

## Atrial Fibrillation and Sepsis: A Life-Threatening Combination



Almost half of the patients with sepsis suffer from myocardial depression and a reduced ejection fraction. Sepsis can also cause changes in circulating volume, vascular tone, and coronary blood flow, all of which affect heart function and heart rate. Serum catecholamine levels and direct measurements of renal sympathetic nerve activity have shown that severe infection activates the sympathetic nervous system. This activation can trigger supraventricular tachyarrhythmias in the presence of a severe infection. Tachyarrhythmias were particularly noticeable in patients with COVID-19.

Tachycardia and atrial fibrillation are predictive key factors for sepsis. Tachycardias of more than 100 beats per minute when admitted to an intensive care unit are a risk factor for a deterioration in the prognosis. In addition, lowering the heart rate to less than 95 beats per minute or decreasing the heart rate within 24 hours of onset is significantly associated with an improved prognosis. Therefore, tachyarrhythmias should be treated with appropriate therapy.

## Beta-Blocker for the Treatment of Tachyarrhythmias in Septic Shock Patients

Although hydration and vasopressor administration improve hemodynamic factors, they also increase the levels of circulating norepinephrine and epinephrine in serum, which increase sympathetic activity, which in turn leads to sympathetic activation of the heart and increased heart rate. The administration of short-acting cardio-selective beta-blockers could therefore help to prevent or reverse the effects on the sympathetic nervous system, and is widely used today for the treatment of various cardiovascular diseases. The use of beta-blockers to treat arrhythmias in patients with septic shock has also been successfully initiated in view of their anti-arrhythmic and anti-inflammatory effects.

Landiolol, an ultra-short-acting beta-adrenergic receptor antagonist, is often used to treat atrial fibrillation and atrial flutter in critically ill patients who are admitted to an intensive care unit, and to treat peri-operative tachyarrhythmias. In addition, landiolol is approved in Japan for the treatment of ventricular fibrillation. Evidence already supported the use of landiolol to treat sepsis-related tachyarrhythmias in case reports, retrospective studies, and animal studies. These studies provided compelling evidence that landiolol can lower the heart rate in patients with sepsis. Now the results of a randomized controlled prospective phase 2/3 study confirming the effectiveness and safety of landiolol in the treatment of sepsis-related tachyarrhythmia are also available, the effects of landiolol on heart rate, mortality and safety in patients with sepsis conditional tachyarrhythmias, including atrial fibrillation, atrial flutter and sinus tachycardia, compared to patients receiving conventional therapy.

This study, which was recently published in the renowned journal *Lancet Respiratory*, showed that significantly more patients with sepsis-related tachyarrhythmias reached a heart rate of 60-94 beats per minute within 24 hours with landiolol. It is important to mention that the blood pressure profiles of the patients in the landiolol arm did not differ from those in the control arm, the proof that a rapid reduction in heart rate can be achieved with landiolol without having to accept a drop in blood pressure. Other important results of the study were the significantly less frequent occurrence of new-onset atrial fibrillation at day 7 with landiolol, shorter ICU and hospital stays, in addition to a clinically relevant lower mortality rate with landiolol at day 28 (12% versus 20%).

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