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Review Article

Practical Prevention of Heart Failure Across Stages A and B: A Scientific Statement From the Japanese Heart Failure Society

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ABSTRACT

Heart failure (HF) is a growing health problem in Japan, associated with substantial morbidity, mortality, recurrent hospitalization, impaired quality of life, and increasing health care costs. Early prevention before the onset of signs and symptoms has therefore become a major priority in cardiovascular medicine. This scientific statement from the Japanese Heart Failure Society provides practical prevention strategies for patients with HF stage A and stage B in Japan. Particular emphasis is placed on biomarker-guided screening using brain (B-type) natriuretic peptide and N-terminal pro-brain natriuretic peptide to facilitate earlier detection of stage B (pre-HF) and identification of patients at increased risk of progression to symptomatic HF. The statement summarizes evidence-based management of major cardiovascular-kidney-metabolic disorders associated with HF development, including hypertension, diabetes mellitus, chronic kidney disease, obesity, coronary artery disease, left ventricular dysfunction, valvular heart disease, and atrial fibrillation. It also addresses disease-specific approaches for optimizing blood pressure, glycemic control, renal protection, lipid management, and weight reduction. Preventive strategies include lifestyle modification, pharmacologic therapy, serial reassessment of natriuretic peptide levels, and appropriate use of cardiovascular imaging and timely specialist referral. Because many patients at risk for HF are managed outside specialized cardiovascular centers, practical pathways for collaboration between cardiologists and noncardiologist physicians are essential. The importance of timely referral, shared risk recognition, and multidisciplinary care is therefore emphasized. Implementation of clinically applicable prevention strategies may help reduce progression to symptomatic HF, facilitate earlier therapeutic intervention, and improve long-term cardiovascular outcomes. (*J Cardiac Fail 2026;00:1–12*)

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See page XXX for disclosure information.
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Introduction

Heart failure (HF) has become a major global health problem associated with increasing morbidity, mortality, recurrent hospitalization, and health care expenditures.[1–3] With the progressive aging of populations worldwide, the burden of HF continues to increase.[1,4] Because HF is associated with impaired quality of life, functional decline, and poor clinical outcomes, its prevention has become a major priority in cardiovascular medicine.

Most cases of HF develop on the basis of cardiovascular-kidney-metabolic risk factors such as hypertension, diabetes mellitus, chronic kidney disease (CKD), obesity, and atherosclerotic cardiovascular disease,[5–7] which are categorized as stage A according to the contemporary HF staging system.[8] In addition, many conditions classified as stage B (pre-HF), including asymptomatic left ventricular dysfunction, previous myocardial infarction, atrial fibrillation (AF), and valvular heart disease, frequently are managed in routine clinical practice by noncardiologist physicians. Importantly, patients with stages A and B are asymptomatic, making early recognition of progression to stage C (symptomatic HF) challenging. Consequently, progression to stage C is often recognized only after irreversible cardiac dysfunction or clinical decompensation has developed. Earlier detection of the transition from stage A to stage B and timely intervention before symptom onset may therefore represent an important opportunity to reduce future HF burden.

Recent guidelines and scientific statements increasingly have emphasized the importance of HF prevention.[8–11] Efforts to prioritize the primary prevention of HF also have been proposed internationally, encompassing risk-based strategies across the cardiovascular-kidney-metabolic spectrum and dedicated approaches for prevention after myocardial infarction.[12–14] Similarly, a joint scientific statement from the Heart Failure Society of America and the American Society for Preventive Cardiology proposed reframing prevention as a continuum spanning the entirety of HF care, from primary prevention in stages A and B to secondary and tertiary prevention in established and advanced HF.[15] In parallel, previous natriuretic peptide–guided screening studies have suggested the potential value of biomarker-guided approaches for earlier detection of stage B and prevention of cardiovascular events.[16,17] However, substantial implementation gaps remain between contemporary guideline recommendations and routine clinical practice. Most patients with stages A and B are managed by primary care physicians, diabetologists, nephrologists, or general internists rather than cardiologists. Therefore, practical and clinically applicable strategies are needed to facilitate earlier detection of stages A and B, guide referral timing, and support multidisciplinary collaboration between cardiologists and noncardiologist physicians.

This scientific statement from the Japanese Heart Failure Society aims to provide practical approaches for HF prevention focused on management for stages A and B. Particular emphasis is placed on biomarker-guided detection using brain (B-type) natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (NT-proBNP), serial reassessment, referral strategies, and disease-specific interventions that can be implemented in routine clinical practice.

Conceptual framework of HF prevention

Stage A and Stage B

The contemporary concept of HF prevention extends beyond the treatment of symptomatic disease and emphasizes intervention across the continuum from cardiovascular risk factors to asymptomatic structural/functional heart disease and ultimately symptomatic HF. According to the contemporary HF staging system, stage A includes patients at risk for HF but without current or previous signs or symptoms of HF, structural or functional heart disease, or abnormal cardiac biomarkers.[8,9] Conditions include hypertension, cardiovascular disease, diabetes, CKD, obesity, exposure to cardiotoxic agents, genetic variants associated with cardiomyopathy, and a family history of cardiomyopathy. Stage B includes patients without current or previous signs or symptoms of HF but with evidence of 1 or more of the following: structural heart disease, increased cardiac filling pressure, or elevated cardiac biomarkers.[8,9] Structural abnormalities associated with stage B include reduced left or right ventricular systolic function (reduced ejection fraction or strain), ventricular hypertrophy, chamber enlargement, wall motion abnormalities, valvular heart disease, previous myocardial infarction, and AF.

Trajectory of HF Progression Across Stages

HF progression is a dynamic and continuous process extending from cardiovascular risk factors to pre-HF and ultimately symptomatic HF. Persistent hemodynamic stress, neurohormonal activation, metabolic dysfunction, systemic inflammation, myocardial fibrosis, endothelial dysfunction, and renal impairment contribute to progressive cardiovascular remodeling over time.[5,18–20] HF

development and progression are increasingly recognized within a broader spectrum of interconnected cardiorenal and metabolic disorders, including obesity, diabetes mellitus, CKD, dyslipidemia, hypertension, atherosclerotic cardiovascular disease, pulmonary disease, and metabolic dysfunction–associated steatotic liver disease, which frequently coexist and share overlapping pathophysiological pathways.[6] Because patients with stages A and B remain asymptomatic, progression toward symptomatic HF may not be clinically recognized until advanced cardiac dysfunction or clinical decompensation develops. In contrast, prognosis worsens with progression across HF stages, and patients with stage B have increased risks of cardiovascular mortality and progression to symptomatic HF compared with those remaining in stage A.[21,22] In this context, prevention of progression from stage A to B, as well as prevention of progression to stage C or D, are central goals of contemporary HF management. Earlier recognition of HF progression may provide an important opportunity for timely therapeutic intervention before irreversible myocardial damage or clinical decompensation develops.

Biomarker-guided screening and referral strategy

Role of BNP/NT-proBNP in Early HF Detection

Natriuretic peptides play a central role in the early detection of stage B and progression toward symptomatic HF. BNP and NT-proBNP are established biomarkers reflecting myocardial wall stress and elevated cardiac filling pressure and are strongly associated with future risk of HF hospitalization and cardiovascular events.[23] Among patients with stage A, periodic assessment of BNP or NT-proBNP may facilitate earlier detection of progression to stage B. In a prospective cohort study of community-dwelling adults in Japan with NT-proBNP levels <125 pg/mL, 4.2% of participants with NT-proBNP ≤55 pg/mL and 17.9% of those with NT-proBNP >55 pg/mL progressed to NT-proBNP levels ≥125 pg/mL over a 5-year follow-up period, suggesting transition to stage B.[24] These findings support the value of natriuretic peptide measurement for detecting subclinical progression before the development of overt HF symptoms. Current evidence supports the use of BNP <35 pg/mL or NT-proBNP <125 pg/mL as thresholds indicating low likelihood of HF in non-acute settings.[25] Conversely, BNP ≥35 pg/mL or NT-proBNP ≥125 pg/mL indicates stage B, particularly in patients with cardiovascular risk factors.

Interpretation of Natriuretic Peptides

Interpretation of BNP and NT-proBNP requires careful consideration of clinical context and comorbidities. Advanced age, female sex, CKD, AF, inflammation, anemia, and treatment with angiotensin receptor-neprilysin inhibitor (ARNI) may increase natriuretic peptide levels independent of symptomatic HF. Conversely, obesity[26] and African ancestry may suppress BNP and NT-proBNP concentrations despite elevated cardiac filling pressure. Among patients treated with ARNI, BNP concentrations may transiently increase during the initial treatment period, whereas NT-proBNP is less affected.[8] The 2026 European Society of Cardiology Guidelines for the management of HF have adopted age-stratified NT-proBNP cut-off values for the diagnostic work-up of patients with suspected HF, applying greater thresholds in older age groups.[11] However, these age-stratified cut-offs apply to the diagnostic evaluation of symptomatic HF and do not modify the stage B thresholds described in the previous section, "Role of BNP/NT-proBNP in Early HF Detection." Moreover, previous studies have demonstrated that elevated NT-proBNP remains strongly associated with adverse cardiovascular outcomes regardless of renal function,[27] and therefore elevated natriuretic peptide levels should not be dismissed solely because of renal dysfunction. Serial changes in natriuretic peptide levels also may provide clinically important information, because the progressive elevation of BNP or NT-proBNP over time may indicate worsening cardiac remodeling and increasing risk of transition to symptomatic HF.[16,28]

Serial Monitoring and Timing of Reassessment

Serial reassessment may facilitate earlier recognition of progression across HF stages, particularly the transition from stage A to B. For patients with stage A, annual BNP or NT-proBNP measurement should be considered whenever feasible. In patients classified as stage B, more frequent reassessment, including BNP or NT-proBNP measurement at least twice a year, may facilitate earlier recognition of progression toward symptomatic HF. In addition to natriuretic peptide measurement, physicians should assess for signs and symptoms suggestive of HF progression, including exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, lower-extremity edema, and weight gain. Radiography of the chest and electrocardiography also may provide important complementary information during follow-up, particularly for detection of pulmonary congestion or new electrocardiographic abnormalities.

Referral Strategy and Collaboration With Cardiologists

Collaboration between primary care physicians and cardiologists is essential for effective HF prevention. Previous studies, including the St. Vincent's Screening to Prevent Heart Failure (STOP-HF) study[16] and the NT-proBNP Selected PreventiOn of cardiac eveNts in a populaTion of dIabetic patients without A history of Cardiac disease (PONTIAC) trial,[17] suggested that natriuretic peptide–guided screening combined with collaborative cardiovascular care may be associated with reduced progression to symptomatic HF and cardiovascular events. Although neither trial was specifically designed to validate the serial monitoring strategy or the specific

measurement intervals recommended in this statement, periodic natriuretic peptide reassessment at the aforementioned intervals is considered a pragmatic, consensus-based approach. Patients with elevated natriuretic peptide levels may have underlying structural heart disease even in the absence of overt HF signs or symptoms and should therefore be referred to a cardiologist for further evaluation and echocardiographic assessment. The goal of specialist referral is not only confirmation of HF diagnosis but also earlier identification of stage B phenotypes and optimization of preventive therapies before the development of symptomatic HF. This collaborative care model may facilitate more timely initiation of evidence-based interventions and improve continuity of care across specialties. An overview of the proposed screening, referral, and preventive management strategies for patients with stages A and B is presented in Figures 1 and 2.

Practical Considerations and Potential Limitations of Screening

Natriuretic peptide–based screening across patients with stages A and B has inherent limitations that warrant careful consideration in clinical practice. Because the prevalence of echocardiographic structural or functional abnormalities is relatively low in the general population,[29] a certain proportion of confirmatory echocardiograms performed after biomarker-based screening may be negative. However, an elevated natriuretic peptide level itself constitutes 1 of the criteria for stage B and reflects an increased risk of future progression to symptomatic HF. Such patients therefore warrant longitudinal follow-up rather than reassurance alone.

The increased demand for echocardiographic referral associated with biomarker-based screening also raises concerns regarding overmedicalization and the capacity of cardiology services to absorb these referrals. These are important and valid concerns, particularly given finite health care resources. Nevertheless, HF prevalence and hospitalization rates continue to increase, placing substantial strain on cardiovascular care systems and driving up health care expenditure. Earlier identification and management of patients with stages A and B may help mitigate this trajectory by reducing progression to symptomatic HF and subsequent hospitalization, potentially offsetting the burden of referral and patient follow-up over the longer term.

Prevention strategies in stage A

Throughout stages A and B, patients should maintain healthy lifestyle habits to prevent progression to stage C, including regular exercise and physical activity, weight management, salt reduction, a healthy diet, smoking cessation, moderation of alcohol intake, and infection prevention. In addition to lifestyle modification, appropriate management of cardiovascular and metabolic diseases plays a central role in preventing progression across HF stages. The sections that follow describe practical

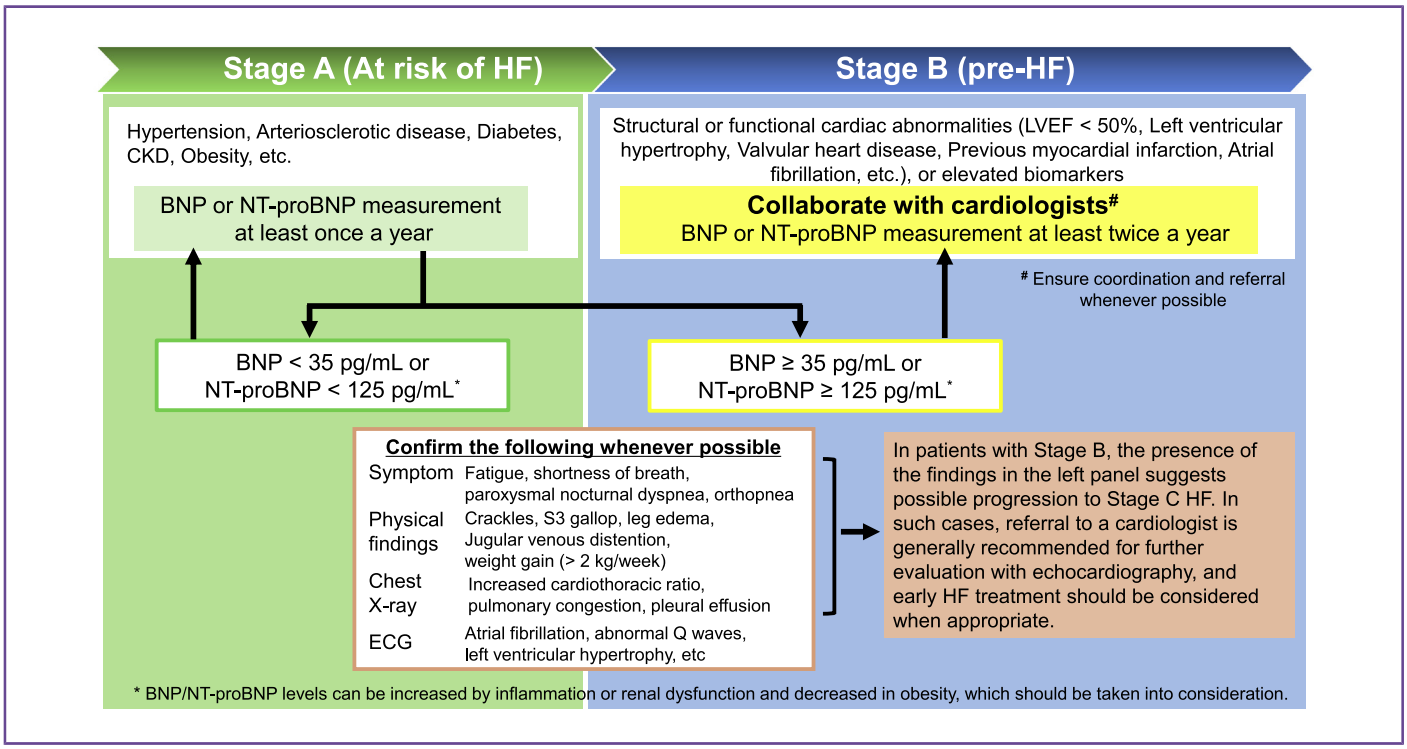


Fig 1. Clinical flowchart for screening, risk assessment, and referral in stage A and stage B. BNP, brain natriuretic peptide; ECG, electrocardiogram; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide.

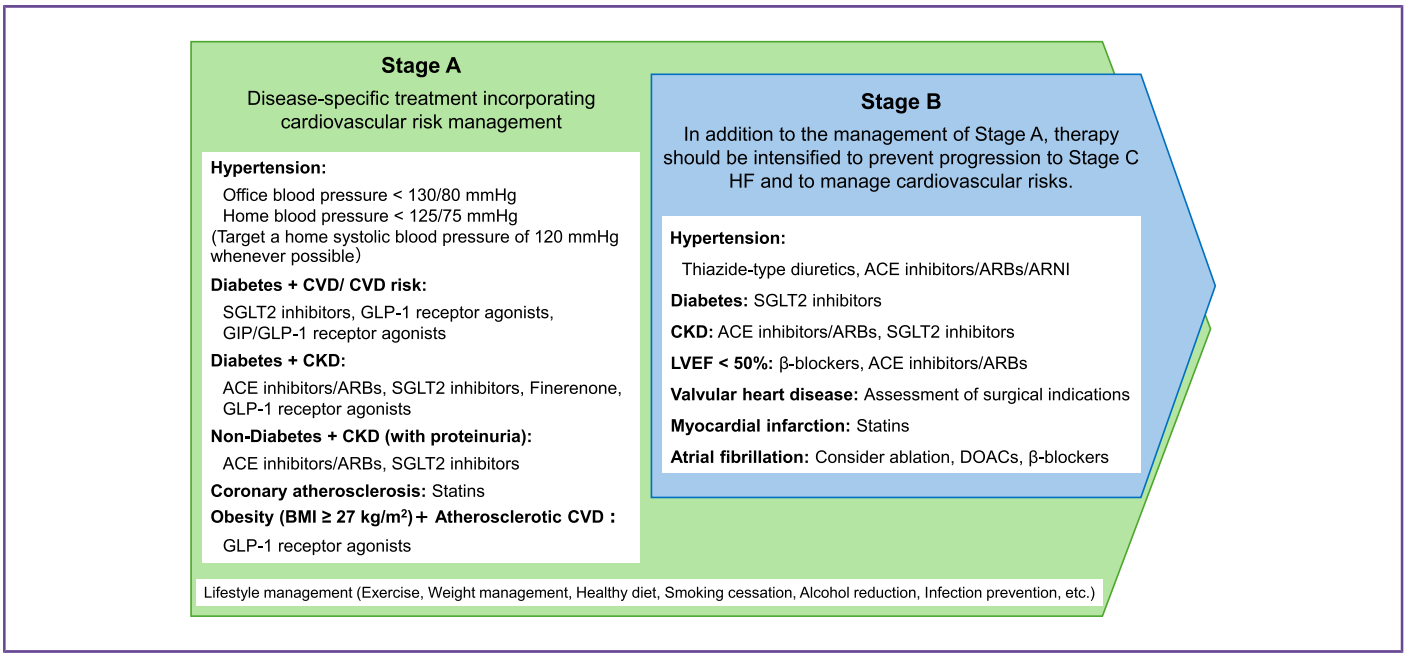


Fig 2. Clinical flowchart for preventive management in stage A and stage B. ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BMI, body mass index; BNP, brain natriuretic peptide; CKD, chronic kidney disease; CVD, cardiovascular disease; DOAC, direct oral anticoagulant; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; SGLT2, sodium-glucose cotransporter 2.

preventive strategies for major conditions associated with HF progression.

Hypertension

The therapeutic goal for patients with hypertension in stage A is to prevent progression to stage B. To achieve this, appropriate blood pressure control and achievement of target blood pressure levels are essential. For all patients with hypertension, the target office blood pressure is <130/80 mm Hg (target home blood pressure is <125/75 mm Hg), and efforts should be made to achieve these targets while taking tolerability and comorbidities into consideration. When feasible, further lowering of blood pressure to <120 mm Hg is encouraged.[30] Lifestyle modifications should be recommended for all patients, regardless of whether pharmacologic therapy is initiated (see Chapter 7 of the current Japanese Society of Hypertension Guidelines[31] for detailed recommendations). If blood pressure targets are not achieved despite lifestyle modifications, antihypertensive drug therapy should be promptly initiated in accordance with current hypertension guidelines[30,31] (see Chapter 8 of the current Japanese Society of Hypertension Guidelines[31] for detailed recommendations on drug selection and treatment algorithms). First-line antihypertensive agents include major classes such as long-acting dihydropyridine calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs), thiazide-type diuretics, and β-blockers. If adequate blood pressure control is not achieved with a single agent, combination therapy using antihypertensive drugs with different mechanisms of action is effective.[32] and treatment intensification should be implemented as early as possible. In this case, 2 first-line drugs are combined, but ARNI (switching from ACE inhibitors or ARB) or a mineral corticoid receptor antagonist also may be administered.

Because an increased number of medications may reduce adherence and thereby impair achievement of blood pressure targets, the use of fixed-dose combination agents should also be considered.[33] Clinical inertia represents a major barrier to achieving blood pressure targets; therefore, health care providers should clearly communicate the significance of blood pressure management and target values to patients and provide treatment based on shared decision-making.

Diabetes and Cardiovascular Disease Risk

Patients with diabetes have a 2- to 4-fold greater risk of developing HF compared with those without diabetes,[34] and HF is a major determinant of prognosis in this population.[35] The risk of incident HF is also elevated in individuals with asymptomatic coronary artery disease or acute coronary syndrome,[34,36] highlighting the need for regular risk assessment and preventive strategies.

For patients with diabetes and cardiovascular disease (CVD) or CVD risk factors, appropriate blood pressure control,[37] glycemic management that minimizes hypoglycemia, and the use of cardioprotective agents, such as sodium-glucose co-transporter 2 (SGLT2) inhibitors,[38] glucagon-like peptide-1 (GLP-1) receptor agonists,[39] and dual glucose-dependent insulinotropic polypeptide (GIP)

and GLP-1 receptor agonist,[40] should be considered for cardiovascular risk reduction. Hypoglycemia may adversely affect the cardiovascular system through sympathetic activation and inflammation,[41] making avoidance of hypoglycemia essential when using agents such as sulfonylureas, glinides, or insulin. Continuous glucose monitoring is useful for detecting nocturnal or unrecognized hypoglycemia.[42] Awareness and management of HF risk in patients with diabetes should be shared across multidisciplinary teams, including primary care physicians, cardiologists, diabetes specialists, and home health care nurses.[43]

Chronic Kidney Disease

In addition to estimated glomerular filtration rate (eGFR), proteinuria assessment, commonly performed using the urinary albumin-to-creatinine ratio (UACR), is a key component of CKD evaluation.[44] However, such testing remains substantially underused in clinical practice. A large laboratory-based analysis in the United States found that 80% of at-risk individuals did not undergo guideline-concordant testing over a 6-year period, and among those tested, only 20% received UACR assessment.[45] Although Japan-specific data are lacking, similar challenges are likely present. In Japan, UACR is currently reimbursed only for diabetic nephropathy. Measurement of the urinary protein-to-creatinine ratio is therefore more practical for screening patients without diabetes. Treatment strategies for CKD differ according to the presence or absence of diabetes and proteinuria.

Diabetes Plus CKD. ACE inhibitors/ARBs, SGLT2 inhibitors, finerenone, and GLP-1 receptor agonists have demonstrated preventive effects against the development of HF in patients with diabetes with CKD. Therefore, combination therapy with these drugs is recommended. The selection of each drug according to CKD stage is summarized in Table 1.

ACE inhibitors/ARBs. ACE inhibitors/ARBs have been proven to reduce the risk of HF development in patients with diabetes and CKD[46–48] and are recommended when appropriate. An initial decrease in eGFR may be observed after initiation (initial dip); therefore, eGFR should be reassessed at an early stage (2–8 weeks after initiation). Even in patients who progress to CKD stages G4 or G5 (eGFR <30 mL/min/1.73 m^2) during treatment, routine discontinuation of ACE inhibitors/ARBs is not necessarily required.[49]

SGLT2 inhibitors. SGLT2 inhibitors have been proven to reduce the risk of HF development in patients with diabetes and CKD[50–53] and are recommended when appropriate. Combination therapy with SGLT2 inhibitors and ACE inhibitors/ARBs has been shown to provide a greater preventive effect against HF. An initial decrease in eGFR may occur after initiation and early reassessment of eGFR (2–8 weeks after initiation) is recommended.

Finerenone. Finerenone has been proven to reduce the risk of HF development in patients with diabetes with CKD[54–56] and is recommended when appropriate. As with other drugs, an initial decrease in eGFR may occur and early reassessment (2–8 weeks after initiation) is recommended. When used in combination with ACE inhibitors/ARBs, careful monitoring of serum potassium levels is required due to the risk of hyperkalemia.

GLP-1 receptor agonists (semaglutide). In patients with diabetes with CKD, subcutaneous semaglutide has been proven to reduce the risk of HF development.[57] GLP-1 receptor agonist therapy should be considered, especially in patients for whom intensification of glycemic control is indicated or who have comorbid obesity meeting the treatment criteria (see the section "Obesity Plus Atherosclerotic CVD").

Nondiabetes Plus CKD (With Proteinuria). Combination therapy with ACE inhibitors/ARBs and SGLT2 inhibitors is

Table 1 Indications for drug therapy across CKD stages

Drug	CKD Stage G1–3 eGFR ≥30 mL/min/1.73m^2	CKD Stage G4 eGFR 15–29 mL/min/1.73m^2	CKD Stage G5 eGFR <15 mL/min/1.73m^2
ACE inhibitors/ARBs	●	○	△
SGLT2 inhibitors	●	● (eGFR ≥20 mL/min/1.73m2)	△
Finerenone*	●	○ (eGFR ≥25 mL/min/1.73m2)	△
GLP-1 RAs* (semaglutide)	●	○ (eGFR ≥25 mL/min/1.73m2)	△

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT2, sodium-glucose cotransporter 2.

●Sufficient evidence supports its use.

○Evidence is limited, but its use is considered based on efficacy and safety.

△Insufficient evidence; no definitive conclusion.

*Limited to patients with diabetes.

recommended. Recently, the FIND-CKD (Ferinject assessment in patients with Iron deficiency anaemia and Non-Dialysis-dependent Chronic Kidney Disease) trial demonstrated that finerenone attenuated the annual rate of eGFR decline and reduced the risk of a composite cardiorenal endpoint in patients without diabetes plus CKD with proteinuria.[58] However, finerenone does not currently have health insurance coverage for this indication in Japan, and this limitation should be kept in mind.

ACE inhibitors/ARBs. ACE inhibitors/ARBs have been shown to reduce cardiovascular events in patients without diabetes with CKD and proteinuria[59,60] and are recommended when appropriate. Clinical considerations after initiation are as described in the section "Diabetes Plus CKD."

SGLT2 inhibitors. SGLT2 inhibitors have been shown to reduce the risk of HF development in patients without diabetes with CKD and proteinuria[50,51] and are recommended, when appropriate, on the basis of their renal and cardiovascular protective effects.[49] Clinical considerations after initiation are as described in the section "Diabetes Plus CKD."

Coronary Artery Disease

Coronary artery disease (CAD) is one of the major causes of HF, and prevention of its progression from an early stage is essential. CAD without regional wall motion abnormalities is categorized as one of the atherosclerotic diseases in stage A. Even in the absence of structural or functional cardiac abnormalities, active intervention and management should begin once CAD is identified. For patients with CAD, antiplatelet therapy and statins should be implemented as appropriate.[61] In accordance with current guideline recommendations, clinicians should provide comprehensive risk factor control, including management of blood pressure, glucose, and lipid levels, together with appropriate pharmacological therapy and lifestyle modification.

Obesity Plus Atherosclerotic CVD

In Japan, obesity is defined as a condition characterized by a body mass index (BMI) $\geq$25 kg/m^2 accompanied by visceral fat accumulation or obesity-related comorbidities.[62] Obesity is classified as stage A and has been reported to confer an increased future risk of HF development.[63,64] Therefore, in patients with obesity, particularly those with a BMI $\geq$27 kg/m^2 and concomitant atherosclerotic CVD, appropriate risk assessment and lifestyle management are required as part of a comprehensive strategy for HF prevention, and pharmacologic treatment may be considered in those who meet the approved indication in Japan (hypertension, dyslipidemia, or type 2 diabetes, together with a BMI $\geq$27 kg/m^2 with $\geq$2 obesity-related comorbidities or a BMI $\geq$35 kg/m^2, each after $\geq$6 months of nutritional counseling and diet and exercise intervention[26]). In particular, people of Asian descent are known to have greater visceral fat accumulation than Western populations even at BMI levels below 30 kg/m^2, which is associated with a greater CVD risk.[65] A 10-year follow-up study from the Circulatory Risk in Communities Study (CIRCS) trial[66] demonstrated that individuals with a BMI of 27$-$30 kg/m^2 had a risk of stage B or symptomatic HF comparable with that of individuals with a BMI $\geq$30 kg/m^2. Accordingly, appropriate dietary and exercise interventions should be implemented for HF prevention. In Japan, 2 injectable agents are currently approved for the treatment of obesity: the long-acting GLP-1 receptor agonist semaglutide and the long-acting dual GIP/GLP-1 receptor agonist tirzepatide. In the SELECT trial, the efficacy of semaglutide was evaluated in patients without diabetes with a BMI $\geq$27 kg/m^2 and established atherosclerotic CVD.[67] The trial demonstrated a significant reduction in the primary composite endpoint of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke), as well as a significant reduction in HF-related composite events, which was a secondary endpoint. Whereas the dual GIP/GLP-1 receptor agonists have been shown to reduce the composite endpoint of cardiovascular death or worsening HF in patients with obesity-associated stage C HF with preserved ejection fraction, evidence supporting a primary preventive effect on HF development in patients with obesity remains limited.[68]

Prevention strategies in stage B

Hypertension

Patients with hypertension in stage B require strict blood pressure control that takes comorbidities into account. The target blood pressure is the same as that for stage A: office blood pressure <130/80 mm Hg (home blood pressure <125/75 mm Hg). Antihypertensive agents should be selected on the basis of comorbidities and underlying pathophysiology, prioritizing drugs with compelling indications while considering contraindications and conditions requiring special caution, and treatment should follow current hypertension guidelines[30,31] (see Chapter 8 of the current Japanese Society of Hypertension Guidelines[31] for detailed recommendations on drug selection and treatment algorithms). Patients with hypertension and CVD are classified as a high-risk group, and it is recommended that antihypertensive therapy be initiated promptly in parallel with lifestyle modification.[31] If monotherapy is insufficient, early initiation of combination therapy with 2 agents is recommended. ACE inhibitors/ARBs and thiazide-type diuretics have strong evidence for preventing the development of HF,[69,70] and their proactive use is recommended. β-blockers should be used with caution, because they may provoke coronary vasospasm. ARNI is effective in hypertension associated with fluid retention, excessive salt intake, or salt sensitivity and

therefore represents a favorable therapeutic option for hypertensive patients in stage B.[31] It should be noted that ARNI should not be used in combination with ACE inhibitors/ARBs.

Diabetes

In patients with diabetes, symptoms of HF may remain unrecognized even after progression to stage C,[71] making careful assessment on the basis of history-taking and physical examination essential to avoid missing early signs. Serial assessment of BNP or NT-proBNP may facilitate earlier recognition of HF progression in patients with diabetes.[72] Reducing CVD risk in patients with diabetes requires not only glycemic control but also comprehensive and proactive management of blood pressure and lipid levels, which has been shown to be effective.[73] Although direct evidence supporting lifestyle interventions for HF prevention is limited, such interventions remain fundamental in diabetes care and are expected to contribute to reduction of HF risk.[74] Management strategies for preventing HF in patients with diabetes should follow the principles outlined in the section "Diabetes Plus Cardiovascular Disease Risk."

Chronic Kidney Disease

Diabetes Plus CKD. Management of patients with diabetes and CKD should follow the recommendations described in the section "Diabetes Plus CKD."

Nondiabetes Plus CKD (With Proteinuria). Management of patients without diabetes with proteinuria should follow the section "Nondiabetes Plus CKD (With Proteinuria)."

Nondiabetes Plus CKD (Without Proteinuria). In patients without diabetes with CKD without proteinuria in stage B, treatment with ACE inhibitors/ARBs and SGLT2 inhibitors should be considered. Table 2 summarizes drug selection for the prevention of HF according to diabetes status and the presence or absence of proteinuria in patients with CKD.

ACE inhibitors/ARBs. In the African American Study of Kidney Disease and Hypertension study (AASK) trial, which enrolled patients without diabetes with CKD (hypertensive nephrosclerosis; 32% without proteinuria), ramipril was shown to improve renal outcomes and reduce all-cause mortality.[75] Renal protective effects of ramipril were observed regardless of the presence of proteinuria. In the EMPA-KIDNEY trial,[51] which partly included patients with nondiabetic CKD without proteinuria, ACE inhibitors/ARBs were considered baseline therapy.

SGLT2 inhibitors. In a subanalysis of the EMPA-KIDNEY trial,[51] which enrolled patients with CKD (54% without diabetes and 20% without albuminuria), empagliflozin was shown to improve the annual rate of eGFR decline (eGFR slope).[76] This renal protective effect was consistent irrespective of the presence of albuminuria. Renal events, including eGFR decline and worsening of eGFR slope, have been associated with increased risk of HF.[77,78] Although evidence in patients without diabetes with CKD without proteinuria remains limited, considering the renal protective effects, ACE inhibitors/ARBs and SGLT2 inhibitors should be considered in patients with stage B. Clinical considerations after initiation are as described in the section "Diabetes Plus CKD."

Left Ventricular Ejection Fraction <50%

Patients with reduced left ventricular ejection fraction (LVEF) are known to have an increased risk of hospitalization for HF, cardiovascular death, and sudden cardiac death during follow-up. In asymptomatic patients with reduced LVEF in the absence of previous myocardial infarction, evidence supporting the efficacy of guideline-directed medical therapy for HF remains limited. Nevertheless, ACE inhibitors/ARBs and β-blockers have been suggested to confer benefit in preventing the development of overt HF.[8]

Valvular Heart Disease

In patients with valvular heart disease, echocardiography should be performed every 6–12 months, and indications

Table 2 Drug selection for HF prevention in patients with CKD, categorized by diabetes and proteinuria status

Drug	Diabetes With CKD	Non-Diabetes CKD (with proteinuria)	Non-Diabetes CKD (without proteinuria)
ACE inhibitors/ARBs	●	●	○
SGLT2 inhibitors	●	●	○
Finerenone	●	–†	–
GLP-1 RAs (Semaglutide)	○	–	–

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; SGLT2, sodium-glucose cotransporter 2.

●Recommended based on sufficient evidence.

○Use may be considered; however, evidence is limited regarding efficacy and safety.

†Limited evidence exists; however, not currently covered by health insurance in Japan for this indication.

for surgical intervention should be assessed according to current guidelines.[79] on the basis of symptoms and other clinical findings.

Previous Myocardial Infarction

A history of myocardial infarction leads to structural cardiac abnormalities through left ventricular remodeling and scar formation. Antiplatelet therapy and statin-based lipid-lowering therapy constitute the cornerstone of secondary prevention to reduce the risk of recurrent myocardial infarction.[61] In patients with reduced LVEF, initiation of ACE inhibitors/ARBs together with β-blockers is recommended.[8] In addition, comprehensive management of blood pressure, glucose, and lipid levels together with lifestyle modification is essential to prevent further myocardial injury and progression to stage C HF.

Atrial Fibrillation

AF increases in prevalence with advancing age, and patients with AF have a 2- to 5-fold greater risk of developing HF. Therefore, in individuals aged $\geq$65 years, regular pulse checks and electrocardiographic screening are recommended to facilitate early detection of previously unrecognized AF.[80] When AF is identified, early determination of an appropriate management strategy is essential, and referral to a cardiologist is recommended. Treatment options include oral anticoagulation as well as rhythm-control strategies such as antiarrhythmic drug therapy or catheter ablation, which should be considered according to the clinical context, including the presence of symptoms (eg, palpitations or dyspnea) and the AF pattern (paroxysmal or persistent).[81] To date, no randomized controlled trials have directly examined whether specific treatment strategies for AF in patients with stage B reduce the subsequent risk of HF development. However, meta-analyses and observational studies, including studies involving patients with stage B, have demonstrated that early rhythm control using antiarrhythmic drugs or catheter ablation is associated with lower risks of cardiovascular death, stroke, and HF hospitalization compared with rate-control strategies.[82] Furthermore, in a propensity score–adjusted analysis of patients with stage B with a previous history of antiarrhythmic drug therapy, those who subsequently underwent catheter ablation had a 57% lower risk of incident HF compared with those in whom a new alternative antiarrhythmic drug was initiated.[83] Accordingly, close collaboration with cardiologists from an early stage is recommended to ensure optimal treatment selection for HF prevention. When rate control is chosen for AF with rapid ventricular rate, a resting heart rate $<$110 beats per minute should be targeted. β-blockers are recommended as first-line agents irrespective of LVEF. Although digitalis glycosides traditionally have been considered second-line therapy for rate control in patients with AF and impaired LVEF, the RAte control Therapy Evaluation in permanent Atrial Fibrillation (RATE-AF) trial demonstrated that quality of life after treatment was comparable between digoxin and bisoprolol in patients with AF and HF symptoms.[84] Although the effect of digoxin used for rate control in patients with AF on the prevention of HF remains unclear, oral digoxin therapy may be considered under regular monitoring of serum concentrations for heart rate control or improvement of quality of life in selected patients.[85]

Future directions

This scientific statement recommends a practical clinical pathway for HF prevention in patients with stages A and B that consists of routine measurement of BNP or NT-proBNP, timely referral to cardiologists when natriuretic peptide levels are elevated, and evidence-based management according to HF stage. Future research should focus on the implementation and optimization of this practical HF prevention strategy in routine clinical practice. Implementation studies evaluating natriuretic peptide–guided collaborative care pathways in routine clinical practice may help establish more effective systems for HF prevention. Further evidence is also needed regarding pharmacologic strategies to optimize the prevention of incident HF in high-risk asymptomatic populations. Aldosterone synthase inhibitors, a novel drug class, in combination with SGLT2 inhibitors have been proposed as a potential strategy for HF prevention. Several ongoing phase 3 trials, including PREVENT-HF (NCT06677060) and EASi-PROTKT (NCT07064473), are currently investigating this combination, and their results are eagerly awaited.[86,87] Beyond implementation of the proposed clinical pathway, advances in precision medicine and digital health may improve HF prevention. Personalized prevention strategies integrating biomarkers, imaging, genetic information, and cardiovascular-kidney-metabolic phenotyping may improve risk stratification and facilitate more individualized preventive therapies. Digital health technologies, monitoring devices, remote screening strategies, and artificial intelligence–assisted risk prediction may further enhance early detection of stage B. Cost-effectiveness analyses and healthcare system-based implementation research will also be important for translating preventive strategies into routine clinical practice.

Conclusions

HF prevention requires earlier detection and intervention before the development of symptomatic disease. Stages A and B represent important opportunities for preventive therapy because patients remain asymptomatic despite progressive cardiovascular remodeling. Biomarker-guided strategies using BNP and NT-proBNP may facilitate earlier identification of stage B and support timely initiation of preventive therapies. Comprehensive management of cardiovascular and metabolic diseases together with multidisciplinary collaboration between cardiologists and noncardiologist physicians is essential for reducing future HF burden. Implementation of the practical and clinically applicable prevention strategies proposed in this scientific

statement may help prevent or delay progression to symptomatic HF and improve long-term cardiovascular outcomes.



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CRediT authorship contribution statement

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HANATANI: Writing — review & editing, Writing — original draft, Formal analysis, Data curation. TOMOYUKI KUNISHIMA: Writing — review & editing, Supervision. MASANARI KUWABARA: Supervision. TAKAYUKI INOMATA: Writing — review & editing, Supervision. KOICHIRO KINUGAWA: Writing — review & editing, Supervision, Conceptualization.

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Patient consent

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