Age-specific differences in non-cardiac comorbidities among elderly patients hospitalized with heart failure: a special focus on young-old, old-old, and oldest-old

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Abstract

Background: Despite the growing epidemic of heart failure (HF), there is limited data available to systematically compare non-cardiac comorbidities in the young-old, old-old, and oldest-old patients hospitalized for HF. The precise differences will add valuable information for better management of HF in elderly patients.

Methods: A total of 1053 patients aged 65 years or older hospitalized with HF were included in this study. Patients were compared among three age groups: (1) young-old: 65 to 74 years, (2) old-old: 75 to 84 years, and (3) oldest-old: ≥85 years. Clinical details of presentation, comorbidities, and prescribed medications were recorded.

Results: The mean age was 76.7 years and 12.7% were 85 years or older. Most elderly patients with HF (97.5%) had at least one of the non-cardiac comorbidities. The patterns of common non-cardiac comorbidities were different between the young-old and oldest-old group. The three most common non-cardiac comorbidities were anemia (53.6%), hyperlipidemia (45.9%), and diabetes (42.4%) in the young-old group, while anemia (73.1%), infection (58.2%), and chronic kidney disease (44.0%) in the oldest-old group. Polypharmacy was observed in 93.0% elderly patients with HF. Additionally, 29.2% patients were diagnosed with infection, and 67.0% patients were prescribed antibiotics. However, 60.4% patients were diagnosed with anemia with only 8.9% of them receiving iron repletion.

Conclusions: Non-cardiac comorbidities are nearly universal in three groups but obviously differ by age, and inappropriate medications are very common in elderly patients with HF. Further treatment strategies should be focused on providing optimal medications for age-specific non-cardiac conditions.

Keywords: Heart failure; Elderly; Non-cardiac comorbidity; Polypharmacy

Introduction

Heart failure (HF) is a major public health problem, primarily because of the aging of the population.[1] Its prevalence has doubled from 6% in those aged from 60 to 79 years to approximately 14% in those aged 80 years or older.[2] HF rarely occurs in isolation or represents a single maladaptive process that affects elderly patients. Cardiac and non-cardiac comorbidities, polypharmacy, and geriatric conditions all contribute to the health outcomes of elderly patients with HF.[3-8] These factors and their complex interplay are essential aspects in older patients with important implications on management and prognosis.[9-11] Thus, unlike the general population, clinicians caring for elderly patients with HF must consider all factors mentioned above in addition to the evaluation of the etiology, stage, and chronicity of HF.

Although there is a perception that elderly patients hospitalized for HF are becoming more medically complex, and non-cardiac comorbidities and inappropri-

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ate treatment differ by age in elderly patients with HF, there is a lack of evidence on the precise differences among young-old, old-old, and oldest-old patients in non-cardiac comorbidities and medication regimens.[12] Therefore, a comprehensive and multidimensional assessment of elderly patients with HF in different age groups is essential for optimizing clinical management and treatment decision making.

To address the major issues mentioned above, this study had two objectives. The first was to give a comprehensive assessment of non-cardiac conditions among elderly patients with HF stratified by age, which are frequently overlooked during routine HF management. The second objective was to compare the medication regimen complexity in different age groups, including the number of medications, potentially inappropriate medications for non-cardiac conditions, and the use of guideline-directed therapies.

Methods

Ethical approval

This study was approved by the Ethics Committee of China-Japan Friendship Hospital (No. 2019-83-k54). Given its retrospective nature and the fact that data analysis was performed anonymously, it was exempt from obtaining informed consent from patients.

Study population

This was a real-world research at the Heart Failure Center in China-Japan Friendship Hospital. Patients admitted to hospital and aged 65 years or older were recruited consecutively between January 1, 2013, and December 31, 2017. The diagnosis of HF (new-onset HF or decompensation of chronic HF) was determined according to the clinical practice guidelines by the Chinese Society of Cardiology,[13,14] and was briefly based on: (1) symptoms, for example, dyspnea, fatigue, or decreased exercise capacity; (2) signs, for example, edema or rales; (3) B type natriuretic peptide or N-terminal pro-B type natriuretic peptide, to differentiate the HF diagnosis for patients with dyspnea; (4) structural and functional abnormalities on echocardiography.

A total of 1053 patients were enrolled for further analysis. They were categorized as three groups according to their age: (1) young-old: 65 to 74 years ($n = 401$), (2) old-old: 75 to 84 years ($n = 518$), and (3) oldest-old: ≥85 years ($n = 134$).

Data collection

For patients hospitalized with HF, clinical details of presentation (eg, demographics, echocardiographic, and biochemical data) at admission and discharge were recorded.

We also extracted information about comorbidities. Because all patients had HF, this condition was not considered a comorbidity. To describe comorbidities, we categorized comorbidities as cardiac and non-cardiac. Cardiac comorbidities were defined as any of the following: coronary heart disease, hypertension, atrial fibrillation, cardiomyopathy, and valvular disorders. To describe non-cardiac comorbidities, we selected 13 most common conditions: anemia, diabetes, chronic kidney disease (CKD), stroke, dyslipidemia, infection, chronic obstructive pulmonary disease (COPD) or asthma, cancer, osteoporosis, sleep apnea, thyroid disease, depression, and cognitive impairment. For each condition, we reported prevalence as the percentage of patients with a diagnosis recorded in their hospital discharge record. Patients without a diagnosis were assumed to be free from that condition.

Admission and discharge medications details were collected, including guideline-directed medications (eg, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], β-blockers, and mineralocorticoid receptor antagonists [MRAs]), symptomatic relieved medications (eg, diuretics, digitalis, nitrates), and other prescription medications (eg, iron repletion, antibiotic, anti-platelet, oral anti-coagulant etc). The number of co-administered medications of every patient was counted. Polypharmacy was defined as the use of at least 5 co-administered medications.[15]

Statistical analysis

Data are presented as frequencies (%) for categorical data, means, and standard deviation for normally distributed continuous variables, or medians and interquartile range for non-normally distributed continuous variables. Comparisons were performed by analysis of variance and followed up with a *post hoc* Bonferroni test for symmetrical continuous, Mann-Whitney *U* or Kruskal-Wallis *H* test for non-symmetric continuous, and χ^2 tests or Continuity correction or Fisher exact test for categorical variables. All $P < 0.05$ from two-sided tests were accepted as statistically significant. All statistical analyses were performed using SPSS 23.0 software (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of elderly patients hospitalized with HF

A total of 1053 elderly patients hospitalized with HF were included in the present analysis. Demographic, echocardiographic, and biochemical data on the three groups were given in Table 1 and Table S1, http://links.lww.com/CM9/A132. The mean age was 76.7 ± 6.6 years and 52.9% were male. There were 401 (38.1%) young-old patients (median age 70.0 years), 518 (49.2%) old-old patients (median age 79.1 years), and 134 (12.7%) oldest-old patients (median age 87.7 years). Age distribution of elderly patients hospitalized with HF was given in Figure S1, http://links.lww.com/CM9/A130.

Elderly patients with HF were inclined to unplanned admissions with age, and the emergency admission proportion in the oldest-old group was up to 41.0%, nearly doubled compared with the young-old group

Table 1: Clinical characteristics of elderly patients hospitalized with heart failure by age group.

Indices	Total	Young-old (65–74 years)	Old-old (75–84 years)	Oldest-old (≥85 years)	*P* values
Patients, *n* (%)	1053 (100)	401 (38.1)	518 (49.2)	134 (12.7)	–
Age, years	76.7 ± 6.6	70.0 ± 2.9	79.1 ± 2.8†	87.7 ± 2.8†	<0.001
Male, *n* (%)	557 (52.9)	198 (49.4)	294 (56.8)†	65 (48.5)	0.047
BMI, kg/m^2	24.3 ± 4.2	24.7 ± 4.2	24.2 ± 4.2	23.5 ± 3.8†	0.043
Underweight	77 (7.3)	28 (7.0)	34 (7.3)	15 (11.2)	0.44
SBP, mmHg	131.5 ± 21.9	130.1 ± 22.8	132.7 ± 21.9	131.4 ± 19.1	0.201
DBP, mmHg	72.7 ± 12.4	74.9 ± 11.8	71.7 ± 12.7†	69.9 ± 12.3†	<0.001
Heart rate, bpm	78.2 ± 16.0	77.5 ± 14.8	77.8 ± 15.8	82.0 ± 19.7†	0.013
BNP, pg/mL*	543.0 (199.0, 1238.0)	405.0 (140.8, 1034.5)	503.2 (196.0, 1393.0)	926.0 (437.0, 1339.1)†	0.001
NT-proBNP, pg/mL*	2082.0 (794.8, 6156.0)	1939.0 (669.6, 3645.5)	1995.0 (655.6, 6409.5)	2670.0 (1343.0, 11241.0)†	0.045
Hemoglobin, g/L	118.7 ± 22.4	121.2 ± 23.0	118.4 ± 22.2	112.5 ± 19.8†	<0.001
eGFR, mL/min/1.73 m^2	67.1 ± 29.0	71.8 ± 28.8	64.6 ± 29.5†	62.6 ± 25.7†	<0.001
Glucose, mmol/L	7.5 ± 3.3	7.5 ± 3.5	7.6 ± 3.3	7.2 ± 2.9	0.536
LVEF, %	50.3 ± 8.5	48.3 ± 9.2	50.8 ± 7.9*,†	54.4 ± 6.4†	<0.001
LVEF ≤40%	286 (27.2)	116 (28.9)	137 (26.4)	33 (24.6)	0.009
40%< LVEF <50%	183 (17.4)	I87 (21.7)	80 (15.4)	16 (1.9)†	–
LVEF ≥50%	584 (55.5)	198 (49.4)	301 (58.1)	85 (63.4)†	–
Length of stay, days	16 (10–24)	15 (10–21)	16 (10–24)	18 (12–29)†	0.004
Emergency admission, *n* (%)	332 (31.5)	97 (24.2)	180 (34.7)†	55 (41.0)†	<0.001

Values are mean ± standard deviation or number (%) unless indicated otherwise. * Median [interquartile range]. † Significant difference compared with the young-old group ($P < 0.025$). BMI: Body mass index; underweight defined as BMI <18.5 kg/m^2; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BNP: B-type natriuretic peptide; NT-proBNP: N-terminal pro-B-type natriuretic peptide; eGFR: Estimated glomerular filtration rate; LVEF: Left ventricular ejection fraction.

($P < 0.001$). The median hospital length of stay was longest in the oldest-old group (18 days), and the shortest in the young-old group (15 days) ($P = 0.004$).

Cardiac and non-cardiac comorbidities of elderly patients hospitalized with HF

The elderly patients with HF typically have extensive comorbidities with the number ranged from 0 to 11. Overall, 97.1% of the elderly patients with HF had two or more additional conditions [Table 2]. Not surprisingly, the number of comorbidities in the elderly patients with HF was increased with age [Figure 1A].

The burden of non-cardiac comorbidities was obviously greater than that of cardiac comorbidity in all the three groups [Figure 1B]. It is noteworthy that the number of individual non-cardiac comorbidities was increased with age; the oldest-old group had a higher prevalence of ≥3 non-cardiac morbidities (68.7% *vs.* 65.8% and 53.1%) compared with the old-old and the young-old group, respectively ($P < 0.001$).

The common non-cardiac comorbidity patterns among the three groups were different [Figure 1C and 1D]. The three most common non-cardiac comorbidities in the young-old group were anemia (53.6%), hyperlipidemia (45.9%), and diabetes (42.4%). While in the oldest-old group, the three most common non-cardiac comorbidities were anemia (73.1%), infection (58.2%), and CKD (44.0%).

A total of 60.4% elderly patients with HF had anemia which was the highest represented non-cardiac comorbidity in all the three groups. Almost three-quarters of the oldest-old patients with HF had anemia, but less than 1% measured the serum ferritin to diagnose iron deficiency. A dramatical increase in the prevalence of infection with age was observed, doubling in prevalence from 29.2% in the young-old group to 58.2% in the oldest-old group ($P < 0.001$). In addition, the average prevalence of stroke was 26.8%, with a significant increase in the oldest-old group, nearly twice higher compared with the young-old group (35.1% *vs.* 19.0%, $P < 0.001$). Besides, the prevalence of CKD, COPD or asthma, cancer, and osteoporosis was also greatly increased from the young-old to the oldest-old groups (all $P < 0.05$) [Table 2 and Figure 1C].

Medications at admission and discharge of the elderly patients hospitalized with HF

Prescribed medications among three groups were given in Table 3 and Table S2, http://links.lww.com/CM9/A133. On average, the elderly patients with HF take 9.4 prescription medications per day, not including over-the-counter or complementary and alternative medications. The number of medications prescribed was increased with age. Polypharmacy (≥5 medications) occurred in 93.0% of the elderly patients with HF and 43.0% of them was prescribed at least ten medications. The proportion of the elderly patients prescribed at least ten medications was approaching twice higher in the oldest-old group compared with that in the young-old group (65.7% *vs.* 33.7%, $P < 0.01$). Of note, there were 5 (3.7%) patients in the oldest-old group taking 20 or more medications.

Additionally, underuse and overuse of medications were very common in the elderly patients with HF [Figure 2]. The overuse of medications was mainly observed for

Table 2: Cardiac and non-cardiac comorbidities of elderly patients hospitalized with heart failure by age group.

Indices	Total $n = 1053$	Young-old (65–74 years), $n = 401$ (38.1%)	Old-old (75–84 years), $n = 518$ (49.2%)	Oldest-old (≥85 years), $n = 134$ (12.7%)	*P* value
Cardiac comorbidities					
Coronary heart disease	728 (68.9)	244 (60.8)	387 (74.7)*	97 (72.4)*	<0.001
Cardiomyopathy	75 (7.1)	45 (11.2)	25 (4.8)*	5 (3.7)*	<0.001
Valvular disorders	84 (8.0)	44 (11.0)	30 (5.8)*	10 (7.5)*	0.016
Hypertension	806 (76.5)	292 (72.8)	414 (79.9)*	100 (74.6)	0.036
Atrial fibrillation	365 (34.7)	129 (32.2)	180 (34.7)	56 (41.8)	0.128
Non-cardiac comorbidities					
Anemia	636 (60.4)	215 (53.6)	323 (62.4)*	98 (73.1)*	<0.001
Dyslipidemia	476 (45.2)	184 (45.9)	240 (46.3)	52 (38.8)	0.279
Infection	424 (40.3)	117 (29.2)	229 (44.2)*	78 (58.2)*	<0.001
Diabetes	423 (40.2)	170 (42.4)	217 (41.9)	36 (26.9)*	0.003
Chronic kidney disease	401 (38.1)	126 (31.4)	216 (41.7)*	59 (44.0)*	0.002
Stroke	282 (26.8)	76 (19.0)	159 (30.7)*	47 (35.1)*	<0.001
COPD or asthma	204 (19.4)	60 (15.0)	110 (21.2)*	34 (25.4)*	0.010
Cancer	141 (13.4)	43 (10.7)	72 (13.9)	26 (19.4)*	0.034
Osteoporosis	62 (5.9)	17 (4.2)	29 (5.6)	16 (11.9)*	0.004
Sleep apnea	58 (5.5)	21 (5.2)	27 (5.2)	10 (7.5)	0.569
Thyroid disease	55 (5.2)	20 (5.0)	31 (6.0)	4 (3.0)	0.367
Depression	31 (2.9)	11 (2.7)	16 (3.1)	4 (3.0)	0.953
Cognitive impairment	19 (1.8)	2 (0.5)	13 (2.5)	4 (3.0)*	0.023
No. of comorbidities					
≥2	1022 (97.1)	376 (93.8)	512 (98.8)*	134 (100)*	<0.001
≥5	504 (47.9)	165 (41.1)	299 (57.7)*	85 (63.4)*	<0.001
No. of non-cardiac comorbidities					
≥1	1027 (97.5)	383 (95.5)	511 (98.6)*	133 (99.3)*	0.004
≥3	646 (61.3)	213 (53.1)	341 (65.8)*	92 (68.7)*	<0.001

Values are *n* (%). * Significant difference compared with the young-old group ($P < 0.025$). COPD: Chronic obstructive pulmonary disease.

antibiotics among all the three groups, with 29.2%, 44.2%, and 58.2% diagnosed with infection, while 64.8%, 65.1%, and 81.3% prescribed with antibiotics in the young-old, old-old, and oldest-old group, respectively. The underuse of medications was mainly observed for the iron repletion; 60.4% patients were diagnosed with anemia in our study, but only 8.9% of them received iron repletion. Compared to the young-old patients, the oldest-old patients were more likely to underuse iron repletion.

There was an inadequacy of guideline-directed HF medications in elderly patients with HF at admission [Table 3], especially in the oldest-old group; ACE inhibitors/ARBs, β-blockers, and MRAs were prescribed in the lowest rate of 39.8%, 53.0%, and 38.8%, respectively. Indeed, few patients appear to receive all the three medications simultaneously. There was an apparent further decrease of discharge medications in comparison with admission medications [Figure S2, http://links.lww.com/CM9/A131].

Discussion

In this study, we evaluated age-specific clinical profile, cardiac and non-cardiac comorbidities, and medication regimens among elderly patients hospitalized with HF. Our analysis identified that, unlike the general population, the burden of non-cardiac comorbidities was noticeably greater in elderly patients with HF compared with that of cardiac comorbidities, and the prevalence of these conditions particularly increased with age. Interestingly, the patterns of the most common non-cardiac comorbidities were apparently different between the young-old and oldest-old patients with HF. The presence of anemia, infection, CKD, and stroke was more common in the oldest-old patients. However, the frequency of dyslipidemia and diabetes was higher in the young-old patients. To our knowledge, this has not been adequately investigated in the previous studies. Our findings also confirmed that polypharmacy and inappropriate medications have increased dramatically in the elderly patients, especially in the oldest-old. Additionally, administration of unnecessary antibiotics for infection and inadequate administration of iron repletion for anemia were the most frequent inappropriate therapies. Our study complements the knowledge in regard to age-related changes in the clinical features among elderly patients hospitalized with HF.

Our study showed that the burden of non-cardiac comorbidities in elderly patients hospitalized with HF, particularly in the oldest-old patients, was greater than that of cardiac comorbidities. We observed that, among elderly patients, HF without non-cardiac comorbidities is very rare, occurring in only 2.5% of the patients and more than 60% of the elderly patients have three or more non-cardiac comorbidities. Our analysis was consistent with the prior studies which have identified that patients with HF have a large burden of non-cardiac

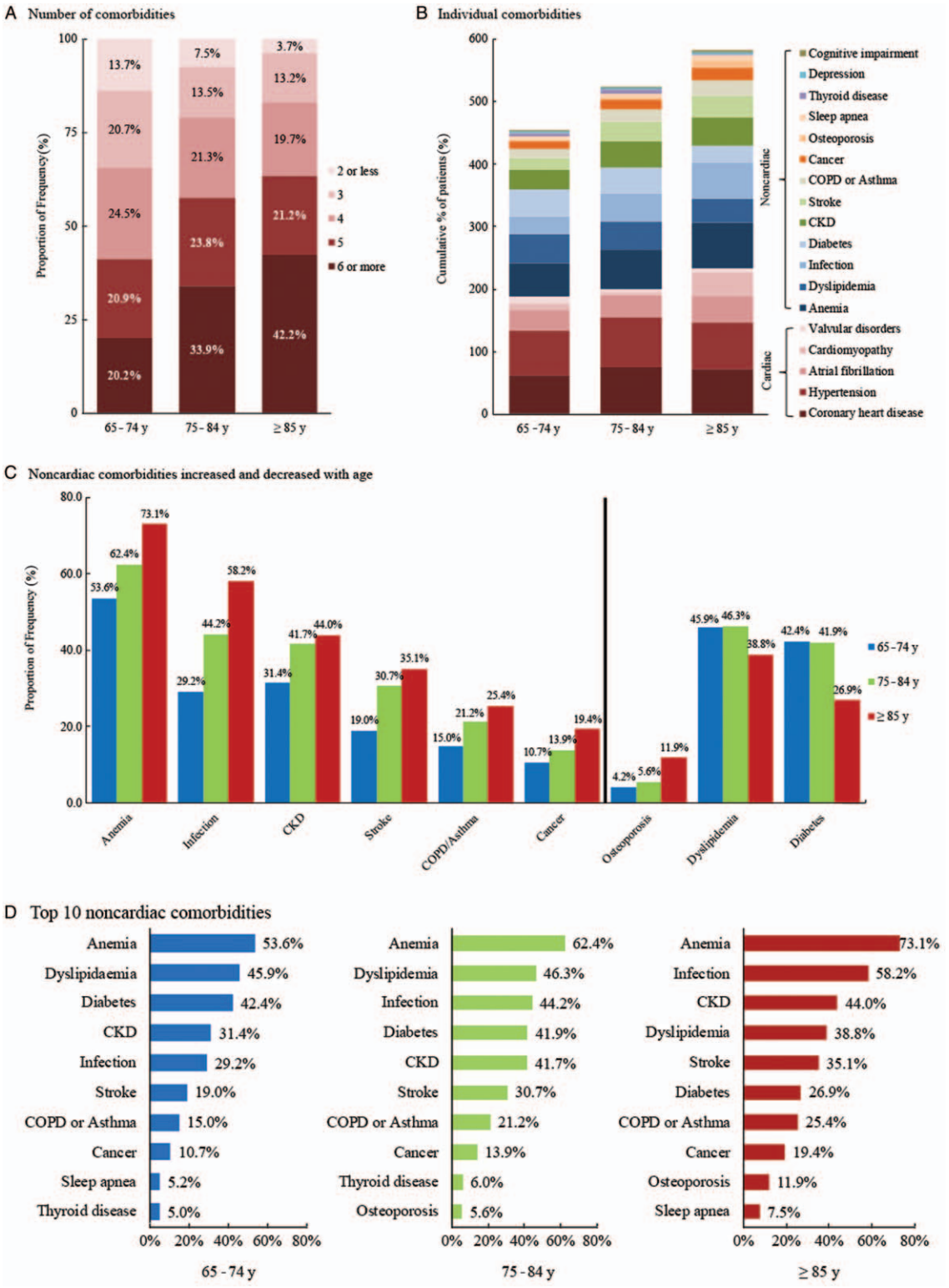

Figure 1: Comorbidities of elderly patients hospitalized with HF by age group. (A) The number of comorbidities in patients with HF. (B) Cumulative percentage of individual comorbidities in patients with HF. (C) Non-cardiac comorbidities in patients with HF. (D) The ten most common non-cardiac comorbidities in patients with HF. CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; HF: Heart failure; y: Years.

comorbidities.[16,17] According to the Get With The Guidelines-Heart Failure Registry, among patients admitted to hospital for HF, 82% had at least one non-cardiac comorbidity.[16] In the European Society of Cardiology HF Pilot survey, it was shown that the majority of patients (74%) with chronic HF had at least one of the non-cardiac comorbidities.[17]

The previous studies mainly focused on the comparison of the clinical features of HF between older and younger

Table 3: Medications at admission and discharge of elderly patients hospitalized with HF by age group.

Indices	Total $n = 1053$	Young-old (65–74 years), $n = 401$ (38.1%)	Old-old (75–84 years), $n = 518$ (49.2%)	Oldest-old (≥85 years), $n = 134$ (12.7%)	*P* value
Admission medications					
ACE-inhibitors/ARBs	620 (59.0)	248 (62.2)	319 (61.6)	53 (39.8)*	<0.001
β-Blockers	678 (64.4)	281 (70.1)	326 (62.9)*	71 (53.0)*	0.001
MRAs	436 (41.4)	184 (45.9)	200 (38.6)	52 (38.8)	0.069
Diuretics	847 (80.4)	324 (80.8)	403 (77.8)	120 (89.6)*	0.009
Digitalis	452 (42.9)	186 (46.4)	203 (39.2)	63 (47.0)	0.054
Nitrates	855 (81.2)	319 (79.6)	420 (81.1)	116 (86.6)	0.197
Anti-platelet	713 (67.7)	261 (65.1)	370 (71.4)*	82 (61.2)	0.028
Anti-coagulant	163 (15.5)	73 (18.2)	74 (14.3)	16 (11.9)	0.127
Statins	501 (47.6)	195 (48.6)	265 (51.2)	41 (30.6)*	<0.001
CCB	407 (38.7)	136 (33.9)	223 (43.1)*	48 (35.8)	0.014
Iron repletion	94 (8.9)	24 (6.0)	48 (9.3)	22 (16.4)*	0.001
Antibiotic	706 (67.0)	260 (64.8)	337 (65.1)	109 (81.3)*	0.001
Discharge medications					
ACE-inhibitors/ARBs	464 (44.1)	181 (45.1)	249 (48.1)	34 (25.4)*	<0.001
β-Blockers	529 (50.3)	226 (56.5)	262 (50.6)	41 (30.8)*	<0.001
MRAs	300 (28.5)	121 (30.2)	142 (27.4)	37 (27.6)	0.636
Diuretic	507 (48.1)	211 (52.6)	239 (46.1)	57 (42.5)	0.057
Digitalis	193 (18.3)	84 (20.9)	88 (17.0)	21 (15.7)	0.213
Nitrates	508 (48.2)	193 (48.1)	258 (49.8)	57 (42.5)	0.324
Anti-platelet	541 (51.4)	201 (50.1)	285 (55.0)	55 (41.0)*	0.013
Anti-coagulant	163 (15.5)	73 (18.2)	74 (14.3)	16 (11.9)	0.127
Statins	442 (42.0)	175 (43.6)	234 (45.2)	33 (24.6)*	<0.001
CCB	306 (29.1)	109 (27.2)	162 (31.3)	35 (26.1)	0.289
Iron repletion	72 (6.8)	20 (5.0)	36 (6.9)	16 (11.9)*	0.022
Number of medications	9.4 ± 4.0	8.7 ± 3.6	9.7 ± 4.2*	10.3 ± 4.0*	0.001
≥5	979 (93.0)	366 (91.3)	483 (93.2)	130 (97.0)	0.154
≥10	453 (43.0)	135 (33.7)	243 (46.9)*	88 (65.7)*	<0.001

Values are mean ± standard deviation or *n* (%). * Significant difference compared with the young-old group ($P < 0.025$). ACE: Angiotensin-converting enzyme; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker; MRAs: Mineralocorticoid receptor antagonists.

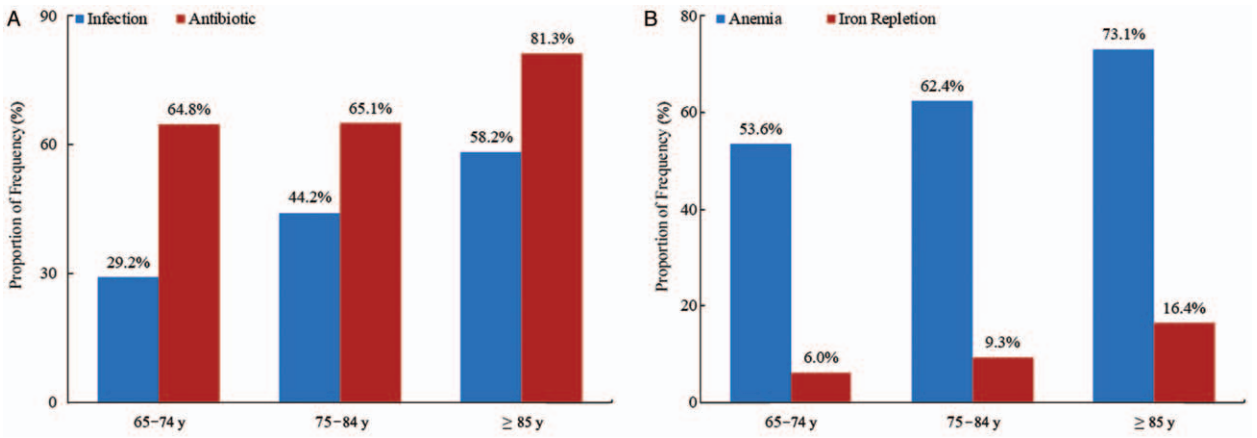

Figure 2: Non-cardiac comorbidities and medications of elderly patients hospitalized with HF by age group. (A) Infection diagnosed and antibiotic prescribed in patients with HF. (B) Anemia diagnosed and iron repletion prescribed in patients with HF. HF: Heart failure; y: Years.

patients with HF, or between patients <75 years and those ≥75 years. Our results identified that patients ≥85 years were obviously different from the young-old patients, even from those aged 75 to 84 years, with respect to the non-cardiac comorbidities. The oldest-old patients appear to be less likely to have traditional risk factors such as diabetes and dyslipidemia, as compared with the young-old patients. Anemia, infection, CKD, and stroke were the most common non-cardiac conditions in these patients. Accordingly, our results suggest that routine risk factors intervention was needed for the young-old patients; however, other non-cardiac conditions management such

as conservation of renal function and infection prevention was more important for the oldest-old patients.

In our study, more than 60% of the elderly patients were diagnosed with HF combined with anemia, which was higher than that in the previous surveys and registries with a range of 22% to 47%.[16,18,19] An increase of anemia prevalence with age was observed in our analysis and was supported by the recent studies.[18,20] Nearly two-thirds of the subjects were over 75 years in the current survey, which may partly explain higher anemia prevalence in the study. The results may also be associated with the poor clinical status (eg, hospitalized of decompensation HF) and malnutrition (eg, lower body mass index and albumin level) in our study population. As confirmed previously, compared with non-anemic patients with HF, anemic patients are more likely to have CKD, severe HF with worse functional status, lower exercise capacity, and increased mortality.[21,22] Therefore, anemia in elderly patients with HF, especially in the oldest-old, should definitely be taken seriously.

Stroke is the most common cause of disability in adult life and a major cause of death in China.[23,24] As an important non-cardiac comorbidity in the present study, the prevalence of stroke in elderly patients with HF was 26.8%, and up to 35.1% in the oldest-old adults, which was five- to six-fold compared with the general elderly population (5.2%) in China.[23] The prevalence of stroke was also noticeably higher than the previous trials conducted in western countries (7%–10%).[25-27] The observed results in high stroke prevalence may be associated with the fact that the heart and the brain share many pathophysiological mechanisms, such as atherosclerotic and thrombotic processes, which lead to acute damage and/or chronic organ dysfunction. But more likely, it was due to the current stroke incidence and mortality rates in China, which appear to be the highest in the world.[23] Stroke sequelae worsen performance status and quality of life, which in turn substantially contributes to mortality in HF patients.[28] This finding highlights the importance of clinical attention to stroke among elderly HF patients, and further studies on potential prevention strategies are warranted.

In accordance with the previous studies, polypharmacy was nearly universal in elderly patients with HF, especially among the oldest-old patients with a multimorbidity burden.[29,30] Our study showed that polypharmacy existed in more than 90% of elderly patients with HF, with 65.7% of the oldest-old patients with HF prescribed with at least ten medications, and 3.7% were even prescribed with more than 20 medications.

In addition to polypharmacy, inappropriate treatment was another profound problem in the management of HF among elderly patients.[31] For instance, infection was one of the main precipitating factors leading to HF admissions. As a result, broad-spectrum antibiotic prescriptions were common. In the present study, approximately 67.0% of the patients with HF were treated with antibiotics; however, only 40.3% have concomitant infection. Although our results of infection were more common compared with the previous surveys and registries both in Europe and the USA with a range of 10% to 21%,[32,33] routine use of empirical antibiotics in patients with HF was exacerbated in the absence of convincing evidence of infection. Previous studies provided evidence for the potentially harmful effects of antibiotics, particularly promoting anti-microbial resistance and life-threatening events, when used indiscriminately in clinically symptomatic HF patients without underlying infection.[16,34] The problem of administration of unnecessary antibiotics appeared to be even worse in the oldest-old patients than in the other two groups. The oldest-old patients got more infections (58.2%) and received more antibiotics (81.3%). Reasons for antibiotic overuse in the oldest-old patients are myriad, including diagnostic uncertainty, physicians' desire for an improved outcome, treatment of conditions caused by colonizing or contaminating organisms, and concern for bacterial superinfection, suggesting that infection indicators (eg, neutrophils, procalcitonin) should be used to exclude bacterial infection and guide antibiotic treatment in oldest-old patients suspicion for infection.

In contrast to the overuse of antibiotics, treatment of anemia was extremely rare in our study, despite the high prevalence. Anemia in the elderly patients is often iron deficiency anemia because of inadequate iron intake and iron absorption disorders.[35] In our study, approximately three-quarters of the oldest-old patients were with anemia, whereas less than 1% of the patients took serum ferritin detection and a significantly lower proportion of the patients (16.4%) were prescribed with an iron repletion than expected, suggesting that iron deficiency inspection and iron repletion is generally ignored during the management of patients with HF, especially among the oldest-old patients. These results were largely due to the lack of recommendations about screening and treatments for iron deficiency in the previous Chinese HF guideline,[13] making clinicians pay less attention to iron deficiency. Elderly patients with HF are at increased risk for anemia and iron deficiency, and should, therefore, be screened for ferritin and transferrin saturation and be prescribed iron repletion accordingly. Iron replacement is appropriate in patients with anemia resulting from iron deficiency, especially in oldest-old patients to improves symptoms and exercise capacity.[36-39]

There were several limitations in this study. First, although our results showed a significant difference in the clinical features among elderly patients with HF among different age groups, due to the cross-sectional nature, we were unable to analyze the effect of these differences on the outcomes of HF. Second, there was growing recognition that geriatric conditions such as disability, cognitive impairment, and frailty were essential and affect the management and outcome of elderly patients with HF. Unfortunately, these geriatric conditions were not adequately assessed in our study. Finally, despite a single-center study, a comprehensive assessment of clinical features (eg, symptoms, signs, comorbidities), hemodynamics, imaging including echocardiography, and treatment was available in our study; hence, we were able to provide more detailed information and to identify HF more accurately than International Classification of

Diseases, 9th Revision, making our study more representative of the elderly population with HF.

Conclusions

The results of our study demonstrated that the burden of non-cardiac comorbidities was nearly universal and obviously greater than that of cardiac comorbidities in elderly patients hospitalized with HF. Besides, the patterns of the non-cardiac comorbidities differed by age. The oldest-old patients appeared to be less likely to have traditional risk factors such as diabetes and dyslipidemia as seen in the young-old patients, while anemia, infection, CKD, and stroke were more common. Moreover, polypharmacy and inappropriately prescribed medications, especially on non-cardiac conditions (eg, administration of unnecessary antibiotics and inadequate administration of iron repletion), were very common in elderly patients. In this regard, a better understanding of the age-related difference of clinical features and more comprehensive care of non-cardiac comorbidities are vital for further improving prognosis in elderly patients with HF. We need more information on elderly patients with HF stratified by age in a large cohort to design preventive and therapeutic strategies specifically directed toward them.

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Conflicts of interest

None.

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