

## Beta-adrenergic receptor blockade in congestive heart failure

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Both basic and clinical experiences in congestive heart failure have established that protracted sympathoadrenal activation over time adversely affects pathophysiology and survival in patients with heart failure. In this regard, beta-adrenergic receptor blockers are accepted as a powerful tool for the management of such patients in addition to renin-angiotensin-aldosterone blockade. Clinical trials on beta-blockers have established that such agents are useful in prolonging life expectancy in overall population of mild to moderate congestive heart failure. However, several controversial issues remain to be answered. One of the greatest concerns is which beta-blocker to be used. It is likely that carvedilol exerts a more potent antiadrenergic effect during stress than metoprolol, since metoprolol but not carvedilol elicits up-regulation of adrenergic receptors. Recently published clinical trial on head-to-head comparison between metoprolol and carvedilol has shown that carvedilol is more efficacious in prolonging life in patients with congestive heart failure. Another concern is introduction of beta-adrenergic blockade in patients with severe congestive heart failure, in whom considerable number of such population are not tolerant to the inherent negative inotropic effect. Inverse agonism, an agonist-independent receptor inactivation effect, may play a pivotal role in mediating such adverse events during introduction of beta-blockers. Finally, therapeutic strategy in patients who exhibit worsening heart failure under the treatment with beta-adrenergic blockers is also controversial. It would be preferred that phosphodiesterase inhibitors or adenylyl cyclase activators are temporarily used under the treatment with beta-blockers, if circulatory failure is not serious.