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CONSENSUS

Chinese expert consensus on the diagnosis and treatment of chronic heart failure in elderly patients (2021)

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Abstract

Heart failure is a clinical syndrome caused by ventricular insufficiency, which results in decreased activity tolerance and repeated hospitalization, seriously affecting quality of life, and it is the main cause of death in elderly people. In recent years, great progress has been made in the treatment of heart failure, but the prevalence, mortality, and readmission rate among elderly patients with heart failure remain high. Because elderly patients have multiple cardiovascular disease risk factors, coexistence of multiple diseases accompanied by multiple syndromes, multiple medications, and natural decline of body functions, the clinical diagnosis, treatment, rehabilitation, and long-term management of these patients differ from those in other populations. To facilitate clinical practice and application of clinical geriatric medicine, especially among community physicians, experts from the Cardiovascular Group, Geriatrics Branch of the Chinese Medical Association have drafted this consensus to summarize the diagnosis and treatment regimens for elderly patients with chronic heart failure and provide guidance for its clinical diagnosis and treatment in China.

KEYWORDS
Chinese experts consensus, chronic heart failure, elderly

1 | OVERVIEW AND EPIDEMIOLOGY

1.1 | Overview

Heart failure (HF) in **volves**a set of complex clinical syndromes with ventricular ejection and/or filling dysfunction caused by abnormal changes in cardiac structures and/or functions, with the main manifestations being fatigue, dyspnea, and fluid retention (pulmonary congestion, systemic congestion, and peripheral edema). Chronic heart failure (CHF) refers to a persistent HF state that can be stable, worsening, or decompensated. Compared with younger adults, elderly patients with CHF are more likely to be admitted to hospital

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See Appendix 1 for the members of Cardiovascular Group, Geriatrics Branch, Chinese Medical Association; Editing Group of the Chinese Expert Consensus on the Diagnosis and Treatment of Chronic Heart Failure in Elderly Patients.

[Correction added on 16 June 2022: The DOI ID for the Chinese publication was corrected].

owing to repeated deterioration of cardiac function or acute decompensation, thereby accelerating the progression of HF.

Based on the left ventricular ejection fraction (LVEF), CHF is classified into HF with reduced ejection fraction (HFrEF), HF with preserved ejection fraction (HFpEF), and HF with mid-range ejection fraction (HFmrEF).[1] Compared with the proportion of HFrEF, the proportion of HFpEF is higher among elderly patients with HF. The extent of HF is usually measured using the New York Heart Association (NYHA) functional classification. In recent years, staging of the HF process (Table 1) is used to facilitate early prevention and control and effectively reduce the morbidity of HF.[2]

1.2 | Epidemiology

The global overall prevalence of HF ranges between 1% and 2%; in developed countries, the morbidity of HF in elderly adults over age 70 years reaches 10%.[1] A Chinese epidemiological survey in 2003 revealed that the HF prevalence among Chinese urban and rural residents was 0.9%; this was 0.4%, 1.0%, 1.3%, and 1.3% in the age groups 35–44, 45–54, 55–64, and 65–74 years, respectively.[3] Data from a hypertension survey showed that the overall prevalence of HF among adults in China over 35 years old between 2012 and 2015 was 1.3%; the prevalence among those aged 55–64, 64–74, and ≥75 years was 1.6%, 2.1%, and 3.2% respectively. The overall HP prevalence has increased by 44% in China over the past 15 years.[4]

The dramatic increase in HF morbidity among elderly adults is related to aging; chronic diseases such as hypertension, coronary heart disease, and diabetes; as well as prolonged patient survival owing to the improvement in health care. The prevalence of left ventricular diastolic dysfunction in elderly adults has increased rapidly and is significantly higher than that of systolic dysfunction.[5] Hospitalized patients with HF in the Chinese HF Center Registration Study who had HFrEF, HFmrEF, and HFpEF accounted for 35.2%, 21.8%, and 43.0%, respectively. The main causes of HFrEF are coronary heart disease, hypertension, and dilated cardiomyopathy. Compared with patients who have HFmrEF and HFrEF, those with HFpEF are older, more frequently women, and are more likely to have hypertension, stroke/transient ischemic attack, atrial fibrillation/flutter, anemia, and chronic obstructive pulmonary disease (COPD).[6]

In recent years, the overall in-hospital mortality of HF has exhibited a downward trend in China, but the mortality rate among elderly patients with HF is significantly higher than that of younger adult patients during the same period. According to one retrospective dataset of 7319 hospitalized patients with HF from 1993 to 2007, the total mortality rates in the age groups 50–59, 60–69, 70–79, 80–89, and ≥90 years were 2.1%, 5.1%, 7.8%, 12.3%, and 16.9%, respectively.[7] With the increasing trend in aging of population in China, cardiovascular diseases and their risk factors are on the rise, and it is expected that the HF prevalence in elderly populations will continue to increase in the future.

2 | CAUSES OF DISEASE

2.1 | Causes

The causes of HF in elderly adults mainly include cardiomyopathy, cardiac overload, and valvular heart disease as well as structural abnormalities, and arrhythmia, together with common diseases such as coronary heart disease, hypertension, diabetes, valvular disease, cardiomyopathy, and atrial fibrillation.[2] Age-specific cardiac changes such as degenerative valvular disease, degenerative changes in the conduction system, and cardiac amyloidosis are also important causes of HF in elderly populations.[8,9]

TABLE 1 Stages of heart failure

Stage	Definition	Patient populations	New York Heart Association (NYHA) functional class
Stage A (risk stage)	High-risk group for heart failure; no cardiac structural or functional abnormalities; no symptoms and/or signs of heart failure	Patients with hypertension, chronic heart disease, diabetes, obesity, metabolic syndrome, history of use of cardiotoxic drugs, history of alcoholism, history of rheumatic fever, family history of cardiomyopathy	None
Stage B (preclinical stage)	Has developed to structural heart disease but no symptoms and/or signs of heart failure	Patients with left ventricular hypertrophy, old myocardial infarction, asymptomatic heart valve disease, chamber enlargement	I
Stage C (clinical stage)	Structural heart disease, with symptoms and/or signs of heart failure in the past or at present	Patients with structural heart disease accompanied by reduced exercise tolerance (dyspnea, fatigue) and fluid retention	I–IV
Stage D (end stage)	Structural heart disease is progressing, despite aggressive medical treatment; symptoms persist at rest and require special interventions	Patients who have been hospitalized repeatedly owing to heart failure and cannot be safely discharged; patients who require long-term intravenous medication; patients who are awaiting heart transplantation; patients who use cardiac mechanical assist devices	IV

2.2 | Precipitating factors

The causes of HF in elderly adults are more widespread, including common factors like infections, acute myocardial ischemia, rapid/slow arrhythmias, fluctuations of blood pressure, excessive sodium intake, rapid and/or excessive infusion and blood transfusion, emotional stress, and medications such as those inhibiting myocardial contractility and those causing water and sodium retention.

2.3 | Comorbidity

Elderly patients with HF usually have a combination of chronic diseases, such as COPD, hypertension, diabetes mellitus, chronic renal insufficiency, and anemia. More than 75% of elderly patients with HF have three or more comorbidities, and 50% have five or more comorbidities. The presence and exacerbation of these chronic diseases are an important basis and factor influencing the onset of HF. Data of the National Heart Lung and Blood Institute on 37,054 patients aged 21 years and older with confirmed HF between 2005 and 2008 showed that the proportion of patients with HFpEF and HFrEF who had five or more comorbidities was 58% and 45%, with a significant difference in the degree of comorbidity burden; the overall disease burden of patients with HFpEF was higher than that in patients with HFrEF.[10]

3 | CLINICAL FEATURES AND DIAGNOSTIC ASSESSMENT

3.1 | Clinical features

Clinical manifestations of HF include atypical signs and symptoms and the coexistence of multiple illnesses, mostly accompanied with geriatric syndromes such as frailty, multiple drug use, and cognitive impairment. Main manifestations include the following.

3.1.1 | Insidious symptoms

Acute decompensated elderly patients with HF are more likely to develop acute pulmonary edema and blood pressure fluctuations. In contrast, most elderly patients with CHF may present with cough, weakness, fatigue, general malaise, loss of appetite, abdominal discomfort, nausea, diarrhea, inattention, and unresponsiveness, and they may not have typical dyspnea.[11–13]

3.1.2 | Atypical signs

Signs such as third heart sound (S3), pulmonary rales, and distention of the jugular vein are nonspecific in elderly patients. Peripheral edema in elderly patients is mostly caused by venous valve insufficiency in the lower extremities, drugs such as calcium channel blockers, or other causes that must be differentiated.[1]

3.1.3 | Geriatric syndromes

HF in elderly patients is mostly accompanied by clinical manifestations such as frailty, sarcopenia, malnutrition, falling, cognitive impairment, delirium, sleep disorders, anxiety, depression, urinary and fecal incontinence, and multiple drug use, which require comprehensive judgment. HF itself is also a geriatric syndrome.[14–16]

3.1.4 | Coexistence of multiple diseases

HF is often combined with hypertension, diabetes, chronic kidney disease, coronary heart disease, COPD, atrial fibrillation, stroke, sleep apnea, anemia, tumors, peripheral vascular disease, and geriatric syndromes. Elderly patients with HF often have two, three, or more comorbidities.[17]

3.2 | Auxiliary examinations

Routine tests include electrocardiogram (ECG), chest radiograph, natriuretic peptide (NP) levels, and ultrasonic cardiogram (UCG), among others. Patients with newly diagnosed HF should undergo examinations including routine blood testing, electrolytes, liver and kidney function, glucose and glycated hemoglobin tests, assessment of thyroid function, serum ferritin and total ferritin binding, and markers of myocardial injury to identify possible causes, influencing factors, and comorbidities, which form the basis for selecting the treatment for HF.[1]

3.2.1 | Routine tests

1. **ECG:** Conventional 12-lead ECG[1] is used to detect HF.
2. **Biomarkers:**

NP: NP is important for excluding HF in elderly patients. The glomerular filtration rate (GFR) decreases gradually with increasing age starting from age 30–40 years and decreases more substantially from age 65–70 years. Studies have shown that the average decrease in GFR is 0.96 ml/min per year or 10 ml/min every 10 years.[18] Thus, NP levels are elevated in elderly adults without HF, and plasma NP concentrations can be elevated two to three times in adults older than 75 years who do not have HF.[1] The NP diagnostic cutoff value for HF has only been validated in young and middle-aged adults and should be assessed individually in elderly patients. If plasma NP levels are normal, HF is unlikely but cannot be ruled out. The cutoff values for diagnosing brain natriuretic peptide (BNP) and amino

terminal proB-type NP (NT-proBNP) in chronic and acute HF[1,2,19,20] are shown in Table 2.

Cardiac troponin: For the diagnosis and prognostic evaluation of patients with HF who have acute myocardial infarction and acute myocarditis.

Myocardial fibrosis markers such as soluble growth-stimulated expression gene 2 protein and galactose lectin 3 contribute to HF risk stratification and prognostic evaluation. The combined use of multiple biological markers can improve the accuracy of diagnosis and prognosis of HF in elderly patients.[1,21,22]

1. **Chest radiography:** Chest radiographs can detect pulmonary disease with respiratory distress and can reveal pulmonary venous congestion or pulmonary edema.[23]
2. **Transthoracic ultrasonic cardiogram (UCG):** UCG should be performed in all elderly patients with HF. UCG provides information on cardiac morphology, structure, and function, which is valuable for the etiological diagnosis of HF, volume status, and prognosis. LVEF is an important basis for the diagnosis of HFrEF, HFmrEF, and HFpEF.[1,24]
3. **Arterial blood gas analysis:** For patients who require accurate measurement of partial pressure of oxygen and partial pressure of carbon dioxide, especially patients with acute pulmonary edema, accompanied by COPD or cardiogenic shock.[1]
4. **Comprehensive geriatric assessment:** A comprehensive geriatric assessment is recommended for elderly patients with HF.[16,25,26]

3.2.2 | Special examinations

1. **Coronary angiography or coronary computed tomography angiography(CTA):** For patients with (1) angina with poor drug efficacy, (2) a history of symptomatic ventricular arrhythmia or cardiac arrest, and (3) suspected coronary artery disease.
2. **Cardiac magnetic resonance (CMR):** The gold standard for measuring ventricular volume, mass, and ejection fraction. CMR delayed gadolinium enhancement and T1 imaging are the preferred methods for assessing myocardial fibrosis in diagnosing the causes of HF. CMR is also used to assess myocardial ischemia and myocardial survival in coronary HF.[1]
3. **Nuclear ventriculography and nuclear myocardial perfusion and/or metabolic imaging:** Single photon emission computed tomography (SPECT) can be performed to assess myocardial ischemia and myocardial survival. Gated SPECT can measure ventricular volumes and their functions. Adoption of 3,3-diphosphino-1,2-propanedioic acid scintigraphy is recommended for the detection of cardiac amyloidosis of the thyroxine transporter.
4. **Cardiopulmonary exercise test (CPET):** CPET can simultaneously test cardiopulmonary metabolic function, distinguish HF from other organ failure, assess the severity of cardiovascular disease and HF prognosis, and guide prescribed cardiac rehabilitation exercise.[21]
5. **6-min walk test (6MWT):** In the absence of conditions for CPET, the 6MWT can be used for risk stratification to assess HF: (1) degree: 6-min walk distance (6MWD) <150 m indicates severe HF, 150–450 m moderate HF, and >450 m mild HF; (2) prognosis: 6MWD <300 m suggests a poor prognosis of HF; (3) an ancillary diagnostic method when the diagnosis of HFpEF in elderly patients is uncertain; and (4) can be used to assess the effect of exercise rehabilitation interventions.[19,27,28]
6. **Invasive or noninvasive hemodynamic test:** Cardiac catheterization is used for: (1) failure to definitively diagnose HFpEF, (2) evaluation prior to cardiac transplantation or mechanical circulatory support, (3) determination of pulmonary hypertension prior to correction of valvular/structural heart disease and assessment of its reversibility, and (4) patients with severe symptoms and unclear hemodynamic status despite standard treatment.[1,19]

The noninvasive hemodynamic test with impedance differential cardiography can be selected for elderly patients with HF and is convenient, safe, and suitable for widespread implementation in primary hospitals.[29]

3.3 | Diagnosis

3.3.1 | Diagnosis of HFrEF

Symptoms or signs of HF with LVEF <40% can be diagnosed as HFrEF.[17]

3.3.2 | Diagnosis of HFmrEF and HFpEF

(1) Signs or symptoms of HF; (2) LVEF: HFmrEF 40%–49%; HFpEF LVEF ≥50%.

The H_2FPEF scoring system, shown in Table 3, includes three indicators of cardiac morphology, function, and NP levels, with 2 points for each major criterion, a maximum of 2 points for each item, and 1 point for each minor criterion (only 1 point can be scored for

TABLE 2 Diagnostic cutoff values for brain natriuretic peptide (BNP) and amino terminal proB-type natriuretic peptide (NT-proBNP) precursors in heart failure

	BNP (ng/L)	NT-proBNP (ng/L)
Chronic	Sinus rhythm, >80 Atrial fibrillation rhythm, >240	Sinus rhythm, >220 Atrial fibrillation rhythm, >660
Acute	>100	Age <50 years, >450 Age 50–75 years, >900 Age >75 years, >1800

the same item). Scores of different items can be added together but not for the same item. HFpEF is clearly diagnosed with a score ≥5 and is not diagnosed with a score ≤1. Diastolic dysfunction is diagnosed with a score of 2–4 and cardiopulmonary exercise stress test or invasive hemodynamic test.[13,19,24] In elderly patients, HFpEF can be diagnosed with a 6MWT <300 m, but non-cardiac disease such as COPD or peripheral vascular disease should be excluded.[19]

Figure 1 shows a flow chart for diagnosis of HF.

Hospitals that are not equipped to perform UCG examinations, exercise stress tests, or invasive examinations can make a clinical diagnosis of HFpEF by referring to the H_2FPEF score, as shown in Table 4. With scores 0–1, HFpEF can be excluded; scores 6–9, HFpEF can be confirmed; and scores 2–5, further examinations are required.[23]

3.4 | Differential diagnosis

HF in elderly adults is not a typical clinical manifestation; therefore, in patients with dyspnea, peripheral swelling, unexplained fatigue, decreased exercise tolerance, loss of appetite, inattention, and unresponsiveness, possible HF should be considered and distinguished from pulmonary pathologies such as COPD, interstitial fibrosis, primary pulmonary hypertension, non-thromboembolic disease, severe anemia, chronic kidney disease, cirrhosis, venous insufficiency, lymphedema, and adverse drug reactions. Differential diagnosis requires comprehensive analysis of the patient's history, symptoms, signs, routine blood tests, urine, liver and kidney function, ECG, UCG, biomarkers, and results of other ancillary examinations. In elderly patients, attention should be paid to the possibility of HF combined with noncardiovascular comorbidities such as COPD, anemia, chronic kidney disease, or geriatric syndrome.

3.5 | Elderly patients with HF and other syndromes

It is recommended that a comprehensive geriatric assessment (Figure 2) be performed along with the diagnosis of HF in elderly individuals to better manage HF in elderly patients individually.[16,24,25] Common geriatric syndromes and their assessment are briefly described below.

3.5.1 | Activities of daily living (ADL)

This should include basic activities of daily living (BADL) and instrumental activities of daily living (IADL). The most commonly used clinical assessment method for BADL is the Barthel Index. IADL are most commonly assessed using the Lawton IADL scale.[30]

3.5.2 | Frailty

The most commonly used assessment tool is the Fried criteria. This measure includes five items; frailty is diagnosed if three or more of the five criteria are met, and pre-frailty is diagnosed if one or two are met.

3.5.3 | Dementia and cognitive impairment (CI)

Recommended tools for the assessment of CI are: (1) the Mini Mental State Examination; and (2) the Mini-Cog test, which has the advantage of being simple and quick.[16]

3.5.4 | Depression

The recommended tool is the Geriatric Depression Scale.[31]

3.5.5 | Malnutrition

All elderly inpatients with HF should be assessed for nutritional risk using tools such as the geriatric Mini Nutritional Assessment – Short Form and the Nutritional Risk Screening 2002.[32]

3.5.6 | Multiple medications

Medications should be periodically reviewed and adjusted in elderly patients with HF to avoid potentially irrational drug use, referring to the 3rd version of Beers Criteria.[11]

4 | TREATMENT AND COMPREHENSIVE MANAGEMENT

4.1 | Treatment goal and principle

The treatment goal is to relieve symptoms, improve exercise tolerance, improve quality of life, and to reduce complications, readmission rate, and mortality.

Treatment should follow the principle of individualization and dynamic assessment of changes in concomitant diseases among patients as well as adjustment of concomitant medications. The patient's cognitive function, liver and kidney function, and electrolytes should be monitored and evaluated regularly; the choice of medications and auxiliary devices should be considered comprehensively; and the treatment regimen should be adjusted in a timely manner.

4.2 | Drug therapy for chronic heart failure (CHF) in elderly patients

4.2.1 | Drugs for the treatment of CHF in elderly patients include the following

Diuretics

Diuretics are currently the sole drug that can completely relieve fluid retention, and as such, these are one of the cornerstones of HF treatment. Diuretics are recommended to relieve symptoms in

TABLE 3 UCG-based HFpEF scores for cardiac function, morphology, and NP levels

	Functional	Morphological	Biomarker (Sinus rhythm)	Biomarker (Atrial fibrillation)
Major	Septal e' <7 cm/s or lateral e' <10 cm/s or average E/e' ≥15 or TR velocity >2.8 m/s (PASP >35 mmHg)	LAVI >34 ml/m^2 or LVMI ≥149/122 g/m^2 (M/W) and RWT >0.42	NT-proBNP >220 pg/ml, or BNP >80 pg/ml	NT-proBNP >660 pg/ml, or BNP >240 pg/ml
Minor	Average E/e' 9–14 or GLS <16%	LAVI >29–34 ml/m^2, or LVMI ≥115/95 g/m^2 (M/W) or RWT >0.42 or LV thickness ≥ 12 mm	NT-proBNP 125–220 pg/ml, or BNP 35–80 pg/ml	NT-proBNP >660 pg/ml, or BNP >240 pg/ml

Abbreviations: BNP, brain natriuretic peptide; GLS, overall longitudinal strain; HFpEF, heart failure with preserved ejection fraction; LAVI, left atrial volume index, left ventricular relative thickness: 2 times posterior wall thickness divided by left ventricular end diastolic internal diameter; NP, natriuretic peptide; NT-proBNP, amino terminal proB-type natriuretic peptide; UCG, ultrasonic cardiogram.

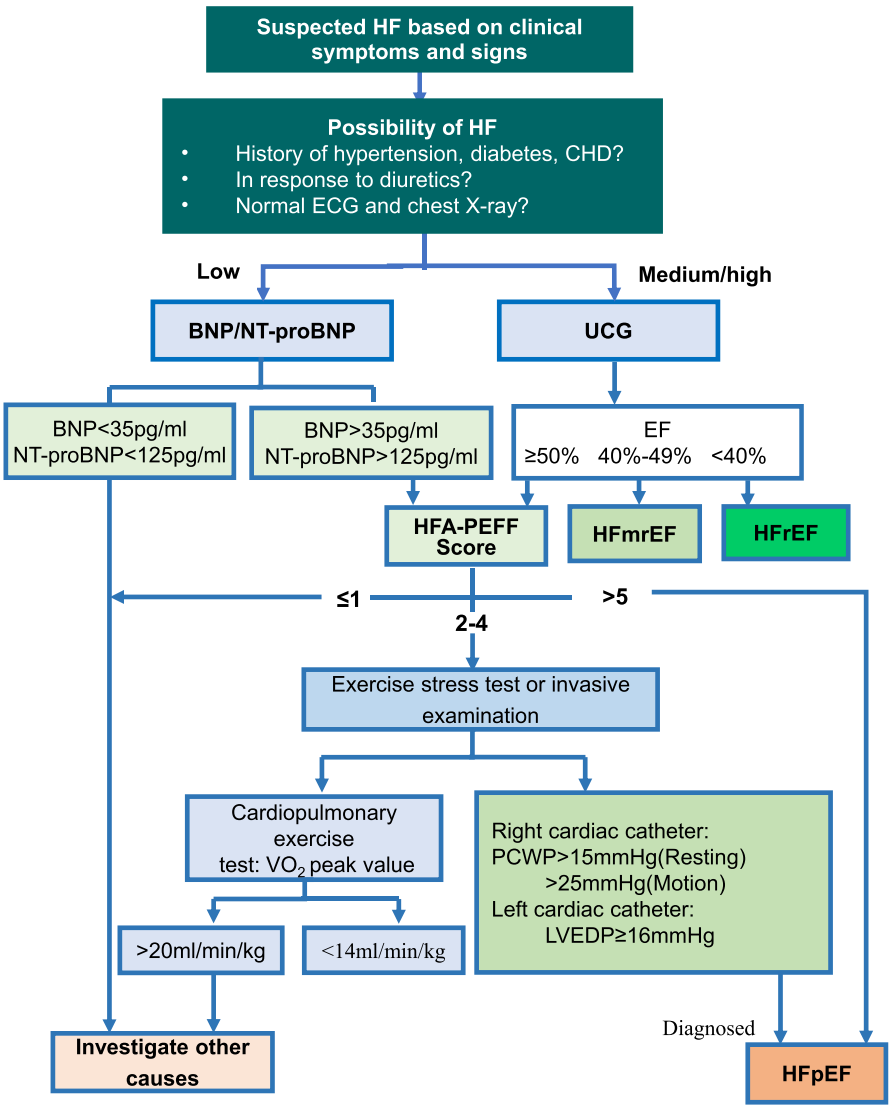

FIGURE 1 Flow chart of HF diagnosis. BNP, brain natriuretic peptide; ECG, electrocardiogram; EF: ejection fraction; HF, heart failure; HFA-PEFF, Heart Failure Association Pre-test assessment, Echocardiography & natriuretic peptide, Functional testing, Final etiology; HFmrEF, HF with mid-range ejection fraction; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction; LVEDP, left ventricular end diastolic pressure; NT-proBNP, amino terminal proB-type natriuretic peptide; PCWP, pulmonary capillary wedge pressure; UCG, ultrasound cardiogram; VO_2, volume of oxygen

patients with HFrEF who have fluid retention; however, there is no evidence as yet that the use of diuretics can reduce mortality or morbidity.[1]

The most commonly used loop diuretic is furosemide. Thiazide diuretics are indicated for hypertensive patients with mild fluid retention, but gout is a contraindication. Diuretics should be administered starting with a low dose, which can be increased gradually until urine volume increases. The patient's symptoms should be closely observed, and changes in urine volume and body weight should be monitored and the dose adjusted in a timely manner. Patients' blood pressure, renal function, electrolytes, and uric acid levels should be monitored during medication administration to avoid hypotension,

TABLE 4 H_2FPEF scores

	Clinical variable	Value	Score
H2 (Heavy, Hypertension)	Obesity	Body mass index >30 kg/m^2	2
	Hypertension	≥2 antihypertensive drugs	1
F (Atrial fibrillation)	Atrial fibrillation	Persistent or paroxysmal	3
P (Pulmonary hypertension)	Pulmonary arterial hypertension	Doppler ultrasound estimation of pulmonary artery systole >35 mmHg	1
E (Elderly)	Age	>60 years old	1
F (Filling pressure)	Left ventricular filling pressure	Doppler ultrasound E/e' >9	1
Total score			0–9

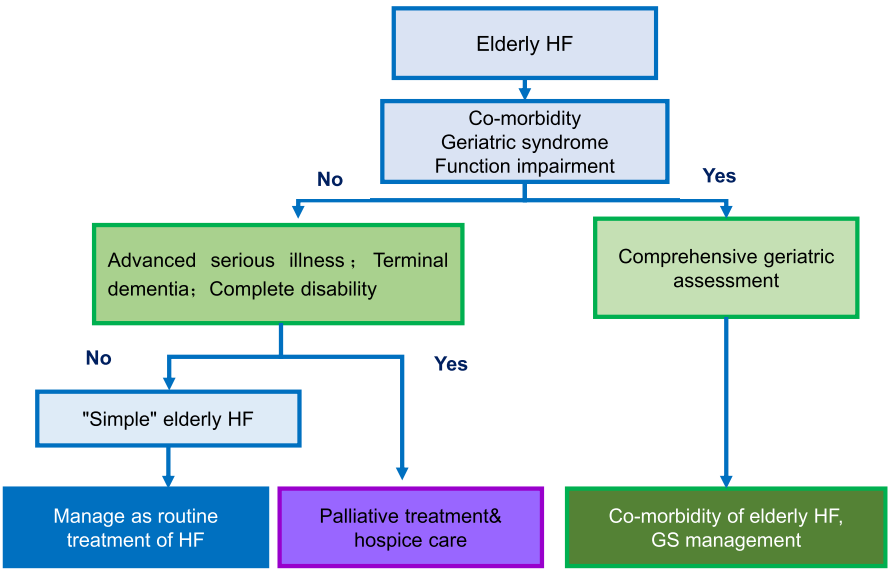

FIGURE 2 Diagnosis and treatment process of heart failure (HF) in elderly patients. GS, geriatric syndrome

worsening of renal function, electrolyte loss, or hyperuricemia. Diuretics should be avoided in patients without symptoms and signs of fluid retention and those who are allergic or have adverse reactions to certain diuretics.

Tolvaptan is a novel aquaretic diuretic vasopressin V2-receptor antagonist. Clinical trials have shown that the addition of tolvaptan on the basis of loop diuretics can increase urine output and improve symptoms; this regimen does not activate the renin–angiotensin–aldosterone system (RAAS) or increase the risk of electrolyte imbalance and renal insufficiency, making it a good option for elderly patients with hyponatremia.

Renin–angiotensin receptor antagonists

Renin–angiotensin receptor antagonists can reduce the readmission rate and mortality of worsening HF in elderly patients and are indicated for all symptomatic patients with HFrEF. If there are no contraindications, an initial low-dose angiotensin-converting enzyme inhibitor (ACEI) is recommended.[33–36] Angiotensin II receptor blockers (ARBs) can be used for patients with HFrEF who cannot tolerate ACEIs when there are no contraindications.[37,38] Additionally, ACEIs can reduce the occurrence of atrial fibrillation caused by HFpEF.[39] In terms of the efficacy of ACEIs or ARBs in patients with HFpEF, especially elderly ones, large-scale clinical trials should be conducted. Elderly patients should be closely monitored for adverse reactions such as postural hypotension, renal function, and hyperkalemia. ACEIs or ARBs should be used with caution in patients with serum creatinine >265.2 μmol/L (3 mg/dl), serum potassium >5.5 mmol/L, symptomatic hypotension (systolic blood pressure <90 mmHg; 1 mmHg = 0.133 kPa) and severe aortic valve stenosis.

Angiotensin receptor–enkephalinase inhibitors (ARNIs)

ARNIs are a class of drugs that act on RAAS and enkephalinase; the representative drug is sacubitril/valsartan. Presently, the guidelines recommend giving ARNI directly instead of ACEIs or ARBs as a priority in patients with NYHA class II or III and patients with HFrEF who can tolerate ACEIs or ARBs to further reduce morbidity and mortality. Compared with ACEIs (such as enalapril), ARNIs can further reduce the level of NT-proBNP in patients with stable acute HF[40] and improve the survival rate in patients of all ages, including those aged ≥75 years.[41–43] The TRANSITION trial showed that the use of ARNI had similar safety outcomes before and after discharge in patients who were hospitalized for worsening HF.[44] ARNIs were well tolerated in elderly patients with HFrEF and showed absolute superiority in cardiovascular mortality among patients with HFrEF. For elderly patients with HFrEF who are still symptomatic after using ACEIs, β-blockers, and aldosterone receptor antagonists, ARNIs are

recommended as replacements for ACEIs and ARBs to reduce the risk of hospitalization and mortality in patients with HFrEF; ARNI can be used only after ACEIs are discontinued for no less than 36 hours. The recommended starting dose is 50 mg bid; the dose is doubled once every 2–4 weeks, until reaching the target dose of 200 mg bid. Elderly patients with low blood pressure should start at a reduced dose. The dose should be adjusted individually according to blood pressure levels and patient tolerance. Elderly patients should be alerted to possible adverse reactions such as symptomatic hypotension, hyperkalemia, worsening renal function, and angioneurotic edema. ARNIs should not be used in elderly patients whose blood pressure is too low during ACEI therapy.[45] Patients should be monitored for renal function and serum potassium within 1–2 weeks of starting ARNI therapy or during dose titration. Additionally, ARNI therapy may increase BNP levels in elderly patients, but it does not affect NT-proBNP. The PARAGON-HF study[46] compared the efficacy of ARNI and valsartan in patients with HFpEF aged over 50 years; ARNI therapy showed a trend of reducing the risk of primary outcomes and the HF readmission rate but had no obvious benefits for the risk of cardiovascular death. Recently, the American College of Cardiology updated its expert consensus on the management of patients with HFrEF and recommended the use of sacubitril/valsartan without pre-treatment using ACEIs/ARBs, further emphasizing the importance of ARNIs as first-line therapy.[47]

β-blockers

The first-line treatment drug can bring definite benefits to elderly patients with HF.[48–50] To reduce morbidity and mortality in all patients with symptoms of HFrEF, β-blockers (bisoprolol, carvedilol, or sustained-release metoprolol succinate) are recommended if there are no contraindications. For patients with fluid retention, diuretics can be used together. A highly selective β1-blocker should be chosen for patients with COPD and benign prostate hyperplasia (BPH). To avoid bradycardia and hypotension, the treatment should start from the lowest recommended dose; the titration interval should be no less than 2 weeks, and the time to target dose can be appropriately extended. The target dose or maximum tolerated dose is the dose used when the patient's resting heart rate is 55–60 beats/min. If the volume load increases after increasing the dose, it is necessary to use the original dose and increase the dose of diuretics. β-blockers are not recommended for patients with bronchial asthma, second-degree or higher atrioventricular block, or heart rate less than 50 beats/min. The patients' blood pressure and heart rate should be monitored to avoid bradycardia, hypotension, and worsening HF during the use of β-blockers. Because there are great differences among elderly patients, the use of β-blockers should be individually tailored.

Aldosterone receptor antagonists (MRAs)

MRAs can reduce mortality in elderly patients with HF.[51–53] For elderly patients with moderate to severe HF (NYHA classes II-IV) who remain symptomatic after use of ACEIs and β-blockers, and symptomatic or diabetic patients with LVEF <40% after myocardial infarction, MRAs such as spironolactone (20 mg/day) or eplerenone (25–50 mg/day) are recommended.[51,53] However, the patient's GFR should be more than 30 ml/min and serum potassium should be less than 5 mmol/L. Patients with advanced age should be closely followed up after MRA treatment to monitor blood pressure, serum potassium, and renal function, and close attention should be paid for adverse reactions such as hyperkalemia and deterioration of renal function.

Digitalis drugs

Digitalis drugs can reduce the readmission rate of worsening HF in elderly patients and are indicated for patients with HFrEF who still have HF symptoms after standard treatment, especially those who have atrial fibrillation with a fast ventricular rate. However, use of digitalis drugs should be avoided in patients with second-degree or higher atrioventricular block, sinus node dysfunction, pre-excitation syndromes with atrial fibrillation or atrial flutter, and hypertrophic myocardial infarction. Elderly patients have a higher risk of digitalis poisoning owing to decreased liver and kidney function. The dose for patients with advanced age or those with impaired renal function is halved to 0.125 mg once a day or every other day, and adverse reactions including arrhythmia and gastrointestinal reactions should be closely monitored. The blood concentration of digitalis should be monitored periodically (<0.9 μg/L).[2]

Sodium glucose cotransporter 2 (SGLT-2) inhibitors

SGLT-2 inhibitors are novel drugs for the treatment of HF, which can increase the excretion of glucose in renal tubules and have diuretic and antihypertensive effects. SGLT-2 inhibitors can effectively reduce mortality in patients with HF[54–57] and are indicated for adult patients who have HFrEF of NYHA classes II-IV.[57,58] During use of SGLT-2 inhibitors, patients' blood pressure, blood sugar, and renal functions should be monitored to avoid adverse reactions such as hypotension, ketoacidosis, and renal function impairment. SGLT-2 inhibitors may interact with loop diuretics and the dose should be adjusted when these are used in combination for elderly patients. If patients develop clinical hypovolemia or ketoacidosis, SGLT-2 inhibitors and diuretics can be temporarily discontinued and the water and electrolyte balance can be adjusted. Precautions against genitourinary infections are needed in elderly patients. For patients with severe renal impairment, end-stage renal disease, or those requiring dialysis, SGLT-2 inhibitors are contraindicated.

Ivabradine

In patients who have HF with sinus rhythm, ivabradine reduces cardiovascular mortality and the HF hospitalization rate, with no significant difference between elderly people and younger adults. There are also no differences in the incidence of adverse events, such as symptomatic bradycardia, asymptomatic bradycardia, and phosphene between elderly individuals and adults.[59,60] Ivabradine should be considered for patients with NYHA classes II-III and LVEF ≤35% or those with CHF and a resting sinus heart rate ≥70 beats/

min who still have symptoms after optimal treatment with the maximum tolerated doses of ACEIs, β-blockers, and MRAs. The starting dose is 2.5 mg bid, and the maximum dose is 7.5 mg bid, which can be adjusted according to the heart rate. The resting heart rate is controlled at 55–60 beats/min. Ivabradine should be used with caution in patients with acute HF, sinus node dysfunction, second-degree atrioventricular block, or a pretreatment resting heart rate <60 beats/min.

Other drugs

1. **Calcium ion antagonists:** Nondihydropyridine calcium channel blockers can prolong ventricular filling time, improve treatment with calcium ion, and reduce arterial stiffness in elderly adults. These agents can be used for the treatment of elderly patients with HFpEF.[61] However, calcium channel antagonists, such as diltiazem and nifedipine, may be associated with poor prognosis in patients with HFrEF owing to their negative inotropic effects; therefore, these should be avoided in elderly patients with HFrEF.[62]
2. **Vasodilators:** Vasodilators (such as isosorbide dinitrate and hydralazine) can adjust the nitric oxide system and improve endothelial function through combined use. These can be administered in symptomatic patients with HFrEF who cannot use ACEIs/ARBs/ARNIs, gradually increasing from a low starting dose to a target dose.[63] However, owing to poor compliance with combined therapy and a high incidence of adverse reactions, routine use of this regimen in addition to standard therapy is not recommended in elderly patients with HFrEF.
3. **Statins:** Statins can theoretically benefit patients with HFpEF owing to their effects on comorbidities such as coronary artery disease, diabetes, and renal insufficiency. Studies have shown that statins may reduce the occurrence of atrial fibrillation and reduce the risk of HFpEF but these agents have no obvious effects on improving the prognosis of patients with HFrEF.[64–66]
4. **Myocardial energy-metabolizing drugs:** These drugs can improve the symptoms of HF and cardiac function in patients. Commonly used drugs are trimetazidine, coenzyme Q10, coenzyme I, levocarnitine, and creatine phosphate.
5. **Novel soluble polynucleotide cyclase stimulator (vericiguat):** This drug can improve the composite endpoint of HF hospitalization and cardiovascular death in patients with HFrEF.[67]
6. **Traditional Chinese medicine:** Standard treatment combined with traditional Chinese medicine treatment can further improve the cardiac function of patients with HF, enhance their exercise tolerance, and improve their quality of life. For patients with CHF of NYHA classes II-IV, Chinese patent medicines, such as Qishen Yiqi Dropping Pills, can be used in combination on the basis of standard treatment.[68] Elderly patients have multiple diseases and are likely to be taking multiple medications, increasing the incidence of adverse drug reactions in this patient population. Special attention must be paid regarding interactions between and adverse reactions to multiple drugs during treatment combining traditional Chinese and Western medicines. Clinical observation and blood concentration monitoring should be enhanced during combined use of traditional Chinese and Western medicines. For example, Radix codonopsis, Panax ginseng, and Angelica sinensis have cardiotonic effects, and when used in combination with digoxin, the blood concentration and cardiotoxicity will be affected. As other examples, licorice can enhance the diuretic effect of spironolactone and the herb Chinese ephedra can weaken the effect of β-blockers.

4.2.2 | Drug treatment for chronic HFrEF in elderly patients

The recommended route for the treatment of chronic HFrEF is shown in Figure 3. For specific drug treatments, refer to the descriptions above

4.2.3 | Drug therapy for elderly patients with HFpEF

Currently, there are limited clinical trials among elderly patients with HFpEF, and conventional drugs for the treatment of HF have not been demonstrated to reduce the morbidity and mortality of HFpEF.[69] Medications targeting RAAS (including ACEIs, ARBs, MRAs) fail to benefit patients with HFpEF. β-blockers reduce all-cause mortality and cardiovascular mortality in patients with HFpEF compared with placebo.[70] However, drugs such as digoxin, ivabradine, and isosorbide mononitrate cannot improve the prognosis of patients with HFpEF.[71] In contrast, sacubitril and valsartan tend to reduce the risk of cardiovascular events.[72] The treatment of elderly patients with HFpEF should focus on aggressive comorbidity management as well as optimization of blood pressure control and volume status.

4.3 | Nondrug treatment

4.3.1 | Strengthening health education and self-management

Health education should be provided to patients and their families, including basic knowledge related to HF, information about medications, symptom monitoring, guidance on diet and exercise, and lifestyle improvement. Patient education should be conducted throughout the HF management process. Patient self-monitoring should also be enhanced, especially regarding changes in daily body weight and urine output, and reasonable limitation of sodium intake. Medication adherence should be improved and unnecessary nontherapeutic health care treatments and medications should be minimized.[1,73]

4.3.2 | Improving sleep disorders

Patients with sleep apnea should sleep in a lateral position and use continuous positive airway pressure to increase LVEF and improve their sleep function and status.

4.3.3 | Device therapy

1. **Mechanical ventilation:** Noninvasive ventilation can not only relieve symptoms but it can also reduce the likelihood of endotracheal intubation. It is recommended that patients with severe pulmonary edema and respiratory failure who can manage with ventilator ventilation be given noninvasive ventilation as soon as possible; however, this is not recommended for patients with hypotension. When necessary, invasive ventilation is applied.
2. **Ultrafiltration and renal replacement therapy:** This is suitable for patients with high volume load who are resistant to diuretics. For elderly patients with acute HF or refractory HF, ultrafiltration and renal replacement therapy can enhance their cardiac function and improve the clinical treatment effect.[74,75]
3. **External counterpulsation:** External counterpulsation therapy enhances exercise capacity, improves cardiac function, and considerably improves quality of life in patients with CHF (NYHA classes II-III) caused by ischemic heart disease. This therapy yields more benefits in elderly patients with HF.[76]
4. **Mechanical circulatory assist devices:** An implantable cardioverter defibrillator (ICD) can be installed for elderly patients with appropriate indications.[77–79] Cardiac resynchronization therapy (CRT) can reduce mortality and hospitalization rates by 12% compared with the optimal medical therapy alone.[80] CRT can be considered for elderly patients with appropriate indications.[81] Use of a left ventricular assist device has become a common treatment for advanced HF. Long-term assistance is only used as a transition in heart transplantation, and this should be used with caution in patients with advanced age.[82]

4.3.4 | Exercise rehabilitation

Improving exercise tolerance is an important means for elderly patients to maintain their ability to live independently. Reasonable exercise rehabilitation training in elderly patients with HF can improve their cardiopulmonary function, exercise tolerance, quality of life, and their prognosis.[83] Rational aerobic exercise is recommended for patients with CHF (including those with HFrEF and HFpEF) of NYHA classes I-III. Because elderly patients have degeneration of body functions and many comorbidities and complications, often combined with sarcopenia, bone and joint diseases, and cognitive dysfunction, the risks involved with exercise are considerably higher than those among younger adults. Therefore, comprehensive assessment and exercise risk stratification must be carried out before exercise rehabilitation in elderly patients to guide the formulation and implementation of individual exercise prescriptions. The main form of exercise is aerobic exercise, focusing on the role of muscle force training and balance coordination training in improving sarcopenia and reducing the risk of falls in elderly patients. Respiratory muscle training is equally important for elderly patients with CHF. Patients with high risk stratification, extremely advanced age, being bedridden long term, disability, weakness, or unwillingness to engage in subjective movement, should exercise mainly in passive rehabilitation.[84,85]

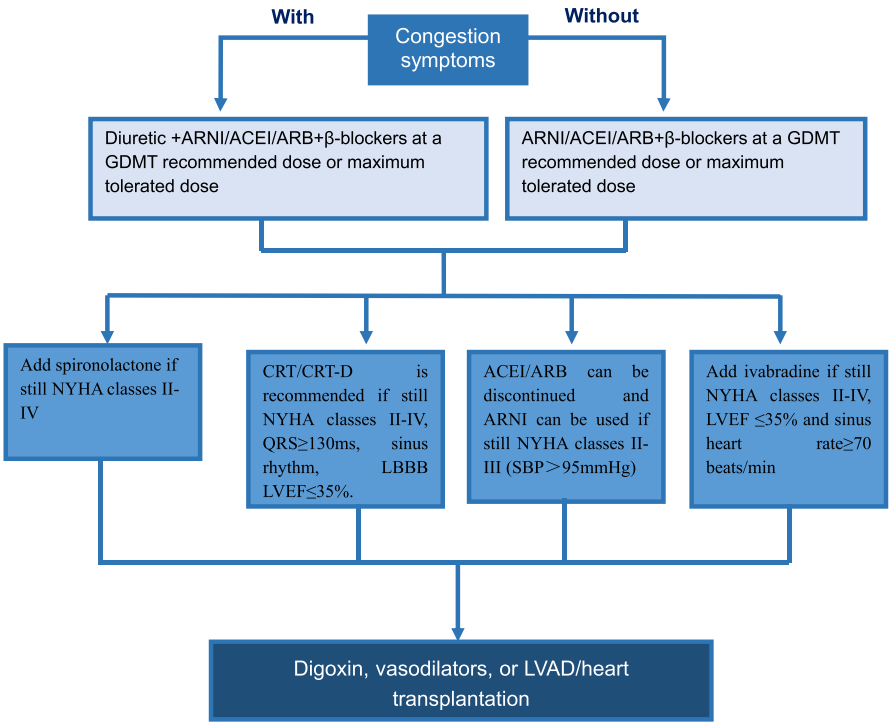

FIGURE 3 Recommended treatment for chronic HFrEF. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; ARNI, angiotensin receptor–enkephalinase inhibitor; CRT, cardiac resynchronization therapy; CRT-D, CRT with cardioverter and defibrillation function; GDMT, guide-directed medical therapy; LBBB, left bundle branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; HFrEF, heart failure with reduced ejection fraction; SBP, systolic blood pressure

4.4 | Management of comorbidities in elderly patients with HF

4.4.1 | Hypertension

Hypertension is the most common cause of CHF in elderly individuals, and blood pressure fluctuation is a main influencing factor in the aggravation and deterioration in HF. Aggressive antihypertensive therapy can reduce the morbidity of HF and prevent or delay HF progression.[86] For hypertensive patients with HF, ARNIs, RAAS blockers (ACEIs/ARBs), and β-blockers are the preferred options to control blood pressure. If blood pressure is not well controlled, diuretics, amlodipine, or felodipine can be used in combination. It is recommended that blood pressure be controlled to below 140/90 mmHg and even below 130/80 mmHg if tolerated by the patient.[87]

4.4.2 | Atrial fibrillation

Atrial fibrillation is the most common arrhythmia in patients with HF. CHF combined with atrial fibrillation substantially increases the risk of cerebral embolism. Rapid atrial fibrillation can lead to further deterioration of cardiac function, which interact with each other to form a vicious circle, resulting in a substantial increase in patient hospitalization and mortality. The incidence of HF complicated with atrial fibrillation is higher in elderly patients. In terms of treatment, modifiable factors (electrolyte imbalance, hypertension, infection, hypoxia, abnormal thyroid function) should be actively screened to treat the primary diseases. The risk of cerebral embolism is evaluated according to the CHA2S2-VAS, and bleeding risk is evaluated using HES-BLED. An individualized diagnosis and treatment plan should be formulated, including anticoagulation, ventricular rate control, and maintenance of sinus rhythm. Figure 4 shows the specific process.

4.4.3 | Diabetes

Diabetes is an independent risk factor for HF. SGLT-2 inhibitors can effectively reduce the risk of all-cause mortality, mortality of cardiovascular disease, and the risk of HF readmission in patients with diabetes and cardiovascular disease, with especially greater benefits in people aged ≥65 years.

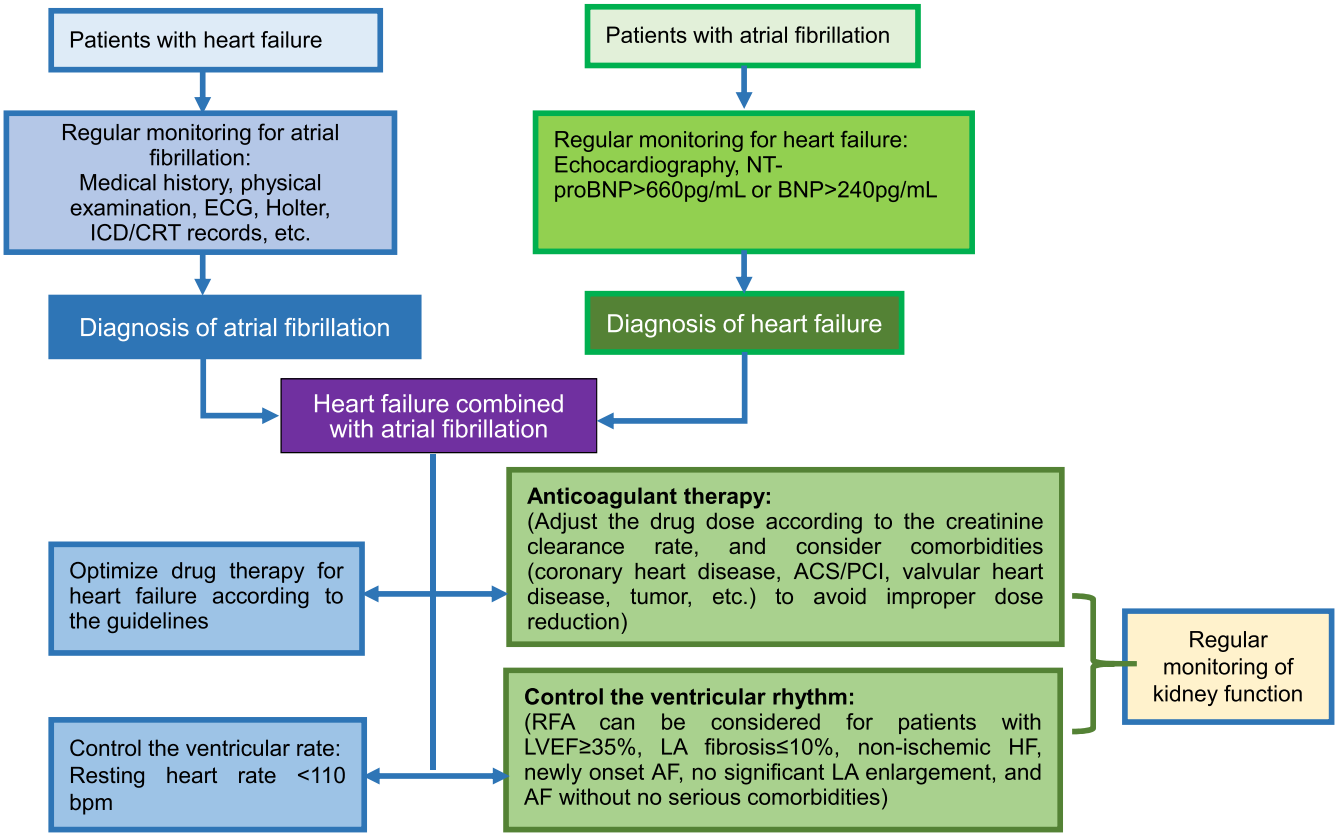

FIGURE 4 Treatment route for chronic heart failure (CHF) complicated with atrial fibrillation. ACS, acute coronary disease; AF, atrial fibrillation; BNP, brain natriuretic peptide; bpm, beats per minute; CRT, cardiac resynchronization therapy; ECG, electrocardiogram; HF, heart failure; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NT-proBNP, amino terminal proB-type natriuretic peptide; PCI, percutaneous coronary intervention; RFA, radiofrequency ablation

4.4.4 | Cognitive impairment, anxiety, depression, and delirium

Approximately one-third of patients with HF aged more than 80 years have cognitive impairment. Delirium is more common in elderly patients with HF and is associated with mortality risk and length of hospital stay in these patients.[88]

4.4.5 | Anemia

Anemia is closely related to the severity of symptoms, quality of life, and prognosis of elderly patients with HF. Iron deficiency is the most common cause of anemia. Patients with HF should be checked for iron deficiency if their hemoglobin is <14 g/dl, regardless of whether their LVEF is reduced.[89] Intravenous iron therapy may be considered for patients with HF of NYHA classes II-III and iron deficiency.[90]

4.4.6 | Frailty

Frail patients with CHF have a higher risk of death, HF readmission, and impaired quality of life.[91] HF readmission and limited mobility among elderly patients can exacerbate frailty. Frail patients should be assessed and individualized treatment regimens developed in a timely fashion.

4.4.7 | Malnutrition

Malnutrition affects the prognosis of patients with HF. All patients should undergo nutritional risk assessment during hospitalization. Nutritional interventions are recommended for patients at risk of malnutrition.

4.4.8 | Polypharmacy

Polypharmacy can lead to decreased compliance and worsening of HF. Therefore, monitoring of HF symptoms, adverse drug reactions, liver and kidney function, and electrolytes should be enhanced. The medication regimen should be simplified.

4.5 | Comprehensive management

HF is a complex cardiovascular disease syndrome with multiple etiologies, multiple mechanisms, and multiple manifestations. For elderly patients with HF, multi-aspect and multi-level comprehensive management should be implemented to address the causes of HF aggravation, lifestyle, drug treatment, rehabilitation, and nursing care before, during, and after hospitalization.

4.6 | Referral and follow-up

When various factors lead to the occurrence of acute decompensated HF, the patient's condition worsens and their vital signs become unstable. In this case, immediate admission to the hospital is required for medical intervention. Patients in community-based medical and health institutions that do not have cardiac emergency capabilities and intensive care units should be transferred to the nearest large- or medium-sized hospital as soon as possible.

Elderly patients with CHF should be followed up periodically. A patient file should be established, and the patient's condition should be followed. Health education and exercise rehabilitation guidance should be provided via outpatient follow-up, community visits, telephone and network home monitoring, and remote monitoring using wearable devices. The initial follow-up can be performed once every 1–2 weeks and once every 1–2 months when the patient is stable. The content of follow-up includes assessing the patient's condition and medication status, monitoring HF symptoms, NYHA classification, blood pressure, heart rate, heart rhythm, body weight, renal function, electrolytes, and other indexes, as well as monitoring adverse drug reactions and medication compliance and making appropriate adjustments to medication regimens. At the same time, the patient's abilities of daily living, cognitive function, psychological state, and dietary habits should be assessed to guide standardized exercise rehabilitation, and HF-related factors should be controlled while actively treating underlying diseases.

Morbidity and mortality are greatly increased in elderly patients with HF owing to the natural decline of organ functions, long-term accumulation of various chronic diseases, interactions among various comorbidities and geriatric syndromes, and a decline in adaptability to different social environments and psychological conditions. It is crucial that the fully understanding of clinical characteristics, early diagnosis of atypical HF, patient's overall condition assessing, as well as the individualized rational drug treatment and rehabilitation. In conclusion, all of these factors formed important basis for improvement in the comprehensive treatment of elderly patients with HF.

AUTHOR CONTRIBUTIONS

Initiate and organization of this consensus: Prof. Xiaoming Wang and Prof. Cuntai Zhang. Preparation and presentation of the published work, specifically critical review and revision, including pre- or post-publication stages: Cardiovascular Group, Geriatrics Branch, Chinese Medical Association; Writing the initial draft (including substantive translation: Editing group of the Chinese Expert Consensus on the Diagnosis and Treatment of Chronic Heart Failure in Elderly Patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Cuntai Zhang is an Editorial Board member of Aging Medicine and a co-author of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication.

ETHICS STATEMENT

Not applicable.

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APPENDIX 1

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