# **Comparative National Prescriptive and Dosimetric Characteristics of Beta-Blocker Therapy in Asian Heart Failure Patients**

**Abstract.**

Contemporary evidence challenges established paradigms surrounding beta-blocker therapy in heart failure management, particularly among Asian populations. The accumulated data demonstrates that beta-blockers exhibit remarkable therapeutic efficacy across diverse heart failure phenotypes when dosing strategies account for population-specific pharmacokinetic properties. Regional prescription disparities—ranging from 61% adoption in Indonesia to 91% in Japan—belie the consistent mortality benefits observed throughout Asian cohorts. The pharmacogenetic distinctions between Asian and Western populations warrant substantive reconsideration of dosing protocols. Japanese patients achieve equivalent clinical outcomes at reduced doses compared to their Western counterparts, necessitating a departure from universal dosing standards. Safety profiles among Asian populations further support tailored therapeutic approaches. The reduced discontinuation rates and favorable adverse event profiles observed in Asian cohorts suggest that concerns regarding beta-blocker tolerability may be less pronounced when dosing strategies reflect population-specific characteristics. The absence of statistical differences in serious adverse events between various beta-blocker formulations provides clinicians with reasonable latitude in agent selection. The compatibility between beta-blockers and contemporary heart failure therapeutics, particularly SGLT2 inhibitors, presents opportunities for synergistic treatment approaches. Dapagliflozin maintains consistent efficacy irrespective of background beta-blocker utilization, suggesting these therapeutic modalities operate through complementary rather than competitive mechanisms. Such observations support combination therapy strategies that may yield superior outcomes compared to monotherapy approaches. Guideline discordance between major cardiology organizations reflects the evolving understanding of heart failure therapeutics, particularly in HFpEF management. Cardioselective beta-blockers demonstrate promise in Asian populations, especially when prescribed considerations account for comorbid conditions and left ventricular function. Future investigations should prioritize the refinement of population-specific dosing algorithms and combination therapy protocols, ultimately advancing precision medicine approaches that acknowledge both regional and individual patient characteristics in therapeutic decision-making.

**Keywords:** ventricular function, heart failure, beta-blocker tolerability, therapeutic approaches

**Introduction**

Beta-blocker therapy persists as a foundational intervention for heart failure management in Asia and around the world, with contemporary investigations demonstrating utilization rates of 83% across multiple national cohorts [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007). Interestingly, the therapeutic landscape reveals considerable heterogeneity in prescriptive practices, clinical effectiveness, and patient outcomes among distinct population groups. Clinical trial participants in the US commonly receive bisoprolol (30%), carvedilol (30%), or metoprolol (40%) for treatment durations averaging 27.54 weeks [[2]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11604132/). According to the National Institutes of Health (NIH), the mortality burden among heart failure patients in the US extends to 44.2% across comprehensive study populations, but no statistically significant differences emerge among the three primary beta-blocker classifications (p = 0.301) [[2]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11604132/). More compelling evidence surfaces when examining beta-blocker utilization through covariate-adjusted analytical frameworks, where these agents associate with reduced risk for primary composite outcomes (HR: 0.70; 95% CI: 0.60-0.83) [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007). The safety and efficacity of co-administration of beta-blockers with sodium glucose co-transporter 2 inhibitors (SGLT2) like dapagliflozin warrants careful examination. The DELIVER investigation, encompassing 6,263 patients with symptomatic heart failure and preserved ejection fraction (HFpEF), provides evidence that beta-blocker therapy does not augment the risk of worsening heart failure events, cardiovascular mortality, or deterioration in health-related quality of life measures [[3]](https://www.sciencedirect.com/science/article/pii/S2213177923006157). These observations challenge longstanding concerns regarding potential antagonistic interactions between beta-blockers and contemporary heart failure pharmacotherapy.

## **Prescriptive Patterns Among Asian Populations with HFmrEF and HFpEF**

Prescriptive practices for beta-blocker therapy across Asian territories exhibit marked heterogeneity, with substantive disparities in both adoption frequencies and dosing methodologies relative to Western therapeutic frameworks. Such regional variation necessitates systematic investigation to optimize treatment paradigms for heart failure patients presenting with mid-range ejection fraction (HFmrEF) and preserved ejection fraction (HFpEF) phenotypes. The ASIAN-HF registry data reveals pronounced geographic disparities in beta-blocker utilization throughout the region. Indonesia demonstrates the most conservative adoption patterns at 61% [[4]](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30306-1/fulltext), whereas Japan exhibits remarkably elevated usage frequencies approaching 91% [[4]](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30306-1/fulltext). Intermediate adoption patterns emerge across other territories—China reports 84.2% utilization among hospitalized HFrEF patients [[5]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11153617/), Southeast Asian nations demonstrate 70.2% overall usage [[6]](https://www.scienceopen.com/hosted-document?doi=10.15212/CVIA.2024.0026), and South Korea maintains prescription frequencies exceeding 65% [[4]](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30306-1/fulltext).

Economic stratification exerts considerable influence upon prescriptive behaviors. High-income territories including Singapore (71%), Hong Kong (70%), Korea (65%), and Japan (63%) demonstrate enhanced propensity for dual first-line therapeutic approaches combining ACE inhibitors or ARBs with beta-blockers compared to lower-income nations [[4]](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30306-1/fulltext). This economic stratification engenders treatment disparities with potential prognostic implications.

Regional heterogeneity extends beyond elementary prescription frequencies. Among HFpEF populations, where evidentiary support for beta-blocker efficacy remains less established, prescription rates nonetheless achieve 78.9% across Southeast Asian countries [6]. The DELIVER trial cohort indicates approximately 80% of HFmrEF and HFpEF patients receive beta-blockers [[3]](https://www.sciencedirect.com/science/article/pii/S2213177923006157), predominantly for comorbid conditions rather than heart failure management *per se*.

### **Carvedilol-Equivalent Dosing Strategies Among Asian Cohorts**

Carvedilol (37%), bisoprolol (30%), and metoprolol (11%) comprise the most frequently prescribed beta-blockers across Asian territories [[4]](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30306-1/fulltext). Administered dosages consistently fall below guideline recommendations, however. Median prescribed dosages across Asian cohorts achieve merely 25% of recommended targets, with 65% of patients receiving less than half the guideline-recommended dosage [[4]](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30306-1/fulltext). This pattern of reduced dosing may represent appropriate therapeutic strategy for Asian populations. Japanese patients demonstrate equivalent clinical effectiveness compared to American counterparts despite receiving lower carvedilol dosages [[7]](https://www.ahajournals.org/doi/10.1161/circ.146.suppl_1.13725). Initial carvedilol dosing in Japanese patients averages 4.3 mg daily compared to 14.5-19.1 mg daily among American patients, while one-year dosages average 11.2 mg daily versus 30.9-34.5 mg daily [[7]](https://www.ahajournals.org/doi/10.1161/circ.146.suppl_1.13725). Pharmacogenetic considerations have influenced regional guideline development. Japanese national guidelines recommend lower target dosages (20 mg daily) compared to American guidelines (50 mg daily) [[8]](https://pmc.ncbi.nlm.nih.gov/articles/PMC10919845/). Despite these reduced dosages, Japanese patients demonstrate comparable improvements in left ventricular ejection fraction and heart rate reduction [[7]](https://www.ahajournals.org/doi/10.1161/circ.146.suppl_1.13725). Asian patients appear to achieve clinical benefits at lower dosages while potentially minimizing adverse effects. Regional dosing heterogeneity extends beyond initial recommendations. Malaysia and Thailand administer the highest beta-blocker dosages throughout Asia, whereas Japan, despite elevated uptake (91%), maintains the lowest dosages with 41% of patients receiving less than 25% of guideline-recommended quantities [[4]](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30306-1/fulltext).

### **Alternative Therapeutic Indications: Hypertension, Coronary Disease, and Atrial Fibrillation**

Beta-blockers serve multiple therapeutic functions beyond heart failure management among Asian populations. ESC guidelines indicate 80% of HFpEF patients receive beta-blockers for indications other than frank heart failure [[9]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11802620/). Alternative therapeutic applications encompass:

1. **Coronary Artery Disease**: Beta-1 selective agents (atenolol, metoprolol, bisoprolol) reduce heart rate and blood pressure, diminishing myocardial oxygen demand and attenuating future myocardial infarction risk [[10]](https://bnrc.springeropen.com/articles/10.1186/s42269-024-01208-z).
2. **Hypertensive Management**: Beta-blockers maintain relevance as initial therapeutic options for hypertensive patients with cardiovascular comorbidities [[10]](https://bnrc.springeropen.com/articles/10.1186/s42269-024-01208-z), although their role as first-line therapy has diminished within contemporary guidelines.
3. **Atrial Fibrillation**: Beta-blockers facilitate heart rate regulation, reduce cardiac strain, and may contribute to thromboembolic prevention and stroke risk reduction [[10]](https://bnrc.springeropen.com/articles/10.1186/s42269-024-01208-z).

Given these multiple indications, beta-blocker utilization frequently persists regardless of heart failure classification. This practice aligns with emerging evidence suggesting potential benefits among HFpEF patients. One nationwide investigation identified statistically significant survival improvement following three years of beta-blocker therapy among HFpEF patients [[9]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11802620/), supporting continued utilization as guideline recommendations continue to evolve.

## **Mortality Reduction and Cardiovascular Event Prevention**

Contemporary investigations examining mortality outcomes provide evidence supporting beta-blocker utilization among Asian heart failure populations. Clinical trials demonstrate consistent benefits across multiple cardiovascular endpoints, with profound implications for therapeutic strategies within these populations. Beta-blocker therapy produces marked reductions in adverse outcomes among Asian heart failure patients across multiple investigational frameworks. The primary composite of worsening heart failure events or cardiovascular death correlates inversely with beta-blocker utilization, yielding a hazard ratio of 0.79 (95% CI: 0.68-0.92) [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007). After adjustment for baseline demographics and established prognostic variables, this protective effect persists with a hazard ratio of 0.70 (95% CI: 0.60-0.83) [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007). Peritoneal dialysis patients represent a particularly compelling cohort for beta-blocker investigation. Among this population, beta-blocker prescription associates with a 43% reduction in adjusted hazard ratio for heart failure death (95% CI: 0.36–0.89; p = 0.013) [[11]](https://pmc.ncbi.nlm.nih.gov/articles/PMC10913941/). Early beta-blocker administration yields even more dramatic results, reducing in-hospital composite endpoints by 58% (RR: 0.42; 95% CI: 0.30–0.58; p < 0.001) and in-hospital all-cause mortality by 57% (RR: 0.43; 95% CI: 0.31–0.61; p < 0.001) [[12]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11399533/). Non-cardioselective beta-blockers demonstrate superior mortality reduction in certain Asian cohorts, with cardiovascular mortality decreasing both in unadjusted models (HR: 0.36; 95% CI: 0.18–0.73; p = 0.004) and following statistical adjustment (HR: 0.37; 95% CI: 0.19–0.73; p = 0.005) [[13]](https://onlinelibrary.wiley.com/doi/10.1002/ehf2.13489). Competing risk analytical frameworks further substantiate beta-blocker benefits among Asian populations. When incorporating competing risk events, the hazard ratio for primary composite outcomes remains 0.68 (95% CI: 0.58-0.79) [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007). Patients receiving beta-blockers maintain a lower cumulative risk for heart failure-related mortality compared to non-users even after accounting for competing risk events (p = 0.007) [[11]](https://pmc.ncbi.nlm.nih.gov/articles/PMC10913941/). Regional heterogeneity within Asia reveals stark disparities in outcomes. Southeast Asian patients experience higher risk profiles, with death or hospitalization rates reaching 25.4% (345 per 1000 person-years) compared to 4.5% (55 per 1000 person-years) among South Asian populations (p < 0.001) [[14]](https://onlinelibrary.wiley.com/doi/full/10.1002/ejhf.1227). Ethnic stratification demonstrates that Malay patients face worse outcomes relative to Chinese patients (HR 2.13, 95% CI 1.34–3.37) [[14]](https://onlinelibrary.wiley.com/doi/full/10.1002/ejhf.1227).

Beta-blocker therapy extends beyond mortality benefits to encompass total heart failure event reduction among Asian populations. Patients receiving beta-blockers demonstrate reduced risk for heart failure events, cardiovascular death, and total heart failure events across crude, covariate-adjusted, and propensity score–based analytical models [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007). Cumulative survival probabilities illustrate these benefits with striking clarity:

* Beta-blocker users: 89.7% survival at 3 years, 86.5% at 5 years
* Non-users: 77.4% survival at 3 years, 75.3% at 5 years [[11]](https://pmc.ncbi.nlm.nih.gov/articles/PMC10913941/)

The relationship between beta-blocker benefits and left ventricular ejection fraction (LVEF) merits particular attention. Beta-blocker associations with clinical outcomes demonstrate consistency regardless of LVEF categorization (LVEF ≤49% versus ≥50%), with interaction p-values exceeding 0.47 [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007). This finding suggests that beta-blocker benefits transcend traditional heart failure classifications, providing therapeutic value across the spectrum of ventricular dysfunction.

## **SGLT2 Inhibitors and Beta-Blocker Combination Therapy**

SGLT2 inhibitors like dapagliflozin represent a contemporary pharmaceutical development constructed to address metabolic and cardiovascular pathophysiology through novel mechanisms. The interaction between these agents and established beta-blocker therapy demands rigorous examination, particularly when considering potential synergistic effects or therapeutic conflicts in Asian patient populations. The DELIVER trial, comprising 6,263 patients with heart failure and left ventricular ejection fraction exceeding 40%, furnishes essential data regarding combination therapeutic strategies. Among study participants, 83% received concurrent beta-blocker therapy, with notable regional variations [[15]](https://pubmed.ncbi.nlm.nih.gov/37767674/). Dapagliflozin demonstrated consistent therapeutic efficacy irrespective of simultaneous beta-blocker utilization. The primary composite endpoint of cardiovascular death or worsening heart failure showed comparable reduction in patients receiving beta-blockers (HR: 0.82; 95% CI: 0.72-0.94) and those without beta-blocker therapy (HR: 0.79; 95% CI: 0.61-1.03) [[15]](https://pubmed.ncbi.nlm.nih.gov/37767674/). The interaction p-value of 0.85 substantiates the statistical consistency of these benefits across both therapeutic groups [[15]](https://pubmed.ncbi.nlm.nih.gov/37767674/). Beta-blocker therapy is associated with diminished risk for the composite outcome (adjusted HR: 0.70; 95% CI: 0.60-0.83) [[16]](https://www.thecardiologyadvisor.com/news/%CE%B2-blocker-use-does-not-affect-dapagliflozin-safety-or-efficacy-in-hfpef-or-hfmref/), suggesting these pharmaceutical interventions operate through complementary rather than competing mechanisms.

The Kansas City Cardiomyopathy Questionnaire (KCCQ) assessments revealed improvements with dapagliflozin therapy independent of background beta-blocker status. At 8 months, multiple domains demonstrated statistically significant enhancements at the 0.01 confidence level:

1. Total Symptom Score: 2.4-point improvement versus placebo (p<0.001)
2. Physical Limitations Score: 1.9-point improvement versus placebo (p<0.001)
3. Clinical Summary Score: 2.3-point improvement versus placebo (p<0.001)
4. Overall Summary Score: 2.1-point improvement versus placebo (p<0.001) [[17]](https://www.jacc.org/doi/10.1016/j.jacc.2022.11.006)

These improvements emerged within one month and amplified throughout the observation period [[17]](https://www.jacc.org/doi/10.1016/j.jacc.2022.11.006). A greater proportion of patients receiving dapagliflozin achieved clinically meaningful KCCQ improvements regardless of concurrent beta-blocker therapy [[17]](https://www.jacc.org/doi/10.1016/j.jacc.2022.11.006).

Safety analyses reveal no reported pharmacodynamic interference between beta-blockers and dapagliflozin. The DAPA-HF investigation demonstrated that dapagliflozin reduced the combined risk of cardiovascular death and heart failure hospitalization by 26%, with cardiovascular mortality alone declining by 18%—benefits that remained unaffected by concomitant beta-blocker utilization [[18]](https://pmc.ncbi.nlm.nih.gov/articles/PMC7327531/). Adverse events were equally prevalent in dapagliflozin and placebo groups irrespective of background beta-blocker therapy (all interaction p-values ≥0.07) [[16]](https://www.thecardiologyadvisor.com/news/%CE%B2-blocker-use-does-not-affect-dapagliflozin-safety-or-efficacy-in-hfpef-or-hfmref/). Comprehensive safety assessments revealed no significant differences at the 0.05 confidence level between treatment groups regarding serious adverse events, volume depletion symptoms, acute kidney injury, or hyperkalemia rates [[19]](https://pmc.ncbi.nlm.nih.gov/articles/PMC9301591/). Although tentative, this evidence supports further research into the clinical efficacy of co-administration of beta-blockers and SLGT2 inhibitors heart failure management in Asian populations.

## **Safety Profiles and Adverse Event Patterns Among Asian Heart Failure Patients**

Safety evaluation of beta-blocker therapy among Asian populations demonstrates distinctive adverse event profiles that merit careful consideration. These patterns inform clinical decision-making processes and provide essential context for treatment optimization. Bradycardia and hypotension constitute the predominant adverse reactions associated with beta-blocker therapy, totaling 3,778 and 3,264 reported cases respectively across different agents [[20]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11566443/). The distribution of bradycardia incidence reveals marked variation by specific drug type. Metoprolol accounts for the highest proportion (29.9%) of bradycardia cases [[20]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11566443/). Bisoprolol emerges as the second most frequent contributor to bradycardia (23.9%), while carvedilol occupies second position for both hypotension and dizziness manifestations at 18.6% and 26.3% respectively [[20]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11566443/). Clinical experience demonstrates bradycardia incidence ranging from 0.4% to 12% among beta-blocker recipients, contrasted with 0-5% in placebo cohorts [[21]](https://pmc.ncbi.nlm.nih.gov/articles/PMC5122500/). Notably, asymptomatic bradycardia during treatment typically does not warrant therapeutic discontinuation according to randomized controlled trial evidence [[21]](https://pmc.ncbi.nlm.nih.gov/articles/PMC5122500/). This finding suggests that heart rate reduction alone should not prompt treatment cessation without accompanying symptomatic manifestations. Japanese clinical investigations reveal superior titration success rates for bisoprolol, with 90.3% of patients achieving maintenance dosing compared to 85.7% for carvedilol [[22]](https://pubmed.ncbi.nlm.nih.gov/23559359/). More striking is the observation that Japanese patients exhibited substantially lower discontinuation and dose reduction rates relative to United States populations, with a relative rate of 0.406 (0.086 vs. 0.212, 95% CI: 0.181 to 0.911, p = 0.035) [[8]](https://pmc.ncbi.nlm.nih.gov/articles/PMC10919845/). Discontinuation patterns differ according to specific agent characteristics. Bisoprolol discontinuation occurred in 2.6% of cases, predominantly attributed to hypotensive episodes, while dose modifications were necessary in 18.4% of patients [[8]](https://pmc.ncbi.nlm.nih.gov/articles/PMC10919845/). Carvedilol presented a contrasting profile, requiring dose reductions in merely 2.2% of cases, primarily due to bradycardia and hypertensive heart disease complications [[8]](https://pmc.ncbi.nlm.nih.gov/articles/PMC10919845/). The absence of marked differences in serious adverse events between beta-blocker types among Asian populations represents a crucial clinical finding. Event-free survival rates for the composite outcome of cardiovascular death or heart failure hospitalizations reached 92.4% with bisoprolol and 94.7% with carvedilol—a statistically insignificant difference at the 0.05 confidence level [[22]](https://pubmed.ncbi.nlm.nih.gov/23559359/). Hospital-based adverse events, including bradyarrhythmias and hypotensive episodes, demonstrated no significant differences between early beta-blocker administration and control groups (RR: 0.75; 95% CI 0.52–1.09; p = 0.13) [[12]](https://pmc.ncbi.nlm.nih.gov/articles/PMC11399533/). Treatment discontinuation rates remained comparable with concurrent dapagliflozin therapy regardless of beta-blocker utilization [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007).

## **Guideline Discordance and the Pursuit of Individualized Therapy**

Contemporary guideline recommendations for beta-blocker therapy demonstrate profound inconsistencies across major cardiology organizations, a situation that demands judicious clinical interpretation rather than blind adherence. The European Society of Cardiology (ESC) and American Heart Association/American College of Cardiology/Heart Failure Society of America (AHA/ACC/HFSA) present starkly divergent approaches to HFpEF management. The AHA/ACC/HFSA guidelines explicitly discourage beta-blocker utilization for HFpEF treatment [[1]](https://www.jacc.org/doi/10.1016/j.jchf.2023.09.007), yet paradoxically endorse these agents for HFmrEF patients based upon meta-analytical evidence demonstrating reduced cardiovascular mortality [[23]](https://www.sciencedirect.com/science/article/pii/S2666602221000513). The ESC guidelines, perhaps more honestly, offer no definitive recommendations regarding beta-blocker therapy for HFpEF [[24]](https://www.acc.org/Latest-in-Cardiology/ten-points-to-remember/2024/04/16/15/08/contemporary-american-and-european). This regulatory ambiguity is troublesome given the body of evidence supporting beta-blocker efficacy across the heart failure spectrum. The reluctance to provide clear guidance likely stems from the heterogeneous nature of HFpEF itself—a syndrome encompassing diverse pathophysiological mechanisms that resist uniform therapeutic approaches.

### Cardioselective beta-blockers demonstrate markedly superior clinical outcomes compared to non-selective agents in Asian populations. Rigorous investigations reveal that cardioselective formulations associate with reduced all-cause mortality (HR: 0.93; 95% CI: 0.89-0.96), major adverse cardiovascular events (HR: 0.96; 95% CI: 0.93-0.998), heart failure hospitalizations (HR: 0.84; 95% CI: 0.78-0.91), and pulmonary complications (HR: 0.94; 95% CI: 0.90-0.98) [[25]](https://pubmed.ncbi.nlm.nih.gov/35135688/). This therapeutic advantage derives from beta-1 selectivity, which circumvents bronchospasm risk among patients with concurrent respiratory conditions [[26]](https://www.sciencedirect.com/science/article/pii/S0025619621006224). Treatment individualization based upon patient-specific comorbidity profiles yields optimal clinical outcomes [[27]](https://www.jacc.org/doi/10.1016/j.jchf.2021.06.011). Several key considerations merit emphasis:

1. Chronic Obstructive Pulmonary Disease: Beta-1 selective agents (bisoprolol, metoprolol, nebivolol) prevent exacerbation of respiratory symptoms while preserving cardiovascular benefits [[28]](https://pmc.ncbi.nlm.nih.gov/articles/PMC8468030/).
2. Diabetes Mellitus: Carvedilol and bisoprolol warrant preference given their neutral effects upon glycemic control profiles [[28]](https://pmc.ncbi.nlm.nih.gov/articles/PMC8468030/).
3. Atrial Fibrillation: Despite conflicting evidence from randomized trials, real-world observational data suggests prognostic advantages independent of rhythm status [[28]](https://pmc.ncbi.nlm.nih.gov/articles/PMC8468030/).

The complexity of these considerations underscores why algorithmic approaches to beta-blocker selection often prove inadequate. Clinical judgment, informed by population-specific evidence and individual patient characteristics, remains paramount.

## **References**

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