JACC: ASIA VOL. ■, NO. ■, 2026

STATE-OF-THE-ART REVIEW

HFpEF in Asia—Clinical Characterization and Therapeutic Strategies

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ABSTRACT

Heart failure with preserved ejection fraction (HFpEF) prevalence is increasing in Asia, driven by aging populations and rising cardiometabolic risk. Asian patients with HFpEF present a decade earlier than Western counterparts, carry a disproportionate burden of diabetes, chronic kidney disease, and visceral adiposity at lower body mass index thresholds, and exhibit marked regional heterogeneity in clinical subtypes and outcomes. Diagnosis remains challenging, as algorithms derived in Western populations perform suboptimally in Asian patients, and access to echocardiography and natriuretic peptide testing is highly variable across the region. Artificial intelligence-enabled tools can bridge these diagnostic gaps. Therapeutically, sodium-glucose cotransporter 2 inhibitors demonstrate consistent benefit across Asian subgroups, whereas glucagon-like peptide-1 receptor agonists and nonsteroidal mineralocorticoid receptor antagonists represent important emerging options, though evidence in lean Asian subtypes remains limited. This review examines the diagnosis, clinical heterogeneity, clinical outcomes, and treatment of HFpEF across Asia, highlighting priorities for future research and quality of care. (JACC Asia. 2026;■:■–■) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

The prevalence of heart failure (HF), including HF with preserved ejection fraction (HFpEF), is increasing in Asia.[1,2] This increasing prevalence is driven by aging populations and an increasing burden of risk factors for HFpEF, such as diabetes and obesity.[3-6] HFpEF is not a specific histopathologic diagnosis, but a clinical syndrome driven by overlapping comorbidity-linked inflammatory and metabolic pathways.[7,8] The demographic profile of HFpEF varies markedly across Asia: patients in South and Southeast Asian cohorts often present at a younger age than Western counterparts, whereas registries from Japan, South Korea, and China describe a predominantly elderly HFpEF population.[9-13] Across the region, patients have a high burden of diabetes and chronic kidney disease (CKD), and manifest "lean-diabetic HFpEF" characterized by disproportionate visceral adiposity at lower body mass index (BMI) thresholds (see **Central Illustration**).[6,14-17]

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received May 21, 2026; revised manuscript received July 16, 2026, accepted August 3, 2026.

ISSN 2772-3747 https://doi.org/10.1016/j.jacasi.2026.08.009

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

AI = artificial intelligence

ASIAN-HF = Asian Sudden Cardiac Death in Heart Failure

AUC = area under the curve

BMI = body mass index

CKD = chronic kidney disease

CKM = cardiovascular-kidney-metabolic

CV = cardiovascular

DELIVER = Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure

DM = diabetes mellitus

ECG = electrocardiography

ESC = European Society of Cardiology

GLP-1 = glucagon-like peptide-1

H_2FPEF = heavy, hypertensive, atrial fibrillation, pulmonary hypertension, elderly, and filling pressure

HF = heart failure

HFA-PEFF = Heart Failure Association pretest assessment, echocardiography and natriuretic peptide, functional testing, and final etiologic assessment

HFpEF = heart failure with preserved ejection fraction

HFrEF = heart failure with reduced ejection fraction

HRQoL = health-related quality of life

LA = left atrial

LV = left ventricle

LVEF = left ventricular ejection fraction

ns-MRAs = nonsteroidal mineralocorticoid receptor antagonists

NT-proBNP = N-terminal-pro hormone B-type natriuretic peptide

PARAGON-HF = Prospective Comparison of ARNI With ARB Global Outcomes in Heart Failure With Preserved Ejection Fraction

RV = right ventricle

SGLT2i = sodium/glucose cotransporter 2 inhibitors

WHtR = waist-to-height ratio

Diagnosis of HFpEF remains challenging.[18,19] Published diagnostic algorithms, such as the Heart Failure Association pretest assessment, echocardiography and natriuretic peptide, functional testing, and final etiologic assessment (HFA-PEFF) and heavy, hypertensive, atrial fibrillation, pulmonary hypertension, elderly, and filling pressure (H_2FPEF) scores, can help with diagnosis.[20,21] However, a previous report in Asian patients from Singapore showed that these diagnostic scores have reasonable specificity but limited sensitivity in Asian populations.[22] This lower sensitivity is likely caused by the lower prevalence of atrial fibrillation (AF) and obesity. Furthermore, Asian patients with HFpEF often have increased N-terminal-pro hormone B-type natriuretic peptide (NT-proBNP) concentrations because of their low prevalence of obesity—the H_2FPEF does not include raised natriuretic peptides. These challenges are further compounded in Asia by the highly variable access to echocardiography and natriuretic peptide testing, especially in lower-middle-income settings across South and Southeast Asia.[23-26]

Sodium/glucose cotransporter 2 inhibitors (SGLT2i) and nonsteroidal mineralocorticoid receptor antagonists (ns-MRAs) have proven effective in improving outcomes in patients with HFpEF.[27-29] Furthermore, recent trials showed the effectiveness of glucagon-like peptide-1 (GLP-1) agonists in improving outcomes in patients with obesity with HFpEF.[30,31] Yet, unfortunately, Asian patients remain under-represented in global clinical trials.[32]

Within this context, this review examines the diagnosis, clinical subtypes, outcomes, and treatment of HFpEF in Asia, a region home to the world's largest and most diverse group of patients with HFpEF.

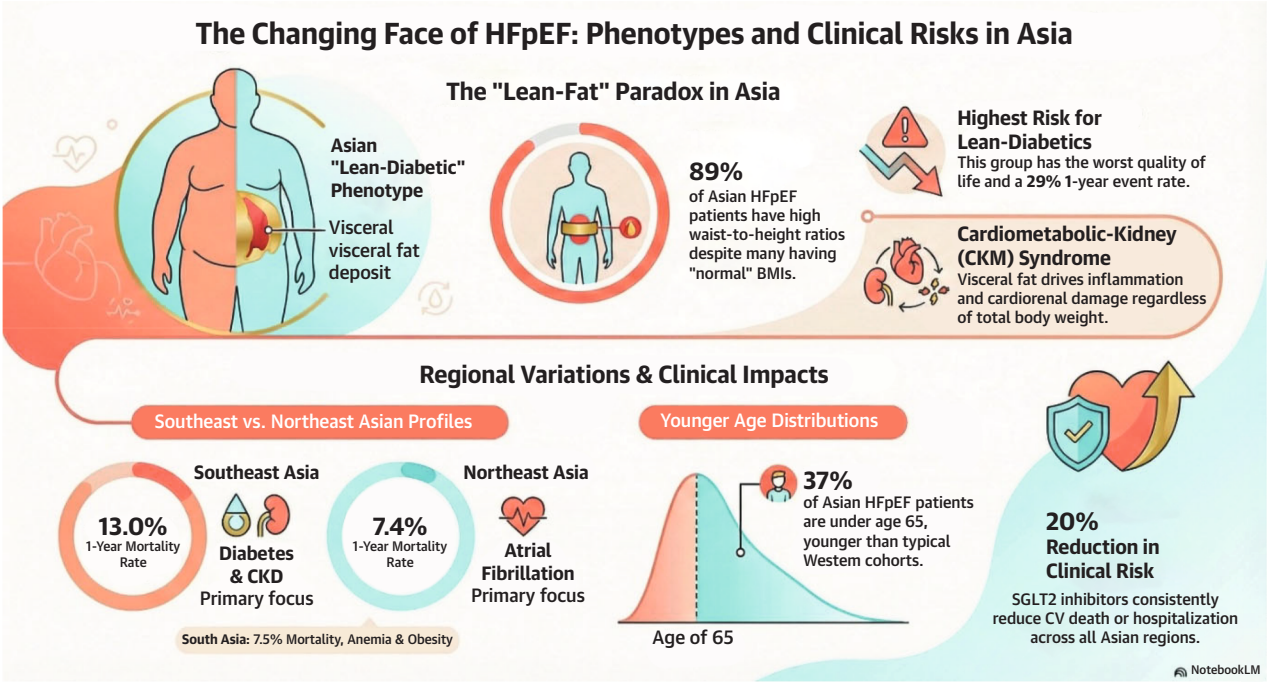
DIAGNOSIS OF HFpEF IN ASIA

STANDARDS OF DIAGNOSIS. Diagnosing HFpEF remains one of cardiology's most challenging conundrums.[33] The 2021 Universal Definition of Heart Failure, endorsed by the Japanese Heart Failure Society and the Chinese HFA, defines HFpEF as a clinical syndrome with signs and symptoms of HF, a left ventricular ejection fraction (LVEF) ≥50%, and corroborating evidence of elevated natriuretic peptide levels (Table 1).[18] In line with the Universal Definition, the 2021 European Society of Cardiology (ESC) and 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America guidelines require patients with HFpEF to have signs and symptoms of HF, an LVEF ≥50%, increased natriuretic peptides, and objective evidence of cardiac structural and/or functional abnormalities consistent with left ventricular (LV) diastolic dysfunction and raised LV filling pressures (Table 1).[34,35]

Several regional (Asia Pacific Society of Cardiology) and national (Japan, Korea, China) cardiovascular (CV) or HF organizations have published guidelines (Table 1). Regional and national guidelines' diagnostic criteria largely align with the Universal Definition, ESC, and American College of Cardiology/American Heart Association/Heart Failure Society of America guidelines (Table 1).[36-39] However, regional guidelines are commonly less specific on structural or functional cutoff points for identifying patients with evidence of increased filling pressures or diastolic dysfunction. This absence likely relates to the unmet need for Asian-specific cutoff points. This is particularly pertinent because Asian patients have lower LV mass than White patients, even after correcting for body surface area.[40] Lower LV mass indexed to height has likewise been reported in Asian compared with American patients with HFpEF.[41] Furthermore, the Echocardiographic Normal Ranges Meta-Analysis of the Left Heart collaboration, analyzing data from 22,404 adults across 43 studies, found that LV end-diastolic volumes, LV end-systolic volumes, and left atrial (LA) volumes are consistently smaller in South and East Asian populations than in European populations, with differences persisting after body surface area indexation.[42] The World Alliance of Societies of Echocardiography study confirmed that Asians have smaller chamber sizes, higher LVEFs, and higher absolute strain values than both Black and White participants.[43] Using Western-derived thresholds for LV hypertrophy or LA enlargement in Asian patients may therefore result in systematic misclassification. Resource constraints compound these challenges: in the Acute Decompensated Heart Failure National Registry International-Asia Pacific registry, LV function was assessed in only 50% of hospitalized patients with HF.[44]

The HFA-PEFF algorithm by the ESC HFA and the H_2FPEF score use a score-based approach to assess the probability of HFpEF.[20,21] The H_2FPEF includes natriuretic peptide levels and echocardiographic

CENTRAL ILLUSTRATION **Summary of Key Characteristics of Heart Failure With Preserved Ejection Fraction (HFpEF) in Asia**



Tromp J, et al. JACC Asia. 2026;■(■):■–■.

A "lean-fat" phenotype predominates in Asia, with 89% of individuals having a high waist-to-height ratio despite a normal body mass index (BMI). Among patients with diabetes, this subtype is associated with the highest risks of mortality and heart failure hospitalization. HFpEF subtypes and their clinical impact vary across regions, with Southeast Asia bearing a higher disease burden and distinct comorbidity profiles. Asian individuals with HFpEF are, on average, a decade younger than their Western counterparts. Despite limited Asian representation in clinical trials, sodium-glucose cotransporter 2 (SGLT2) inhibitors have demonstrated significant therapeutic benefit in HFpEF. Disclaimer: This image was generated using artificial intelligence and subsequently reviewed by the authors for accuracy and scientific validity. CKD = chronic kidney disease; CKM = cardiovascular-kidney-metabolic; CV = cardiovascular.

structural and functional parameters.[20] In contrast, the HFA-PEFF score includes clinical characteristics, such as obesity (BMI >30 kg/m^2) and AF.[21] In Japanese patients with clinically defined HFpEF, both HFA-PEFF and H_2FPEF showed acceptable performance, with H_2FPEF (area under the curve [AUC] 0.89) having significantly higher diagnostic accuracy for HFpEF than the HFA-PEFF score (AUC: 0.82).[45] A study from Singapore demonstrated reasonable specificity but limited sensitivity. The poor sensitivity might be explained by the younger age, lower prevalence of AF, especially in South Asian patients, and lower prevalence of obesity.[22] The H_2FPEF score assigns substantial weight to obesity, a threshold met by only a minority of Asian patients. Lowering the BMI cutoff from 30 to 27 kg/m^2 to define obesity increased the sensitivity of the H_2FPEF score from 24.9% to 30.9% only, and maintained the same specificity for Asians with HFpEF.[22] Thus, the limited sensitivity of the score cannot be explained by BMI cutoffs alone. To reduce reliance on echocardiography and BMI, the B-type natriuretic peptide, renal function, elderly age, atrial fibrillation, and hypertension[2] score was recently derived and validated in Japanese patients; it combines age ≥65 years, coronary artery disease, elevated natriuretic peptides, anemia, cardiomegaly on chest radiography, LV high-voltage on electrocardiography (ECG), and AF, achieving good discrimination.[46]

Natriuretic peptides, including B-type natriuretic peptide and NT-proBNP, remain essential for HFpEF diagnosis and prognostication.[47] Natriuretic peptides are consistently recommended for diagnosis in HFpEF, including in Asian patients (**Table 1**). A few studies have looked at the differential performance of natriuretic peptides in Asian vs White

TABLE 1 Comparison of Diagnostic Criteria for Heart Failure With Preserved Ejection Fraction Across International and Regional Guidelines

Diagnostic Criteria	Universal Universal Definition	Europe ESC 2021	United States 2022 AHA/ACC/HFSA	Japan 2025 JCS/JHFS	Korea 2023 KSC	Asia Pacific 2023 APSC	China 2018 CCA
Signs and symptoms	Required	Required	Required	Required	Required	Required	Required
Natriuretic peptide thresholds	BNP >35 pg/mL; NT-proBNP >125 pg/mL	BNP >35 pg/mL; NT-proBNP >125 pg/mL	Signs and symptoms NP: BNP >35 pg/mL; NT-proBNP >125 pg/mL	Signs and symptoms NP: BNP >35 pg/mL; NT-proBNP >125 pg/mL	Signs and symptoms NP: BNP >35 pg/mL; NT-proBNP >125 pg/mL	Signs and symptoms NP: BNP >35 pg/mL; NT-proBNP >125 pg/mL	Signs and symptoms NP: BNP >35 pg/mL; NT-proBNP >125 pg/mL
Structural abnormalities	Objective evidence, not specified	LAVi >34 mL/m^2; LVMi ≥115 g/m^2 (M)/≥95 g/m^2 (W); RWT >0.42; LV wall thickness ≥12 mm	LAVi, LVMi per ASE/EACVI 2016 norms; or elevated LV filling pressures	Objective evidence, not specified	LAVi >34 mL/m^2; LVMi ≥115 g/m^2 (M)/ ≥95 g/m^2 (W) RWT >0.42	Objective evidence, not specified	Objective evidence, not specified
Functional abnormalities	Objective evidence, not specified	E/e' ≥13 and mean e' <9 cm/s or TRV >2.8 m/s	E/e' ≥15 (definitive); E/e' 9-14 (indeterminate, needs supporting criteria) ASE 2016 framework	Objective evidence, not specified	TRV >2.8 m/s	Objective evidence, not specified	Objective evidence, not specified

Summary of key characteristics of HFpEF in Asia. Disclaimer: This image was generated using artificial intelligence and subsequently reviewed by the authors for accuracy and scientific validity.

ACC = American College of Cardiology; AHA = American Heart Association; APSC = Asian Pacific Society of Cardiology; ASE = American Society of Echocardiography; BNP = B-type natriuretic peptide; CCA = Chinese Cardiology Association; EACVI = European Association of Cardiovascular Imaging; E/e' = ratio of early mitral inflow velocity to early diastolic mitral annular velocity; ESC = European Society of Cardiology; HFSA = Heart Failure Society of America; JCS = Japanese Circulation Society; JHFS = Japanese Heart Failure Society; KSC = Korean Society of Cardiology; LAVi = left atrial volume index; LV = left ventricle; LVMi = left ventricular mass index; M = men; NP = natriuretic peptide; NT-proBNP = N-terminal pro-B-type natriuretic peptide; RWT = relative wall thickness; TRV = tricuspid regurgitation velocity; W = women.

patients.[48,49] Previous studies found that NT-proBNP had similar prognostic performance but better diagnostic performance in dyspneic patients at the accident and emergency.[48,49] However, natriuretic peptides are not always available in resource-constrained settings. For example, natriuretic peptide testing was available in only 18% of patients who visited the accident and emergency in the Philippines.[50]

EMERGING TECHNOLOGIES TO ADDRESS DIAGNOSTIC CHALLENGES IN ASIA. Artificial intelligence (AI) solutions can help address diagnostic challenges in Asia, especially in resource-limited settings.

AI-based risk prediction models are increasingly being developed in Asian countries. A recent study using an AI risk-prediction model trained on 840 patients in China reported an AUC of 0.85 for predicting HFpEF using readily available clinical variables.[51] Similarly, models have been developed in different settings, accurately predicting both prognosis and diagnosis of patients with HFpEF.[52,53]

Data-driven multibiomarker strategies can provide incremental diagnostic value. A panel of high-sensitivity troponin-I, B-type natriuretic peptide, and galectin-3 achieved an AUC of 0.82 for predicting future HFpEF in the St Vincent's Screening to Prevent Heart Failure study.[54] However, relatively a few studies have validated these results. However, despite this progress, a few studies have been translated into clinical practice. Notably, a 2019 study involving patients from New Zealand and Singapore demonstrated that an 8-MicroRNA panel accurately discriminated acute from less acute patients, including those with HFpEF.[55]

AI applied to 12-lead ECGs has emerged as a scalable, low-cost screening tool for HFpEF. An early 2019 study found that AI-based ECG reading could identify patients with systolic dysfunction, with an AUC of 0.93.[56] In 2024, this was extended to include the detection of diastolic dysfunction: a deep learning neural network trained on 98,736 patients achieved an AUC of 0.91 for HFpEF.[57] Similar high diagnostic performance of AI-ECG for diagnosing HFpEF was shown in other studies.[58] Although previous studies were predominantly conducted in Western Europe and the United States, 2 recent studies from Korea reported similar results and feasibility in Asian patients.[59,60]

AI-assisted echocardiography also shows promise.[61-65] Recently published algorithms showed high agreement with human expert measurements for LV and LA segmentation,[61,65] estimating diastolic dysfunction,[61,65] and for predicting HFpEF.[62-64] Importantly, although most recently published algorithms were trained and validated in largely

Caucasian patients[62-64] recent studies with algorithms trained on Asian patients from Singapore showed consistent performance in both Asian and White patients.[61,65] A subsequent prospective noninferiority study against 3 expert core-laboratory readers confirmed that deep learning performance was statistically noninferior across all measured parameters, including those assessing diastolic dysfunction.[65] A recent study from Taiwan showed that AI-based analysis of echocardiographic images using intrabeat dynamics had an AUC of 0.91 for detecting HFpEF.[66]

Remote monitoring and digital health for HFpEF remain nascent in Asia. Implantable hemodynamic monitoring has demonstrated efficacy in HFpEF. The CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) trial CardioMEMS subgroup analysis of 119 patients with LVEF ≥40% showed a 46% reduction in HF hospitalizations with pulmonary artery pressure-guided management.[67] Similarly, the Hemodynamic-GUIDEd Management of Heart Failure trial (1,000 patients, including 398 with HFpEF) showed consistent benefit across LVEF groups in pre-COVID analyses.[68] However, no Asian data on implantable hemodynamic monitors exist, and device availability remains limited across the region. In addition to implantable hemodynamic monitoring, cardiac implantable electronic devices equipped with multiparameter remote monitoring algorithms can detect early decompensation. The HeartLogic algorithm (Boston Scientific) integrates heart sounds, thoracic impedance, respiration rate, heart rate, and activity to predict worsening HF.[69,70] A recent study from Japan showed the feasibility of using HeartLogic in Asia.[71] Notably, in this Japanese study, patients had a lower HeartLogic score at admission, possibly reflecting a lower admission threshold of patients in Japan compared with previous data from the United States of America.[71] Further studies from Asia-Pacific settings are needed to validate its performance and clinical utility in patients with HFpEF.[72]

Other algorithms with future potential include AI detection of HF with the Apple Watch single-lead ECG.[73] However, these algorithms can currently only detect a reduction in LVEF and are therefore not suitable for HFpEF. A few Asia-specific studies on the detection or diagnosis of HFpEF using wearables have been conducted. The combination of AI-automated echocardiography, validated AI-ECG models, and expanding digital infrastructure across Asia creates an opportunity to build integrated screening pathways.

SUBTYPES AND KEY SUBGROUPS

INTRODUCTION TO HFpEF HETEROGENEITY. The pathophysiologic understanding of HFpEF has shifted beyond the conventional view of hypertension-induced ventricular hypertrophy to include systemic inflammation, endothelial dysfunction, coronary microvascular disease, and altered myocardial energetics as converging biological pathways.[74,75] Most recently, the adipokine hypothesis has been proposed as a framework for explaining the pathophysiology of HFpEF.[76] This framework groups adipokines into 3 mutually exclusive domains. Domain 1 adipokines are cardioprotective yet suppressed in patients with excess adiposity. Domain 2 adipokines are cardioprotective and upregulated by adiposity. Lastly, domain 3 adipokines are harmful through proinflammatory, prohypertrophic, profibrotic, and antinatriuretic effects. The overarching hypothesis of this framework is that HFpEF results from an adiposity-driven imbalance in adipokines, leading to increased domain 3 adipokines, suppression of domain 1 adipokines, and inadequate regulatory responses from domain 2 adipokines.[76]

How well this new framework translates to Asian patients with HFpEF remains unclear. A previous analysis of the Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry found 3 subtypes among patients with heart failure with reduced ejection fraction (HFrEF) and HFpEF, with HFpEF more likely to be present.[16] The first was an elderly/AF/hypertensive subtype. This patient group had the oldest average age, a high prevalence of AF, and hypertension. The second group was an adipose subtype. All of these patients had obesity, with a high prevalence of hypertension and diabetes. The last subtype was a unique Asian “lean diabetic” group. These patients were generally lean but had a very high prevalence of diabetes and CKD.[16] The next section discusses these subtypes in detail.

ELDERLY/AF/HYPERTENSIVE SUBTYPE. The elderly/AF/hypertensive subtype was the most prevalent in the ASIAN-HF registry. These patients were the oldest and had a high prevalence of hypertension and AF.[16]

Hypertension remains the most prevalent risk factor for HFpEF, accounting for 60% to 89% of cases.[77] The traditional paradigm suggests that longstanding hypertension leads to LV hypertrophy, pathologic myocardial fibrosis, and diastolic dysfunction.[74,75] However, contemporary data indicate that fewer than 50% of HFpEF patients meet the

criteria for ventricular hypertrophy, and myocardial fibrosis, although present, is only modestly elevated (median 9.6% vs 7.1% in control patients). In Asia, regional variations in blood pressure control and target achievement are significant. Southeast Asian patients in the ASIAN-HF registry often presented with the highest hypertension burden, despite being younger; South Asian patients showed the most prominent concentric remodeling, and Northeast Asians had proportionally more AF.[9,10]

Current guidelines advocate for a target of <130/80 mm Hg.[74,77] Of note, this recommendation rests on evidence from broader hypertension trials rather than HFpEF specifically. Importantly, reducing hypertension in at-risk populations reduces HFpEF incidence by up to 40% over 2 to 8 years, making hypertension control one of the most evidence-supported preventive strategies available.[74] However, clinicians must be wary of a J-shaped relationship, where a systolic blood pressure <120 mm Hg may paradoxically increase the risk of adverse events in older adults.[78] Management often requires multiple agents and sodium restriction to mitigate the exaggerated hypertensive response to exercise seen in this subtype.[77,78]

AF is strongly associated with HFpEF, even more so than HFrEF, with AF prevalence ranging from 15% to 65%.[10,79-81] Significant geographic variations exist in Asia, with patients with HFpEF in Southeast Asia exhibiting the highest AF prevalence (49%), followed by Northeast Asians (37%), and lowest in South Asians (12%).[82] The relationship is truly bidirectional: HFpEF increases AF risk by a factor of 6, whereas AF itself promotes a unique "atrial-dominant" HFpEF subtype characterized by LA myopathy and poor LA compliance.[79,83,84] The ASIAN-HF echocardiographic clustering analysis identified that an "atrial dominant" subtype constituted 10% of patients with HFpEF, characterized by marked LA myopathy and occurring predominantly in elderly women with multiple comorbidities.[83]

Patients with HFpEF and AF are typically older, have higher NT-proBNP levels, larger LA volumes,[79] and experience more severe congestion and right ventricle (RV) failure.[84,85] Ten-year progression to permanent AF is common, particularly from paroxysmal AF (52%), with the likelihood increasing with higher AF stage, poorer LA compliance, and lower LA strain.[84] As AF progresses to a permanent state, patients experience a significant decline in cardiac output and exercise capacity because of the loss of atrial kick and the inability to increase stroke volume during exertion.[84] Pathophysiologic changes include increased heart volume because of atrial dilatation, elevated filling pressures because of heightened pericardial restraint, greater congestion, greater pulmonary vascular disease, and lower cardiac output.[84]

ADIPOSITY-RELATED HFpEF. The interplay between obesity and HFpEF is highly complex. Obesity is well-established as an independent risk factor for incident HFpEF, affecting approximately 60% to 80% of HFpEF patients and conferring a dose-dependent relationship that does not extend to HFrEF.[75,77,86] Visceral adiposity precedes and predicts HFpEF development in both experimental models and community-based studies.[86] This distinction reinforces the central etiologic role of adiposity in shaping this specific HF subtype.[76] This complexity is further compounded by the "obesity paradox" observed in established HF, wherein patients with elevated adiposity appear to experience more favorable outcomes than their leaner counterparts.[87]

Patients with adiposity-related HFpEF are characteristically younger, more symptomatic, and demonstrate worse exercise capacity than their nonobese counterparts.[75,88] Exercise intolerance is multifactorial, ranging from lower peak exercise capacity to higher LV and RV filling pressures during exertion and reduced pulmonary-artery vasodilator reserve.[75,77] This syndrome is often accompanied by a clustering of cardiometabolic comorbidities, including hypertension, insulin resistance, dyslipidemia, and obstructive sleep apnea, reflecting the broader cardiometabolic milieu associated with excess adiposity.[75,77] Key hemodynamic features include increased plasma volume, concentric LV remodeling, RV dilatation and dysfunction, greater epicardial fat thickness, and heightened pericardial restraint with ventricular interdependence.[75,77,89]

Multiple interrelated pathophysiologic mechanisms may contribute to the development of obesity-related HFpEF. Adiposity-driven hypertension, systemic inflammation, insulin resistance, and metabolic dysregulation interact to impair diastolic, systolic, arterial, and skeletal muscle domains.[75,77] Epicardial and pericardial fat accumulation contribute to pericardial restraint and enhanced ventricular interdependence, which together exacerbate cardiac filling pressures and mechanical coupling between the ventricles.[75] Previous results from an Asian cohort demonstrated that the relative mass of epicardial fat was increased in patients with HFpEF and that epicardial fat mass was associated with worse cardiac fibrosis.[15]

Furthermore, Asia is home to a specific lean-fat subtype (**Central Illustration**), in which patients have

a low BMI (<24.5 kg/m^2) but a high waist-to-height ratio (WHtR ≥0.55).[90,91] Among patients with HFpEF in the ASIAN-HF cohort, 11% had the lean-fat subtype.[6] Patients with this subtype were predominantly women from South and Southeast Asian countries, had a high diabetes prevalence, and experienced the worst composite outcomes.[6]

Importantly, data from ASIAN-AF revealed a BMI paradox, wherein higher BMI was associated with lower risk by traditional classification. Yet, obesity, indexed by WHtR, showed the opposite: higher WHtR correlated with higher composite event rates in both HFpEF and HFrEF.[6] Among Asian patients with HFpEF, 89% had increased WHtR despite only 60% meeting a BMI threshold of ≥30 kg/m^2,[6] underscoring that visceral adiposity, not total body mass, is the relevant driver of cardiometabolic risk in Asian populations with HF.

A plausible mechanistic framework linking these observations is the adipokine hypothesis. Hypertrophied and inflamed visceral adipose tissue disseminates dysfunctional cellular stress to the heart, vasculature, and kidneys through aberrant secretion of biologically active adipokines.[76] Particularly, epicardial and paracardial fat appear to play a central pathogenic role and show the strongest predictive value for HF events.[76] Downstream pathways include sodium retention, neurohormonal activation via the leptin-aldosterone-neprilysin axis, systemic inflammation, end-organ fibrosis, and enhanced pericardial restraint, collectively promoting HFpEF.[76]

Cardiovascular-kidney-metabolic (CKM) syndrome, arising from excess or dysfunctional adipose tissue that secretes proinflammatory and prooxidative mediators, accelerates the pathophysiology of HFpEF through augmented inflammation, dyslipidemia, hypertension, and insulin resistance.[92] Adipose depots in pericardial, myocardial, and perirenal compartments exert direct effects on cardiac remodeling through inflammatory, fibrotic, and energetic pathways.[92] Asian populations display a distinctive CKM profile with: 1) visceral adiposity despite lower BMI; 2) earlier-onset diabetes; and 3) greater cardiorenal disease burden than Western counterparts. These underscore the need for Asia-specific risk-stratification frameworks.[30,76]

LEAN DIABETIC HFpEF AND CKD. Diabetes is highly prevalent in HFpEF, with a global prevalence of 30% to 45% that increases to 75% when prediabetes is included.[78,93] The ASIAN-HF registry documented a 45.0% diabetes prevalence across HFpEF patients from 11 Asian regions,[94] with the lean-diabetic subtype conferring the worst prognosis.[16] Asia is now the epicenter of the diabetes epidemic worldwide. Irrespective of HF subtype, Asian patients with HF had a 3-fold higher prevalence of diabetes mellitus (DM), despite a lower BMI and age, compared with their White counterparts.[14] Regional heterogeneity is substantial. Southeast Asians in ASIAN-HF carried the highest diabetes burden despite being younger than their Northeast Asian counterparts.[9,10]

The ASIAN-HF registry identified a distinct lean-diabetic subtype characterized by diabetes, hypertension, low obesity prevalence, and high CKD burden.[16,95] Importantly, patients with lean diabetes had the worst quality of life and highest 1-year mortality rates compared with other subtypes.[16]

The "lean diabetic" subtype had a high prevalence of CKD. The prevalence of CKD was highest in Southeast Asia, which also has the highest prevalence of diabetes and visceral adiposity.[10] The pathophysiology is multidirectional across HFpEF, CKD, and visceral adiposity.[96,97] Importantly, given the high level of visceral adiposity in Asian patients at a lower BMI, this might give rise to a "lean" version of the CKM syndrome, where HFpEF and CKD coexist in the absence of overt obesity but underlying presence of visceral fat.

CKD complicates the diagnosis of HFpEF by elevating natriuretic peptides (because of reduced kidney clearance), independently of hemodynamic congestion, thereby lowering the specificity of standard diagnostic thresholds.[77] On the other hand, serum creatinine may be falsely depressed because of sarcopenia or volume expansion (common in elderly patients with HFpEF), resulting in an overestimation of estimated glomerular filtration rate, leading to underdiagnosis of CKD.[77] Although reliance on creatinine alone may incompletely capture CKD, complementary markers like albuminuria (albumin-to-creatinine ratio/urine albumin-to-creatinine ratio) and secondary hyperparathyroidism, which rise with diuresis, may provide important information to identify true CKD severity.[77]

Emerging therapies, including SGLT2 inhibitors, ns-MRAs, and GLP-1 receptor agonists, offer concurrent CV and kidney benefits in patients with a lean-diabetic phenotype and CKD. However, this remains to be specifically tested in Asian populations.

CLINICAL OUTCOMES AND PROGNOSIS

MORTALITY AND HOSPITALIZATION RATES. HF is associated with significant mortality and morbidity. Despite advances in medical therapy, clinical outcomes of patients with HF remain dismal, with 1- and 5-year mortality rates of approximately 20% to

30%[98-102] and 50% to 75%,[103] respectively. Earlier studies had shown variation in mortality across HF subgroups, with better 1-year survival among patients with HFpEF compared with those with HFrEF.[2,104-106] Long-term mortality rates among these EF subgroups, however, were similar.[100,103,107] Furthermore, the composite outcome of mortality or all-cause rehospitalization was also similar in HF subgroups in risk-adjusted analyses.[103]

Hospital readmissions, as a hallmark of HF, were as high as 45% to 60% at 1-year from diagnosis based on large population-based studies and meta-analyses.[98,99,108] CV rehospitalization was higher among patients with HFrEF, in contrast to higher non-CV rehospitalization and all-cause rehospitalization among patients with HFpEF,[103] driven largely by their comorbidities in the latter. Notably, few global clinical trials and registries (eg, PARAGON-HF [Efficacy and Safety of LCZ696 Compared to Valsartan, on Morbidity and Mortality in Heart Failure Patients With Preserved Ejection Fraction],[109] ASIAN-HF [Asian Sudden Cardiac Death in Heart Failure],[9,110] EMPULSE [Empagliflozin in Patients Hospitalized for Acute Heart Failure],[111] and REPORT-HF [International REgistry to assess medical Practice and lOngitudinal obseRvation for Treatment of Heart Failure][2]) have identified regional and country-level differences in mortality and rehospitalization rates, even among countries within the same continent.[99] Significant heterogeneity in mortality and readmissions observed was not fully explained by the country's health expenditure, economic indices, or income disparity,[99] alluding to a myriad of other macro and patient-level factors[109] influencing outcomes, such as varying access to health care facilities, differences in admission thresholds for hospitalization, health policies across countries, geographic factors, management, medical infrastructure, and differences in patients' characteristics (eg, race, in vs out-patients).

Until about a decade ago, outcomes data in HF subgroups, especially on HFpEF, had been predominantly from Western countries. Yet important differences in clinical characteristics, medical management, and health care infrastructure between patients from Western countries and those from Asia have contributed to the significant heterogeneity observed in mortality and hospitalization rates.[99,109] A better understanding of the contributing factors can elucidate mitigating factors to reduce the burden associated with HF. At 1 (high) end of the regional/country income spectrum with an advanced health system, a report from the Japanese Heart Failure Syndrome With Preserved Ejection Fraction Registry,[112] a multicenter study across 15 sites in Japan between November 2012 and March 2015, N = 535 (median age: 80 years; 50% women), showed 17.9% (experienced all-cause death or HF hospitalization), 7.6% (all-cause death), 2.9% (CV death), 4.6% (non-CV death), and 10.3% (HF hospitalization) at 1-year postdischarge.[113] Two-year mortality rate was 20.9%, similar to that (19%) from the Jichi Medical University Center of Excellence, Community Medicine Cardiovascular Research and Development registry, but significantly lower than the 26.6% reported among hospitalized patients with HFpEF in Singapore.[113] Significant variation in outcomes across geographic regions was also observed in the ASIAN-HF,[9] with the poorest outcomes from patients (with HFpEF) in Southeast Asia as compared with Northeast Asia (including Japan), despite being younger (mean age: 67.4 vs 71.6 years), independent of differences in comorbidity burden and cardiac geometry.[9] In particular, the younger, more metabolically impaired patients (lean diabetes subtype) had the worst outcomes.[20] Notably, known variables accounted for only 49% of the risk of death, with contributions mainly from demographics and geographic region.[9]

CAUSE-SPECIFIC MORTALITY. A better understanding of the causes driving terminal events in HFpEF can provide insight into the pathophysiology of this complex syndrome and aid in therapeutic development. A meta-analysis showed that most deaths in HFpEF are CV deaths, accounting for 58.5% (median, pooled) of deaths in registries and approximately 70% in clinical trials.[114,115] Among CV deaths, sudden cardiac death and HF death are the leading cardiac modes of death in clinical trials. However, compared with HFrEF, the proportions of these cause-specific deaths are lower in HFpEF.[114] Sudden deaths account for a quarter of all-cause deaths and 40% of CV deaths in HFpEF.[115]

In Asia, CV deaths account for as much as half (50%-60%) of all deaths, driven by HF exacerbation and sudden death.[112,116] Cancer, infection, respiratory diseases, and renal failure are leading causes of non-CV deaths, especially among elderly patients.[116,117] In the PARAGON-HF trial, the proportion of CV and sudden cardiac death was higher in those with lower LV EF, and the proportion of non-CV death rose with increasing EF.[118]

QUALITY OF LIFE AND FUNCTIONAL STATUS. Patients with HFpEF have a reduced quality of life, often worse than many forms of cancer.[119] The presence and severity of signs and symptoms are

important drivers of health-related quality of life (HRQoL). Importantly, patient-reported HRQoL and its change are superior indicators of prognosis compared with signs and symptoms.[120]

Asian patients with HFpEF often report a high burden of symptoms such as dyspnea, fatigue, and anxiety.[120] A study conducted in Vietnam found that shortness of breath (95.5%) and fatigue (94.8%) were the most frequently reported symptoms among hospitalized older patients with HF.[121] This high symptom burden is consistent with findings from other Asian regions, where comorbidities such as hypertension, diabetes, and CKD are prevalent and contribute to the overall symptomatology.

Asian patients with HFpEF generally report lower HRQoL and functional status than other populations. This is supported by several studies that highlight ethnic differences in perceived HRQoL among HF patients.[120,122] The ASIAN-HF registry study found that Asian patients with HFpEF often have a high burden of comorbidities, which significantly impacts their quality of life. The Kansas City Cardiomyopathy Questionnaire scores were used to assess QoL, and patients in the "lean diabetic" group had the worst QoL among the identified multimorbidity groups.[16] Another study comparing multinational and multiethnic variations in HRQoL using the Kansas City Cardiomyopathy Questionnaire found that Asian patients, particularly Chinese, Malay, and Japanese/Korean, had lower HRQoL scores compared with White and Black patients.[122] This was after adjusting for demographic characteristics and HF severity. Specifically, self-efficacy, which measures confidence in managing symptoms, was notably lower in Asian patients.[122] Even within Asia, variation in findings was observed, with Japanese patients reporting higher self-efficacy than those from Southeast Asia.[122] Indeed, a growing body of evidence supports the fact that optimal HRQoL is largely dependent on patient competence in symptom perception.

Poor HRQoL also impacts depression or anxiety. However, psychological effects, for example, depression or anxiety, are not often reported in Asia,[123] likely because of fear of stigmatization. A multicenter study (N = 263) compared anxiety, depression, insomnia, and HRQoL between women and men with HFpEF.[124] The investigators found no sex differences in depression, insomnia, and QoL in patients with HFpEF after adjusting for confounders. However, women (vs men) with HFpEF experienced more severe anxiety and sleep quality after adjustment.[124]

TREATMENT

HISTORICAL CONTEXT: THE TREATMENT GAP. Initial trials of medications proven effective in HFrEF were unsuccessful in patients with HFpEF.[125-129] Use of perindopril in HFpEF investigated in PEP-CHF (The perindopril in elderly people with chronic heart failure) study did not improve mortality outcomes.[125] CHARM-PRESERVED (Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-Preserved Trial), testing the use of candesartan in 3,023 patients, did not reduce a combined outcome of CV death or HF hospitalization.[126] However, covariate-adjusted analyses were borderline statistically significant ($P = 0.051$).[126] I-PRESERVE (Irbesartan in Patients with Heart Failure and Preserved Ejection Fraction) (n = 4,128, irbesartan) was the largest and most adequately powered RAAS (the renin-angiotensin-aldosterone-system)-inhibitor trial in HFpEF and proved definitively neutral.[127] Subsequent analyses showed that 23% of patients had NT-proBNP levels <125 pg/mL, with half of them obese.[130] Subsequent covariate-adjusted analyses suggested a potential beneficial effect of Irbesartan in a subgroup of patients.[131]

TOPCAT (The Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial, which investigated the use of spironolactone, was overall neutral.[128] However, subsequent analyses found that 30% of Russian patients assigned to the spironolactone arm had undetectable drug levels on canrenone metabolite analysis.[132] Subsequent analyses in the Americas subgroup of the trial suggested an 18% relative risk reduction in the primary composite endpoint.[133]

PARAGON-HF narrowly missed its primary endpoint, a composite of total HF hospitalizations and CV death.[129] Prespecified subgroup analyses identified differential benefit in patients with LVEF below the median of approximately 57% and in women.[129,134,135] PARAGLIDE-HF (Prospective comparison of ARNI with ARB Given following stabiLization In DEcompensated HFpEF) (n = 466) subsequently demonstrated that sacubitril/valsartan reduced NT-proBNP by 15% relative to valsartan when initiated within 30 days of a worsening HF event.[136] A prespecified pooled analysis of PARAGON-HF and PARAGLIDE-HF suggested a significant reduction in the primary composite endpoint of HF hospitalization and CV events in both patients with HFrEF and heart failure with mildly reduced ejection fraction.[137]

Many of the neutral trials share common lessons: clinical heterogeneity of HFpEF, including metabolic, fibrotic, and inflammatory HFpEF subtypes; failures in diagnostic criteria that enrolled patients without confirmed diastolic dysfunction or elevated natriuretic peptides; and inclusion of patients with noncardiac dyspnea. Later successful trials built on these lessons by mandating elevated natriuretic peptide levels and by including evidence of structural heart disease.

BREAKTHROUGH: SGLT2 INHIBITORS. EMPEROR-Preserved (Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction) trial was the first trial to demonstrate unequivocal benefit in HFpEF, reducing the composite of CV death or HF hospitalization by 21%. This reduction was primarily driven by a 27% reduction in HF hospitalization.[27] LVEF subgroup analysis showed graded benefit across the ejection fraction spectrum, with no significant benefit in patients with LVEF ≥60% (HR: 0.87; 95% CI: 0.69-1.10). However, the *P* value for interaction was nonsignificant ($P = 0.27$).[138] Subsequent regional and ethnic analyses showed consistent efficacy in Asian patients.[139]

Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure (DELIVER) confirmed and extended the results from EMPEROR-Preserved, showing an 18% reduction in CV death and worsening HF.[28] Critically, benefit was consistent across the full LVEF spectrum, including LVEF ≥60%, without the attenuation observed in EMPEROR-Preserved. Notably, DELIVER enrolled 19.6% of patients in Asia. A post hoc analysis of Asian patients demonstrated the consistency of results.[140] The DAPA-HF (Dapagliflozin in Patients With Heart Failure and Reduced Ejection Fraction) plus DELIVER pooled analysis (n = 11,007) demonstrated that dapagliflozin reduced CV death across the LVEF spectrum.[141] A geographic analysis of pooled data confirmed a consistent benefit in Asia.[142]

Asia-specific studies showed consistent benefits. The EMPRISE (EMPagliflozin compaRative effectIveness and SafEty) East Asia study, across Japan, South Korea, and Taiwan (28,712 matched pairs), found that empagliflozin vs dipeptidyl peptidase-4 inhibitors inhibitors reduced the risk of HF hospitalization and all-cause mortality by 24% in patients with established CV disease.[143] Japan approved empagliflozin for HF regardless of ejection fraction in April 2022 and dapagliflozin in January 2023, with full national health insurance coverage.[144] Nevertheless, costs can remain a significant barrier to prescribing SGLT2 inhibitors in Asia. In India, SGLT2 inhibitors were not cost-effective at branded prices in patients with HFrEF.[145] In Thailand, SGLT2i were not cost-effective in patients with HF and diabetes.[146] However, the expiration of empagliflozin's patent could significantly reduce costs. Estimated sustainable cost-based manufacturing prices of SGLT2i are US$1.30 to US$3.45 per month.[147] In 2021, the World Health Organization included SGLT2i on its Essential Medicines List, though only for the treatment of diabetes.[148]

Yet, diagnostic infrastructure presents an additional barrier. HFpEF diagnosis requires echocardiography and natriuretic peptide measurement, which remain inaccessible in rural settings across most Asian low-middle-income countries.

MINERALOCORTICOID RECEPTOR ANTAGONISTS (250). The FINEARTS-HF (Finerenone Trial to Investigate Efficacy and Safety Superior to Placebo in Patients With Heart Failure) trial was the first study showing the effectiveness of ns-MRAs in patients with HFpEF. Over a median follow-up of 32 months, finerenone reduced the primary composite of total worsening HF events plus CV death by 16% in 6,001 patients with HFpEF (LVEF ≥40%). This benefit was primarily driven by a reduction in worsening HF events rather than CV deaths.[29] Importantly, this benefit was consistent across the LVEF spectrum and in men and women.[149,150] Furthermore, benefits were consistent even in patients with concomitant SGLT2i use.[151] Compared with steroidal MRAs, finerenone exhibited greater mineralocorticoid receptor selectivity and lacked antiandrogenic effects (eg, gynecomastia and menstrual irregularities).[152] In FINEARTS, hyperkalemia occurred more frequently (serum potassium >5.5 mmol/L in 14.3% vs 6.9%), though hyperkalemia requiring hospitalization was rare (0.5% vs 0.2%), and finerenone was protective against hypokalemia (4.4% vs 9.7%).[29] A pooled analysis of RALES (Randomized Aldactone Evaluation Study), EMPHASIS-HF (Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure), TOPCAT, and FINEARTS trials showed a significant improvement in patient outcomes, including death and hospitalization, regardless of region and LVEF phenotype.[153]

EMERGING THERAPIES: GLP-1 RECEPTOR AGONISTS. STEP-HFpEF (Semaglutide Treatment Effect in People With Obesity and HFpEF) was the first study demonstrating that GLP-1 inhibitors can improve clinical outcomes in patients with obesity and HFpEF without diabetes.[154] In this trial, a 52-week treatment with GLP-1 inhibitors improved HRQoL, reduced body weight by 10.7%, improved the 6-minute walk

distance by 20.3 m (95% CI: 8.6-32.1), and decreased C-reactive protein by 39% compared with placebo.[154] A separate study, STEP-HFpEF DM, replicated the findings of STEP-HFpEF in patients with type 2 DM.[155] A subsequent pooled analysis demonstrated consistent results regardless of age, sex, and BMI subgroups. A second post hoc pooled analysis combined patients from STEP-HFpEF, STEP-HFpEF DM, and patients with physician-reported HFpEF from the SELECT (Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity) and FLOW (Evaluate Renal Function with Semaglutide Once Weekly) trials.[156] In this study involving 3,743 patients with HFpEF, treatment with semaglutide also reduced the risk of long-term outcomes, including a 31% relative risk reduction of HF hospitalization or CV death. This effect was primarily driven by a reduction in HF hospitalizations, because the effect on CV death alone was nonsignificant.[156] The SUMMIT (A Study of Tirzepatide [LY3298176] in Participants With Heart Failure With Preserved Ejection Fraction [HFpEF] and Obesity) trial was the first single HFpEF trial showing an improvement in a hard clinical endpoint: GLP-1 inhibitors reduced the primary endpoint of CV death or worsening HF by 38%. A cardiac magnetic resonance imaging substudy ($n = 106$) showed tirzepatide reduced LV mass by 11 g ($P = 0.004$) and paracardiac adipose tissue by 45 mL ($P < 0.001$).[157]

The generalizability of these findings to Asian patients is challenging. STEP-HFpEF patients were 96% White and only 4% Asian.[154] Patients in the STEP program had a mandatory BMI threshold of ≥30 kg/m^2 for obesity.[154,155] This threshold excluded the majority of Asian patients with HFpEF, who commonly have a lower BMI.[10] The World Health Organization Asia-Pacific classification defines obesity at BMI ≥27.5 kg/m^2 (or ≥25 in many Asian guidelines), yet Asians develop metabolic complications—including visceral adiposity-driven diastolic dysfunction—at substantially lower BMI thresholds.[14] Furthermore, Asian patients with HFpEF commonly present with a lean-diabetic subtype, driven by visceral fat, which has particularly worse outcomes.[16,158] A prior investigation of the thresholds of BMI and waist circumference that associate with subclinical cardiac dysfunction in Asian adults revealed even lower cutoffs of 26.4 kg/m^2 and 87.5 cm in men and 23.4 kg/m^2 and 83 cm in women, respectively. Therefore, therapeutic evidence of GLP-1 inhibitor efficacy at lower BMI thresholds is an urgent unmet need. Safety also warrants attention. Asian patients could have lower weight below healthy ranges and unmask or worsen sarcopenia, which is common in older Asian patients with HFpEF.

TREATMENT GAPS AND UNMET NEEDS. Given Asia's specific HFpEF profile, several treatment gaps and unmet needs remain. Patients with lean and normal-weight HFpEF, especially those with a lean diabetic subtype, are very common in Asia.[10,16] For example, in the DELIVER trial, Asian participants had a mean BMI approximately 6 kg/m^2 lower than non-Asian participants.[140] SGLT2 inhibitors are effective in normal-weight patients,[27] but GLP-1 receptor agonists remain untested in lean (Asian) patients with HFpEF.

Many Asian countries are highly aged societies, which is associated with greater frailty. Dapagliflozin was beneficial regardless of frailty status.[159] In a post hoc analysis of DELIVER, dapagliflozin's absolute benefit almost doubled in the frailest patients. Furthermore, in absolute terms, the Quality-of-life improvements were greatest among the frailest patients.[159] An important caveat is that frailty in the DELIVER population was largely coupled with higher BMI,[160] whereas frailty in Asian HFpEF more commonly coexists with low BMI and sarcopenia. Therefore, these findings may not translate directly to the sarcopenic, low-body-mass-index frailty phenotype prevalent in Asia.

Asia is also home to some of the richest and poorest countries, leading to stark disparities in access to treatment and diagnosis of HFpEF. The International Congestive Heart Failure study documented 1-year mortality ranging from 7% in China to 23% in India to 34% in Africa, with only 46% of the variation explained by measured variables, suggesting that health system variation is a major determinant.[161] ASIAN-HF also confirmed big regional differences in outcomes. Southeast Asian patients with HFpEF, despite being younger, had a 2.7-fold higher risk of death or HF hospitalization than Northeast Asians.[10] In DELIVER, China had the highest risk of HF hospitalization in Asia, but—together with Japan—the lowest risk of death. In contrast, Vietnam had a relatively lower risk of HF hospitalization but a significantly higher risk of CV death.[140] Collectively, these results suggest that regional variation in outcomes of patients with HFpEF in Asia is influenced by differences in health systems.

Variations in health systems are also clear in differences in costs and access to novel HF therapies. At branded prices, SGLT2 inhibitors had an incremental cost-effectiveness ratio of US$7,318/quality-adjusted life-year in India in patients with HFrEF, against a willingness-to-pay threshold of US$2,710, which was

HIGHLIGHTS

- Marked regional heterogeneity in clinical subtypes and outcomes of HFpEF in Asia.
- Limited access to echocardiography & natriuretic peptide testing complicate diagnosis.
- Diagnostic algorithms for HFpEF perform suboptimally in Asian patients.
- Artificial intelligence solutions can bridge these diagnostic gaps.
- Accurate diagnosis of clinical subtypes & equitable access to therapies are vital.

not cost effective.[145] Given the smaller absolute risk benefit of SGLT2 inhibitors in patients with HFpEF, they are even less likely to be cost-effective in this patient population. Similar results were found in Thailand. There are currently no cost-effectiveness studies on GLP-1 receptor agonists in HFpEF. Yet, cost-effectiveness thresholds vary significantly across Asia, meaning therapies considered standard in high-income settings remain inaccessible across much of the region.

CONCLUSIONS

This review highlights the clinical heterogeneity of HFpEF in Asia and underscores the importance of accurate diagnosis, subtype-informed risk stratification, and equitable access to emerging therapies. Continued regional research, improved representation of Asian populations in global clinical trials, and health system-level interventions will be essential to close existing care gaps and optimize outcomes for patients with HFpEF across diverse Asian settings.

ACKNOWLEDGMENTS The authors would like to thank the Guest Associate Editor Tao Li and the Guest Editor-in-Chief Rong Tian.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Tromp is supported by the National University of Singapore Start-up grant and the CS-IRG from the National Medical Research Council; has received research support from AstraZeneca and consulting or speaker fees from Roche Diagnostics, and owns a patent US-10702247-B2 unrelated to the present work. Dr Lam has received research grants from the National Medical Research Council of Singapore, Novo Nordisk, and Roche Diagnostics; has served in advisory, consulting, and trial leadership roles for Alnylam Pharma, AnaCardio AB, Applied Therapeutics, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, BridgeBio, Corteria, CPC Clinical Research, Cytokinetics, Eli Lilly, EvlaBio, ICON Clinical Research, Impulse Dynamics, Intellia Therapeutics, Janssen Research & Development LLC, Klyv Therapeutics, Medscape/WebMD Global LLC, Merck, Novartis, Novo Nordisk, Pfizer, Radcliffe Group, Ribocure, Roche, and Us2.ai; has patent PCT/SG2016/050217 pending and patent US Patent No. 10,631,828 B1; US 10,702,247 B2; US 11,301,996 B2; US 11,446,009 B2; US 11,931,207 B2; US 12,001,939; US 12,400,762 B2; and is a cofounder and nonexecutive director of Us2.ai. Dr Schiattarella reports research agreements and/or speaker honoraria and/or consultancy agreements from Boehringer Ingelheim, Pfizer, Novo Nordisk, e-Therapeutics, Sanofi, and Preload Therapeutics, not related to the content of this work. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS Asia, heart failure, regional differences