International Journal of Advances in Medicine
Sawhney JP et al. Int J Adv Med. 2023 Jul;10(7):527-537
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20231872

Original Research Article

Management of heart failure patients with systolic dysfunction in a real-world setting-a physician-based survey

J. P. Sawhney[1], Peeyush Jain[2]*, Kiran Kantanavar[3]

[1]Department of Cardiology, Sir Ganga Ram Hospital, Delhi, India
[2]Department of Preventive Cardiology, Fortis Escorts, Delhi, India
[3]Medical Affairs, Abbott Healthcare Pvt. Ltd., Mumbai, Maharashtra, India

Received: 11 April 2023
Accepted: 24 May 2023

***Correspondence:**
Dr. Peeyush Jain,
E-mail: dpn2005@gmail.com

ABSTRACT

Background: The objective of this study was to understand cardiologists' perspectives on heart failure (HF) management with an emphasis on heart rate (HR) optimization and practice patterns among different medical specialties.
Methods: A digital, cross-sectional, questionnaire-based survey involving 149 Indian cardiologists who were experienced in the management of patients with HF in their clinical practice was conducted. The survey questionnaire included 53 items divided into five sections. Responses were analyzed and data were represented as summary statistics.
Results: According to most cardiologists, majority of patients belong to the New York Heart Association (NYHA) categories II and III, with ischemia being the most prevalent cause of HF. For patients with HF with reduced ejection fraction (HFrEF), HR>70 beats per minute and sinus rhythm, 38.9% of clinicians strongly agreed to include ivabradine in the treatment regimen. According to 56.4% of clinicians, 26%-50% of patients with HFrEF were receiving ivabradine therapy at <50% guideline-directed target dose of β-blockers. At the highest therapeutic dosage of ivabradine, 46.3% of clinicians noticed a 6-10 bpm reduction in HR. Additionally, it was reported that a stable HFrEF patient consumed an average of 4-6 tablets daily (67.1%), which increased the pill burden. Overall, 58.4% and 67.1% of clinicians strongly believed that cutting back on medications will assist with therapy adherence and that improved therapy adherence and compliance aid with clinical outcomes, respectively. Majority of the clinicians strongly agreed or agreed that patients should be switched from twice-daily to once-daily ivabradine.
Conclusions: Clinical outcomes of patients with HF could be improved by reducing the pill burden and improving compliance.

Keywords: Cardiologists, Ivabradine, HFrEF, Ischemia

INTRODUCTION

Heart failure (HF) has emerged as a major cause of death and morbidity in this era of non-communicable illnesses. Any abnormalities of the heart structure or function can result in chronic HF, a complicated and progressive clinical condition.[1] Worldwide, HF affects more than 60 million individuals. These figures will, however, rise in the upcoming years, mostly because of the aging population, but also because of the increasing incidence of specific comorbidities, such as hypertension or diabetes, and the improved management of acute cardiovascular problems.[2] The prognosis for HF is poor; approximately 50% of patients diagnosed with HF die within 5 years.[3] Worldwide, the cost of HF health expenditures is US$31 billion.[4] The prevalence of HF is equally distributed between HF with reduced ejection fraction (HFrEF), which is defined as a left ventricular ejection fraction (LVEF) <35–40%, and HF with preserved ejection fraction (HFpEF), which is defined as an LVEF >40%,

with 53% of patients having impaired systolic function and the remaining 47% having preserved systolic function.[5-7]

The burden of HF in low- and middle-income (LMIC) nations is distinct from that in high-income ones. In LMICs, the "double burden" of HF is extensively recognized.[4]

In India, there are ~22.7 million patients with HF, and among these patients, HFrEF is the predominant type.[7,8] Although the prognosis for HFrEF has improved due to the availability of evidence-based medications, readmission rates and consequent death rates have remained unchanged in the last two decades.[4] A better knowledge of existing practice patterns, drug delivery gaps, and impediments to accessing guideline-directed medical therapy (GDMT) is essential for establishing focused initiatives to improve patient outcomes and quality of care. However, findings from the change in the management of patients with HF (CHAMP-HF) registry that included a cohort of 3,518 patients with HFrEF on angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs), angiotensin receptor neprilysin inhibitors (ARNIs), β-blockers (BBs), or mineralocorticoid receptor antagonists (MRAs), revealed that there were large disparities in the usage and dose of HFrEF medications.[9] Findings from the Asian sudden cardiac death in HF (ASIAN-HF) registry involving 11 Asian countries revealed that guideline-directed medical therapies at recommended doses were underutilized in patients with HFrEF.[10] Despite guidelines, educational efforts, and quality improvement initiatives, a comparison with prior registry data from approximately a decade ago shows that outpatient use and dosing of GDMT have generally not improved, and there is a significant gap between GDMT and real-world clinical practice.[9]

It is known that better use of evidence-based treatments has the potential to avert a significant number of HF fatalities each year.[11] HR optimization is one of the evidence-based strategies in HFrEF. Results from the Systolic HF Treatment with the I_f Inhibitor Ivabradine Trial (SHIFT) study indicated that the risk of cardiovascular death and HF hospitalization increased by 3% for every bpm increase from baseline HR and by 16% for every 5 bpm increase.[12] Thus, it is important to understand clinicians' viewpoints on the idea of HR reduction in real-world clinical practice.

Medical treatment for patients with CHF is offered in India by a variety of healthcare specialists from several healthcare sectors, including hospital-based interventional cardiologists, office-based cardiologists, and/or consultant clinicians. As a result, it is crucial to investigate practice trends across a broad group of healthcare practitioners treating patients with HF in the Indian clinical setting. A cross-specialty physician-based survey, namely, 'Management of HF patients with systolic dysfunction in a real world setting milestone', was conducted to understand clinicians' perspectives regarding HF management with an emphasis on HR optimization as well as to know practice patterns among different medical specialties.

METHOD

Survey design

This was a digital, cross-sectional, questionnaire-based survey designed to assess the attitudes of Indian clinicians with at least 5 years of experience in HF management and HR optimization from different regions across India. A total of 149 cardiologists and consulting clinicians were included. Each clinician was asked to respond to the survey questions based on their clinical experience in managing patients with HFrEF (LVEF<40%) with a disease duration of ≥3 months, or those with stable HFrEF (no major change in the symptoms and signs of HF for at least one month on treatment) or those that had no hospitalization for HF in the 3 months before survey participation. The survey was conducted from 7 to 29 January 2022. Clinicians who provided written informed consent received an online questionnaire with standardized questions regarding HF patient profile, recommended pharmacotherapies, and their attitudes related to HR or HR optimization, and adherence to therapy.

The survey was conducted in conformance with the principles of the declaration of Helsinki and the International Conference on Harmonization-Good Clinical Practice (GCP) guidelines. In accordance with local legislation and national guidelines, as this survey did not involve any intervention to patients, ethical approval by an independent ethics review board was not required. The confidentiality and identity of cardiologists and clinicians were preserved throughout the survey and data processing.

Survey questionnaire

The survey questionnaire consisted of 53 items grouped into 5 sections that assessed the HF patient profiles, etiology of HF, comorbidities associated with HF, recommended pharmacotherapy (in newly diagnosed patients), guideline-directed target dose, maximally tolerated doses, perspectives related to HR in patients with HF, target resting HR range, HR optimization, and treatment adherence in HF patients. The detailed survey questionnaire is depicted in supplementary Table 1.

Statistical analysis

Because the current survey was designed to learn about the clinical practice and treatment recommendations of cardiologists and consulting clinicians, a formal sample size estimate was not done. The survey comprised 53 questions aimed at 149 clinicians, which corresponded to a respondent-to-item ratio of >2.[13] The collected responses were compiled and recorded, and statistical analyses were performed using Microsoft Excel. Each question's overall response percentage was calculated.

RESULTS

A total of 149 clinicians were approached for this survey, and all gave consent to participate. All 149 clinicians responded to the survey, yielding a response rate of 100%.

Profiles of patients with HF in clinical practice

Survey revealed that 2%, 46.3%, 43.6%, and 8.1% of clinicians saw patients with HFrEF of NYHA categories I, II, III, and IV, respectively. Most common etiology of HF wass ischemia according to 75.8% of clinicians, followed by hypertension (14.1%), dilated cardiomyopathy (9.4%), and rheumatic heart disease (RHD; 0.7%).

For patients with HFrEF, regular follow-up was advised every 1 month by 45.6% of clinicians, every 3 months by 42.3% of clinicians, every 15 days by 10.1% of clinicians, and every 6 months by 2.0% of clinicians. Majority of clinicians (53.7%) reported that patients with HF had at least 3-4 comorbidities, 22.8% reported that patients have at least 1-2 comorbidities, 14.8% reported 5-6 comorbidities, and 8.8% reported that patients with HF >6 comorbidities. Most common cardiovascular comorbidity in patients with HF was CAD according to 40% of clinicians. Most common non-cardiac comorbidity in patients with HF was diabetes mellitus, according to 81.5% of clinicians, followed by chronic kidney disease (CKD; 11.4%), iron deficiency/anemia (4.0%), and chronic obstructive pulmonary disease (COPD; 3%).

With regard to hospitalization due to worsening HF, 51.7%, 40.3%, and 8.0% of clinicians reported that 26%-50%, 0%-25%, and 51%-75% of patients with HFrEF undergo one or more hospitalizations in an year, respectively.

Pharmacotherapy for patients with HF

Regarding newly diagnosed patients with HFrEF, BBs, and ACEIs/ARBs/ARNIs were the initial therapy of choice of 59.7% of cardiologists, followed by ACEIs/ARBs/ARNIs (26.8%), and BBs (13.4%; Figure 1). For HF management, 38.9% and 32.2% of cardiologists reported that 26%-50% of their patients were being prescribed two and three drugs, respectively, and the most preferred ACEI was ramipril (76.5%), and most preferred ARB was telmisartan (53.0%).

For patients with HFrEF, 36.9% and 43.6% of cardiologists reported that 26%-50% of their patients received guideline-directed targeted doses of ACEIs and BBs, respectively. The guideline directed target dose of ACEIs was enalapril 10-20 mg b.i.d, lisinopril 20-40 mg o.d., perindopril 8-16 mg o.d., and ramipril, 10 mg o.d, whereas that of BBs was bisoprolol 10 mg o.d., carvedilol 25-50 mg b.i.d., metoprolol succinate (controlled release/extended-release 200 mg o.d., and nebivolol, 10 mg o.d. Among patients who were on ARB therapy, 39.5% of cardiologists reported that 51%-75% of patients with HFrEF received guideline-directed target doses (candesartan 32 mg o.d., losartan 50-150 mg o.d., and valsartan 160 mg b.i.d.). The survey also showed that 42.3% of cardiologists reported that <25% of patients with HFrEF were on ARNIs (sacubitril/valsartan) therapy and 53.02% of clinicians reported that these patients received guideline-directed targeted dose (200 mg b.i.d sacubitril/valsartan). Loop diuretics were prescribed by 43.0% of cardiologists in patients with HFrEF once they become stabilized on the core medications of ACEIs/ARBs/ARNIs, BBs, and MRAs.

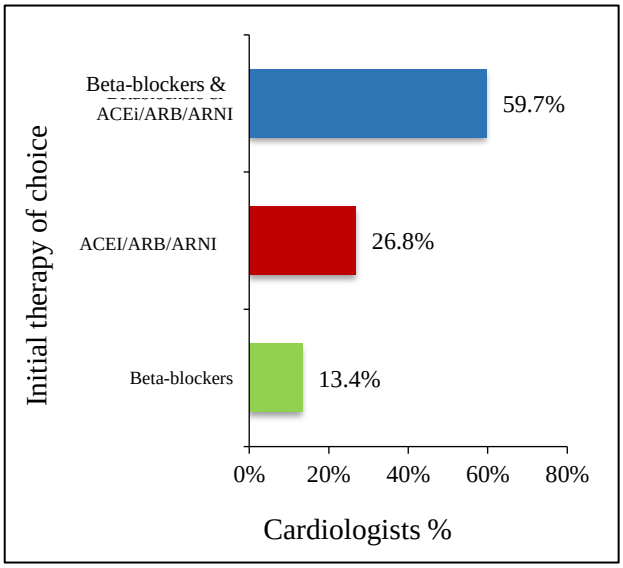

Figure 1: Initial therapy of choice in newly diagnosed HFrEF patients by cardiologists.

Less than 25% of patients with HFrEF receiving the three core medications per targeted dose of ACEI/ARB, BB, and MRA, remained symptomatic as reported by 44.3% of cardiologists and <25% of those receiving guideline-directed targeted dose of ARNI, BB, or MRA remained symptomatic as per 53% of cardiologists.

When asked about screening patients for iron deficiency, 41.6%, 31.5%, and 19.4% of clinicians reported that they screened patients often, always, and sometimes, respectively.

Regarding the treatment of choice in HF patients with iron deficiency, 53.7% of cardiologists recommended intravenous ferric carboxymaltose whereas ferrous ascorbate oral therapy, intravenous iron sucrose, and ferrous fumarate oral therapy were recommended by 28.6%, 9.4%, and 8.0% of cardiologists.

For patients on BBs, 38.9% of cardiologists recommended bisoprolol or metoprolol succinate in 26-50% of patients for HF management. Clinicians were found recommending carvedilol (45.6%) in 26-50% of patients and nebivolol (73.1%) in <25% of patients for HF management. The most common barrier to up-titration of

BBs was found to be bradycardia (62.4%), followed by hypotension (25.5%), fatigue (8.7%), and dyspnea (3.4%).

To achieve the target dose, 54.4% of clinicians mentioned that they up-titrated BB doses every 4 weeks, while 30.9%, 11.4%, and 3.3% of clinicians up-titrate doses of BB every 2 weeks, 8 weeks, and 12 weeks. Similarly, to achieve the target dose of ACEI/ARB/MRA, 61.7% of clinicians mentioned that they up-titrated the dose every 4 weeks, while 24.2%, 10.1%, and 4% of clinicians mentioned that they up titrated doses every 2 weeks, 8 weeks, and 12 weeks, respectively.

Among patients undergoing device treatment for HF, 44.9% of clinicians reported that they often down-titrate GDMT, whereas 13.4% of clinicians reported that they always down-titrate the GDMT. Furthermore, 33.5% of clinicians reported that they sometimes down-titrated GDMT, and 8.0% of clinicians never down-titrated the GDMT.

In HF patients with 'recovered ejection fraction' (i.e., patients who previously had reduced ejection fraction but showed improvement or recovery by natural history or in response to therapy), 46.3% clinicians reported that they often down-titrate/downsize GDMT, whereas 14.7% clinicians reported that they always down-titrate/downsize GDMT. The 34.8% of clinicians reported that they sometimes down-titrate/downsize GDMT, and 4.2% of clinicians never down-titrate/downsize GDMT.

Perspectives related to HR patients with HF

Most of the surveyed clinicians (80.5%) revealed that they recorded the HR of patients with HFrEF during each follow-up visit. Regular self-monitoring of HF, BB, and ivabradine for HR modulation was very frequently encouraged by 39.6% of clinicians.

When asked about their target resting HR (RHR), clinicians were mostly found to aim for 64-60 bpm (44.3%) and 69-65 bpm (36.2%). In addition, 48.3%, 20.1%, 26.2%, and 5.4% of clinicians reported that 51%75%, >75%, 26%-50%, and <25% of their patients achieved the target RHR, respectively.

HR optimization in HF

In this survey, it was observed that 38.9% of clinicians strongly agreed and 34.2% of clinicians agreed that in HFrEF patients with >70 bpm and sinus rhythm, ivabradine should be added even before the maximum tolerated dose of BB is reached, whereas 20.1% of cardiologists disagreed and 6.7% strongly disagreed with it. For patients with HFrEF, 56.4%, 23.5%, 16.1%, and 4.0% of clinicians also revealed that 26%-50%, 51%-75%, <25%, and >75% of their patients receiving ivabradine therapy were at<50% guideline-directed target dose of BB, respectively.

In patients with HFrEF on ivabradine therapy, 43.6% of clinicians revealed that they occasionally up-titrated ivabradine dose to 15 mg per day, whilst 27.5%, 22.1%, and 6.7% of clinicians revealed that they rarely, frequently, and very frequently up titrated ivabradine dose (Figure 2). For patients with >70 bpm, 61.1% of cardiologists revealed that they titrated the ivabradine dose every 4 weeks, while 24.2%, 12.1%, and 2.7% revealed that they titrated the dose every 2 weeks, 8 weeks, and 12 weeks, respectively.

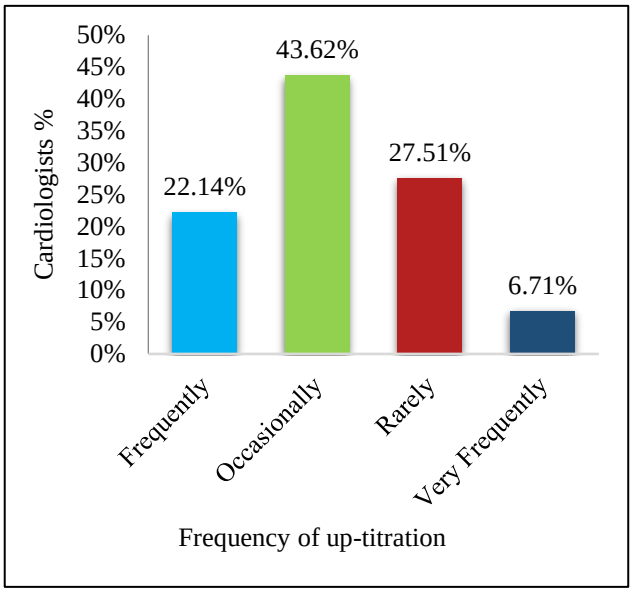

Figure 2: Frequency of up-titration of ivabradine therapy to 15 mg/day by cardiologists in patients with HFrEF.

When clinicians were asked about what level of bradycardia is of serious concern in patients receiving BB and/or ivabradine therapy, 36.2% of physicians reported that 44-40 bpm is of serious concern, whereas 26.8%, 26.1%, and 10.7% clinicians reported that 49-45 b.p.m., 54-50 bpm, and 60-55 bpm is of serious concern.

In addition, 46.3%, 35.6%, 9.4%, and 8.7% of clinicians revealed that HR reductions of 6-10 bpm, 11-15 bpm, 0-5 bpm, and 16-20 bpm were observed with a maximum therapeutic dose of ivabradine, respectively (Figure 3).

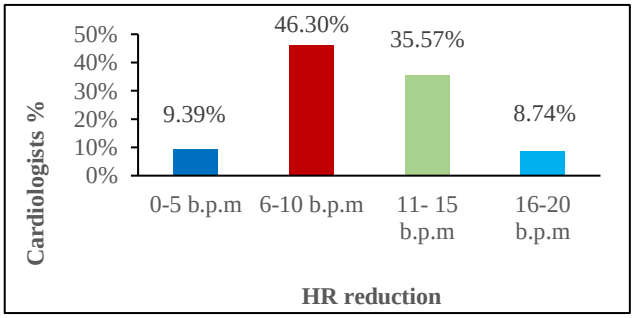

Figure 3: HR reduction with a maximum therapeutic dose of ivabradine.

Adherence to therapy in HF

With regard to adherence to treatment, 16% of clinicians revealed that 10-20% of their HFrEF patients were non-adherent to treatment, whereas 23.5%, 19.5%, and 15.4% of clinicians revealed that 21%-30%, <10%, and >30% of their patients were non-adherent to treatment. Among the core HF medications, 51.0% of clinicians revealed that their patients were non-adherent to ARNIs, while 14.8%, 14.1%, 12.7%, and 7.4% revealed that their patients were non-adherent to ACEIs, ARBs, BBs, and MRAs. The main reasons for non-adherence among HFrEF patients were found to be pill burden (37.6%), discontinuation of medication when feeling better (33.6%), cost of therapy (14.1%), frequency of dosing (12.1%), and drug side effects (2.7%). Among the side effects of HF medications, the most common reasons for discontinuation were hypotension (43%), bradycardia (25.5%), hypokalemia (16%), renal dysfunction (11.4%), and angioedema (4%).

Most clinicians opined that a stable HFrEF patient consumes 4-6 pills on average (67.1%), while 22.1%, 6.0%, and 4.7% clinicians that stable patients were consuming 7-9, ≤3, and >9 pills, respectively. This survey also revealed that 58.4% and 67.1% of clinicians strongly agree that a reducing in the number of pills will help improve adherence to therapy and that good adherence and compliance to therapy help improve clinical outcomes, respectively. When clinicians were asked about whether patients become non-adherent to medication after device therapy, 47.6% agreed and 19.4% strongly agreed, while 30.8% disagreed and 2% strongly disagreed.

In this survey, most cardiologists and clinicians strongly agreed (55.0%) or agreed (43.0%) that shifting patients from ivabradine twice daily to a once daily (10/15 mg prolonged-release formulation) regimen would help improve adherence to therapy (Figure 4).

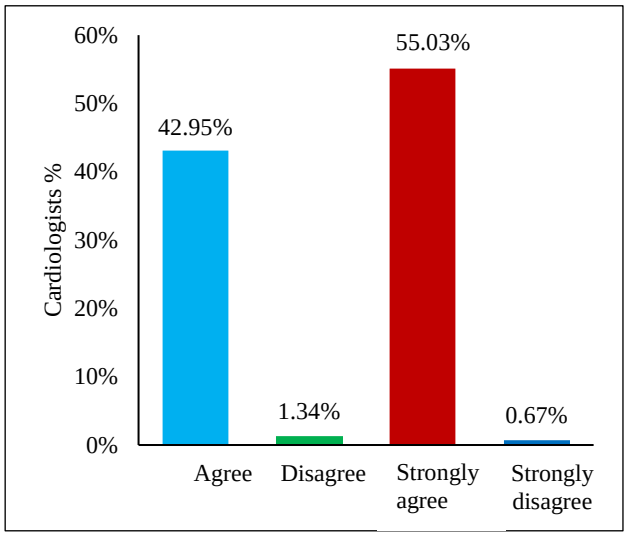

Figure 4: Cardiologists opinion on the benefit of shifting patients from ivabradine twice daily to a once-daily regimen.

DISCUSSION

India exhibits a greater burden of mortality from HF that might be attributed to the difference in the demographic, clinical, and genetic profile of the Indian population.[14] Nevertheless, very limited data about HF in India are available.[15] Contemporary HF data from developing and low-middle-income countries are sparse, and the epidemiology of HF in India is largely unexplored.[16] Few registries that have subsequently included Indian patients include Asian Sudden cardiac death in HF registry (ASIAN-HF), international congestive HF registry (INTER-CHF), and Trivandrum HF registry (THFR).[17-21] Apart from these, the American College of Cardiology's Practice Innovation and Clinical Excellence (PINNACLE) India quality improvement program also collected data on the prescription of guideline-directed medical therapy to ambulatory HF patients.[22]

In the national heart failure registry involving a total of 10,851 study populations in 53 tertiary care facilities in 21 states in India, HFrEF (>two-thirds of the patients had NYHA class III)) was the most common presentation and ischemic events were found to be the major etiology for HF (72%).[23] This observation was also evident from our survey wherein the majority of HFrEF patients who were in the NYHA II and NYHA III categories, and the most common etiology for HF was ischemia.

HF patients are remarkably complex with a large burden of cardiac and non-cardiac comorbidities. Atrial fibrillation, CAD, obesity, CKD, diabetes mellitus, hypertension, and diabetes mellitus are among the comorbid diseases that are present in more than half of HF patients. These comorbidities are linked to an increase in total symptom load and poor clinical outcomes.[24] Moreover, data from 207,984 patients with the guidelines-HF registry showed that the prevalence of 0, 1, 2, and ≥3 non-CV comorbidities was 18%, 30%, 27%, and 25%, respectively. From 2005 to 2014, there was a decline in patients with no non-CV comorbidities (22-16%; $p<0.0001$) and an increase in patients with ≥3 non-cardiovascular comorbidities (18-29%; $p<0.0001$).[25] Our survey also revealed that majority of HF patients visiting the clinicians had 1-4 comorbidities. CAD and hypertension were the dominant cardiac comorbidities, and diabetes and CKD were the non-cardiac comorbidities seen in HF patients in this survey, with nearly 50% of patients having one or more hospitalizations in a year due to worsening HF.

Several randomized controlled studies have shown that neuro-hormonal modulators, including ACEI, ARBs, MRAs, BBs and the recently authorized ARNIs, reduce mortality in HF patients. Diuretics are primarily used to treat congestion symptoms and may enhance therapeutic results.[7]

To maximize the potential benefits of treatment for patients with HFrEF, GDMT should be started and

adjusted throughout all care settings. Optimum benefit is derived at the target dosing achieved in clinical trials, but lower than target doses still confer significant benefit.[26] In all patients with chronic symptomatic HFrEF, ACEI (or ARB) and BB were considered to be the first-line agents. In patients who remain symptomatic despite optimal therapy with an ACEI, BB, and MRA, ACEI was replaced with ARNI. In patients who can tolerate ACEI (or ARB) well, replacement by ARNI may be considered on an individualized basis.[8] The guidelines strongly recommend the use of a combination of all these agents (ACEI/ARB/ARNI+BB+MRA) in most HF patients.[27] Combined ARB+ARNI therapy with sacubitril/valsartan has more recently demonstrated superiority to ACEI in well-treated patients with HFrEF.[28]

As per our survey, among newly diagnosed HFrEF patients, BBs and ACEI/ARB/ARNI were the initial therapy of choice by clinicians, followed by ACEI/ARB/ARNI, and in those patients who were receiving HFrEF medications, clinicians were mostly prescribing two- and three core HF medications (ACEI/ARB/ARNI, BB, or MRA). The most preferred ACEI and ARB for HF management by cardiologists were ramipril and telmisartan, respectively. The most preferred BBs recommended by the clinicians were bisoprolol and metoprolol.

Iron deficiency is common in HF patients with and without anemia. If serum ferritin level is <100 or transferrin saturation is <20%, IV ferric carboxymaltose is used.[7] The European recommendations propose treating symptomatic iron-deficient HF patients with IV ferric carboxymaltose to improve HF symptoms and quality of life (QoL).[29] The suggested IV ferric carboxymaltose dosage is 500-1000 mg in 50 ml saline over 10-15 min.[7] As observed in the survey, the majority of clinicians recommended IV ferric carboxymaltose.

ESC and ACCF/AHA international guidelines recommend up-titration of evidence-based medications (ACEI/ARB and β-blockers) in patients with HF and HFrEF to target doses. The recommendations are based on data from large randomized clinical studies demonstrating that both ACEI and BBs enhance clinical outcomes in individuals with mild to moderate HFrEF when up-titrated to respective target dosages. Additionally, higher doses of ACEI/ARB and BB were better doses.[30] In our survey, the majority of clinicians up-titrated the dose of BB and ACEI/ARB/MRA every 4 weeks to achieve the target dose.

HR is an important hallmark of long-term clinical outcomes in patients with HFrEF. A lower HR was associated with lower mortality.[31] In a retrospective study by Barwani and Petzold, reduction in resting HR to as low as ≤65 bpm was associated with improved survival from all-cause mortality among octogenarians with HFrEF and concomitant AF.[32] This observation was also evident from our survey with most physicians aiming for a target HR of 64-60 bpm.

Ivabradine is approved to reduce hospitalizations for patients with symptomatic HF, HFrEF, and persistently elevated HRs despite otherwise maximal medical therapy.[33] In our survey, majority of clinicians strongly believed that in HFrEF patients with >70 bpm and sinus rhythm, ivabradine should be added before the maximum tolerated dose of BB is reached. This therapy-related decision is supported from the results of the SHIFT study involving patients with HFrEF. The study demonstrated that reductions in HR due to ivabradine benefit patients with HFrEF who have HRs of >70 bpm, despite receiving guideline-directed therapies, including BBs. The rates of major adverse CV events, namely hospitalization for HF and CV death, were significantly lower in the ivabradine group than in the placebo group, especially among the patients with higher baseline HRs.[34]

Ivabradine reduces HR in a dose-dependent manner. At prescribed dosages, the HR is reduced by around 10 bpm, whether the patient is at rest or active. The HR drops almost linearly with increasing dosages of ivabradine up to 15 mg to 20 mg twice a day.[35] In the survey, 46.3% of clinicians observed a decrease of 6-10 bpm at the maximum therapeutic dose of ivabradine, while 35.6% of clinicians observed a decrease of 11-15 bpm.

Non-adherence is a growing concern to clinicians and the healthcare system. A complex medication regimen, high pill burden, medication discontinuation, cost of therapy, and drug side effects can lead to non-adherence and poor management of chronic conditions.[36-38] This observation was also evident from the survey wherein the majority of HFrEF patients were non-adherent to treatment (patients were found non-adherent to ARNIs, followed by ACEIs, ARBs, BBs, and MRAs). The main reasons for non-adherence were pill burden and medication discontinuation. Among the side effects of HF medications, the most common reasons for discontinuation of drugs were hypotension and bradycardia. The survey also revealed that most patients were taking an average of 4-6 pills for HFrEF management.

The use of combination and once-daily formulations, as well as patient education and monitoring, have all been found to be successful techniques for managing polypharmacy, reducing pill load, and improving medication management.[36] As observed in our survey, most cardiologists strongly agreed that reducing the number of pills would help improve adherence and compliance with therapy. Furthermore, the survey findings suggested that all cardiologists and clinicians strongly agreed that switching patients from ivabradine twice daily to a once-daily regimen will aid in medication adherence.

The lack of questions on occupational exposure history, socioeconomic position, generic differences, past hospitalization that may have influenced treatment patterns, are some of the survey limitations. The total patient percentile based on which each cardiologist provided their responses was also not accounted for.

CONCLUSION

Findings from the current survey provide a comprehensive view of HFrEF from the cardiologists' perspectives. Ramipril, telmisartan, bisoprolol, metoprolol, carvedilol, and nebivolol were the most recommended HF drugs by cardiologists. However, pill burden is an issue in Indian clinical practice. This increases the risk of hospitalization, medication errors, and costs both for the pharmaceuticals involved and for the treatment of adverse events. One way to get around the regimen complexity issue is to make a drug regimen less complicated. Other is by choosing long-acting drugs. The survey results can ultimately serve to inform clinicians and policymakers about the specific factors and methods that should be taken into consideration to optimize medication use and promote better results from the patients' perspectives within the framework of the continually expanding standard of care in HFrEF.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Manish Varma and Dr. Gulshan from Spirant Communication Pvt. Ltd. for their medical writing and editorial assistance.

Funding: The study was funded by Abbott Healthcare Pvt. Ltd.
Conflict of interest: P. Sawhney is a member of European Society of Cardiology Heart Failure Association, European Association of Preventive Cardiology, and European Atherosclerosis Society. Peeyush Jain has received research grants from Sun Pharmaceuticals, speakers' honoraria from Abbott for participation in international speaker program and advisory board meetings. Kiran Kantanavar is an employee of Abbott. The remaining authors received research grant from Abbott for participation in the survey
Ethical approval: Not required

REFERENCES

1. Jain D, Pandey UK, Tripathi S, Kaushley A, Verma B, Ghosh S et al. Benefits of angiotensin receptor-neprilysin inhibitor in heart failure with reduced ejection fraction: A longitudinal study. J Clin Diagn Res. 2022;16(4):8-13.
2. Escobar C, Palacios B, Varela L, Gutiérrez M, Duong M, Chen H et al. Prevalence, characteristics, management and outcomes of patients with heart failure with preserved, mildly reduced, and reduced ejection fraction in Spain. J Clin Med. 2022;11(17):1-18.
3. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M et al. Heart-disease and stroke statistics-2016 update: a report from the American Heart Association. Circulation. 2016;133(4):e38-60.
4. Harikrishnan S, Bahl A, Roy A, Mishra A, Prajapati J, Nanjappa MC et al. National Heart Failure Registry, India: design and methods. Indian Heart J. 2019;71(6):488-91.
5. Riello I. Heart failure with reduced ejection fraction. Cardiology. 2021;77:772-810.
6. Störk S, Handrock R, Jacob J, Walker J, Calado F, Lahoz R et al. Treatment of chronic heart failure in Germany: a retrospective database study. Clin Res Cardiol. 2017;106(11):923-32.
7. Mishra S, Mohan JC, Nair T, Chopra VK, Harikrishnan S, Guha S et al. Management protocols for chronic heart failure in India. Indian Heart J. 2018;70(1):105-27.
8. Guha S, Harikrishnan S, Ray S, Sethi R, Ramakrishnan S, Banerjee S et al. CSI position statement on management of heart failure in India. Indian Heart J. 2018;70(1):S1-72.
9. Greene SJ, Butler J, Albert NM, DeVore AD, Sharma PP, Duffy CI et al. Medical therapy for heart failure with reduced ejection fraction: The CHAMP-HF registry. J Am Coll Cardiol. 2018;72(4):351-66.
10. Teng TH, Tromp J, Tay WT, Anand I, Ouwerkerk W, Chopra V et al. Prescribing patterns of evidence-based heart failure pharmacotherapy and outcomes in the ASIAN-HF registry: a cohort study. Lancet Glob Health. 2018;6(9):e1008-18.
11. Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J. 2011;161(6):1024-30.
12. Swedberg K, Komajda M, Böhm M, Borer JS, Ford I, Dubost-Brama A, Lerebours G, Tavazzi L. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. Lancet. 2010;376(9744):875-85.
13. Anthoine E, Moret L, Regnault A, Sébille V, Hardouin JB. Sample size used to validate a scale: a review of publications on newly-developed patient reported outcomes measures. Health Qual Life Outcomes. 2014;12(1):1-10.
14. Mehrotra S, Sharma TM, Bahl A. Impact of comorbidities in heart failure–prevalence, effect on functional status, and outcome in Indian population: A single-center experience. J Clin Prev Cardiol. 2019;8(4):166-72.
15. Chopra VK, Mittal S, Bansal M, Singh B, Trehan N. Clinical profile and one-year survival of patients with heart failure with reduced ejection fraction: The largest report from India. Indian Heart J. 2019;71(3):242-8.
16. Shukkoor AA, George NE, Radhakrishnan S, Velusamy S, Gopalan R, Kaliappan T et al. Clinical characteristics and outcomes of patients admitted with acute heart failure: Insights from a single-center heart failure registry in South India. Egyptian Heart J. 2021;73(1):38-48.
17. Lam CS, Anand I, Zhang S, Shimizu W, Narasimhan C, Park SW et al. Asian Sudden Cardiac Death In Heart Failure (ASIAN-HF) registry. Eur J Heart Fail. 2013;15(8):928-36.

18. Dokainish H, Teo K, Zhu J, Roy A, AlHabib KF, ElSayed A et al. Global mortality variations in patients with heart failure: results from the International Congestive Heart Failure (INTER-CHF) prospective cohort study. Lancet Glob Health. 2017;5(7):e665-72.
19. Dokainish H, Teo K, Zhu J, Roy A, Al Habib KF, El Sayed A et al. Heart failure in Africa, Asia, the Middle East and South America: The INTER-CHF study. Int J Cardiol. 2016;204:133-41.
20. Sanjay G, Jeemon P, Agarwal A, Viswanathan S, Sreedharan M, Vijayaraghavan G et al. In-hospital and three-year outcomes of heart failure patients in South India: The Trivandrum Heart Failure Registry. J Card Fail. 2018;24(12):842-8.
21. Harikrishnan S, Sanjay G, Anees T, Viswanathan S, Vijayaraghavan G, Bahuleyan CG et al. Clinical presentation, management, in-hospital and 90-day outcomes of heart failure patients in Trivandrum, Kerala, India: The Trivandrum Heart Failure Registry. Eur J Heart Fail. 2015;17(8):794-800.
22. Pokharel Y, Wei J, Hira RS, Kalra A, Shore S, Kerkar PG et al. Guideline-directed medication use in patients with heart failure with reduced ejection fraction in India: American College of Cardiology's PINNACLE India Quality Improvement Program. Clin Cardiol. 2016;39(3):145-9.
23. Harikrishnan S, Bahl A, Roy A, Mishra A, Prajapati J, Manjunath CN et al. Clinical profile and 90 day outcomes of 10 851 heart failure patients across India: National Heart Failure Registry. ESC Heart Fail. 2022;9(6):3898-908.
24. Khan MS, Samman Tahhan A, Vaduganathan M, Greene SJ, Alrohaibani A, Anker SD et al. Trends in prevalence of comorbidities in heart failure clinical trials. Eur J Heart Fail. 2020;22(6):1032-42.
25. Sharma A, Zhao X, Hammill BG, Hernandez AF, Fonarow GC, Felker GM et al. Trends in noncardiovascular comorbidities among patients hospitalized for heart failure: insights from the Get with The Guidelines-Heart Failure Registry. Circ Heart Fail. 2018;11(6):e004646.
26. Inpatient Initiation of HFrEF Therapies. Available at: https://www.acc.org/Latest-in-Cardiology/Articles/2022/06/01/12/11/Inpatient-Initiation-of-HFrEF-Therapies. Inpatient Initiation of HFrEF Therapies-American College of Cardiology. Accessed on 12 February, 2023.
27. Joseph J, PS S, James J, Abraham S, Abdullakutty J. Guideline-directed medical therapy in heart failure patients: impact of focused care provided by a heart failure clinic in comparison to general cardiology out-patient department. Egyptian Heart J. 2020;72:1-8.
28. Haydock PM, Flett AS. Management of heart failure with reduced ejection fraction. Heart. 2022;108(19):1571-9.
29. Iron Deficiency in Heart Failure. Available at: Iron Deficiency in Heart Failure - American College of Cardiology (acc.org)
30. Ouwerkerk W, Teng TH, Tromp J, Tay WT, Cleland JG, van Veldhuisen DJ, et al. Effects of combined renin-angiotensin-aldosterone system inhibitor and beta-blocker treatment on outcomes in heart failure with reduced ejection fraction: insights from BIOSTAT-CHF and ASIAN-HF registries. European J Heart Fail 2020;22(8):1472-82.
31. Yumita Y, Nagatomo Y, Takei M, Saji M, Goda A, Kohno T et al. Personalized target heart rate for patients with heart failure and reduced ejection fraction. J Pers Med. 2022;12(1):50-62.
32. Barywani S, Petzold M. Prognostic impact of heart rate in elderly with systolic heart failure and concomitant atrial fibrillation. Scand Cardiovasc J. 2017;51(4):190-6.
33. Psotka MA, Teerlink JR. Ivabradine: role in the chronic heart failure armamentarium. Circulation 2016;133(21):2066-75.
34. Böhm M, Swedberg K, Komajda M, Borer JS, Ford I, Dubost-Brama A et al. Heart rate as a risk factor in chronic heart failure (SHIFT): the association between heart rate and outcomes in a randomised placebo-controlled trial. Lancet. 2010;376(9744):886-94.
35. Tse S, Mazzola N. Ivabradine (Corlanor) for heart failure: the first selective and specific IF inhibitor. P T. 2015;40(12):810-4.
36. Farrell B, French Merkley V, Ingar N. Reducing pill burden and helping with medication awareness to improve adherence. Can Pharm J (Ott). 2013;146(5):262-9.
37. Iuga AO, McGuire MJ. Adherence and health care costs. Risk management and healthcare policy. Risk Manag Healthc Policy. 2014;7:35-44.
38. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. Circulation. 2009;119(23):3028-35.

Cite this article as: Sawhney JP, Jain P, Kantanavar K. Management of heart failure patients with systolic dysfunction in a real-world setting-a physician-based survey. Int J Adv Med 2023;10:527-37.

APPENDIX

Supplementary Table

Table 1: Survey questionnaire.

S. no.	Questionnaire			
Section 1: Profiles of patients with HF				
01	Majority of your patients with HFrEF fall in which NYHA category?			
	NYHA I	NYHA II	NYHA III	NYHA IV
02	What is the most common etiology of HF in your clinical practice?			
	Ischemia	Hypertensive	Dilated cardiomyopathy	Rheumatic heart disease
03	Mostly, routine follow-up of a stable HFrEF patient is advised every:			
	15 days	1 month	3 months	6 months
04	On an average, the number of comorbidities [such as hypertension, diabetes mellitus, CKD, CAD, COPD, OSA), iron deficiency etc.] in your heart failure patients is:			
	1-2	3-4	5-6	>6
05	In your clinical practice, the most common cardiovascular comorbidity among patients with HF is (one or more options can be selected):			
	Hypertension	CAD	Atrial fibrillation/flutter	Dyslipidemia
06	The most common non-cardiovascular comorbidity among patients with heart failure is (one or more options can be selected):			
	Diabetes mellitus	CKD	Iron deficiency/anemia	COPD
07	On an average, what percentage of HFrEF patients undergo one or more than one hospitalization due to worsening of heart failure in a year?			
	0%-25%	26%-50%	51%-75%	>75%
Section 2: Pharmacotherapy of HF				
08	In a newly diagnosed patient with HFrEF, what is your initial therapy of choice?			
	β -blockers	ACEI/ARB/ARNI	MRA	β-blocker and ACEI/ARB/ ARNI
09	What percentage of your HFrEF patients receive any two of the core heart failure medications (ACEI/ARB/ARNI, β-blocker or MRA)?			
	<25%	26%-50%	51%-75%	>75%
10	What percentage of your HFrEF patients receive all three of the core heart failure medications (ACEI/ARB/ARNI, β-blocker and MRA)?			
	<25%	26-50%	51%-75%	>75%
11	What is your most preferred ACE-I for managing heart failure?			
	Enalapril	Lisinopril	Perindopril	Ramipril
12	What is your most preferred ARB for managing heart failure?			
	Olmesartan	Losartan	Valsartan	Telmisartan
13	In patients on ACEI therapy, what percentage of patients receive guideline directed target dose*/maximally tolerated dose of ACEI?			
	<25%	26%-50%	51%-75%	>75%
14	In patients on ARB therapy, what percentage of patients receive guideline directed target dose**/maximally tolerated dose of ARBs?			
	<25%	26%-50%	51%-75%	>75%
15	In patients on β-blocker therapy, what percentage of patients receive guideline directed target dose***/maximally tolerated dose of β-blockers?			
	<25%	26%-50%	51%-75%	>75%
16	What percentage of HFrEF patients remain symptomatic despite optimal medical therapy involving three core medications (on maximally tolerated doses/ guideline directed target doses) of ACEI/ARB, β-blocker and MRA?			
	<25%	26%-50%	51%-75%	>75%
17	What percentage of your HFrEF patients are on ARNI (sacubitril/valsartan) therapy?			
	<25%	26%-50%	51%-75%	>75%
18	In patients on ARNI (sacubitril/valsartan) therapy, what percentage of patients receive guideline directed target dose (200 mg BID [sacubitril/valsartan])/maximally tolerated dose of ARNI?			
	<25%	26%-50%	51%-75%	>75%
19	What percentage of HFrEF patients remain symptomatic despite optimal medical therapy involving three core medications (on maximally tolerated doses/ guideline directed target doses) of ARNI, β-blocker and MRA?			
	<25%	26%-50%	51%-75%	>75%
20	In your clinical practice, what percentage of patients on β-blockers receive bisoprolol for management of heart failure?			
	<25%	26%-50%	51%-75%	>75%

Continued.

S. no.	Questionnaire			
21	In patients on β-blockers therapy, what percentage of patients receive carvedilol for management of heart failure?			
	<25%	26%-50%	51%-75%	>75%
22	In your clinical practice, what percentage of patients on β-blockers receive metoprolol succinate (CR/XL) for management of heart failure?			
	<25%	26%-50%	51%-75%	>75%
23	In patients on β-blockers, what percentage of patients receive nebivolol for management of heart failure?			
	<25%	26%-50%	51%-75%	>75%
24	Which is the most common barrier for up-titration of β-blockers?			
	Hypotension	Bradycardia	Fatigue	Dyspnea
25	In order to achieve target dose (or maximally tolerated doses), how frequently do you up titrate the dose of β-blocker?			
	Every 2 weeks	Every 4 weeks	Every 8 weeks	Every 12 weeks
26	In order to achieve target dose (or maximally tolerated doses), how frequently do you up titrate the dose of ACEI/ARB/MRA?			
	Every 2 weeks	Every 4 weeks	Every 8 weeks	Every 12 weeks
27	How often do you continue to prescribe loop diuretics in HFrEF patients once they become stabilized on core medications of ACEI/ARB/ARNI, β-blockers and/MRA?			
	Very frequently	Frequently	Occasionally	Rarely/never
28	How often do you screen for iron deficiency (serum iron/total iron-binding capacity/ferritin/folate) in your patients with HF?			
	Always	Often	c) Sometimes	Rarely/never
29	What is the treatment of choice in HF patients with iron deficiency (serum ferritin <100 µg/l or ferritin between 100 and 299 µg/L and transferrin saturation <20%)?			
	Intravenous ferric carboxymaltose	Ferrous ascorbate oral therapy	Ferrous fumarate oral therapy	Intravenous iron sucrose
30	In patients receiving device therapy for heart failure, how often do you down titrate (reduction in dosage of HF drugs)/down size (reduction in class of HF drugs) guideline directed medications?			
	Always	Often	Sometimes	Rarely/never
31	In HF patients with 'recovered ejection fraction' (previously had reduced ejection fraction but had improvement or recovery by natural history or in response to therapy), how often do you down titrate (reduction in dosage of HF drugs) / down size (reduction in class of HF drugs) guideline directed medications?			
	Always	Often	Sometimes	Rarely/never
Section 3: Perspectives related to heart rate in patients with HF				
32	You record heart rate of HFrEF patients during each follow up visit:			
	Most likely	Likely	Unlikely	Highly unlikely
33	What is usual method of recording the heart rate in your patients with HF? (one or more options can be selected)			
	Clinical palpation	Automated BP apparatus with HR recording	12 Lead ECG with HR recording	Pulse oximetry
34	Do you encourage your patients on heart rate modulating medications such as β-blockers and ivabradine to do routine self-monitoring of heart rate?			
	Very frequently	Frequently	Occasionally	Rarely
35	What is the target resting heart rate range you aim for in patients with HFrEF?			
	69-65 bpm	64-60 bpm	59-55 bpm	54-50 bpm
36	What percentage of patients achieve target heart rate range set by you?			
	<25%	26%-50%	51%-75%	>75%
Section 4: Heart rate optimization in HF				
37	In HFrEF patients with >70 bpm and sinus rhythm, ivabradine should be added even before reaching maximally tolerated dose of β-blockers?			
	Strongly agree	Agree	Disagree	Strongly disagree
38	In your clinical practice, what percentage of HFrEF patients receiving ivabradine therapy are on <50% guideline directed target dose of β-blockers?			
	<25%	26%-50%	51-75%	>75%
39	In your clinical practice, what percentage of HFrEF patients receiving ivabradine therapy are on maximally tolerated dose of β-blockers?			
	<25%	26-50%	51%-75%	>75%
40	In HFrEF patients on ivabradine therapy, how often do you need to up titrate the dose to the 15 mg per day (maximum dose)?			
	Very frequently	Frequently	Occasionally	Rarely
41	How often do you titrate the dose of ivabradine in patients with >70 bpm?			
	Every 2 weeks	Every 4 weeks	Every 8 weeks	Every 12 weeks
42	In patients on β-blocker and/or ivabradine therapy, what level of bradycardia is of serious concern?			
	60-55 bpm	54-50 bpm	49-45 bpm	44-40 bpm
43	In patients on ivabradine therapy, how much heart rate reduction is expected on a maximum therapeutic dose?			
	0-5 bpm	6-10 bpm	11-15 bpm	16-20 bpm
Section 5: Adherence to therapy in HF				

Continued.

S. no.	Questionnaire				
44	What percentage of HFrEF patients are non-adherent to treatment?				
	<10%	10%-20%	21%-30%		>30%
45	Main reason for non-adherence among HFrEF patients is:				
	More number of pills (pill burden)	Frequency of dosing	Stop taking medications once they feel better	Side effects of medications	Cost of the therapy
46	On an average, number pills consumed by a stable HFrEF patient is:				
	≤3	4-6	7-9		>9
47	Reduction in number of pills will help improve adherence to therapy:				
	Strongly agree	Agree	Disagree		Strongly disagree
48	Good adherence and compliance to therapy helps in improving clinical outcomes:				
	Strongly agree	Agree	Disagree		Strongly disagree
49	Among core heart failure medications, to which class of drugs most of the patients are non-adherent?				
	ARNI	ARB	ACE-I	MRA	β-blockers
50	After device therapy for heart failure, patients become more non-adherent to medications:				
	Strongly agree	Agree	Disagree		Strongly disagree
51	Among side effects of heart failure medications, which is the most common reason for discontinuation of drugs?				
	Hypotension	Hyperkaliemia	Bradycardia	Angioedema	Renal dysfunction
52	Shifting patients from ivabradine twice daily to once daily (10/15 mg-prolonged release formulation) regimen would help in improving adherence to therapy:				
	Strongly agree	Agree	Disagree		Strongly disagree

ACEI, angiotensin-converting enzyme inhibitor; ARNI, angiotensin receptor neprilysin inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; MRA=mineralocorticoid receptor antagonist; NYHA, New York Heart Association. *Enalapril: 10-20 mg b.i.d; lisinopril: 20-40 mg o.d.; perindopril: 8-16 mg o.d.; ramipril: 10 mg o.d. **Candesartan: 32 mg o.d.; losartan: 50-150 mg o.d.; valsartan: 160 mg b.i.d. ***Bisoprolol: 10 mg o.d.; carvedilol: 25-50 mg b.i.d.; metoprolol succinate (CR/XL): 200 mg o.d.; nebivolol: 10 mg o.d.