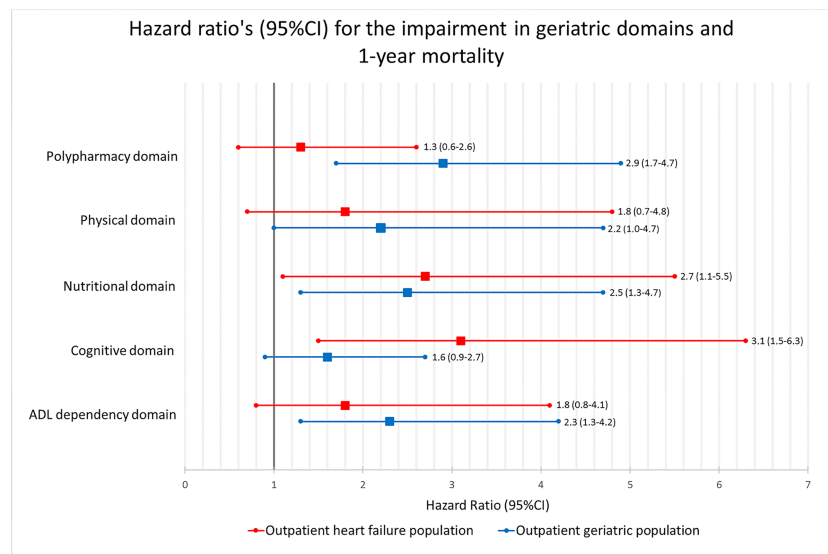

Table 2 Risk of 1 year mortality according to total number of impaired domains for both populations

	Outpatient heart failure population HR (95% CI)[a]	Outpatient geriatric population HR (95% CI)[a]
0–2 domains impaired	Reference	Reference
3 domains impaired	1.6 (0.6–4.2)	1.4 (0.7–2.9)
4 domains impaired	2.8 (1.1–7.3)	3.4 (1.7–6.8)
5 domains impaired	6.5 (2.1–20.1)	7.9 (2.9–21.3)

CI, confidence interval; HR, hazard ratio.
[a]Model 1: adjusted for age and sex.

aortic valve implantation procedure, to the satisfaction of physicians and patients.[32] HF care might benefit even more from a holistic approach, as it is more than a 'go or no go' for a procedure, being more gradual and having more treatment options. Future research should further investigate how the different domains are most effectively assessed and how to optimize personalized care in older patients with HF. To investigate this, we are evaluating a multidisciplinary care programme in an outpatient HF clinic, which involves a geriatric screening and if indicated a multi-domain geriatric assessment by a geriatric nurse. Patients will be discussed in a multidisciplinary team and given individualized care based on the multi-domain impairments. Care consumption, quality of life, and adverse events will be monitored.

This study has several strengths. This study used a standardized work-up for both the geriatric outpatients and the patients with HF, which resulted in a uniformed data collection, making comparison possible. Furthermore, the populations presented in our study are an accurate representation of all older patients referred to an outpatient clinic for medical care, as hardly any exclusion criteria were applied to both cohorts. Lastly, we obtained, although unintentionally, the mortality data of both cohorts before the COVID-19 pandemic, which has caused excess mortality, especially in this older population.

Limitations of the current study must also be addressed. First, the number of patients with HFpEF in our cohort is lower than expected, and this may explain the underrepresentation of women. Patients with HFrEF are preferentially referred for up-titration of guideline-directed medication, while patients with HFpEF are most often referred back to the general practitioner due to the absence of guideline-directed medical therapy for HFpEF. Second, this study failed to include two other important geriatric domains, for example, the psychological and social domains.[28] Although these domains are of added value, especially for quality of life, the domains assessed in this study are more commonly associated with adverse outcomes and thus may be of greater value to assess patients at risk of these adverse outcomes.[5,8] However, assessing these domains to ensure holistic care is recommended in future research and future care.

Third, using polypharmacy as a proxy for multimorbidity might not be sufficient when comparing these specific populations. Due to guideline-directed therapy, the number of prescribed medication is expected to be higher in the HF population. However, using a cut-off value of >10 prescribed medications, we expect to have selected the patients with evident multimorbidity in both cohorts. Another limitation is the use of the MMSE, developed to screen for Alzheimer's disease, to assess impairments in the cognitive domain.[33] The aetiology of cognitive impairment in patients with HF is more likely to be vascular, which mostly results in limitations in planning and reasoning, and to lesser extent in memory function, which are not as easily detected with the MMSE.[34,35] This might have influenced the number of patients with cognitive impairment in the HF population and resulted in a mismatch with earlier research.[36] Proper detection of cognitive impairment is clinically relevant as it limits a patients' ability to comply with complex medical regimes.

In conclusion, to implement holistic care, as called for in the 2016 ESC HF guideline, our data provide evidence to approach an older patient with HF like a geriatric patient and conduct a similar multi-domain geriatric assessment in patients with HF at the outpatient clinic.

Acknowledgements

Conflict of interest

Funding

Supporting information

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

Figure S1. Association one standard deviation increase on geriatric assessment items with 1-year mortality in different patient populations, HR (95% CI).

Table S1. Baseline patient characteristics of patients with HFmrEF or HFrEF (*n* = 168) and patients with HFpEF (*n* = 39).

References

1. van Riet EE, Hoes AW, Wagenaar KP, Limburg A, Landman MA, Rutten FH. Epidemiology of heart failure: the prevalence of heart failure and ventricular dysfunction in older adults over time. A systematic review. *Eur J Heart Fail* 2016; **18**: 242–252.

2. Minamisawa M, Seidelmann SB, Claggett B, Hegde SM, Shah AM, Desai AS, Lewis EF, Shah SJ, Sweitzer NK, Fang JC, Anand IS, O'Meara E, Rouleau JL, Pitt B, Solomon SD. Impact of malnutrition using geriatric nutritional risk index in heart failure with preserved ejection fraction. *JACC Heart Fail* 2019; **7**: 664–675.

3. Doehner W, Ural D, Haeusler KG, Celutkiene J, Bestetti R, Cavusoglu Y, Peña-Duque MA, Glavas D, Iacoviello M, Laufs U, Alvear RM, Mbakwem A, Piepoli MF, Rosen SD, Tsivgoulis G, Vitale C, Yilmaz MB, Anker SD, Filippatos G, Seferovic P, Coats AJS, Ruschitzka F. Heart and brain interaction in patients with heart failure: overview and proposal for a taxonomy. A position paper from the Study Group on Heart and Brain Interaction of the Heart Failure Association. *Eur J Heart Fail* 2018; **20**: 199–215.

4. Gorodeski EZ, Goyal P, Hummel SL, Krishnaswami A, Goodlin SJ, Hart LL, Forman DE, Wenger NK, Kirkpatrick JN, Alexander KP, Geriatric Cardiology Section Leadership Council, American College of Cardiology. Domain management approach to heart failure in the geriatric patient: present and future. *J Am Coll Cardiol* 2018; **71**: 1921–1936.

5. Cacciatore F, Abete P, Mazzella F, Viati L, Della Morte D, D'Ambrosio D, Gargiulo G, Testa G, Santis D, Galizia G, Ferrara N, Rengo F. Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *Eur J Clin Invest* 2005; **35**: 723–730.

6. Kleipool EE, Hoogendijk EO, Trappenburg MC, Handoko ML, Huisman M, Peters MJ, Muller M. Frailty in older adults with cardiovascular disease: cause, effect or both? *Aging Dis* 2018; **9**: 489–497.

7. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016; **37**: 2129–2200.

8. Kleipool EEF, Wiersinga JHI, Trappenburg MC, van Rossum AC, van Dam CS, Liem SS, Peters MJL, Handoko ML, Muller M. The relevance of a multidomain geriatric assessment in older patients with heart failure. *ESC Heart Fail* 2020; **7**: 1264–1272.

9. Mazya AL, Garvin P, Ekdahl AW. Outpatient comprehensive geriatric assessment: effects on frailty and mortality in old people with multimorbidity and high health care utilization. *Aging Clin Exp Res* 2019; **31**: 519–525.

10. SAJvdS HFMR-M, Peters MJL, Kleipool EEF, Trappenburg MC, Muller M. In pressMortality risk and its association with geriatric domain deficits in older outpatients. *Gerontology* 2020 In press.

11. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr* 2017; **17**: 230.

12. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M, European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010; **39**: 412–423.

13. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, Brach J, Chandler J, Cawthon P, Connor EB, Nevitt M, Visser M, Kritchevsky S, Badinelli S, Harris T, Newman AB, Cauley J, Ferrucci L, Guralnik J. Gait speed and survival in older adults. *JAMA* 2011; **305**: 50–58.

14. Lilamand M, Kelaiditi E, Cesari M, Raynaud-Simon A, Ghisolfi A, Guyonnet S, Vellas B, van Kan GA, Toulouse Frailty Platform Team. Validation of the Mini Nutritional Assessment-Short Form in a population of frail elders without disability. Analysis of the Toulouse Frailty Platform population in 2013. *J Nutr Health Aging* 2015; **19**: 570–574.

15. Vellas B, Villars H, Abellan G, Soto ME, Rolland Y, Guigoz Y, Morley JE, Chumlea W, Salva A, Rubenstein LZ, Garry P. Overview of the MNA—its history and challenges. *J Nutr Health Aging* 2006; **10**: 456–463 discussion 63-5.

16. Folstein MF, Robins LN, Helzer JE. The Mini-Mental State Examination. *Arch Gen Psychiatry* 1983; **40**: 812.

17. O'Bryant SE, Humphreys JD, Smith GE, Ivnik RJ, Graff-Radford NR, Petersen RC, Lucas JA. Detecting dementia with the Mini-Mental State Examination in highly educated individuals. *Arch Neurol* 2008; **65**: 963–967.

18. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc* 1983; **31**: 721–727.

19. Warraich HJ, Kitzman DW, Whellan DJ, Duncan PW, Mentz RJ, Pastva AM, Nelson MB, Upadhya B, Reeves GR. Physical function, frailty, cognition, depression, and quality of life in hospitalized adults ≥60 years with acute decompensated heart failure with preserved versus reduced ejection fraction. *Circ Heart Fail* 2018; **11**: e005254.

20. Reeves GR, Whellan DJ, Patel MJ, O'Connor CM, Duncan P, Eggebeen JD, Morgan TM, Hewston LA, Pastva AM, Kitzman DW. Comparison of frequency of frailty and severely impaired physical function in patients ≥60 years hospitalized with acute decompensated heart failure versus chronic stable heart failure with reduced and preserved left ventricular ejection fraction. *Am J Cardiol* 2016; **117**: 1953–1958.

21. Gastelurrutia P, Lupon J, Altimir S, de Antonio M, Gonzalez B, Cabanes R, Rodríguez M, Urrutia A, Domingo M, Zamora E, Díez C, Coll R, Bayes-Genis A. Fragility is a key determinant of survival in heart failure patients. *Int J Cardiol* 2014; **175**: 62–66.

22. Uchmanowicz I, Mlynarska A, Lisiak M, Kaluzna-Oleksy M, Wleklik M, Chudiak A, Dudek M, Migaj J, Hinterbuchner L, Gobbens R. Heart failure and problems with frailty syndrome: why it is time to care about frailty syndrome in heart failure. *Card Fail Rev* 2019; **5**: 37–43.

23. Muntwyler J, Abetel G, Gruner C, Follath F. One-year mortality among unselected outpatients with heart failure. *Eur Heart J* 2002; **23**: 1861–1866.

24. Owen A. Life expectancy of elderly and very elderly patients with chronic heart failure. *Am Heart J* 2006; **151**: 1322 e1–4.

25. Koudstaal S, Pujades-Rodriguez M, Denaxas S, Gho J, Shah AD, Yu N, Patel RS, Gale CP, Hoes AW, Cleland JG, Asselbergs FW, Hemingway H. Prognostic burden of heart failure recorded in primary care, acute hospital admissions, or both: a population-based linked electronic health record cohort study in 2.1 million people. *Eur J Heart Fail* 2017; **19**: 1119–1127.

26. Hernandez Torres C, Hsu T. Comprehensive geriatric assessment in the older adult with cancer: a review. *Eur Urol Focus* 2017; **3**: 330–339.

27. Blom J, den Elzen W, van Houwelingen AH, Heijmans M, Stijnen T, Van den Hout W, Gussekloo J. Effectiveness and cost-effectiveness of a proactive, goal-oriented, integrated care model in general practice for older people. A cluster randomised controlled trial: Integrated Systematic Care for older People—the ISCOPE study. *Age Ageing* 2016; **45**: 30–41.

28. Goyal P, Gorodeski EZ, Flint KM, Goldwater DS, Dodson JA, Afilalo J, Maurer MS, Rich MW, Alexander KP, Hummel SL. Perspectives on

implementing a multidomain approach to caring for older adults with heart failure. *J Am Geriatr Soc* 2019; **67**: 2593–2599.

29. Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment: a meta-analysis of controlled trials. *Lancet* 1993; **342**: 1032–1036.

30. Ellis G, Langhorne P. Comprehensive geriatric assessment for older hospital patients. *Br Med Bull* 2004; **71**: 45–59.

31. Van Craen K, Braes T, Wellens N, Denhaerynck K, Flamaing J, Moons P, Boonen S, Gosset C, Petermans J, Milisen K. The effectiveness of inpatient geriatric evaluation and management units: a systematic review and meta-analysis. *J Am Geriatr Soc* 2010; **58**: 83–92.

32. Khosravi ADW, Wendler O. TAVI 2018: from guidelines to practice. *ESC: e-journal of Cardiologie Practice* 2018; **15**.

33. Arevalo-Rodriguez I, Smailagic N, Roque IFM, Ciapponi A, Sanchez-Perez E, Giannakou A, Pedraza OL, Cosp XB, Cullum S. Mini-Mental State Examination (MMSE) for the detection of Alzheimer's disease and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database Syst Rev* 2015; **3**: CD010783.

34. Dong Y, Sharma VK, Chan BP, Venketasubramanian N, Teoh HL, Seet RC, Tanicala S, Chan YH, Chen C. The Montreal Cognitive Assessment (MoCA) is superior to the Mini-Mental State Examination (MMSE) for the detection of vascular cognitive impairment after acute stroke. *J Neurol Sci* 2010; **299**: 15–18.

35. O'Brien JT, Erkinjuntti T, Reisberg B, Roman G, Sawada T, Pantoni L, Bowler JV, Ballard C, DeCarli C, Gorelick PB, Rockwood K, Burns A, Gauthier S, DeKosky ST. Vascular cognitive impairment. *Lancet Neurol* 2003; **2**: 89–98.

36. Cannon JA, Moffitt P, Perez-Moreno AC, Walters MR, Broomfield NM, McMurray JJV, Quinn TJ. Cognitive impairment and heart failure: systematic review and meta-analysis. *J Card Fail* 2017; **23**: 464–475.