REVIEW ARTICLE

A Consensus Statement on the Role of Bisoprolol across the CV Continuum

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Abstract

Cardiovascular disease (CVD) remains the leading cause of death globally, affecting populations in both developed and low- and middle-income countries. Although age-adjusted mortality rates from coronary artery disease (CAD) have declined in regions such as the United States and Europe, sudden cardiac death continues to account for a significant proportion of CVD-related fatalities. The concept of the "cardiovascular continuum," introduced more than a decade ago, describes the progressive nature of CVD—beginning with modifiable risk factors such as hypertension, diabetes, and smoking, which collectively drive oxidative stress, endothelial dysfunction, and inflammation. Over time, these pathophysiological changes lead to atherosclerosis and end-organ damage, often well before clinical symptoms become apparent.

In India, the burden of CVD has risen sharply in recent decades, particularly due to increasing rates of coronary heart disease and cerebrovascular events. Emerging evidence identifies an elevated resting heart rate as an independent predictor of adverse cardiovascular outcomes, particularly in individuals with hypertension, myocardial infarction (MI), and heart failure (HF). Among available pharmacological options, beta-blockers—particularly bisoprolol—have demonstrated strong efficacy in managing angina, atrial fibrillation (AF), and heart failure with reduced ejection fraction (HFrEF). By acting at multiple stages of the cardiovascular continuum, bisoprolol provides both symptomatic relief and disease-modifying effects, underscoring its importance in contemporary cardiovascular management.

Keywords: Beta-blockers, Bisoprolol, Cardiovascular disease, Heart failure.

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Introduction

Cardiovascular disease (CVD) remains the leading cause of mortality worldwide, exerting a major burden on developed nations and increasingly affecting developing countries as well. Although age-specific mortality rates from CAD have significantly declined in the United States and Europe over the past four decades, sudden cardiac deaths still account for nearly one-fourth of all fatalities.

About 15 years ago, a multidisciplinary panel of experts from various research fields convened to reassess the existing understanding of CVD. They proposed a unifying concept—the cardiovascular continuum—which explains CVD as a progressive sequence of interrelated events driven by the interaction of multiple internal and external risk factors. These factors initiate a cascade of pathophysiological changes that gradually evolve into overt heart disease.

The cardiovascular continuum describes the underlying pathophysiological process of CVD as a continuum of molecular and cellular alterations (Fig. 1). Major contributors to heart disease, including hypercholesterolemia, high blood pressure, elevated blood sugar, and smoking, lead to oxidative stress and endothelial dysfunction. This dysfunction sets off a chain of events in the coronary arteries involving alterations in vasoactive mediators, activation of inflammatory pathways, and vascular remodeling. Over time, these processes culminate in atherosclerosis and organ damage. Importantly, evidence indicates that these changes begin early in life—long before clinical symptoms appear—underscoring that CVD results from a slow, progressive pathophysiological process.[1]

Cardiovascular disease remains a leading cause of premature death and disability; however, its progression is not inevitable. Over the past few decades, significant progress in understanding the pathophysiological mechanisms of heart disease has coincided with remarkable therapeutic innovations. These developments now enable effective interventions across the entire spectrum—from individuals with silent atherosclerotic risk factors to those suffering from advanced, end-stage heart failure.[2]

Heart rate (HR) serves as a powerful predictor of cardiovascular as well as all-cause morbidity and mortality, both in the general population and among individuals with established CVD. For the purpose of this Consensus Statement, the cardiovascular (CV) continuum is defined as a sequence of interlinked events that illustrate the progressive nature of CVD. This progression typically begins with hypertension (HTN) and extends through angina, MI, and AF, ultimately culminating in HF.

As depicted in Figure 1, the CV continuum emphasizes the dynamic and interconnected stages of cardiovascular disease—from early, modifiable risk factors such as hypertension to severe, life-threatening outcomes like HF. This framework underscores the critical importance of early detection,

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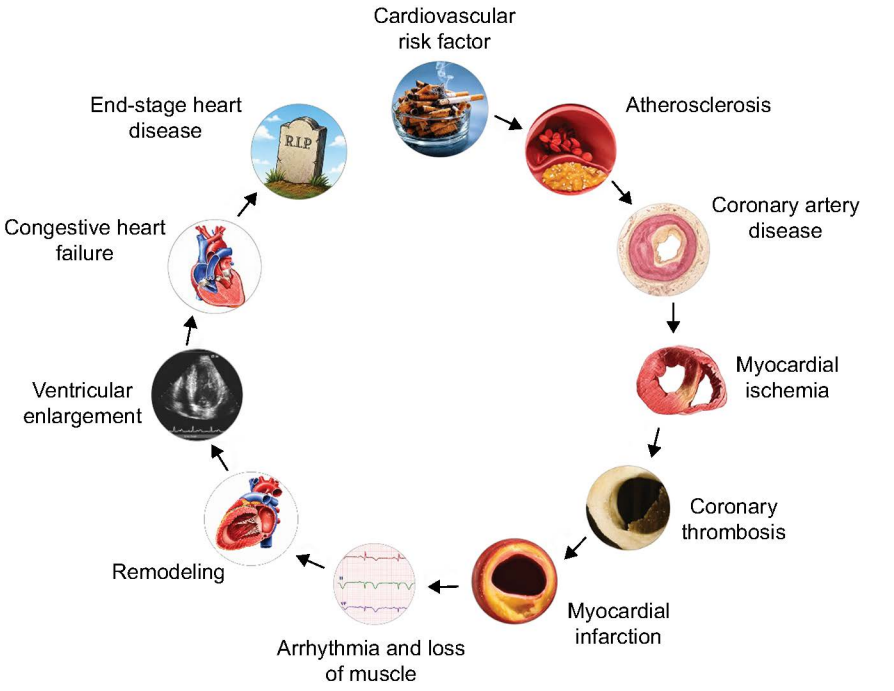

Fig. 1: Cardiovascular continuum. Schematic representation of all processes involved in cardiovascular disease from cardiovascular risk factors to end-stage heart failure

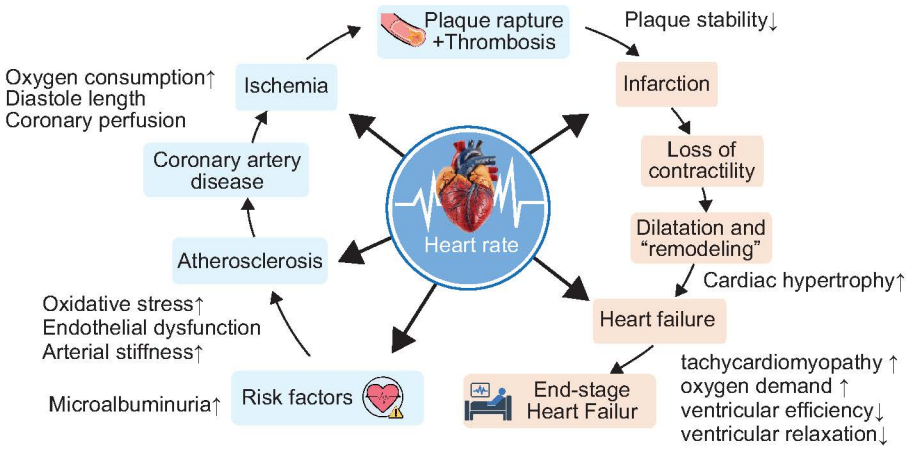

Fig. 2: Pathophysiological effects of heart rate on the cardiovascular disease continuum

timely intervention, and comprehensive management strategies to interrupt or slow the progression of disease at each stage.[2–4]

Cardiovascular Disease in Indians

According to the Global Burden of Disease (GBD) study, the India State-level Disease Burden report indicates that between 1990 and 2016, the prevalence of ischemic heart disease (IHD) and stroke in India increased by 2.3 times. During this period, the number of CVD cases more than doubled—from 25.7 million (95% CI 25.1–26.0) in 1990 to 54.5 million (53.7–55.3) in 2016. However, these figures are likely conservative, given the country's substantial burden of risk factors.[2]

Cardiovascular diseases (CVD), including heart attacks and strokes, remain the leading cause of death and disability worldwide, accounting for one-third of all deaths in India. Uncontrolled blood pressure is a major contributor to CVD risk. Among the estimated 220 million people in India living with hypertension, only 12% have their blood pressure adequately controlled. Hypertension—the leading cause of adult mortality—is both preventable and treatable.[5] The first national-level NCD survey (2018–2019) reported that 28.5% of individuals aged 18–49 years had hypertension. Among them, 27.9% were aware of their condition, 14.5% were receiving treatment, and only 12.6% had their blood pressure under control.[6]

Baseline Pulse Rate: A Predictor of Cardiac Outcomes

Baseline pulse rate (PR) is a well-established prognostic marker in CVD, strongly associated with adverse outcomes across conditions such as hypertension, MI, and HF. Numerous clinical studies have demonstrated that an elevated resting HR correlates with increased morbidity and mortality in these populations. Evidence from the ONTARGET/TRANSCEND trials shows that every 10 beats per minute (bpm) rise in resting HR among patients with stable CVD is associated with a 22–26% higher risk of major cardiovascular events, a 33–41% greater risk of cardiovascular death, and a 33–39% increase in all-cause mortality.[7]

Elevated HR is consistently linked to all stages of the cardiovascular continuum, demonstrating a close relationship with blood pressure in both normotensive and hypertensive individuals.[8] As illustrated in Figure 2, heart rate influences each phase of the continuum—from early vascular risk factors to overt cardiovascular events and the development of HF. This influence stems from its impact on key pathophysiological mechanisms, including increased myocardial oxygen consumption, reduced coronary perfusion time, and enhanced arterial wall stress, all of which accelerate disease progression.[9]

Accordingly, heart rate serves not only as a risk marker but also as a focus for therapy aimed at preventing and managing heart-related disorders. Lowering HR in patients with chronic stable angina improves myocardial perfusion and reduces oxygen demand, thereby enhancing cardiac efficiency. Notably, HR-lowering agents exhibit a use-dependent effect, wherein their therapeutic efficacy strengthens with continued use, providing sustained cardiovascular protection (Fig. 2).[9]

Management of Arterial Hypertension—Insights from the 2023 ESH Guidelines

Preferred Pharmacologic Categories for Initial Therapy

Major clinical practice guidelines (CPGs) consistently recommend agents acting on the renin–angiotensin system (RAS blockers), thiazide and thiazide-type diuretics, and calcium antagonists as initial treatment options for hypertension management (Fig. 3). The European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines additionally include beta-blockers as first-line agents, whereas most other international guidelines reserve their use

Current Practice Guidelines	*Indian CPGs*	
	2016 MoHFW	2019 IGH-IV
BP threshold (mmHg) for adding pharmacological therapy	≥140/90	>140/90 >130/80 if CVD
BP Target (mmHg)	<80 years: <140/90 ≥80 years: <150/90	<60 years: 120–130/70–80 ≥60 years: 130–140/80–90
BP measurement for initial evaluation and monitoring control	Office measurement preferred.	ABPM or HBPM preferred. Alternative is repeated office measurements.
First-line BPLDs	Three classes: 1. RASI 2. CCBs 3. Thiazide	Four classes 1. RASI 2. CCB 3. Diuretics 4. Newer Beta-blockers
Stepwise approach with specific classes/drugs, dose (mg)	1. Enal 5/Los 50 or Amlo 5 or Hctz/Chlo 12.5 2. Add a second drug Enal./Amlo 2.5–5/Hctz 12.5] 3. Enal 5 + Amlo 2.5 + Hctz 12.5 4. Enal 10 + Amlo 10 + Hctz 25 5.Refer to specialist	1. RASI or CCB or Diuretic 2. RASI + CCB/Diuretic 3. RASI + CCB + Diuretic 4. RASI + CCB + Diuretic + MRA 5. Add MRA or α-B; in special cases: centrally acting drugs or direct vasodilators 6. Refer to specialist
Combination therapy/SPC	Initiate with combination only if BP > 180/110. SPCs only after BP is stabilized with two drugs given separately	Initiate with combination if BP > 160/100, preferably a SPC.
Frequency of follow-up	1–2 weeks: after initiation of therapy 2–4 weeks: after change of BPLDs	**Monthly**: after initiation or change of BPLDs until target BP achieved 3 monthly (high risk) or 5 monthly (low–moderate risk): if target BP achieved
Target time for BP control	6–8 weeks	–

Fig. 3: Summary of guideline recommendations for pharmacological management of hypertension

for patients with established CVD or specific clinical indications. The Indian Guidelines on Hypertension-IV (IGH-IV) present a somewhat conflicting stance—stating that beta-blockers are "no longer first-line" for general use, yet still recommending the "newer" beta-blockers as first-line options in younger hypertensive patients.[10]

There are also notable differences among CPGs concerning the preference for thiazide vs thiazide-like diuretics. The ACC/AHA guidelines suggest these two classes can be used interchangeably, while the International Society of Hypertension (ISH) favors thiazide-like diuretics, recommending thiazide diuretics only as alternatives when necessary. Both the ESC/ESH and WHO guidelines mention the use of either class but do not indicate a clear prioritization. Within Indian recommendations, the IGH-IV document broadly refers to diuretics, omitting subclass differentiation, whereas the Ministry of Health and Family Welfare (MoHFW) guideline specifies both but gives priority to thiazide diuretics.[10]

Clinical Conditions Favoring Beta-blocker Use in Hypertensive Patients

Clinical trials and meta-analyses have demonstrated that both first- and second-generation beta-blockers (BBs)—including agents such as propranolol, atenolol, and metoprolol—reduce the risk of cerebrovascular accidents, heart failure, and other significant cardiac events among individuals with hypertension. In relation to alternative classes of antihypertensive drugs, BBs offer comparable protection against major cardiovascular outcomes, though their effectiveness in preventing cerebrovascular events appears slightly lower. This difference may be attributed to subtle variations in blood pressure control, particularly in central systolic blood pressure.[11]

Historically, BBs were listed as one of the five primary categories of blood pressure–lowering medications in earlier guidelines. However, they are now primarily recommended for patients with specific comorbid conditions—including heart failure (HF), post-MI, angina, AF, or for younger women planning pregnancy.[11]

Table 1: Selected diseases and conditions for the use of BBs in patients with hypertension

Selected indications with guideline-directed medical therapy for BBs
Chronic coronary syndromes, anti-ischemic therapy
Post-myocardial infarction: arrhythmias, angina, known incomplete revascularization, HF
Acute coronary syndrome
HFrEF and HFpEF if coronary disease (ischemia), arrhythmias and tachycardia
Atrial fibrillation: prevention, rhythm control, heart rate control
Women with child-bearing potential/ planning pregnancy
Hypertension disorders in pregnancy
Selected other conditions in which therapy with BBs can be favorable
Hypertension with elevated resting heart rate >80 bpm
Emergency, urgency and parenteral administration
Perioperative hypertension
Major noncardiac surgery
Excessive pressor response to exercise and stress
Hyperkinetic heart syndrome
Postural orthostatic tachycardia syndrome
Orthostatic hypertension
Obstructive sleep apnea (OSA)
Peripheral arterial disease with claudication
Chronic obstructive pulmonary disease (COPD)
Portal hypertension, cirrhosis-related esophageal varices and recurrent variceal bleeding
Glaucoma
Thyrotoxicosis, hyperthyroidism
Hyperparathyroidism in uremia
Migraine headache
Essential tremor
Performance anxiety and anxiety disorders
Psychiatric disorders (post-traumatic stress)

Third-generation beta-blockers, such as nebivolol and carvedilol, possess additional vasodilatory properties and a more favorable safety profile, including fewer adverse effects on sexual function. Clinical trials involving BBs such as carvedilol, bisoprolol, and nebivolol have demonstrated clear benefits in patients with HFrEF. However, evidence from hypertension-specific outcome trials remains limited, and findings from real-world studies have been inconsistent regarding their degree of cardiovascular protection (Table 1).[11]

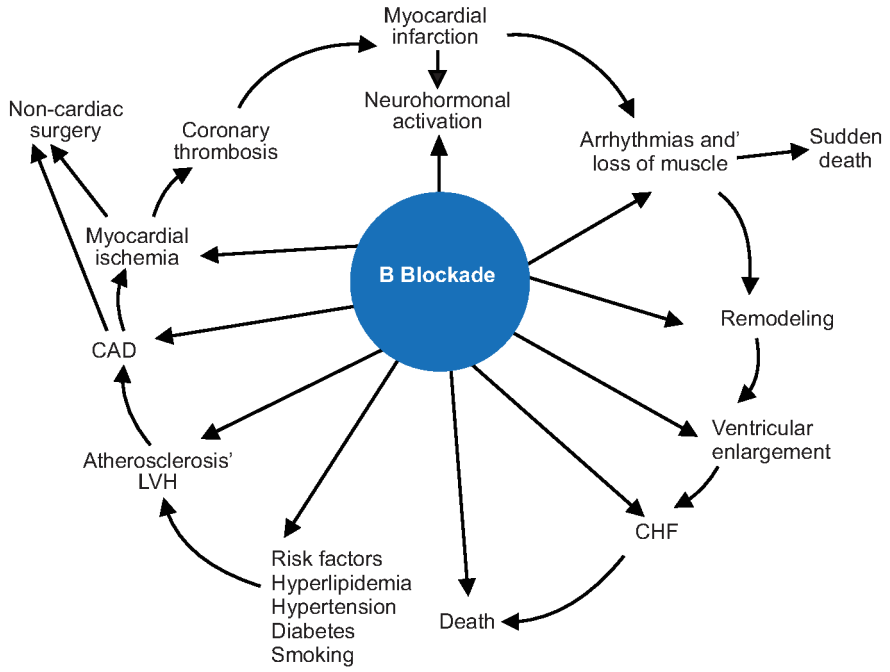

Fig. 4: Beta-blockers can intervene at many points in the cardiovascular continuum

Table 2: Summary of indications, recommendations and considerations

Indication	*Recommendation*	*Comorbidities and considerations*
Angina	All beta-blockers are considered equally effective, although bisoprolol or metoprolol may be preferred. Celiprolol and pindolol tend not to be used.	Cardioselective beta-blockers, e.g. bisoprolol or metoprolol, are less likely to cause adverse effects, e.g. cold extremities or fatigue Celiprolol and pindolol have intrinsic sympathomimetic activity (ISA) which may reduce bradycardia or peripheral vasoconstriction Water-soluble beta-blockers, e.g. atenolol, celiprolol or nadolol, are less likely to cause central nervous system (CNS) adverse effects, such as sleep disturbance Polypharmacy: bisoprolol is less likely to interact with other medicines Renal dysfunction: consider dose adjustments for water-soluble beta-blockers, e.g. atenolol, celiprolol and nadolol; bisoprolol may be preferred Respiratory disease: cardioselective beta-blockers, e.g. bisoprolol and metoprolol, are preferred
Arrhythmias	Metoprolol or bisoprolol	
Heart failure	Bisoprolol, carvedilol or metoprolol	
Hypertension	All beta-blockers are considered to be equally effective (as fourth-line treatment)	
Postmyocardial infarction	Bisoprolol or metoprolol; consider withdrawal after 6–12 months if revascularized and no other indications	

Contribution of β-Blockers (Bisoprolol) to Cardiovascular Disease Management

Beta-blockers (BBs) play a pivotal role in slowing or halting the progression of the cardiovascular continuum. Over the past two decades, extensive research has expanded their therapeutic potential beyond their traditional indications in hypertension and post-MI prevention, to include significant benefits in chronic heart failure (CHF) and in reducing cardiovascular events during surgeries unrelated to the heart. One of the most remarkable paradigm shifts in cardiology has been the repositioning of beta-blockers in CHF, from being previously contraindicated to now serving as a cornerstone of therapy. Their ability to reduce both morbidity and mortality in CHF is well established, and ongoing studies continue to refine their optimal application. The CIBIS III trial demonstrated that initiating treatment with the beta-blocker bisoprolol prior to adding an ACE inhibitor is equally safe and effective as starting therapy in the reverse sequence (Fig. 4).[12]

Beta-blockers exert their cardiovascular benefits primarily through selective blockade of β_1-adrenergic receptors, which constitute approximately 80% of the heart's adrenergic receptors. This mechanism helps counteract the proarrhythmic effects of excessive sympathetic stimulation. Their antiarrhythmic properties are mediated through multiple pathways: they lower heart rate, suppress ectopic pacemaker activity, slow atrioventricular (AV) nodal conduction, and prolong the AV nodal refractory period. Additionally, by reducing sympathetic drive, myocardial ischemia, and mechanical stress, and by enhancing baroreflex sensitivity, beta-blockers effectively prevent arrhythmias and stabilize cardiac rhythm. Unlike many other antiarrhythmic agents that act directly on ion channels, beta-blockers have minimal proarrhythmic potential, offering an excellent balance of safety and efficacy across a broad spectrum of cardiovascular disorders.[13]

Cardiovascular Indications

The clinical role of beta-blockers has evolved considerably over time. Initially introduced as first-line agents for hypertension and considered contraindicated in heart failure, their therapeutic positioning has since changed. Currently, their use in hypertension is more selective, whereas they are well established as a cornerstone therapy in heart failure management. Moreover, the long-term benefits of beta-blockers following myocardial infarction are now viewed with greater uncertainty than in the past. Table 2 summarizes the contemporary indications, recommendations, and clinical considerations for beta-blocker use across cardiovascular conditions.[14]

Main Pharmacokinetic and Pharmacodynamic Properties of β-Blockers

While all beta-blockers act as competitive antagonists at β_1-adrenoceptors, they differ markedly in their pharmacokinetic (PK) and pharmacodynamic (PD) characteristics (Table 3). Key PK variations include gastrointestinal absorption, hepatic first-pass metabolism, lipid solubility, plasma protein binding, penetration into the central nervous system, myocardial tissue distribution, and rates of hepatic metabolism and renal excretion. PD distinctions involve differences in β_1-selectivity, intrinsic sympathomimetic activity, membrane-stabilizing effects, α-receptor blockade, and the presence of direct vasodilatory properties (Table 3).[15–27]

Consensus 1: Elevated Heart Rate in Indian Clinical Practice

In Indian patients, blood pressure often shows evening surges accompanied by elevated

Table 3: Clinical outcomes at follow-up of 3.8 median years

Drug	*Extent of absorption (% of dose)*	*Bioavailability (% of dose)*	*Major first–pass hepatic metabolism*	*Lipid solubility*	*Elimination*	*β1 selectivity*	*Dialyzability*	*Effect on sexual function*	*Effect on insulin resistance*
Bisoprolol	≈90	≈88	No	Low	Renal/hepatic	++++	Low dialyzability	Improves aspects of sexual function, including erection firmness and satisfaction with sexual performance	Neutral effects on the insulin sensitivity index
Atenolol	≈50	≈40	No	Low	Renal	++	High dialyzability	Chronic worsening of sexual activity	Worsens insulin sensitivity, potentially leading to increased fasting blood glucose levels
Carvedilol	>90	≈30	Yes	Moderate	Hepatic	0	Nondialyzable	Chronic worsening of sexual activity	Lowers insulin resistance
Metoprolol	>90	≈50	Yes	Moderate	Hepatic	+	High dialyzability	Metoprolol decreases erectile function	Reduces insulin sensitivity
Nebivolol	>90	12–96	Yes	Low	Hepatic	++++ (increases NO availability)	Nondialyzable	Preserves sexual function	Improve of insulin resistance

++++, More β1 selectivity; +, less β1 selectivity

heart rate and heightened sympathetic activity. The therapeutic objectives are to achieve a 20% decrease from baseline pressure levels and maintain the pulse between 60 and 70 beats per minute. For patients who are hemodynamically stable, therapy can be initiated with bisoprolol 5 mg or metoprolol 50 mg daily. In individuals requiring a more gradual approach, treatment may begin with bisoprolol 1.25 mg, followed by dose escalation every 2 weeks to 2.5 mg, 5 mg, and eventually 10 mg, if target heart rate goals are not achieved. Continuous monitoring for bradycardia is essential, and further dose increases should be avoided if it occurs. Patients with bronchial hyperreactivity or chronic obstructive pulmonary disease (COPD) should be closely observed for worsening respiratory symptoms during titration, and dose escalation should be stopped if any concerning symptoms arise. Regular follow-up visits are recommended to ensure good tolerance, achievement of therapeutic heart rate targets, and absence of adverse effects.

Coronary artery disease, presenting as angina or myocardial infarction, is a leading cause of cardiac failure having preserved or moderately reduced ejection fraction in India. Data obtained through the Indian Heart Failure Registry indicate that 70–80% of cardiac failure patients also have CAD. Clinicians have noted that individuals over 35 years of age and those with hypertension, tremors, hyperhidrosis, tachycardia, or mid-range ejection fraction often respond favorably to beta-blocker therapy. Indian patients frequently exhibit resting tachycardia (80–100 bpm), necessitating vigilant monitoring of blood pressure and pulse in those with hypertension, heart failure, angina, myocardial infarction, or arrhythmias to optimize outcomes and ensure safety.

Bisoprolol in the Management of Hypertension

Recent national hypertension guidelines in India have suggested positioning beta-blockers as a later-line therapy, following diuretics, ACE inhibitors/ARBs, and calcium channel blockers. In contrast, the current ESH and ESC recommendations still recognize beta-blockers as a primary treatment option, advocating their role in both the initiation and continuation of antihypertensive therapy, either alone or in combination with other agents.[12]

Bisoprolol, a highly cardioselective β_1-blocker, offers potential advantages over other selective beta-blockers due to its potency, tolerability, and predictable pharmacokinetics. Although head-to-head trials among selective beta-blockers are generally limited in size, meta-analyses provide useful insights into bisoprolol's role in hypertension management.[28]

The BRIGHT study evaluated bisoprolol as an initial treatment option among Indian adults diagnosed with stage I primary hypertension. The study demonstrated that bisoprolol was both effective and well tolerated, with an average daily dose of 5 mg, achieving target blood pressure in 96.44% of patients, supporting its suitability as a first-line antihypertensive in this population.[29]

The CREATIVE study compared bisoprolol with long-acting metoprolol CR/ZOK in patients with mild-to-moderate primary hypertension, focusing on dynamic HR and blood pressure (BP) control. Bisoprolol showed superior reduction in dynamic HR and was noninferior in controlling dynamic BP, without any new safety concerns.[30]

A pooled analysis comparing bisoprolol against several selective beta-blockers such as atenolol, betaxolol, esmolol, acebutolol, metoprolol, and nebivolol revealed that bisoprolol was more effective in reducing BP and HR, while also showing a beneficial impact on lipid profiles, particularly by elevating HDL cholesterol levels. These findings support bisoprolol's clinical efficacy and role in therapeutic decision-making for hypertension.[31]

The AMCOR study assessed the combination of bisoprolol 5 mg and amlodipine 5 mg in patients whose BP was inadequately controlled by amlodipine monotherapy. Adding bisoprolol significantly enhanced BP management,

producing an additional decrease of 7.2 mm Hg in systolic levels and 3.95 mm Hg in diastolic values, underscoring the effectiveness of this combination in resistant hypertension.[32]

A 30-center, randomized, double-blind study evaluated the antihypertensive efficacy and safety of bisoprolol 5 mg combined with hydrochlorothiazide 6.25 mg (B5/H6.25) vs monotherapy with either agent in stage I–II hypertension. The combination demonstrated sustained 24-hour BP control, a similar safety profile to placebo, and fewer adverse events compared with hydrochlorothiazide (HCTZ) 25 mg, including a lower incidence of hypokalemia.[33]

The HEART study, a cross-sectional survey of hypertension specialists across India (June–December 2022), assessed real-world use of the bisoprolol + telmisartan combination. Findings included:

- 47% of physicians followed American Hypertension Guidelines.
- Telmisartan was preferred by 95% as the ARB.
- 73% favored bisoprolol for newly diagnosed hypertension, with 57% choosing a 5 mg dose for patients at cardiovascular risk.
- 44% estimated that 20–40% of patients required dual therapy.
- 70% reported improved organ function with the bisoprolol + telmisartan combination, confirming its effectiveness in blood pressure control and cardiovascular risk reduction.[34]

Overall, these studies highlight bisoprolol's efficacy, safety, and utility in both monotherapy and combination therapy, reinforcing its role in modern hypertension management, particularly in the Indian population.

Consensus 2: Bisoprolol in the Management of Hypertension in India

In an Indian context, cardiologists tend to use beta-blockers, with bisoprolol being the most commonly used, followed by nebivolol. These beta-blockers are commonly prescribed alongside ARBs, ACEIs, or diuretics in individuals presenting with elevated BP (≥150/100 mm Hg) as well as an increased heart rate (>90 bpm). Some newer combinations are bisoprolol with amlodipine or telmisartan.

Patients with renal or liver issues can take bisoprolol as it prevents surges in hypertension during dialysis. Additionally, it is more sympathetic and more common in younger Indian patients suffering from obesity, which makes beta-blockers such as bisoprolol, which is a cardioselective beta-blocker, more appropriate. Bisoprolol is helpful since it is a selective beta-blocker that has a heart rate-counteracting side effect, which helps with many patients' systemic issues.

Bisoprolol's selectivity makes it easier to treat hypertensive patients with comorbid illnesses like COPD. Treatment during early stages of COPD might enhance the patient's overall health; additionally, use of bisoprolol may lower inflammation, mucus and cytokine secretion, neutrophil activity and bronchoconstrictive endothelin-1 release, thus slowing COPD progression later on.

Antihypertensive medications have an impact on sexual dysfunction, which is a concern for men with hypertension, particularly induced by an increase in blood pressure.

Bisoprolol in the Management of Angina

For many patients, angina is the initial manifestation of CAD, highlighting the need for symptom control and reduction of acute cardiovascular events. Both European and US guidelines recommend beta-blockers as first-line therapy for angina. In the UK, the National Institute for Health and Care Excellence (NICE) advises treating stable angina with either a beta-blocker or a calcium channel blocker (CCB), reserving nitrates for patients who cannot tolerate these agents.[35]

Clinical evidence demonstrates that beta-blockers reduce ischemic and anginal episodes more effectively than placebo, and often outperform CCBs. Meta-analyses also indicate that beta-blockers lower mortality risk and are associated with fewer adverse events compared to CCBs. Bisoprolol, a highly β_1-selective blocker, has been shown to reduce angina attacks, improve exercise tolerance, and decrease ischemic burden, surpassing drugs such as nifedipine and isosorbide dinitrate.[35]

In a study by Terol et al., patients with chronic stable angina were initiated on bisoprolol 10 mg once daily, with subsequent dose adjustments to 5, 15, or 20 mg based on clinical response. Most patients (88%) remained on the 10 mg dose. The study reported that 89% of patients experienced fewer angina attacks, with 56% becoming angina-free. Responses were consistent across age groups and smoking status. Bisoprolol was well tolerated, with only 5.1% reporting side effects, confirming its efficacy and safety in angina management.[36]

A cohort analysis by Sabidó et al., using the UK Clinical Practice Research Datalink (CPRD), compared long-term outcomes of bisoprolol with other beta-blockers and nonbeta-blocker medications in angina patients. The study found that bisoprolol significantly reduced mortality and the risk of cardiovascular events, supporting guideline recommendations for its role as an initial treatment option in routine clinical practice.[35]

The TIBBS study evaluated bisoprolol versus nifedipine in patients with chronic stable angina, focusing on transient myocardial ischemia. Both drugs decreased the frequency and duration of ischemic episodes, but bisoprolol demonstrated superior efficacy, particularly in reducing the morning peak of ischemic activity, highlighting its advantage in controlling ischemia.[37]

Consensus 3: Bisoprolol in the Management of Angina in India

Indian research indicates that beta-blockers (BBs) treat arrhythmias associated with angina. Cardiologists emphasize achieving a target heart rate of 60 bpm in ischemic patients, which can be facilitated by bisoprolol taken once daily.

Cardiologists check heart rate, blood pressure, COPD, diabetes, and other relevant comorbidities prior to starting pharmacological treatment for angina. For patients with borderline readings, they often start with and monitor response to bisoprolol 1.25 mg. Combination therapy with calcium channel blockers and BBs is commonly employed.

When prescribing beta-blockers, some practitioners do not use them even with heart rates at 75–80 bpm—in favor of trimetazidine or coenzyme Q—and this is a common mistake when managing CAD. Given the clear advantages that beta-blockers provide, this approach needs to be adjusted.

Cardiologists prefer bisoprolol due to its selective beta-1 activity, lack of adversely affecting pulmonary function, lipid and glucose metabolism, high bioavailability, rapid absorption, long half-life, and bisoprolol's anticipated fixed-dose combinations with telmisartan, chlorthalidone, and amlodipine to enable comprehensive management. It is documented that beta-blockers are more effective than calcium channel blockers in reducing ischemic episodes since the effect

of BBs is mostly through decreased heart rate and blood pressure.

Bisoprolol in the Management of Myocardial Infarction

Myocardial infarction is defined by acute ischemia and necrosis of the myocardium, usually resulting from prolonged or severe reductions in coronary blood flow. In China, the incidence of acute MI is rising, with rural populations experiencing higher rates than urban areas, and MI-related mortality is increasing. Cardiac insufficiency occurs when myocardial contractility declines, reducing forward blood flow and leading to congestion within the systemic or pulmonary circulation.[31]

Evidence suggests that many patients develop or worsen cardiac insufficiency after MI, primarily due to adverse myocardial remodeling, which compromises cardiac contractility. The coexistence of MI and cardiac insufficiency complicates management and significantly affects prognosis.[38]

Conventional therapies alone are often inadequate for patients with MI complicated by cardiac insufficiency. Bisoprolol, a selective β_1-adrenoceptor blocker, is widely used for moderate to advanced heart failure, ischemic heart conditions, and elevated blood pressure. By selectively blocking β_1 receptors, bisoprolol reduces the effects of adrenaline on the heart, exhibiting greater β_1 selectivity than metoprolol and atenolol. While its efficacy in chronic heart failure is well established, its specific role in MI with cardiac insufficiency has been further investigated.[38]

A meta-analysis evaluating bisoprolol in MI patients with cardiac insufficiency found that, when added to conventional therapy, bisoprolol significantly improved cardiac function and reduced serum homocysteine (Hcy) and C-reactive protein (CRP) levels, without significant adverse effects.[39]

In a randomized study by Poldermans et al., bisoprolol demonstrated long-term cardioprotective effects in high-risk patients following major vascular surgery, significantly lowering the rates of cardiac death and recurrent MI.[40]

Maclean et al. studied early oral beta-blocker therapy in patients with acute non-ST elevation myocardial infarction (NSTEMI). Patients receiving bisoprolol within 4 hours of admission experienced fewer ventricular arrhythmias, cardiac deaths, and major adverse cardiovascular events (MACE) compared to those with delayed treatment, suggesting early low-dose bisoprolol confers protective benefits.[41]

The Tenacity study evaluated postacute coronary syndrome (ACS) patients with left ventricular systolic dysfunction (LVSD) over one year. Bisoprolol, combined with guideline-directed medical therapy (GDMT), significantly reduced heart rate, improved left ventricular ejection fraction (LVEF), and decreased ST segment deviation at the J point, without adversely affecting HbA1C or lipid profiles.[42]

Overall, these studies underscore bisoprolol's role in improving cardiac function, reducing inflammatory markers, preventing arrhythmias, and enhancing long-term outcomes in patients with MI and cardiac insufficiency.

Consensus 4: Bisoprolol in the Management of MI in India

In India, beta-blockers (BBs) are useful in the treatment of STEMI, particularly in the presence of left ventricular (LV) dysfunction. Cardiologists often start with short-acting BBs for hemodynamic monitoring and transition to long-acting BBs such as bisoprolol, metoprolol ER, or carvedilol. These BBs are used in conjunction with ACEi, ARBs, ARNIs, or even SGLT2 inhibitors.

For non-STEMI myocardial infarctions and bronchospasm patients, bisoprolol is better due to its profile. Even in the setting of acute heart failure BBs are usually continued as part of multidrug therapy with ARNIs, ARBs, ACE inhibitors, MRAs, or SGLT2 inhibitors, aiming to reach target doses as quickly as safe. Often, bisoprolol is the first drug of choice for arrhythmias. Should this be ineffective, metoprolol or carvedilol can also be added. Following myocardial infarction, there is a rationale to increase or start bisoprolol since it reduces myocardial oxygen demand and heart rate while decreasing the likelihood of recurrent cardiovascular events. It is protective against post-MI arrhythmias and provides cardioprotection that improves prognosis after MI.

Additionally, as a beta-blocker, bisoprolol aids in stabilizing heart function, making it a valuable option in post-MI management for long-term outcome improvement. In Indian patients, bisoprolol is typically initiated at 2.5 mg, with dose adjustments based on heart rate and clinical response.

Role of Bisoprolol in Atrial Fibrillation Management

Bisoprolol, a highly selective β-blocker, has demonstrated strong efficacy in the management of AF by reducing heart rate, thereby decreasing cardiac workload and enhancing the efficiency of cardiac output. In patients with supraventricular arrhythmias, current evidence supports bisoprolol as a preferred agent, particularly for rate control in AF. It also plays a preventive role in rhythm control strategies, helping to reduce the incidence of postoperative AF in patients undergoing both cardiac and noncardiac surgeries.[43]

In the management of ventricular arrhythmias, bisoprolol contributes significantly to reducing death rates and rehospitalizations, especially among individuals with clinically stable cardiac failure who experience severe arrhythmias such as sustained ventricular tachycardia (VT) or ventricular fibrillation (VF). Early administration—within 4 hours of myocardial infarction—has been associated with lower mortality, a reduced frequency of ventricular arrhythmias, and fewer major adverse cardiac events (MACE) in patients with non-ST elevation myocardial infarction (NSTEMI). Furthermore, bisoprolol effectively decreases the burden of ventricular ectopy in patients with premature ventricular contractions (PVCs).[43]

A comprehensive review by Muresan et al. analyzed the available evidence regarding bisoprolol's efficacy in supraventricular and ventricular arrhythmias. Of 325 studies initially screened, 28 met inclusion criteria—19 focused on supraventricular arrhythmias, 8 on ventricular arrhythmias, and 1 addressed both. The review concluded that bisoprolol is well supported by current evidence for rate control in AF and for prevention and management of ventricular arrhythmias.[43]

A study by Mahrose et al. explored how bisoprolol could help prevent AF after on-pump coronary artery bypass graft (CABG) surgery. Patients were split into two groups: one received bisoprolol alone (Group A), while the other received bisoprolol combined with hydrocortisone (group B). The results were striking—those in group B had a significantly lower rate of postoperative AF and experienced shorter hospital stays. These findings highlight that adding hydrocortisone may enhance bisoprolol's protective effect and support faster recovery following CABG.[44]

The MAIN-AF study further investigated the dose-dependent effects of bisoprolol in patients with chronic (persistent or permanent) AF. All participants initially received 2.5 mg/day of bisoprolol for two weeks; thereafter, 48 patients requiring further rate control were randomized to continue 2.5 mg/day or escalate to 5 mg/day for another two weeks. The results demonstrated a more pronounced reduction in heart rate during daytime compared to nighttime. Although the 5 mg/day group exhibited a greater decrease in systolic blood pressure, the difference was not statistically significant. Importantly, no serious adverse

Drugs	Guideline	Recommendation	COR	LOE
ARNi	ESC 2023	HFrEF	I	A
		HFmrEF	II	B
	ACC/AHA/HFSA 2022	HFpEF	II	B
Beta-blocker	ESC 2023	HFrEF	I	A
	ACC/AHA/HFSA 2022	HFmrEF	II	B
MRAs	ESC 2023	HFrEF	I	A
		HFmrEF	II	B
	ACC/AHA/HFSA 2022	HFpEF	II	B
SGLT2i	ESC 2023	HFrEF	I	A
		HFmrEF	I	A
		HFpEF	I	A
	ACC/AHA/HFSA 2022	HFmrEF	II	A

Fig. 5: Management of Heart Failure in a Resource-Limited Setting: Expert Opinion from India [ACC/AHA/HFSA, American College of Cardiology/American Heart Association/Heart Failure Society of America; ARNi, angiotensin receptor–neprilysin inhibitor; COR, class of recommendation; ESC, European Society of Cardiology; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LOE, level of evidence; MRAs, mineralocorticoid receptor antagonists; SGLT2i, sodium–glucose cotransporter 2 inhibitors]

events were observed. This study provided the first quantitative assessment of β-blocker monotherapy in AF, confirming that bisoprolol induces a safe, dose-dependent reduction in heart rate at 2.5 mg and 5 mg daily.[45]

Collectively, these findings underscore bisoprolol's clinical versatility and safety in arrhythmia management—providing effective rate control in atrial fibrillation, reducing the risk of postoperative AF, and mitigating ventricular arrhythmias while maintaining a favorable safety profile.

Consensus 5: Bisoprolol in the Management of Atrial Fibrillation in India

In India, metoprolol and carvedilol are the go-to options for managing heart rate, controlling rhythm, and preventing heart failure, while bisoprolol is infrequently used for AF. Due to longstanding medical traditions, metoprolol is often used first for AF.

The panel recommends that BBs should predominantly focus on the management of ventricular tachycardia (VT) and only use AF as a secondary focus. Beta-blockers have been proven to improve focal ventricular rate by increasing sympathetic outflow, which is the main driver of ventricular tachycardia. It is true that beta-blockers are routinely prescribed for AF to control the rate; however, their effectiveness for rhythm control in AF is not great. Rather, they are quite effective for rate control in tachycardia as they stabilize ventricular function, thus lowering the probability of rapid heart rate-induced sudden cardiac arrest.

Beta-blockers are not employed for prevention in AF but are used to manage active episodes, especially in patients after cardiac surgeries. The benefit of bisoprolol is its capacity to inhibit excessively fast ventricular rates during episodes of AF. For patients with AF, regulating heart rate during physical activity can be quite difficult, and beta-blockers (BBs) like bisoprolol, occasionally used in conjunction with digoxin, are utilized to control heart rate surges induced by exercise.

Beta-blockers are crucial in the management of various arrhythmias, encompassing both supraventricular and ventricular types. They are also vital during perioperative phases, nonsurgical interventions, and following open-heart surgeries, where their membrane-stabilizing characteristics assist in maintaining rhythm control.

Bisoprolol in the Management of Heart Failure

Management Protocols for HFrEF

Heart failure with reduced ejection fraction requires a personalized treatment approach—one that carefully considers each patient's clinical profile, coexisting conditions, and individual preferences. Tailoring therapy in this way helps optimize outcomes and supports more patient-centered care. Pharmacological therapy remains the cornerstone of treatment, and clinical guidelines continue to evolve as new evidence emerges (Fig. 5).[46]

Beta-Blockers

- Demonstrated to significantly reduce both mortality and morbidity in patients with HFrEF.
- Should be initiated once the patient is clinically stable and euvolemic.
- Effective in patients with either sinus rhythm or AF.
- Require gradual dose titration under close monitoring of heart rate, blood pressure, and symptoms.
- Potential adverse effects include bradycardia, hypotension, and bronchospasm.
- Abrupt discontinuation should be avoided, as it can precipitate clinical deterioration.[39]

Since the early 2000s, BBs have become a fundamental component of HFrEF therapy, typically used alongside angiotensin-converting enzyme inhibitors (ACEi). Among the three beta-blockers recommended for chronic heart failure—bisoprolol, metoprolol succinate, and carvedilol—bisoprolol is distinguished by its high selectivity for β_1-adrenergic receptors. This receptor specificity contributes to its strong clinical efficacy and favorable safety profile in chronic heart failure management.[47–50]

The CIBIS-II trial provided pivotal evidence supporting bisoprolol's role in heart failure therapy. The study demonstrated a 34% reduction in overall mortality and a 44% decrease in sudden cardiac death among patients treated with bisoprolol. In addition to its survival benefits, bisoprolol was shown to improve cardiac performance, enhance physical endurance, and elevate overall well-being in individuals with chronic cardiac failure—establishing it as a cornerstone therapy in CHF management.[47–50]

The CIBIS-II trial provided strong evidence that bisoprolol—a selective β_1-blocker—can significantly reduce the risk of death in patients with stable CHF (chronic heart failure). Compared to a placebo, bisoprolol showed a clear survival benefit, reinforcing its role as a cornerstone in heart failure management. Importantly, the study also reported a marked reduction in the incidence of sudden cardiac death, reinforcing the survival advantage conferred by bisoprolol in this patient population.[51]

The BISOCOR Observational Study evaluated the real-world application of bisoprolol in stable heart failure patients, assessing the alignment between target doses recommended by the CIBIS-II trial and those achieved in clinical practice. The study also analyzed functional outcomes, adverse events, and reasons for treatment discontinuation. Conducted in Spain, it was the first study to confirm that bisoprolol can be safely titrated to its maximum recommended doses in the outpatient management of heart failure, demonstrating both its effectiveness and tolerability in routine care.[52]

Consensus 6: Bisoprolol for the Treatment of Heart Failure among Patients in India

Within the Indian context, bisoprolol is recognized as the primary beta-blocker for heart failure, preferred over carvedilol. Its cardioselective characteristics lead to a less significant hypotensive effect when compared to nonselective beta-blockers. Bisoprolol is deemed more effective than other beta-blockers such as metoprolol, carvedilol, and nebivolol in the treatment of heart failure. It is especially preferred for managing patients with stable HF. Research indicates that bisoprolol should be initiated at a dose of 1.25 mg for HF, with weekly increases to 5 mg daily, targeting a final dose of 10 mg. For effective management of HF, bisoprolol is taken once daily. In patients with heart failure with preserved ejection fraction (HFpEF), beta-blockers are prescribed with caution, while sodium-glucose cotransporter 2 (SGLT2) inhibitors and diuretics are considered the first-line therapies, followed by angiotensin receptor-neprilysin inhibitors (ARNIs). Beta-blockers, including bisoprolol, are now advised alongside ACE inhibitors in the management of heart failure. The usual initiation strength for bisoprolol begins at 1.25 mg and is gradually titrated to 2.5 mg, 5 mg, or higher, depending on patient tolerance, with 5 mg being the most commonly tolerated dose. Bisoprolol has shown effectiveness in lowering mortality and preventing sudden death in patients with heart failure.

Conclusion

The concept of the cardiovascular continuum offers a comprehensive framework for understanding the progressive nature of CVD—from the initial development of risk factors to the eventual onset of heart failure. This continuum underscores the critical importance of early, targeted interventions aimed at preventing or slowing disease progression.

Bisoprolol, a highly selective β_1-adrenoceptor blocker, has demonstrated consistent clinical efficacy across multiple stages of this continuum. By effectively reducing heart rate, improving left ventricular function, and lowering the incidence of major cardiovascular events, bisoprolol serves as a key therapeutic agent in a range of cardiovascular conditions, including hypertension, angina, myocardial infarction, atrial fibrillation, and HFrEF.

In the Indian clinical context, bisoprolol is especially advantageous due to its excellent tolerability, convenient once-daily dosing, and suitability for a wide spectrum of patients—including those with diabetes, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), and older adults. Expert consensus supports its use in real-world practice, emphasizing its effectiveness as part of individualized, combination-based cardiovascular therapy.

With the growing burden of cardiovascular morbidity in India, a comprehensive strategy that integrates optimal heart rate control within guideline-directed medical therapy is increasingly vital. By acting at multiple stages of the cardiovascular disease pathway, bisoprolol not only provides symptomatic improvement but also delivers sustained cardioprotection—reaffirming its pivotal role in modern cardiovascular management.

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