

# Are $\beta$ -blockers Contraindicated in Patients with Congestive Heart Failure?

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Since 1970s, usage of  $\beta$ -blockers in treatment of patients with heart failure was recommended by several investigators but the fact that it reduces myocardial contractility, precluded their use. The past decade has shown significant improvement in the understanding of heart failure, shifting from a hemodynamic to a neurohormonal basis.<sup>1</sup>

Recent primary evidence from randomized clinical trials has demonstrated a significant benefit to patients with heart failure when  $\beta$ -blockers therapy is added to standard therapy.<sup>2</sup> While it is known that  $\beta$ -blockers do not cause overt heart failure, a large proportion of clinical heart failure is diastolic dysfunction, nearly 30-40%, which is improved by  $\beta$ -blocker therapy.<sup>3</sup>

The rationale for their use in heart failure is that the concentration of circulating catecholamines is increased in patients with congestive heart failure (CHF). Thus, constant adrenergic stimulation can adversely affect cardiac myocytes.  $\beta$ -blockers improve left ventricular systolic function, in the long run regress myocardial hypertrophy and normalization of ventricular shape can occur through a 'reverse remodeling effect'.<sup>1</sup> They also reduce oxygen demand and produce bradycardia,<sup>4</sup> which restores contractility in left ventricular dysfunction.

When patients are treated with  $\beta$ -blockers postmyocardial infarction, mortality is lower amongst those who begin with a low ejection fraction.<sup>5</sup> In patients who had previous heart failure, the incidence of sudden cardiac death is significantly lower with  $\beta$ -blockers and overall mortality is considerably reduced.<sup>6</sup> A recent meta-analysis showed that  $\beta$ -blockers reduce all-cause mortality in CHF patients by 29%. Studies like the Randomized Evaluation of Strategies for Left Ventricular Dysfunction (RESOLVD) pilot study have shown metoprolol-induced neurohormonal modifications by decreasing renin and angiotensin II

concentrations. Their effect on exercise capacity and quality-of-life is not convincing. US Carvedilol Program, Cardiac Insufficiency Bisoprolol Study 2 (CIBIS-2) and Metoprolol CR/XL Randomized Intervention Trial in Chronic Heart Failure (MERIT-HF) testing carvedilol, bisoprolol and metoprolol, respectively, impressively established the fact that  $\beta$ -blockers in heart failure have reduced sudden death and total mortality, and led to decrease in hospitalization rate.<sup>1</sup>

Carvedilol was the first  $\beta$ -blocker to be approved by US FDA (Food and Drug Administration) in 1997 for treatment of heart failure. Carvedilol Prospective Cumulative Survival (COPERNICUS) trial demonstrated 35% reduction in mortality by carvedilol versus placebo in patients with severe heart failure.<sup>7</sup> Carvedilol reduced sudden death in patients with symptomatic heart failure and impaired left ventricular functions. It also has a vasoactive profile, increases vasodilatation in peripheries and high compliance, thus, reducing the occurrence of cold hands and feet among patients treated for heart failure.<sup>8</sup>

Hence,  $\beta$ -blockers are indicated in patients with chronic stable mild-to-moderate symptomatic heart failure (New York Heart Association [NYHA] functional class II and III) with depressed left ventricular function.<sup>1</sup> Bisoprolol can be used effectively at the maximum recommended doses for outpatient treatment of heart failure. It significantly improves functional status, quality-of-life and ejection fraction.<sup>9</sup> Carvedilol or Metoprolol European Trial (COMET) was initiated to evaluate effects of carvedilol and metoprolol on mortality in patients with CHF.<sup>7</sup>

In conclusion, it can be said that  $\beta$ -blockers are a heterogeneous group with regard to efficacy, safety profile, tolerability and ancillary properties. Hence, optimal selection and use of agents with better reverse remodeling effects and peripheral vasodilatation in the cardiovascular continuum will assist in providing improved management.<sup>10</sup> Though once contraindicated,  $\beta$ -blockers are now an evidence-based recommendation for the treatment of heart failure.<sup>1</sup>

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# Make sure

## DURING MEDICAL PRACTICE

**SITUATION:** An elderly patient with isolated systolic hypertension developed stroke.



**LESSON:** Make sure to remember that as per the Study on Cognition and Prognosis in the Elderly (SCOPE) trial, in elderly patients with isolated systolic hypertension, antihypertensive treatment based on candesartan resulted in a significant 42% relative risk reduction in stroke in comparison with other antihypertensive treatment, despite little difference in BP reduction.

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