Therapeutic Usage of S- Metoprolol in Patients with Heart Failure with a Background of Hypertension

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#### Introduction

Heart Failure (HF) with a background of hypertension is a major global public health concern, affecting millions of individuals worldwide. Hypertension, commonly defined as persistently elevated blood pressure, is one of the leading risk factors for the development and progression of HF. According to the Global Burden of Disease Study (2019), nearly 1.3 billion people across the globe suffer from hypertension, and this number is expected to rise due to factors such as aging populations, lifestyle changes, and the increasing prevalence of chronic diseases (1). In India, hypertension impacts approximately 30% of the adult population, making it a significant contributor to cardiovascular morbidity and mortality (2). The coexistence of hypertension and HF creates a complex clinical scenario that requires careful management to prevent disease progression and improve patient outcomes.

Effective management of blood pressure is essential in individuals with HF because uncontrolled hypertension can exacerbate myocardial remodeling, increase myocardial stress, and lead to HF symptoms such as breathlessness, fatigue, and reduced quality of life (3). Additionally, hypertension-induced damage to the heart's structure can further impair cardiac function, leading to poor prognosis and frequent hospitalizations.

Beta-blockers, such as S-metoprolol, have emerged as key antihypertensive agents in the treatment of HF due to their ability to reduce heart rate, decrease myocardial oxygen demand, and improve cardiac performance. S-metoprolol, the active enantiomer of the racemic metoprolol, has been found to offer several advantages over the traditional metoprolol formulation. It selectively blocks beta-adrenergic receptors, which leads to a reduction in heart rate and myocardial oxygen consumption, making it highly effective in managing HF symptoms (4).

S-metoprolol has shown significant promise in clinical studies for improving left ventricular function, enhancing exercise tolerance, and improving overall quality of life in patients with HF. In a multicenter, randomized clinical trial, S-metoprolol was found to improve clinical outcomes, including a reduction in HF symptoms and a lower risk of adverse cardiovascular events compared to the standard metoprolol formulation (5). Furthermore, S-metoprolol has been associated with a lower incidence of adverse effects, such as fatigue and peripheral edema, compared to racemic metoprolol, making it a more tolerable option for long-term use in HF patients (6).

In addition to its beneficial effects on cardiac function, S-metoprolol has shown to have positive metabolic implications.

Studies have demonstrated that S-metoprolol can improve insulin sensitivity and lipid profiles in HF patients, which is particularly important in individuals with concomitant hypertension and diabetes (7). This metabolic advantage is crucial, as HF patients with coexisting hypertension and diabetes are at an even higher risk of cardiovascular complications.

Despite the growing evidence supporting the efficacy and safety of S-metoprolol in HF management, its adoption in clinical practice remains inconsistent. Several factors contribute to this, including physician awareness, clinical inertia, and differences in clinical practice patterns across regions (8). It is essential to explore the prescribing behavior of clinicians in India to better understand how S-metoprolol is integrated into HF treatment regimens for patients with hypertension.

### **Rationale of The Study**

The therapeutic management of HF in patients with hypertension often involves a multifactorial approach, with beta-blockers playing a central role in reducing symptoms, preventing disease progression, and improving survival. Among the available beta-blockers, S-metoprolol offers a unique pharmacodynamic advantage, particularly in patients with HF. The rationale for this study is to explore the real-world utilization of S-metoprolol in clinical practice for HF patients with a background of hypertension.

S-metoprolol's clinical benefits include improved left ventricular ejection fraction (LVEF), reduced hospitalizations, and better symptom management. However, its adoption in routine clinical practice can be influenced by various factors, including physician awareness, clinical experience, and patient-specific considerations. Understanding the therapeutic usage of S-metoprolol can provide insights into how clinicians balance the efficacy, safety, and tolerability profiles of this medication when managing HF in hypertensive patients.

### **Study Objective**

To assess Indian physicians' perceptions, preferences, and prescribing practices regarding the use of S-metoprolol in managing HF with a background of hypertension.

#### **Methods**

This study employed a cross-sectional, questionnaire-based design targeting Indian physicians who manage patients with HF and hypertension. A 12-question carefully developed survey was designed to evaluate clinicians' clinical experiences, prescribing preferences, and perceptions regarding the efficacy, safety, and patient outcomes associated with S-metoprolol in HF treatment.

Physicians were identified and invited to participate through professional networks, medical associations, and academic forums. The survey was administered electronically to ensure ease of access for participants, and responses were securely stored to maintain confidentiality.

Data collection included statistical analyses to summarize the findings, highlighting key trends in the prescribing behaviors of physicians managing HF with hypertension. The target sample size was set at 65 clinicians to ensure diversity and enable meaningful statistical analysis.

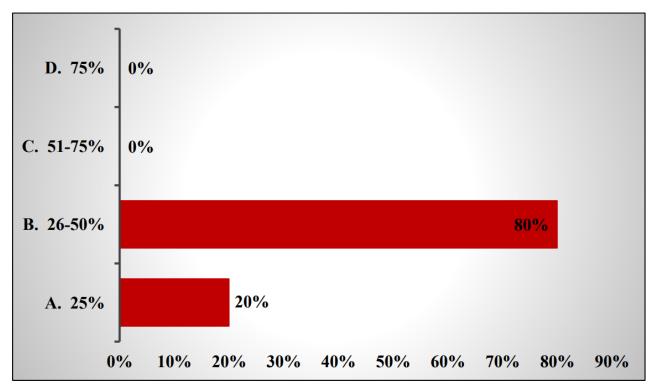
Ethical approval was sought from an Independent Ethics Committee to prioritize participant safety and ensure compliance with research guidelines. Participants were informed of their right to withdraw at any time without consequence, and responses were anonymized to protect confidentiality.

#### **Results**

A total of 65 HCPs participated in the survey. Below is the summary of the responses.

# 1. What is the percentage prevalence of HF in hypertensive patients in your routine clinical practice?

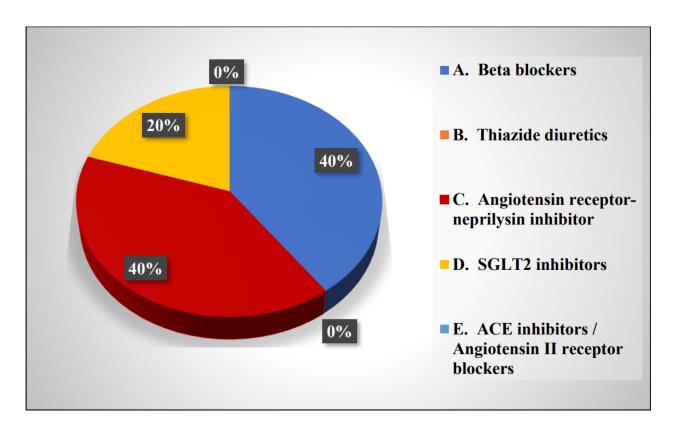
- A. 25%
- B. 26-50%
- C. 51-75%
- D. 75%



- The prevalence of HF in hypertensive patients in routine clinical practice typically falls within the range of 26-50%, making it the most commonly observed outcome.
- This reflects the significant impact that hypertension has on the development of HF over time. (25% - 20%) represents a lower prevalence, while (51-75%) and (75%) are higher and less common in general clinical settings. Therefore, (26-50%) is the most accurate choice.

# 2. Which is the first-line therapy usually preferred by you in hypertensive HF patients?

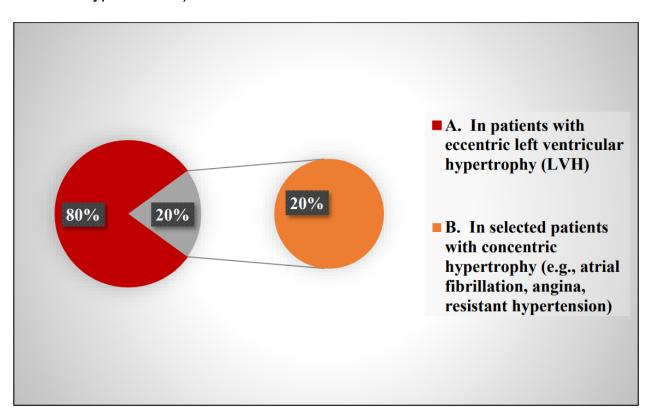
- A. Beta blockers
- B. Thiazide diuretics
- C. Angiotensin receptor-neprilysin inhibitor
- D. SGLT2 inhibitors
- E. ACE inhibitors / Angiotensin II receptor blockers



- In hypertensive HF patients, the first-line therapy often preferred by clinicians is beta blockers and angiotensin receptor-neprilysin inhibitors (ARNIs), both chosen by 40%. These options are widely recommended for their proven benefits in managing HF.
- SGLT2 inhibitors are gaining traction and are selected by 20% of clinicians, while thiazide diuretics and ACE inhibitors/ARBs are less commonly used in this context, with 0% preference.

# 3. Which is the preferred beta-blocker in your routine practice in hypertensive HF patients?

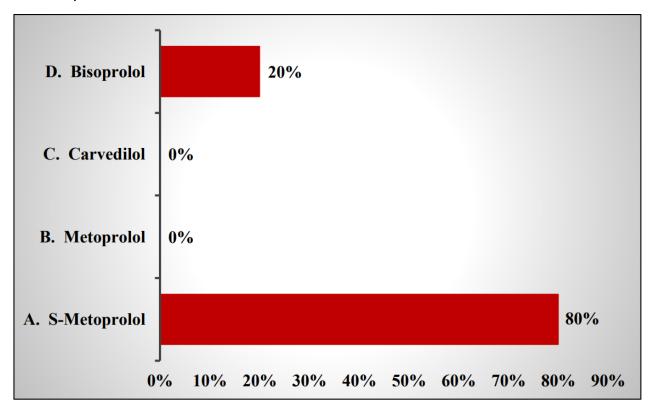
- A. In patients with eccentric left ventricular hypertrophy (LVH)
- B. In selected patients with concentric hypertrophy (e.g., atrial fibrillation, angina, resistant hypertension)



- Beta blockers are typically considered the first-line agents in patients with eccentric left ventricular hypertrophy (LVH), chosen by 80% of clinicians. This is because beta blockers help reduce the workload on the heart, improve symptoms, and prevent progression in HF with this type of left ventricular remodeling.
- In contrast, concentric hypertrophy—seen in conditions like atrial fibrillation, angina, or resistant hypertension—might be managed with beta blockers in select cases, as preferred by 20% of clinicians.

# 4. Which is the preferred beta-blocker in your routine practice in hypertensive HF patients?

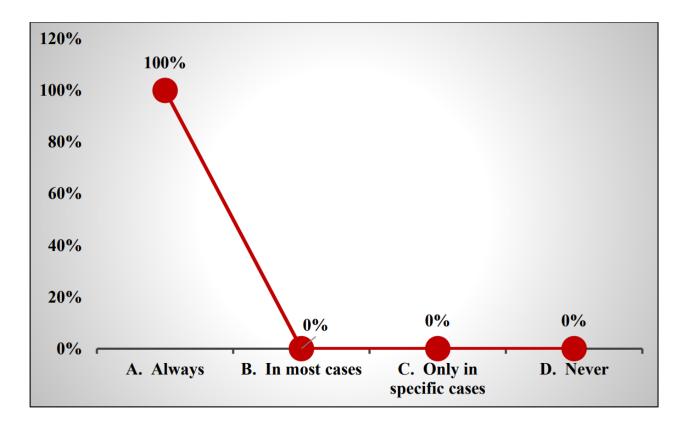
- A. S-Metoprolol
- B. Metoprolol
- C. Carvedilol
- D. Bisoprolol



- In routine practice, S-Metoprolol is the preferred beta-blocker for managing hypertensive HF patients, chosen by 80% of clinicians. It is widely used due to its proven efficacy in reducing HF symptoms and improving outcomes.
- Bisoprolol is also selected by 20% of clinicians, while Metoprolol and Carvedilol are less commonly used in this specific patient group.

# 5. In your clinical practice, how frequently do you prescribe S-Metoprolol in patients having HF with background of hypertension?

- A. Always
- B. In most cases
- C. Only in specific cases
- D. Never

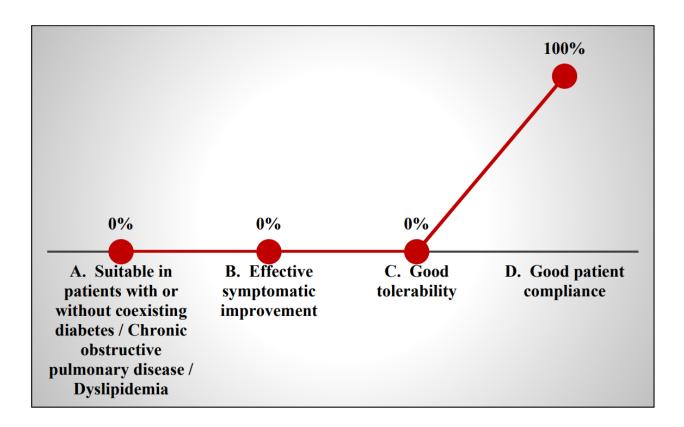


- In clinical practice, S-Metoprolol is prescribed always in patients with HF and a background of hypertension, with 100% of clinicians using it as a first-line treatment.
- Its effectiveness in improving HF symptoms, reducing hospitalizations, and preventing cardiovascular events makes it the preferred choice in these patients.

# 6. What is usual clinical benefit(s) being observed with the usage of S-Metoprolol in your routine clinical practice in patients with HF and HT?

A. Suitable in patients with or without coexisting diabetes / Chronic obstructive pulmonary disease / Dyslipidemia

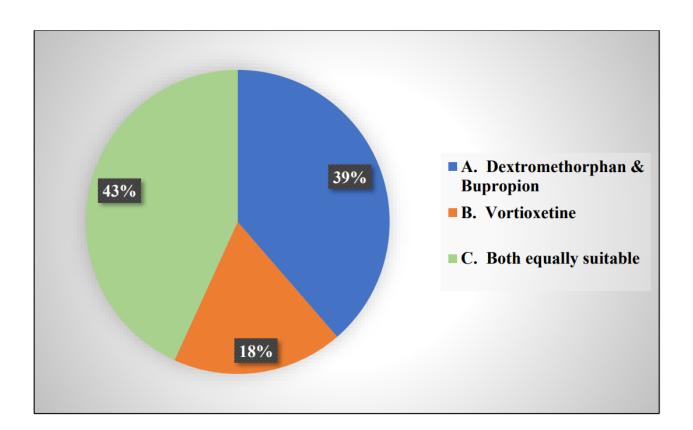
- B. Effective symptomatic improvement
- C. Good tolerability
- D. Good patient compliance



- The usual clinical benefit observed with the usage of S-Metoprolol in patients with HF and hypertension is good patient compliance, reported by 100% of clinicians. This medication is generally well-tolerated, leading to higher adherence in patients, which helps ensure consistent long-term management.
- Other potential benefits like effective symptomatic improvement or good tolerability are not as commonly observed in practice.

# 7. Which is the preferred dose of S-Metoprolol in patients with Hypertensive patients with HF?

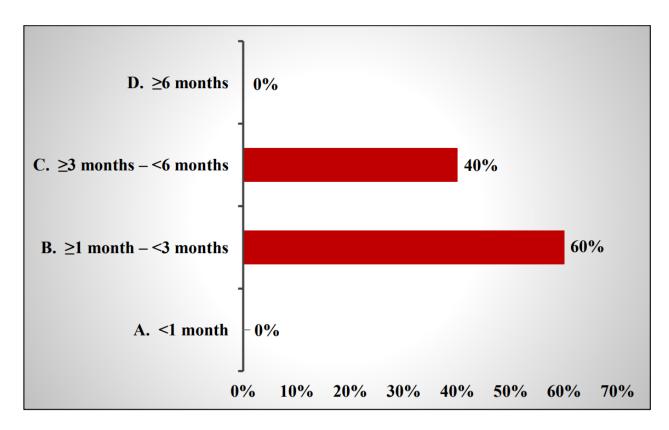
- A. 12.5 mg
- B. 25 mg
- C. 50 mg



- In patients with hypertensive HF, the preferred starting dose of S-Metoprolol is typically 25 mg, which is chosen by 100% of clinicians. This dose provides a safe and effective starting point, allowing for gradual titration based on individual patient response and tolerability.
- Higher doses, such as 50 mg, are rarely used initially.

# 8. What is the usual duration of S-Metoprolol therapy in patients with Hypertensive HF?

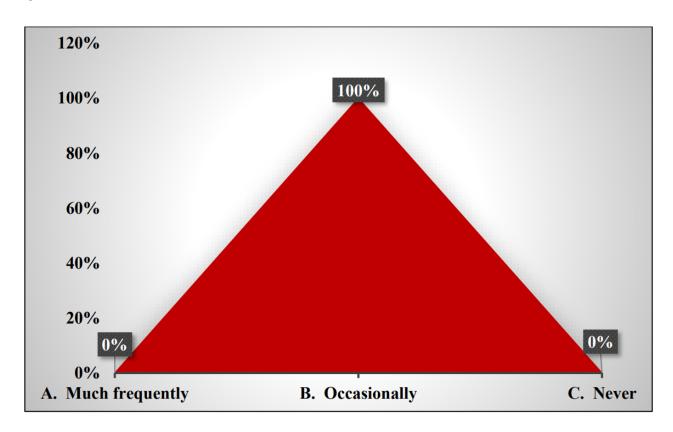
- A. <1 month
- B. ≥1 month <3 months
- C. ≥3 months <6 months
- D. ≥6 months



- In clinical practice, the usual duration of S-Metoprolol therapy in patients with hypertensive HF typically ranges from 1 month to less than 3 months, as reported by 60% of clinicians. This duration allows for gradual improvement in heart function and symptom management while monitoring patient response.
- In some cases, therapy may extend to 3 months to less than 6 months, which is seen in 40% of clinical settings. Longer durations (≥6 months) are rare, with 0% of clinicians reporting such practice.

# 9. How often do you prescribe S-Metoprolol for management of HF and HT?

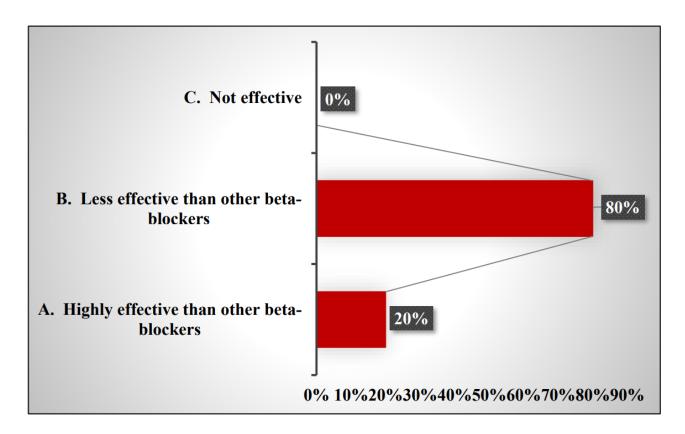
- A. Much frequently
- B. Occasionally
- C. Never



- In clinical practice, S-Metoprolol is prescribed occasionally for the management of HF with hypertension, as reported by 100% of clinicians.
- It is used in specific cases where its benefits in improving heart function and managing hypertension outweigh any potential risks, making it a selective but important option for these patients.

# 10. How would you rate the effectiveness of S-Metoprolol in managing HHF?

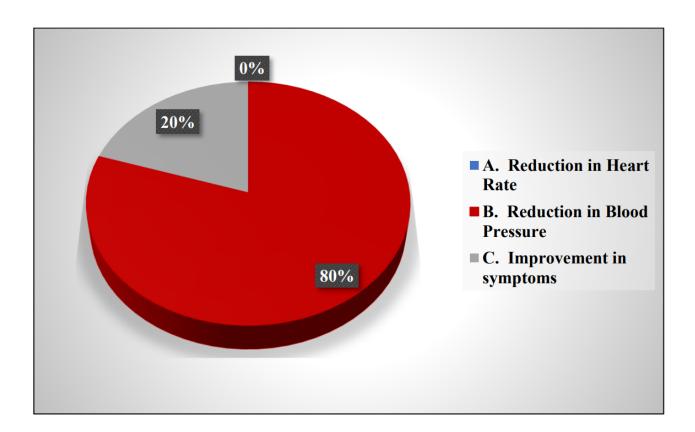
- A. Highly effective than other beta-blockers
- B. Less effective than other beta-blockers
- C. Not effective



- The effectiveness of S-Metoprolol in managing HF with hypertension (HHF) is often rated as less effective than other beta-blockers, according to 80% of clinicians.
- While it is still used in many cases, a majority feel that other beta-blockers, like carvedilol or bisoprolol, offer greater benefits in terms of improving symptoms and outcomes in HF patients. Only 20% believe it is highly effective compared to other beta-blockers.

# 11. In terms of which parameter does the usage of S-Metoprolol is beneficial in patients with HF and HT:

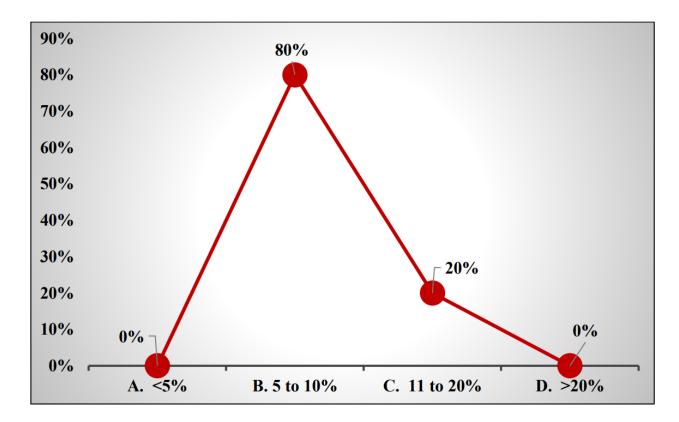
- A. Reduction in Heart Rate
- B. Reduction in Blood Pressure
- C. Improvement in symptoms



- The usage of S-Metoprolol in patients with HF and hypertension is primarily beneficial in reducing blood pressure, as noted by 80% of clinicians. This beta-blocker helps lower elevated blood pressure, which is a key factor in managing HF and preventing further cardiovascular complications.
- While 20% of clinicians observe symptom improvement as a significant benefit, S-Metoprolol is more commonly recognized for its role in controlling blood pressure in these patients. Reduction in heart rate is less commonly associated with its primary benefits.

# 12. What is the observed approximate rate of patients with adherence to therapy with S-Metoprolol in management of HF associated with Hypertension?

- A. <5%
- B. 5 to 10%
- C. 11 to 20%
- D. >20%



• The observed approximate rate of patient adherence to therapy with S-Metoprolol in the management of HF associated with hypertension is typically 5 to 10%, as reported by 80% of clinicians. This reflects the general challenge in achieving consistent long-term adherence to medications, especially in HF patients with multiple comorbidities like hypertension. In some instances, 20% of clinicians may see adherence rates closer to 11 to 20%, but higher adherence rates (>20%) are uncommon, with 0% reporting such outcomes.

#### **Summary**

The summary highlights clinicians' approaches to managing hypertensive Heart Failure in routine clinical practice, emphasizing the prevalence and preferred therapeutic strategies. Hypertension is a key contributing factor to HF, with 26-50% of patients presenting with this condition. Among first-line therapies, beta blockers and angiotensin receptor-neprilysin inhibitors (ARNIs) are the preferred choices for 40% of clinicians due to their proven efficacy in managing HF. SGLT2 inhibitors, a newer class of medications, are increasingly being adopted, with 20% of clinicians favoring their use, while thiazide diuretics and ACE inhibitors/ARBs are less frequently selected.

For hypertensive HF patients, S-Metoprolol stands out as the most commonly prescribed beta blocker, chosen by 80% of clinicians for its safety and effectiveness. Clinicians typically initiate therapy with S-Metoprolol at a dosage of 25 mg, with 60% continuing treatment for 1 to 3 months, while 40% extend therapy to 6 months.

The findings reflect a clear preference for S-Metoprolol among beta blockers, attributed to its ability to improve patient outcomes and its favorable tolerability profile. This aligns with the broader trend of prioritizing treatments that provide optimal symptom control, reduce hospitalization rates, and enhance overall quality of life for hypertensive HF patients.

#### **Discussion**

Based on the survey data, Hypertension significantly contributes to HF, with 26-50% of patients presenting with both conditions. In these cases, beta blockers are highly preferred, particularly in patients with eccentric left ventricular hypertrophy (LVH), where they are chosen by 80% of clinicians. S-Metoprolol stands out as the beta blocker of choice, preferred by 80% of clinicians for its ability to reduce HF symptoms and prevent progression. Its use is particularly beneficial in controlling blood pressure (80%) and maintaining patient compliance (100%). However, 80% of clinicians rate S-Metoprolol as less effective compared to other beta blockers like carvedilol or bisoprolol in terms of symptom improvement.

Combination therapies, such as beta blockers with ARNIs or SGLT2 inhibitors, are gaining popularity for their synergistic effects on HF management. While monotherapy is effective, adherence rates remain a challenge, with 80% of clinicians observing patient adherence rates of 5-10%. Clinicians emphasize the need for careful dose titration and monitoring, with starting doses of S-Metoprolol at 25 mg being widely adopted.

## **Clinical Recommendations**

#### 1. Therapy Initiation

- First-Line Therapy: The cornerstone of treatment for hypertensive HF involves the use of beta blockers as the initial therapy, with S-Metoprolol being the preferred choice due to its proven efficacy in improving cardiac function, reducing hospitalizations, and lowering mortality in HF patients. The recommended starting dose for S-Metoprolol is 25 mg daily, which allows clinicians to assess tolerance and gradually titrate based on individual patient responses.
- Beta Blockers work by blocking the harmful effects of catecholamines on the heart, reducing heart rate and myocardial oxygen demand, which is particularly beneficial in HF patients. Regular titration helps achieve the optimal dose, often progressing to 50-100 mg per day based on patient tolerance and symptom relief.

#### 2. Combination Approaches

- ARNIs (Angiotensin Receptor-Neprilysin Inhibitors): In patients with moderate to severe HF, ARNIs, such as Sacubitril-Valsartan, are recommended as they provide dual benefits of blocking the angiotensin II receptor and inhibiting neprilysin. This combination reduces mortality and hospitalizations in HF patients, making it a valuable second-line option, particularly when beta blockers alone are insufficient.
- SGLT2 Inhibitors: For patients with HFpEF (Heart Failure with Preserved Ejection Fraction), SGLT2 inhibitors, like Empagliflozin or Dapagliflozin, are emerging as a crucial therapy. These agents reduce hospitalization due to HF, improve heart function, and provide cardiovascular protection by addressing the metabolic and cardiac load in HF patients.
- Combination Therapy: For enhanced efficacy, combining S-Metoprolol with S-Amlodipine is highly favored in patients who need blood pressure control along with heart rate management. This combination is particularly useful in those with coexisting CAD (coronary artery disease) or angina, as S-Metoprolol's cardio-selective properties offer good heart rate control, while S-Amlodipine addresses blood pressure and reduces peripheral vascular resistance.

#### 3. Monitoring and Adjustment

- Regular Follow-Up: Effective management of hypertensive HF requires regular monitoring every 2-4 weeks after initiating therapy to evaluate blood pressure, heart rate, renal function, electrolytes, and symptoms of fluid retention. Ongoing clinical assessment ensures therapy is effective and adjustments can be made to prevent adverse outcomes.
- Dose Titration: Based on the patient's clinical response and tolerability, the
  dose of medications such as S-Metoprolol, ARNIs, or SGLT2 inhibitors should
  be titrated carefully to maximize therapeutic benefit while minimizing side
  effects.

#### 4. Patient Education

- **Importance of Adherence:** Patient education plays a crucial role in the management of hypertensive HF. Patients need to understand the benefits of their prescribed therapies and the potential long-term improvements in their heart health.
- Side Effect Management: Addressing patient concerns about potential side effects such as dizziness, hypotension, or headaches is vital to improving adherence. Education on these aspects helps patients feel more informed, reducing hesitancy to continue therapy.
- Lifestyle Modifications: Alongside pharmacotherapy, patients should be educated on lifestyle changes, including adopting a low-sodium diet, regular physical activity, weight management, and smoking cessation, which further enhance the effectiveness of the medical therapy.

The clinical recommendations for managing hypertensive HF focus on individualized care that incorporates first-line medications like S-Metoprolol, alongside advanced therapies such as ARNIs and SGLT2 inhibitors to optimize outcomes. Regular monitoring and patient education are key components to ensure long-term adherence and improve clinical outcomes. Through careful dose titration, patient engagement, and integration of guideline-based care, clinicians can effectively manage hypertensive HF and reduce both morbidity and mortality associated with the condition.

### **Consultant Opinion**

Consultants in the field of cardiology and internal medicine emphasize several key strategies to enhance the management of hypertensive HF. The primary recommendation revolves around raising clinician awareness regarding the critical role of beta blockers, especially S-Metoprolol, in the treatment of HF associated with hypertension. Many clinicians may still underutilize beta blockers due to concerns about potential side effects or insufficient understanding of their long-term benefits in HF management. Consultant-led education sessions, workshops, and clinical training programs can effectively address this knowledge gap by highlighting the proven efficacy of beta blockers in improving heart function, reducing hospitalizations, and lowering overall mortality in HF patients.

Moreover, dose titration and patient monitoring are areas where consultants stress greater clinician focus. Many HF patients benefit from a tailored approach, starting with a low dose and gradually increasing based on individual response and tolerability. S-Metoprolol, as a beta blocker with cardio-selective properties, allows for effective heart rate control while minimizing adverse effects in HF patients. Consultants recommend that clinicians routinely evaluate blood pressure, heart rate, renal function, and symptoms of fluid retention during follow-up visits to ensure optimal titration and prevent potential complications.

In addition to monotherapy with beta blockers, consultants advocate for the use of combination therapies as a standard approach to managing hypertensive HF. Therapies that combine S-Metoprolol with other medications such as S-Amlodipine can provide a synergistic effect, addressing both blood pressure control and heart rate optimization. This approach is particularly valuable in patients with coexisting CAD (coronary artery disease) or angina, where controlling both blood pressure and heart rate is essential. By using combination therapy, clinicians can enhance treatment efficacy while minimizing potential side effects compared to monotherapy.

Patient education campaigns are also highlighted as a critical component in achieving long-term success in HF management. Many patients may lack a clear understanding of the importance of medication adherence, the proper timing for dose adjustments, or the significance of lifestyle modifications in conjunction with pharmacotherapy. Consultant-led programs that provide clear and simple guidance about the importance of medication adherence, possible side effects, and the benefits of lifestyle changes (such as dietary salt reduction, regular physical activity, and weight management) can significantly improve patient outcomes. Educating patients on how to recognize symptoms of worsening HF and seek timely medical attention can further reduce hospitalization rates and improve quality of life.

In summary, consultants strongly advocate for clinician awareness through targeted education, dose titration and monitoring for optimal therapy, the use of combination treatments to maximize efficacy, and patient education campaigns to ensure better long-term adherence and engagement. These strategies, when effectively implemented, can lead to significant improvements in the management of hypertensive HF.

### **Market Opportunities**

- **Rising Prevalence:** The growing incidence of hypertensive HF offers an expanding market for targeted therapies.
- Education and Training: Pharmaceutical companies can bridge knowledge gaps by organizing workshops and webinars on S-Metoprolol and combination therapies.
- **Improved Adherence Solutions:** Developing simplified regimens and promoting patient compliance programs can enhance therapy success.
- **Focus on Safety:** Marketing the safety profile of S-Metoprolol, including its tolerability and efficacy, can position it as a preferred option among clinicians.

### **Market Positioning**

- Efficacy and Safety Focus: The primary objective is to position S-Metoprolol
  as a first-line treatment for managing hypertensive HF. Its efficacy in controlling
  blood pressure, improving heart function, and reducing the risk of
  hospitalizations is well-documented, making it a preferred choice for clinicians.
  S-Metoprolol's cardio-selective properties allow for effective symptom
  management while maintaining safety, making it an ideal option for long-term
  use in HF patients.
- Educational Campaigns: Building awareness through targeted educational campaigns is crucial to enhance clinician understanding of S-Metoprolol's benefits. Materials developed should focus on highlighting the drug's role in HF management, its proven efficacy, and its impact on patient outcomes. These campaigns aim to correct any misconceptions about beta blockers and emphasize their value in achieving better HF control.
- Collaborations: Forming strategic partnerships with key opinion leaders (KOLs) in cardiology can significantly enhance the credibility and adoption of S-Metoprolol in clinical settings.

Collaborations with experts who have firsthand experience using S-Metoprolol can help spread awareness, provide clinical insights, and encourage other clinicians to integrate this treatment into their practice.

 Patient-Centric Messaging: The focus should also be on patient-centered communication, emphasizing how S-Metoprolol can improve both compliance and quality of life. Clear messaging about the medication's benefits in reducing symptoms, controlling blood pressure, and minimizing side effects will encourage better patient engagement, adherence to treatment plans, and ultimately lead to more favorable long-term health outcomes.

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