

## Guidelines Interpretation

# Guidelines for the management of chronic heart failure in dialysis patients in China

In China, the number of dialysis patients is on the rise, and the incidence of heart failure in dialysis patients has remained high.



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### Incidence of heart failure in Chinese multi-center cohort study

**47.3%** in peritoneal dialysis patients

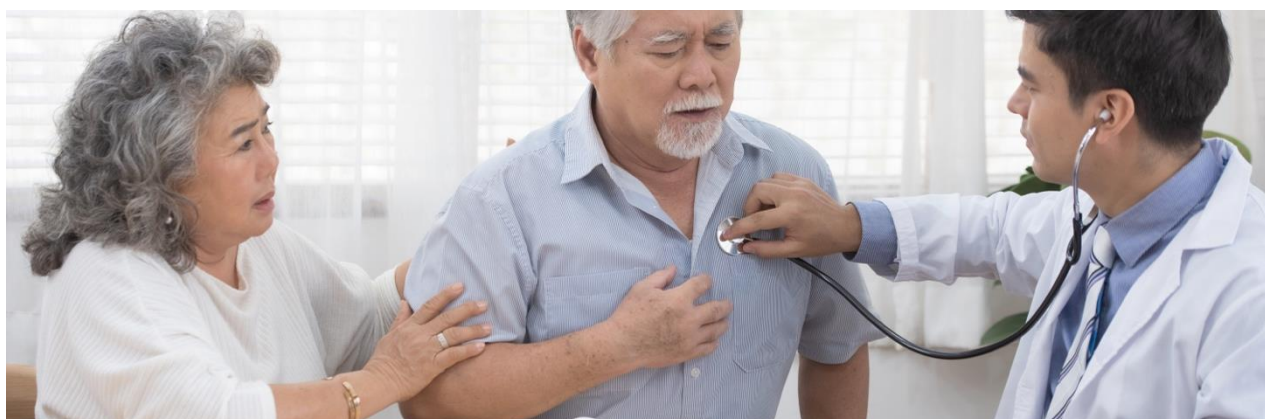
**42.9%** in hemodialysis patients

It is estimated that the number of dialysis patients in China will exceed 870,000 in 2025. A multi-center cohort study of 2388 Chinese dialysis patients (1775 on hemodialysis and 613 on peritoneal dialysis) found that the incidence of heart failure was 47.3% in peritoneal dialysis patients and 42.9% in hemodialysis patients.

Since dialysis patients have almost no residual renal function and many chronic complications, combined with the particularity, variability and limitations of hemodialysis and peritoneal dialysis, it is particularly important to protect the cardiac function of dialysis patients.

The diagnosis, treatment, and management of risk factors differ significantly between dialysis patients and the general population.

Heart failure is the second most common cardiovascular disease in dialysis patients. Once dialysis patients are complicated with heart failure, the survival rate is significantly reduced. Based on medical evidence and clinical experience, the Chinese Medical Association Nephrology Branch and the Zhongguancun Nephrology & Blood Purification Innovation Alliance Working Group jointly drafted the first "Guidelines for the management of chronic heart failure in dialysis patients in China", in order to standardize the clinical management process of heart failure in dialysis patients and improve patient outcomes.



## 1. Diagnosis of heart failure

The diagnosis and evaluation of heart failure depends on history, physical examination, laboratory tests, cardiac imaging, and functional tests.

Table 1. Diagnostic criteria for heart failure

Diagnostic criteria	HFrEF	HFmrEF	HFpEF
1	Symptoms and/or signs	Symptoms and/or signs	Symptoms and/or signs
2	LVEF < 40%	LVEF 40% ~ 49%	LVEF ≥ 50%
3	-	Elevated natriuretic peptide with at least one of the following criteria: (1) left ventricular hypertrophy and/or left atrial enlargement; (2) abnormal cardiac diastolic function	Elevated natriuretic peptide with at least one of the following criteria: (1) left ventricular hypertrophy and/or left atrial enlargement; (2) abnormal cardiac diastolic function

Note: HFrEF: heart failure with reduced ejection fraction, research status on it: randomized clinical trials mainly include such patients, and effective treatment has been proven; HFmrEF: heart failure with median ejection fraction, research status on it: the clinical characteristics, pathophysiology, treatment and prognosis of these patients are still unclear, and the single listing of this group is conducive to relevant studies; HFpEF: heart failure with preserved ejection fraction, research status on it: the patient's symptoms need to be ruled out as being caused by a non-cardiac condition, and effective treatment has not been established; LVEF: left ventricular ejection fraction; elevated natriuretic peptide as B-type natriuretic peptide (BNP) > 35 ng/L and/or N-terminal B-type natriuretic peptide (NT-proBNP) > 125 ng/L; indicators of abnormal diastolic function are shown in the transthoracic echocardiography in the diagnosis and evaluation of heart failure.

## a. Symptoms and signs

Main symptoms: dyspnea, fatigue, and fluid retention.

Characteristic signs include moist rale, peripheral edema, jugular vein engorgement, hepatojugular reflux sign, changes in apical pulsatile position, third heart sound gallop and heart murmur.

It should be noted that since the above symptoms and signs can also be seen in dialysis patients with volume overload, it is clinically difficult to distinguish heart failure from systemic volume overload. As a result, early heart failure symptoms in dialysis patients are often ignored.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Symptoms and signs	Strengthen the monitoring of heart failure-related symptoms and signs in dialysis patients, with particular attention to distinguish it from systemic volume overload.	I	C

## b. Routine examinations

Routine laboratory tests, ECG, chest X-ray, biomarkers, and echocardiography, etc.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Electrocardiogram	For dialysis patients with suspected or newly diagnosed heart failure, an electrocardiogram is recommended to assess heart rhythm, heart rate, QRS wave morphology and time limit, and to determine the presence of underlying conditions such as myocardial ischemia or left ventricular hypertrophy.	I	B
Chest X-ray	For dialysis patients with suspected or newly diagnosed heart failure, a chest x-ray is recommended to detect signs of pulmonary congestion / edema and cardiac enlargement, and to identify other cardiac or noncardiac causes that may be contributing to the patient's symptoms.	I	B



## 2. Biomarker

### a. Natriuretic peptide (NT-proBNP or BNP)

In dialysis patients, elevated BNP levels can still reflect the presence and severity of heart failure and provide prognostic information, but the diagnostic cutoff value should be adjusted according to renal function. The available research evidence suggests that:

- NT-proBNP is more predictive of heart failure than BNP;
- It is suggested to use NT-proBNP as an indicator for evaluating heart failure in dialysis patients: the half-life of NT-proBNP (60-90 min) is longer than that of BNP (20 min), and the concentration of the former in plasma is also higher than the latter, which is more convenient for clinical detection;
- Existing clinical studies have shown that the optimal cutoff value of NT-proBNP for the diagnosis of heart failure in ESRD patients is 11215.2 ng/L; however, the accuracy and validity of this criterion still need to be confirmed in independent prospective studies and clinical practice.

### b. Cardiac troponin (cTn)

Troponin T (TnT) has a higher predictive value for prognosis than troponin I (TnI), and hs-TnT is more widely used because its sensitivity is higher than that of TnT.

hs-TnT increases slightly with the progression of renal insufficiency, and the cutoff value for prognosis evaluation should be adjusted according to renal function: studies have shown that the optimal cutoff value of hs-TnT for predicting all-cause mortality in patients with CKD Stage 4 to 5 is 40 ng/L.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Natriuretic peptide	For dialysis patients with suspected or newly diagnosed heart failure, natriuretic peptide testing is recommended for the early diagnosis or exclusion of heart failure.	I	B
	It is suggested that NT-proBNP at dry weight should be used as the main biomarker for the diagnosis of heart failure in dialysis patients.	IIa	C
Cardiac troponin	For dialysis patients with suspected or newly diagnosed heart failure, hs-cTnT testing is recommended to assist in the etiological diagnosis, risk stratification, and prognostic assessment of heart failure.	I	A
Other biomarkers	For dialysis patients with heart failure, cardiac injury or fibrosis biomarker testing may be considered to assist in literature stratification and prognostic assessment of heart failure.	IIb	C

### c. Echocardiography

Echocardiography is an important examination in the diagnosis of heart failure, and is also the first choice to evaluate the cardiac structure and function. In dialysis patients, echocardiographic indicators that should be of particular concern include left ventricular size and wall thickness (to assess the presence of left ventricular hypertrophy and geometry), LVEF, left ventricular diastolic function, valve appearance and function, left atrial pressure, and pulmonary artery systolic pressure.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Echocardiography	For dialysis patients with suspected or newly diagnosed heart failure, echocardiography is recommended to assess cardiac structure and function, improve diagnostic accuracy, and assist in subtyping to guide management.	I	B
	Echocardiography is recommended when dialysis patients reach dry weight to exclude the influence of volume factors on the results.	IIa	C
	In dialysis patients, the ADQI Working Group echocardiography diagnostic criteria for heart failure may be considered, but attention should be paid to its potential overdiagnosis.	IIb	C
	In dialysis patients with worsening symptoms or signs of heart failure, follow-up echocardiographic evaluation should be performed as clinically necessary to reduce heart failure-related mortality, morbidity, and hospitalization rate.	IIa	B



### 3. Special examination

Special examinations for heart failure are suitable for patients who need to further clarify the etiology and condition evaluation, mainly including cardiac MRI, cardiac CT, coronary angiography, and quality of life assessment.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Cardiac MRI	CMR should be considered for dialysis patients who have no definite diagnosis of heart failure after preliminary clinical evaluation, or need to further clarify the etiology, or need to determine the indications for coronary revascularization, and non-gadolinium imaging should be considered if enhanced scanning is required.	IIb	C
	If gadolinium-enhanced CMR is required, high-throughput HD therapy is recommended as soon as possible after examination and followed by additional high-throughput HD after 24 hours to maximize gadolinium clearance and reduce the risk of nephrogenic systemic fibrosis.	IIa	C
Cardiac CT	For dialysis patients with heart failure who have low to moderate suspected coronary heart disease or for whom the load test fails to definitively diagnose myocardial ischemia, cardiac CT/CTA is feasible to exclude coronary stenosis, but attention should be paid to the effect of calcification on its accuracy, and the effect of iodine-containing contrast agent on residual renal function, volume load, and serum potassium in patients.	IIa	B
Coronary arteriography	Coronary angiography may be considered for dialysis patients with heart failure who have risk factors for coronary heart disease and have myocardial ischemia as indicated by noninvasive examination, but the effects of iodine-containing contrast agent on residual renal function, volume load and serum potassium should be noted.	IIb	C
Life quality assessment	Life quality assessment is helpful for the screening of subclinical heart failure and may be considered for dialysis patients at high risk of heart failure.	IIb	C





## 4. Heart failure management in dialysis patients

Hemodialysis management: prevention of heart failure in maintenance hemodialysis (MHD) patients.

The prevention of heart failure in MHD patients mainly includes optimizing volume status, achieving adequate dialysis, and preventing vascular access-related heart failure.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Optimizing volume status	Optimizing volume status is an important goal in the management of heart failure in MHD patients.	I	C
	For MHD patients, assessment of volume status should be based first on clinical assessment (history review and physical examination).	I	C
	For MHD patients, non-invasive methods such as ultrasound, bioelectrical impedance and relative blood volume monitoring can be considered to assist in the assessment of volume status.	IIb	C
	For MHD patients who have completed volume assessments, it is recommended to gradually achieve the target dry weight over a period of days or weeks.	I	B
	For MHD patients, weight gain during dialysis should be controlled to less than 5% of body weight.	I	B
Achieving adequate dialysis	In order to prevent heart failure, MHD patients should achieve adequate dialysis, and the main strategies are: strict dialysis adequacy management, high-throughput dialysis, online HDF and selection of membrane materials with good biocompatibility.	I	A
Preventing vascular access-related heart failure	Preoperative HF assessment is recommended for all patients for whom vascular access is to be established, and regular follow-up is recommended for patients at high risk for heart failure (significant AVF dilatation, suspected high flow, or high AVF/AVG) after AVF/AVG.	I	B
	For patients with an EF < 30% at preoperative assessment, establishment of AVF/AVG is not recommended.	III	C
	For patients at high risk of heart failure or those with pre-existing heart failure, it is recommended to avoid the location and method of fistula anastomosis that may lead to high blood flow.	IIa	C

## Treatment of heart failure in MHD patients

Intensive dialysis, continuous renal replacement therapy (CRRT), and treatment of vascular access-related heart failure are important aspects of hemodialysis treatment in MHD patients with heart failure.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Intensive dialysis	For MHD patients with heart failure, an intensive dialysis regimen with increased dialysis frequency is recommended.	I	B
CRRT	For MHD patients with heart failure, continuous renal replacement therapy is recommended, especially when they cannot tolerate IHD.	I	B
Treatment of vascular access-related heart failure	For patients with established AVF/AVG, AVF/AVG blood flow monitoring and echocardiography should be performed in time if heart failure is present or the original heart failure is aggravated.	I	C
	For patients with vascular access-related heart failure, internal fistula drainage surgery is recommended when the cardiac index is $\leq 3.9 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ .	IIa	C
	For patients with vascular access-related heart failure, such as refractory heart failure, it is recommended to close the AVF/AVG.	IIa	B
Others	For MHD patients with heart failure who have recurrent hypotension during dialysis, hypothermic dialysate ( $<35^{\circ}\text{C}$ ) may be considered.	IIb	B
	For MHD patients with heart failure who have recurrent hypotension during dialysis, personalized dialysate concentration may also be considered.	IIb	B

## Peritoneal dialysis (PD) management

PD is a home-based therapy that continuously removes sodium and water to maintain good volume status and avoids the risk of heart failure associated with vascular access, so it is considered an appropriate treatment for dialysis patients with heart failure, especially those with refractory heart failure.

Recommendation	Strength of Recommendation	Levels of Evidence
PD is beneficial to improve the cardiac function status and reduce the readmission rate of heart failure in dialysis patients with heart failure, which is an appropriate treatment for such patients.	I	B



### Prevention of heart failure in PD patients

The prevention of heart failure in PD patients mainly includes the optimization of non-drug therapy and PD prescription.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Optimizing non-drug therapy	To prevent heart failure, water and sodium intake should be strictly limited for PD patients.	I	C
	To prevent heart failure, body weight monitoring should be strengthened for PD patients, and daily weight measurement and recording are recommended.	I	C
Optimizing PD prescription	To prevent heart failure, PD patients are advised to adopt an optimized PD mode.	IIa	C
	In order to prevent heart failure, PD patients with insufficient ultrafiltration or uncontrollable volume can be treated with PD combined with HD.	IIa	B

### Treatment of heart failure in PD patients

The treatment of heart failure in PD patients mainly includes adjustment of PD prescription and PD mode.

Item	Recommendation	Strength of Recommendation	Levels of Evidence
Adjusting PD prescription	For PD patients with heart failure, increasing the dialysate glucose concentration, shortening the abdominal storage time of dialysate and increasing the dialysis dose are conducive to improving the volume and correcting the heart failure.	I	C
	For PD patients with heart failure, the use of icodextrin dialysate is recommended to increase ultrafiltration.	I	A
Adjusting PD Mode	For PD patients with heart failure, ultrafiltration can be improved by adjusting PD mode.	IIa	B

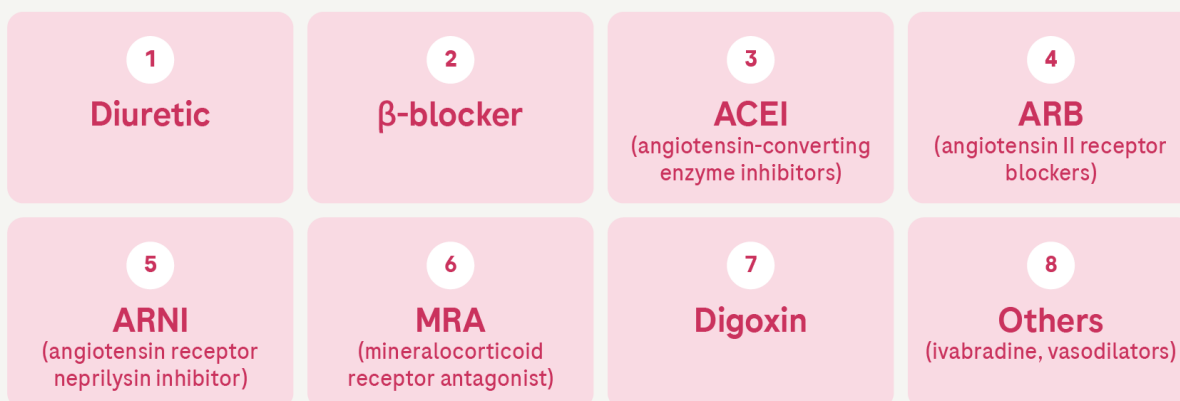


## 5. Drug management

Drug management therapy remains an integral part of the treatment of dialysis patients with heart failure. Experts have formed preliminary consensus opinions on drug therapy based on the limited clinical evidence available, but these opinions still need to be further refined in clinical practice.

Commonly used drugs in the treatment of dialysis complicated with heart failure are diuretics,  $\beta$ -blockers, angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB); angiotensin receptor neprilysin inhibitor (ARNI); mineralocorticoid receptor antagonist (MRA), digoxin and others.

### Commonly used drugs in the treatment of dialysis complicated with heart failure



## Dialysis with reduced ejection fraction

### Drug management in patients with heart failure (HFrEF)

Therapeutic drugs	Recommendation	Strength of Recommendation	Levels of Evidence
Diuretic	For dialysis patients with HFrEF who still have urine volume and fluid retention, diuretic treatment is recommended, and loop diuretic is preferred.	IIa	B
$\beta$ -blocker	For dialysis patients with HFrEF, $\beta$ -blocker treatment is recommended.	I	B
ACEI/ARB	For dialysis patients with HFrEF, it is recommended to use ACEI/ARB in combination with $\beta$ -blocker.	IIa	B
ARNI	For dialysis patients with HFrEF who can tolerate ARB/ACEI treatment, it is recommended to use ARNI instead of ARB/ACEI to further control the symptoms of heart failure and improve myocardial remodeling.	IIa	C
	Concomitant use of ARNI with ACEI should be avoided.	III	B
	It is recommended to use ARNI 36 hours after discontinuation of ACEI.	IIa	C
	For dialysis patients with HFrEF, ARNI can be considered for initial treatment to reduce the risk of short-term adverse events and simplify the management process (avoiding the conversion process from ACEI to ARNI).	IIb	C
MRA	For dialysis patients with HFrEF who have been treated with an optimal dose of $\beta$ -blockers combined with ACEI/ARB/ARNI and still have symptoms of heart failure, MRA therapy can be considered under strict screening and close monitoring.	IIb	B
Digoxin	The routine use of digoxin is not recommended for most dialysis patients with HFrEF.	III	B

### Drug management of dialysis patients with heart failure with mildly reduced ejection fraction (HFmrEF) and heart failure with preserved ejection fraction (HFpEF)

Item	Recommendation	Strength of Recommendation	Levels of Evidence
HFmrEF	For dialysis patients with HFmrEF, $\beta$ -blockers combined with ACEI/ARB/ARNI are recommended.	IIa	C
HFpEF	For dialysis patients with HFpEF, the treatment is mainly to control the volume overload, improve hypertension and myocardial ischemia and other related factors.	I	B
	For dialysis patients with HFpEF, $\beta$ -blockers combined with ACEI/ARB/ARNI therapy may be considered.	IIb	C
	For dialysis patients with HFpEF, MRA therapy should be considered after a full assessment of the potential risks and benefits of treatment.	IIb	C

#### References:

Chinese Medical Association Nephrology Branch, Zhongguancun Nephrology & Blood Purification Innovation Alliance. Guidelines for the management of chronic heart failure in dialysis patients in China [J]. Chinese Journal of Nephrology, 2022, 38(5): 465-496. DOI: 10.3760/cma.j.cn441217-20210812-00068.