

# Contemporary Approach and Current Treatment Modalities for Management of Heart Failure Across Asia: A Literature Review

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## ABSTRACT

With millions being affected, Heart Failure (HF) has become a growing health concern in Asia, especially in South Asia, where it affects a younger population presenting with multiple co-morbidities. Despite global advancements in HF treatments, existing guidelines remain largely based on American and European populations; however, there is a need for tailored strategies in Asia. The present literature-based review provides an overview of the existing HF management guidelines and highlights guidelines specific to Asian countries. It further summarises findings from recent publications that describe current treatment patterns for HF, including pharmacological and non pharmacological strategies as well as the use of medical devices. While older medications continue to remain the standard of care, newer therapies show promising potential to enhance treatment effectiveness and recovery in patients with HF. Developing region-specific HF guidelines is essential, considering Asia's unique genetic, socioeconomic and healthcare-related factors.

**Keywords:** Management of heart failure, Pharmacotherapy, Treatment guidelines

## INTRODUCTION

Heart Failure (HF) affects over 38 million people globally, making it a significant public health concern [1]. Asia is home to 4.4 billion people, representing approximately 60% of the world's population [2]. With a higher prevalence of HF in the Asian population, the condition imposes a substantial burden on the healthcare system [2]. In India alone, the prevalence of HF is estimated to range from 1.3 to 4.6 million [3]. Co-morbidities such as hypertension, diabetes mellitus, hyperlipidaemia and metabolic disorders are commonly observed in patients with HF and are known to impact clinical outcomes [4]. Additionally, individuals in the South Asian region are affected at a significantly younger age compared to those in Western countries [5-7]. Research indicates that two-thirds of these younger individuals present with multimorbidity at the time of diagnosis [6].

Although extensive global research on HF is available, current treatment guidelines are primarily based on data from Western populations. Consequently, gaps remain in understanding the distinct epidemiology and management needs of Asian individuals [2]. Diverse genetic backgrounds, lifestyle factors and varying healthcare infrastructures in Asia influence HF phenotypes and treatment responses [6,8]. Extended hospital stays, frequent outpatient visits and ongoing medication requirements significantly affect patients' Quality of Life (QoL) and productivity [9,10]. Therefore, it is essential to develop tailored strategies for the prevention, diagnosis and management of HF to effectively address its growing burden in this region [11]. Reviewing the literature and updating practices is imperative, especially in light of evolving therapies, newer medications and changing global treatment patterns.

The present review aimed to strengthen the understanding of current trends in HF management in Asia. It evaluates the existing landscape of HF therapies, highlights key advancements and identifies gaps in the literature that must be addressed to improve patient outcomes. By synthesising existing data and analysing recent research, the present review provides insights to support the development of tailored HF management strategies for Asia's diverse and expanding population.

**Guidelines for management of HF:** Treatment guidelines for HF emphasise pharmacological and non pharmacological approaches to significantly improve patient outcomes. According to the 2022

American College of Cardiology (ACC) and American Heart Association (AHA) guidelines and the 2021 European Society of Cardiology (ESC) guidelines, first-line therapy for patients with Heart Failure with Reduced Ejection Fraction (HFrEF) includes Angiotensin-Converting Enzyme Inhibitors (ACEIs), Angiotensin Receptor-Neprilysin Inhibitors (ARNIs), Angiotensin II Receptor Blockers (ARBs),  $\beta$ -blockers, Mineralocorticoid Receptor Antagonists (MRAs), Sodium-Glucose Co-Transporter-2 (SGLT2) inhibitors and diuretics [12-14]. The 2022 ACC/AHA guidelines also recommend additional therapies—ivabradine, vericiguat and digoxin—for patients with HFrEF who do not respond adequately to first-line therapy [12,13].

The 2023 ESC guidelines recommend SGLT2 inhibitors, such as empagliflozin and dapagliflozin, for patients with HF and Left Ventricular Ejection Fraction (LVEF)  $>40\%$ . They also recommend finerenone, a non steroidal MRA, to reduce the risk of HF progression and cardiovascular death in patients with diabetes and Chronic Kidney Disease (CKD), across all ejection fraction categories [14].

Non pharmacological strategies recommended by the ACC/AHA and ESC guidelines include multidisciplinary cardiac rehabilitation programs to enhance functional capacity, manage symptoms and provide psychological support. Regular vaccinations, including influenza and pneumococcal vaccines, are advised to reduce infection-related complications. Restriction of dietary salt intake is recommended, especially for patients with congestion, to minimise fluid retention. Additionally, supervised exercise training is encouraged to decrease HF-related hospitalisations [12-14].

In the Asian context, the Korean Society of Heart Failure (KSHF), the Japanese Circulation Society (JCS)/Japanese Heart Failure Society (JHFS) and the Asian Pacific Society of Cardiology (APSC) have developed guidelines for the management of HF [15-17]. However, these appear to be adaptations of the ACC/AHA and ESC guidelines. According to the KSHF guidelines, patients with HFrEF and mildly reduced ejection fraction (HFmrEF) show considerable benefits from ARNIs, while SGLT2 inhibitors are recommended for all types of HF [15]. The JCS/JHFS 2017 guidelines recommend ACEIs, ARBs,  $\beta$ -blockers and MRAs for chronic HFrEF. In the 2021 revision, additional drugs such as ivabradine, ARNIs (sacubitril/valsartan) and SGLT2 inhibitors were incorporated into the treatment algorithm for patients with HFrEF [16].

The APSC 2022 guidelines emphasise the use of Renin-Angiotensin System (RAS) blockers (ARNIs/ACEIs),  $\beta$ -blockers, MRAs and SGLT2 inhibitors (dapagliflozin and empagliflozin) for patients with HFrEF, HFmrEF and HF with preserved ejection fraction (HFpEF). These guidelines prefer the use of ARNIs over ACEIs for HFrEF. If both ARNIs and ACEIs are intolerable, ARBs may be considered. Patients who cannot tolerate ACEIs, ARBs, or ARNIs may be evaluated for nitrate plus hydralazine therapy. Those who remain symptomatic despite Optimal Medical Therapy (OMT) are advised to receive digoxin. Additionally, for patients with congestion, loop diuretics are recommended to reduce the risk of death and improve exercise capacity in HFrEF [17].

In addition to pharmacological treatment, the JCS/JHFS guidelines recommend percutaneous mitral valve repair systems (MitraClip) and transcatheter aortic valve implantation as non pharmacological treatment options [16]. Similarly, the APSC guidelines include cardiac implantable electronic device therapy along with the multidisciplinary cardiac care strategies recommended by the ACC/AHA and ESC [17]. The ACC/AHA, ESC, KSHF, JCS/JHFS and APSC guidelines is summarised in [Table/Fig-1] [12-17].

## LITERATURE SEARCH

The authors performed a literature search using PubMed to identify relevant articles on HF management in Asian populations. The

search terms used included: HF, chronic HF, Asia (and the names of all Asian countries), treatment, intervention, management and therapy. Among all retrieved references, they restricted the results to full-text or free full-text articles involving human subjects. Case studies, case reports and reviews were excluded. They also excluded studies focused on non Asian populations, those involving participants aged  $<18$  years and studies lacking relevant outcome measures. Publications reporting duplicated treatments/therapies were also excluded. A total of 16 studies meeting the eligibility criteria were included in the present review.

The selected studies primarily consisted of observational cohort studies, retrospective and prospective cohort studies, non randomised and non blinded multicentre global studies, large long-term observational studies, network meta-analyses and nationwide cohort studies evaluating both pharmacological and non pharmacological HF therapies. The outcomes of interest included clinical measures such as mortality, hospitalisation rates, QoL, symptom relief and HF severity.

## Current Treatment Modalities

With a growing body of evidence supporting various treatment modalities, HF management continues to evolve pharmacologically. The RAAS inhibitors and  $\beta$ -blockers remain the foundational therapies for HF, particularly in South Asian populations.

Guidelines	ACC/AHA (2022)12,13	ESC (2023)14	KSHF15	JCS/JHFS (2021)16	APSC (2022)17
<b>Pharmacotherapy for HFrEF</b>					
Standard therapies	<p>ACEi or ARB or ARNi (preferred)- Recommended as first-line therapy.</p> <p><math>\beta</math>-blockers- Bisoprolol, carvedilol, SR metoprolol succinate Recommended in patients with current or previous symptoms to reduce hospitalisation and mortality</p> <p>MRA- Spironolactone or eplerenone Recommended in patients with eGFR <math>&gt;30</math> mL/min/1.73 m<sup>2</sup> and serum potassium is <math>&lt;5.0</math> mEq/L</p> <p>SGLT2 inhibitors (dapagliflozin and sotagliflozin) recommended in patients with symptomatic CHF irrespective of presence of T2DM.</p> <p>Hydralazine and Isosorbide Dinitrate- Recommended in patients with intolerance to ARNi, ACEi, or ARB</p>	<p>ACEi or ARB or ARNi- Recommended as first-line therapy.</p> <p>SGLT2i- Dapagliflozin/ Empagliflozin</p> <p>MRA- Finerenone Recommended in patients with CKD and T2DM</p> <p>IV iron supplementation- Recommended in patients with Iron deficiency</p>	<p>ARNi/ACEi/ARB- Strongly recommended as first-line; start with ACE inhibitors or ARBs and switch to ARNi if tolerated</p> <p>Beta-blocker- Bisoprolol, carvedilol and metoprolol SR tablets Recommended alongside RAAS inhibitors; helps to improve symptoms and reduce mortality</p> <p>MRA- Spironolactone, Eplerenone Recommended in conjunction with RAAS inhibitors and <math>\beta</math>-blockers; reduces mortality and hospitalisations</p> <p>SGLT2 inhibitor- Recommended in patients with or without diabetes; helps to reduce hospitalisation and cardiovascular mortality.</p>	<p>ARNi- Sacubitril/valsartan Recommended in adult patients with CHF</p> <p>I(f) Channel Blocker or HCN Channel Blocker- Ivabradine Recommended in patients of CHF with SR and a resting heart rate at of 75 bpm or higher</p> <p>SGLT2 inhibitor- Dapagliflozin Recommended in patients with T2DM complicated by HF and CKD</p>	<p>ARNi (preferred)/ ACEi/ ARB <math>\beta</math>-blocker MRA SGLT2i</p> <p>These four therapies are considered foundational treatment for HFrEF</p>
Additional pharmacotherapy	<p>Diuretics- Bumetanide, furosemide and torsemide Recommended in patients with fluid retention to relieve the symptoms of congestion</p> <p>Addition of thiazide (metalozone)- Recommended for patients not responding to diuretics alone.</p> <p>Omega-3 PUFA supplementation- Recommended as adjunctive therapy to reduce mortality and cardiovascular hospitalisations</p> <p>Potassium binders- Patiromer, sodium zirconium cyclosilicate Recommended in patients with hyperkalemia (serum potassium level <math>&gt;5.5</math> mEq/L)</p> <p>Ivabradine- Recommended in patients with symptomatic chronic HF (LVEF <math>\leq 35\%</math>) receiving GDMT and who are in SR with a heart rate of <math>\geq 70</math> bpm</p> <p>Vericiguat- Recommended in patients with recent worsening of HF</p> <p>Digoxin- Recommended in patients with irresponsive GDMT</p>	<p>i.v. iron supplementation with ferric carboxymaltose or ferric derisomaltose</p>	<p>Diuretics- recommended in patients with fluid retention to maintain adequate fluid volume</p> <p>Ivabradine- recommended in patients with SR and a resting HR <math>\geq 70</math> beats/min and if symptoms persist after optimising first line therapy and MRA-</p> <p>Vericiguat recommended in patients with LVEF <math>&lt;45\%</math> and recent worsening of HF</p> <p>Digoxin- Recommended in patients with AF, unresponsive beta blockers or contraindicated</p> <p>Tolvaptan- Recommended in patients with volume overload with hyponatraemia refractory to other treatments</p>	<p>Vericiguat- Recommended in patients with outpatient IV diuretics and symptomatic chronic heart failure and an EF of less than 45%.</p> <p>Omecamtiv Mecarbil</p>	<p>Loop diuretics- Recommended in patients with congestion</p> <p>Ivabradine- Recommended in patients with EF <math>\leq 35\%</math> in SR and a resting heart rate <math>\geq 70</math> bpm, symptomatic OMT, those intolerable to <math>\beta</math>-blockers.</p> <p>i.v. ferric carboxymaltose- Recommended in patients with iron deficiency (serum ferritin <math>&lt;100</math> ng/ml or serum ferritin 100-299 ng/ml with TSAT <math>&lt;20\%</math>).</p> <p>Vericiguat- Recommended in patients with worsening HF</p> <p>Digoxin- Recommended in patients who remain symptomatic despite OMT.</p> <p>Nitrate plus hydralazine- Recommended in patients who cannot tolerate ACEi, ARB or ARNI.</p>

## Devices and interventional therapies

	<p>ICDs- Recommended in patients with:</p> <ul style="list-style-type: none"> <li>Non ischaemic DCM or ischaemic heart disease at least 40 days post-MI with LVEF ≤35% and expectation of meaningful survival for &gt;1 year</li> <li>At least 40 days post-MI with LVEF ≤30% while and expectation of meaningful survival for &gt;1 year</li> <li>Genetic arrhythmogenic cardiomyopathy with high-risk features of sudden death, with EF ≤45%</li> <li>CRT-</li> </ul> <p>Recommended in patients with:</p> <ul style="list-style-type: none"> <li>LVEF ≤35%, SR, left LBBB with a QRS duration ≥150 ms</li> <li>LVEF ≤35%, SR, a non-LBBB pattern with a QRS duration ≥150 ms</li> <li>high-degree or complete heart block and LVEF of 36% to 50%</li> <li>LVEF ≤35%, sinus rhythm, LBBB with a QRS duration of 120 to 149 ms</li> <li>LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS duration of 120 to 149 ms</li> <li>GDMT with LVEF ≤35% and undergoing placement of a new or replacement device implantation with anticipated requirement for significant (&gt;40%) ventricular pacing</li> <li>LVEF ≤30%, ischaemic cause of HF, sinus rhythm, LBBB with a QRS duration ≥150 ms</li> <li>Autonomic nervous system modulation</li> <li>Cardiac Contractility Modulation (CCM)</li> </ul>		<p>LVAD, heart transplantation or palliative therapy.</p> <p>ICD- Recommended in patients:</p> <ul style="list-style-type: none"> <li>Recovered from haemodynamically unstable ventricular arrhythmias</li> <li>symptomatic HF of ischaemic origin, if LVEF is ≤35% despite ≥3 months of GDMT and survival is expected for &gt;1 year</li> <li>symptomatic HF of non-ischaemic origin, if LVEF ≤35% despite ≥3 months of GDMT and survival is expected for &gt;1 year</li> </ul> <p>CRT- Induce ventricular resynchronisation, thereby helps to improve QoL, hospitalisation and mortality</p>	<p>Mechanical Circulatory Support- paracorporeal VADs.</p> <p>Catheter-Based Transaortic Microaxial Pumps (Impella)</p>	
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## Pharmacotherapy for HFmrEF

Standard therapies	ARNi, ACEi, or ARB beta blockers MRAs SGLT2i	Diuretics for fluid retention SGLT2i-Dapagliflozin/ Empagliflozin MRA- Finerenone Recommended in patients with CKD and T2DM	ARNi/ACEi/ARB- Considered to reduce cardiovascular mortality Beta-blocker- Considered to reduce cardiovascular mortality MRA- Considered to reduce cardiovascular mortality SGLT2 inhibitor- Empagliflozin or dapagliflozin- Recommended for patients with HF with or without diabetes to reduce hospitalisation or mortality Diuretics- Recommended in patients with symptoms of congestion		ARNi/ACEi/ARB β-blocker MRA SGLT2i
Additional pharmacotherapy		ACEi/ARNi/ARB MRA Beta-blocker i.v. iron supplementation with ferric carboxymaltose or ferric derisomaltose			Loop diuretics i.v. ferric carboxymaltose

## Pharmacotherapy for HFpEF

Standard therapies	ARNi/ACEi/ARB MRA SGLT2i	Diuretics for fluid retention SGLT2i-Dapagliflozin/ Empagliflozin MRA- Finerenone Recommended in patients with CKD and T2DM	ARNi/ACEi/ARB- Recommended to reduce cardiovascular mortality β-blockers- Considered to reduce cardiovascular mortality MRAs- Recommended in patients with symptomatic HFpEF (LVEF ≥45%, elevated BNP level or HF admission within 1 year, eGFR >30 mL/min/1.73 m <sup>2</sup> , creatinine SGLT2 inhibitor- Considered to reduce cardiovascular mortality Diuretics- Considered to reduce cardiovascular mortality		ARNi/ACEi/ARB β-blocker MRA SGLT2i
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Additional pharmacotherapy	Nitrates or phosphodiesterase-5 inhibitors Diuretics				Loop diuretics
<b>Non pharmacological therapies</b>					
	Multidisciplinary care cardiac rehabilitation program. Vaccination. Dietary Sodium Restriction. Exercise training	Multidisciplinary care cardiac rehabilitation program. Vaccination. Dietary Sodium Restriction. Exercise training	Patient self-management. Exercise therapy. Home-based cardiac rehabilitation; telehealth and mobile health intervention	Percutaneous Mitral Valve Repair System (MitraClip)- Recommended for patients at high risk of open-heart surgery Transcatheter Aortic Valve Implantation- Recommended in patients with symptomatic severe aortic stenosis Remote Monitoring Systems. Salt Management. Nutrition; Management Prevention of Infection and Vaccination- Influenza and pneumococcus vaccines	Multidisciplinary care cardiac rehabilitation program. Cardiac implantable electronic devices therapy- Recommended in patients with LVEF $\leq$ 35% after 3 months of achieving OMT

[Table/Fig-1]: Management of HF: Guidelines and Recommendations [12-17].

ACC, American college of cardiology; ACEi: Angiotensin-converting enzyme inhibitor; AF: Atrial fibrillation; AHA: American heart association; APSC: Asian pacific society of cardiology; ARB: Angiotensin II receptor blocker; ARNI: Angiotensin receptor neprilysin inhibitor;  $\beta$ : beta; BNP: B-type natriuretic peptide; CCM: Cardiac contractility modulation; CHF: Chronic heart failure; CKD: Chronic kidney disease; CRT: Cardiac resynchronisation therapy; DCM: Dilated cardiomyopathy; EF: Ejection fraction; ESC: European society of cardiology; eGFR: estimated glomerular filtration; ESC: European society of cardiology; GDMT: Guideline directed medical therapy; HCN: Hyperpolarisation-activated cyclic nucleotide-gated channels; HF: Heart failure; HFmrEF: HF with midrange ejection fraction; HFpEF: HF with preserved ejection fraction; HFrEF: HF with reduced ejection fraction; HR: Hazard ratio/heart rate; ICD: Implantable cardioverter-defibrillator; IV: Intravenous; JCS: Japanese circulation society; JHFS: Japanese heart failure society; KSHF: Korean society of heart failure; LBBB: Left bundle branch block; LVAD: Left ventricular assist device; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction; MRA: Mineralocorticoid receptor antagonist; OMT: Optimal medical therapy; PUFA: Polyunsaturated fatty acid; QoL: Quality of life; QRS: QRS complex with Q wave, R wave and S wave; RAAS: Renin angiotensin aldosterone system; SGLT2: Sodium glucose cotransporter 2; SR: Sinus rhythm; T2DM: Type 2 diabetes mellitus; TSAT: Transferrin saturation; VADs: Ventricular assist devices

Research conducted by Ouwerkerk W et al., and Kubota Y et al., demonstrated that achieving Guideline-Recommended Therapeutic Doses (GRTD) of these medications significantly improves patient outcomes and reduces mortality [18,19]. Their findings highlighted the survival benefits of  $\beta$ -blockers in HFrEF, with a Hazard Ratio (HR) of 0.40. Similarly, results from the ASIAN-HF registry emphasised the importance of non-cardio-selective  $\beta$ -blockers (HR 0.37) in reducing cardiovascular mortality in patients with overlapping Chronic Obstructive Pulmonary Disease (COPD).

A real-world study by Sachdeva A et al., found that the use of ARNI (sacubitril/valsartan) significantly improved Left Ventricular Ejection Fraction (LVEF) by 23% and resulted in a marked reduction in N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels [20]. These findings are consistent with those reported by Xie B et al., and Murphy SP et al., [21,22].

Studies have also demonstrated the beneficial effects of MRAs, particularly in patients with End-Stage Renal Disease (ESRD). The use of MRAs has been associated with reduced cardiovascular and all-cause mortality, highlighting their utility in high-risk populations [23,24].

In addition to pharmacological interventions, mechanical devices such as Implantable Cardioverter-Defibrillators (ICDs) and Cardiac Resynchronisation Therapy (CRT) have played a critical role in managing patients with severe HF [25,26]. Zhang S et al., and Naik A et al., reported that ICDs can reduce all-cause mortality by nearly 50%, making them especially beneficial for patients at high risk of ventricular tachycardia or ventricular fibrillation [27,28]. CRT has also been shown to improve clinical scores and reduce morbidity and mortality in HF patients [26]. It is one of the most effective therapies for improving ventricular contractility, reducing functional mitral regurgitation, promoting ventricular remodelling and enhancing overall LV ejection fraction [29].

The CRT is recommended for patients with reduced LVEF, New York Heart Association (NYHA) Class III or ambulatory Class IV symptoms, QRS duration  $>120$  ms and, in particular, those with Left Bundle Branch Block (LBBB) morphology [30,31].

A study conducted by Mischke K et al., found reduced intrinsic QRS durations in patients following CRT, indicating reverse electrical

remodelling in responders and those with dilated cardiomyopathy [32]. Similarly, Dizon J et al., reported a complete LBBB reverting to a normal QRS pattern after CRT, demonstrating its potential for electrical remodelling in specific cases [33]. In contrast, another study found that patients in the responder and dilated cardiomyopathy groups did not show a reduction in intrinsic QRS duration after CRT. However, in the non-responder and ischaemic cardiomyopathy groups, a prolonged intrinsic QRS duration was observed after two years of follow-up, suggesting that CRT may delay further damage to the cardiac electrical conduction system rather than reverse it [34]. In a study by Ma K et al., the mortality rates for mitral valve repair and replacement were found to be similar (0.2 percent for repair and 0.9 percent for replacement), reflecting a growing use of bioprosthetic valves and minimally invasive techniques [35].

An analysis of data from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) evaluated long-term survival outcomes in HF patients undergoing coronary revascularisation. CABG showed better outcomes compared with percutaneous coronary intervention (PCI) in patients with acute HF [36]. A propensity score-matched cohort study in the Korean population by Lee SE et al., showed that CABG was associated with significantly lower all-cause mortality and fewer cardiovascular-related rehospitalisations compared with PCI. The benefits of CABG were more pronounced in older patients and in those with complex coronary artery disease [37].

Non pharmacological interventions play an important role, particularly in patients with diuretic resistance or intolerance to conventional therapies. Ultrafiltration (UF) provides a viable alternative to high-dose diuretics for managing fluid overload in decompensated HF, resulting in improved fluid removal, shorter hospital stays and fewer rehospitalisations [38]. A position statement from the HF Association of the ESC emphasised the effectiveness of UF in reducing hospital readmissions and fluid overload [39].

Weight management, including dietary modification and physical activity, substantially reduces risk factors for atherosclerotic cardiovascular disease. The Dietary Approaches to Stop Hypertension (DASH) diet recommends 4-5 servings of fruits and vegetables, 6-8 servings of whole grains daily and increased intake of calcium (1250 mg), magnesium (500 mg) and potassium (4700 mg).

It also advises limiting cholesterol intake to 150 mg and restricting saturated fat to 6 percent of daily calories [40,41]. Additional lifestyle changes such as limiting sodium intake to 2300 mg/day (5.84 g Sodium Chloride (NaCl)), maintaining a healthy body weight (BMI 18.5-23 kg/m<sup>2</sup>), limiting alcohol consumption and quitting smoking are effective strategies for controlling hypertension in individuals with Type 2 Diabetes Mellitus (T2DM) [42].

Mobile health (m-health) interventions have shown potential in improving self-care, including weight management and enhancing QoL in HF patients [43]. Research indicates that Weight Management (WM) interventions incorporating education, coping strategies and regular follow-up significantly improve adherence to monitoring, enhance weight management skills and reduce HF-related rehospitalisation rates [44]. These findings align with a study conducted by He S et al., [45].

Fluid intake management is another crucial component of HF care. Non compliance is associated with higher rehospitalisation rates [46]. According to Braunwald E et al., fluid restriction is typically recommended for patients with hyponatraemia (<130 mEq/L), which may result from activation of the renin-angiotensin system, excessive arginine vasopressin secretion, or sodium loss due to prior diuretic use. Fluid restriction (<2 L/day) is advised for hyponatraemic individuals or those with persistent fluid retention despite high-dose diuretics and sodium restriction [47]. While Japanese guidelines provide no strong recommendations on fluid intake, the ESC advises all HF patients to avoid excessive fluid consumption [48,49]. Recent evidence, however, supports more liberalised fluid strategies in both chronic and acute HF, emphasising the need for patient-specific adjustments based on clinical status and environmental factors [12,49,50].

Effective management requires recognising when to adjust fluid intake. Patients should increase fluid consumption during periods of high heat, nausea, or vomiting and reduce intake when experiencing weight gain or congestive symptoms. These adjustments help maintain optimal fluid balance and support effective HF management [51,52].

Exercise interventions, particularly those tailored to culturally specific populations, have been shown to improve HF outcomes. Khandekar JS et al., highlighted the importance of yoga—including postures, breath control and meditation—as a key intervention for reducing blood pressure (BP) in prehypertensive individuals [53]. Engaging in exercise such as brisk walking for 50-60 minutes, three to four times weekly, provides additional benefits for BP management [54]. Similarly, exercises including Tai Chi, Yoga and Baduanjin not only improve general well-being but also enhance exercise tolerance and lower BP levels in HF patients [55]. Previous research, including meta-analyses, has demonstrated that exercise programs in HF patients are associated with significant improvements in both physical function and quality of life (QoL) [56].

Furthermore, culturally relevant interventions, such as those described in the Utah South Asian Cardiovascular Health Initiative (U-SACHI) study, emphasise the importance of lifestyle modifications and exercise in improving cardiovascular health markers, weight

management and reducing the risk of HF [57]. Research conducted in hospitalised HF patients showed fewer adverse outcomes in patients with stable low Geriatric Nutritional Risk Index (GNRI) scores, highlighting the significance of holistic care in improving outcomes [58]. Underweight patients often present with undernutrition, sarcopenia and cardiac cachexia, a phenomenon referred to as the “obesity paradox” [59-61]. Effective nutritional management requires the intervention of a dietitian for comprehensive assessment and to develop individualised modifications addressing undernutrition. Evidence suggests that dietitian-led interventions, including provision of balanced meals, addressing dietary deficiencies and integrating nutritional supplements, significantly improve long-term prognosis [62]. Nutritional supplementation has been shown to improve QoL, maintain balanced body weight and facilitate recovery in patients with cardiac cachexia [63].

In the ACC expert consensus decision pathway on tobacco cessation, Barua RS et al., emphasised that smoking cessation reduces cardiovascular morbidity and mortality, particularly in patients with pre-existing heart conditions [64]. The decreased risk of HF among individuals who quit smoking underscores smoking cessation as an essential component of HF management. In a nationwide cohort study in Korea, Yoo JE et al., reported that heavy smokers who quit experienced the most significant reduction in HF risk, reinforcing the importance of smoking cessation [65].

Telemedicine and community health worker interventions have also shown favourable results in improving symptom management in HF patients. A prospective, randomised, multicentre study in 1,538 HF patients demonstrated that telemedicine-based interventions can effectively monitor patients, reduce hospitalisations and improve outcomes [66]. A systematic review and meta-analysis by Ma Y et al., reported similar findings, highlighting that telehealth interventions can significantly improve the management of chronic diseases, including HF, by providing timely monitoring and reducing the need for in-person visits [67].

Reverse remodelling is a critical factor in HF risk stratification. Improved clinical outcomes, such as reduced mortality risk and HF hospitalisation, are associated with improved LVEF and Left Atrium (LA) reverse remodelling at six months post-hospitalisation, particularly in patients with HF with recovered ejection fraction (HFrecEF) [68]. Furthermore, Vitamin D has been shown to significantly improve cardiac stretch biomarkers, left ventricular dimensions (LVEDD and LVESD) and left ventricular function, contributing to favourable remodelling outcomes [69].

Cardiac remodelling reversibility through changes in energy metabolism has also been demonstrated in animal models, particularly for individuals with diabetic HF and HFpEF [70]. Long-term studies are also needed to assess the durability of interventions and explore newer therapies, such as SGLT2 inhibitors, which have shown promising results in recent trials [71]. A summary of the studies included in this narrative review, focusing on HF treatment modalities, is presented in [Table/Fig-2] [18-20,23,27,28,35,37,38,43,55,57,58,61,65,69].

Author (year)	Study design	Settings and population	Intervention or comparison	Outcomes assessed	Key findings
Ouwerkerk W et al., (2024) [18]	Observational cohort study	European BIOSTAT-CHF and ASIAN-HF registries Patients with HFrEF (N=6787)	RAAS inhibitors and β-blockers	Mortality, adherence to GRTD	14% achieved ≥50% of GRTD; 100% GRTD showed best outcomes, β-blockers (HR 0.40) had better survival outcomes compared to ACEi/ARB (HR 0.75).
Kubota Y et al., (2021) [19]	Retrospective cohort study	ASIAN-HF registry Patients with HFrEF and with/without COPD (N=5232)	Cardio-selective vs. non-cardio-selective β-blockers	Mortality (all-cause, cardiovascular)	Non-cardio-selective β-blockers significantly reduced all-cause mortality (HR 0.37) compared to no β-blocker use.
Sachdeva A et al., (2024) [20]	Real-world retrospective study	Indian patients with newly diagnosed HF (N=60)	Sacubitril/Valsartan	LVEF, NT-proBNP	3-month follow-up showed LVEF improved by 23%, NT-proBNP levels decreased significantly; main dose was 50 mg BD, with <5% experiencing hypotension.

Lin DS et al., (2023) [23]	Retrospective cohort study	Taiwan NHIRD Patients with HF and ESRD (N=50872)	MRAs	Cardiovascular death, all-cause mortality	MRA use was associated with lower cardiovascular death and all-cause mortality (HR 0.88), particularly in patients on hemodialysis.
Zhang S et al., (2020) [27]	Prospective non randomised study	Global multicenter study in patients with VT/VF (N=3889)	ICD therapy for VT/VF	Mortality, ICD therapy utilisation	ICD therapy was associated with a 49% reduction in all-cause mortality among patients with VT/VF.
Naik A et al., (2018) [28]	Long-term observational study	12 hospitals in patients with HF eligible for CRT (N=471)	CRT vs. no CRT	Clinical scores, HF-related metrics, mortality	CRT was associated with improved clinical scores (OR=2, 95% CI 1.25-3.20, p=0.004) and reduced mortality over 24 months.
Lee SE et al., (2020) [37]	Prospective cohort study	Korean registry Patients with AHF undergoing CABG or PCI (N=717)	CABG vs. PCI	Mortality, rehospitalisation	CABG was associated with a lower risk of mortality (HR 0.57) compared to PCI, with benefits more pronounced in patients with severe coronary artery disease.
Teo LY et al., (2024) [38]	Retrospective cohort study	Hospitalised patients with decompensated HF and diuretic resistance (N=44)	UF vs high-dose diuretics	Fluid output, rehospitalisation, quality of life	UF resulted in greater fluid and weight loss, shorter hospital stays and fewer 90-day rehospitalisations, with no adverse events reported.
Xu J et al., (2021) [55]	Network meta-analysis	Network of trials, meta-analysis in patients with CHF using Asian exercise programs	Tai Chi, Baduanjin, Yoga	QoL, exercise tolerance, blood pressure	Exercise programs improved QoL; Tai Chi significantly lowered blood pressure, Baduanjin reduced cardiac load and Yoga increased peak $VO_2$ .
Chakraborti K et al., (2024) [57]	Observational cohort study	Multicenter study in South Asian patients with CVD (N=5000)	Culturally specific lifestyle interventions	Cardiovascular health markers, risk factor reduction	Lifestyle modifications improved cardiovascular health markers, supporting HF prevention.
Sunaga A et al., (2024) [58]	Prospective observational study	Registry of hospitalised patients with decompensated HF (N=982)	Nutrition status (GNRI) assessment	Adverse outcomes based on GNRI score	Patients with stable low GNRI scores had fewer adverse outcomes compared to those whose nutritional status worsened.
Yoo JE et al., (2023) [65]	Nationwide cohort study	Korean health screenings in smokers (N=778608)	Smoking cessation vs. continued smoking	HF risk	Smokers who quit had a lower risk of developing HF (adjusted HR 0.86). Heavy smokers who quit had the most significant risk reduction, while reducing smoking without quitting did not significantly decrease HF risk.
Ma K et al., (2020) [35]	Retrospective cohort study	Patients from East China undergoing mitral valve surgery (N=3238)	Mitral valve repair vs. replacement	Mortality, surgical trends	Mortality rates were consistent across procedures, with repair at 0.2% and replacement at 0.9%; use of minimally invasive and bioprosthetic techniques increased.
Lalithanuamti HT et al., (2024) [43]	Observational study	Patients from south India with HF (N=90)	Mobile application-based remote patient management	Patient acceptance, management strategies	Post-discharge management strategies, showed positive acceptance of mobile application-based remote patient management in HF care.
Nochioka K et al., (2010) [61]	Cohort study	Japanese CHF patients (N=972)	Body mass index	Prognosis, heart failure outcomes	Both high and low BMI were found to be prognostic risks in patients with CHF, highlighting the importance of balanced weight management.
Mohanty V et al., (2022) [69]	Retrospective study	North Indian patients with congestive HF (N=97)	Vitamin D supplementation	Vitamin D levels, HF outcomes	Vitamin D supplementation in HF patients led to improved clinical outcomes, demonstrating its role in managing HF.

**[Table/Fig-2]:** Summary of the shortlisted studies on heart failure management interventions and outcomes in Asian context [18-20,23,27,28,35,37,38,43,55,57,58,61,65,69]. ACEi: Angiotensin-converting enzyme inhibitor; AHF: Acute heart failure; ARB: Angiotensin II receptor blockers; BD: Twice daily;  $\beta$ : beta; BMI: Body mass index; CABG: Coronary artery bypass grafting; CHF: Chronic heart failure; CI: Confidence interval; COPD: Chronic pulmonary obstructive disease; CRT: Cardiac resynchronisation therapy; CVD: Cardiovascular disease; ESRD: End-stage renal disease; GNRI: Geriatric, nutritional risk index; GRTD: Guideline-recommended therapeutic dose; HF: Heart failure; HFREF: Heart failure with reduced ejection fraction; ICD: Implantable cardioverter-defibrillator; LVEF: Left ventricular ejection fraction; MRA: Mineralocorticoid receptor antagonist; NHIRD: National health insurance research database; NT-proBNP: N-terminal pro-B-type natriuretic peptide; OR: Odds ratio; PCI: Percutaneous coronary intervention; QoL: Quality of life; SGLT2: Sodium glucose cotransporter 2; UF: Ultrafiltration; VF: Ventricular fibrillation; VT: Ventricular tachycardia

## Limitation(s)

Despite advancements, several gaps remain in HF treatment. Most studies are observational or retrospective, limiting the ability to draw conclusive evidence. Additionally, the studies included in the present review often focus on specific populations, such as those with CKD or specific ethnic groups, including Asian populations, which may not fully represent the broader HF population. Future research should address these gaps by conducting randomised controlled trials that include diverse populations, particularly those from low-income regions and underrepresented groups.

## CONCLUSION(S)

The HF remains a complex, multifaceted condition requiring a comprehensive management approach tailored to the patient's condition. Current treatment modalities—including pharmacological interventions such as RAAS inhibitors,  $\beta$ -blockers, ARNIs, MRAs and SGLT2 inhibitors—have significantly improved outcomes in

HF patients. Advanced interventions, including CRT and surgical options, continue to provide substantial benefits for those with severe disease. Lifestyle modifications and exercise programs offer valuable support in enhancing overall well-being and QoL.

Alongside the need for medications that provide long-term benefit, there is a growing need for personalised treatment strategies. Continued research is essential to optimise care and address gaps in HF management. Given the diversity of the Asian population, there is a clear need for treatment guidelines focused on the demographic and disease characteristics of HF patients in this region.

## Acknowledgement

The authors would like to acknowledge Harpreet Kaur and Lakshya Untwal (Textometry Pvt. Ltd., India) for providing medical writing support in accordance with GPP 2022 guidelines (DeTora LM, Torosier D, Sykes A, et al., Good Publication Practice [GPP]

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#### AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

#### PLAGIARISM CHECKING METHODS:

- Plagiarism X-checker: Apr 06, 2025
- Manual Googling: Jul 10, 2025
- iThenticate Software: Jul 12, 2025 (11%)

#### ETYMOLOGY:

Author Origin

#### EMENDATIONS:

5

Date of Submission: **Mar 25, 2025**

Date of Peer Review: **May 22, 2025**

Date of Acceptance: **Jul 15, 2025**

Date of Publishing: **Mar 01, 2026**