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Antibiotic Resistance

Short Acting Beta-Blockers in Critically Ill Patients With Heart Failure

An overview of the clinical evidence demonstrating the effectiveness of landiolol for the treatment of atrial fibrillation or atrial flutter with heart failure and effective heart rate control during arrhythmias.

Supraventricular arrhythmias (SVTs) are common in post-operative and cardiac ICUs. SVTs increase the risk of death as well as the risk of neurological sequelae. Some common risk factors for atrial fibrillation (AF) include age, male sex, history of arrhythmias, hypertension, post-operative atrial pacing, post-operative pneumonia and mechanical ventilation for more than 24 hours. In addition, patients in the ICU often have underlying heart disease. This increases their risk for cardiac arrhythmias (Annane et al. 2008).

Epidemiology data from 26 French ICUs shows that 12% of patients developed arrhythmias. 8% developed supraventricular arrhythmias, and little more than 2% developed ventricular arrhythmias. Among the critically ill patients, 2% also developed conduction abnormalities with low heart rate. Patients with no arrhythmias had a mortality rate of 17%, compared to patients that developed supraventricular tachycardia, who had a mortality of nearly 30%. Patients with ventricular arrhythmias had very high mortality of 73%. The study also reported some hypoxic brain injury in patients with ventricular tachycardia and strokes in patients with supraventricular tachycardia (Annane et al. 2008).

AF and acute heart failure (AHF) often co-exist, leading to increased morbidity and mortality. The development of AF in HF can be due to multiple factors. AF induces electrical and haemdoydnamic deterioration and causes tachycardia-mediated cardiomyopathy. The presence of AF can increase the likelihood of HF. At the same time, AHF is one of the strongest risk factors for AF.

Studies show that AF is present in approximately 35% of patients with AHF. There are several clinical scenarios of AF with AHF. In some cases, AF is the only predominant trigger for AHF. In other cases, AF is the consequence of AHF. Sometimes, AF is an innocent bystander in AHF. The goal, in every clinical situation, should be to identify AF and AHF and treat it (Halvorsen et al. 2020).

> **landiolol can treat acute disorders, including supraventricular tachycardia, and is indicated for the rapid control of ventricular rate in patients with atrial fibrillation or atrial flutter in perioperative, postoperative, or other circumstances where short-term control of the ventricular rate with a short acting agent is desirable**

According to the 2020 ESC Guidelines for the diagnosis and management of AF, beta-blockers are the first-line rate-controlling agents based on better acute rate control. Digoxin is not effective in patients with increased sympathetic drive, and studies have associated the use of digoxin with excess mortality in AF patients. Therefore, beta blockers are preferred over digoxin in acute settings because of their rapid onset of action and effectiveness (Hindricks et al. 2021).

Landiolol in Acute Decompensated Heart Failure Due to Atrial Fibrillation

AF and atrial flutter (AFL) are especially common in patients with left ventricular (LV) dysfunction. Landiolol is an ultra-short-acting β-blocker that selectively binds to β1 receptors. It is metabolised in the blood and liver and has a short half-life of approximately 4 minutes. The drug has been shown to be useful for treating several acute disorders, including arrhythmias in critical conditions (Nagai et al. 2013).

The J-Land study compared the efficacy and safety of landiolol with digoxin for the control of tachycardia in AF/AFL in patients with LV dysfunction. The study included two hundred patients with atrial fibrillation or atrial flutter. Findings showed that continuous intravenous administration of landiolol effectively controlled rapid heart rate in patients with AF/AFL and LV dysfunction. Landiolol was effective in 48% of the patients, while digoxin was effective in 13.9% of patients. These results show that landiolol was more useful than slow-acting digoxin. Landiolol reaches a steady state rapidly and has a half-life of 4min; therefore, the risk of hypotension is low because its dose can be adjusted according to the patient's condition (Nagai et al. 2013).

Another study evaluated the clinical usefulness of landiolol for rapid AF in patients with acute decompensated heart failure (ADHF) with reduced ejection fraction (HFrEF). Study findings show that landiolol was

safe and effective in decreasing heart rate in these patients. Landiolol has a minimum negative inotropic effect. Treatment with landiolol has been shown to be beneficial in terms of heart rate reduction (Iwahashi et al. 2019).

Furthermore, an AF-CHF landiolol survey also reported the safety and effectiveness of landiolol when it was used for the treatment of AF or atrial flutter with heart failure. No safety concerns were reported, and most patients achieved effective heart rate control after treatment (Yamashita et al. 2019).

In another study, the researchers investigated whether landiolol could effectively control heart rate in septic patients with supraventricular tachyarrhythmias. Findings showed a substantial reduction in heart rate in the landiolol group compared to the control group, and there was no deterioration of haemodynamics. In addition, the conversion to sinus rhythm was observed more frequently in the landiolol group than in the control group (Okajima et al. 2015).

There is an ongoing trial of landiolol in sepsis patients (LANDI-SEP trial) which recently finished enrollment. Study patients have AF and/or tachycardia in sinus rhythm. Results are expected soon (Unger et al. 2018).

Another study demonstrated the benefit of using a low-dose β1-blocker in combination with milrinone. The combination rapidly improved the cardiac function of ADHF patients with tachycardia, and the addition of low-dose landiolol eliminated pulsus alternans. Landiolol with milrinone improved cardiac function through the slowing of the heart rate. In addition, the cardioprotective effect of the β-blocker improved haemodynamics. Therefore, the addition of low-dose β-blockers like landiolol may be an effective cardioprotective therapy in patients with ADHF (Kobayashi et al. 2012).

The above clinical evidence demonstrates that landiolol should be the gold standard for rapidly lowering heart rhythm. It has a better pharmacokinetic and pharmacodynamic profile. It also has a very good safety profile to slow heart rate with no negative inotropic effect. In addition, there is a long range of adjustable dosages. ■

Key Points

- Ultrashort-acting ß-blockers, such as landiolol, can rapidly control heart rate.
- The effectiveness of landiolol has been comprehensively assessed and proven in atrial fibrillation/atrial flutter patients with heart failure.
- The safety of landiolol has been shown to be acceptable without any major concerns.
- Most patients with arrhythmias treated with landiolol achieved effective heart rate control.

Disclaimer

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References

Annane D, Sébille V, Duboc D et al. (2008) Incidence and prognosis of sustained arrhythmias in critically ill patients. Am J Respir Crit Care Med. 178(1):20-5.

Halvorsen S, Kudaiberdieva G, Bueno H et al. (2020) Atrial fibrillation in acute heart failure: A position statement from the Acute Cardiovascular Care Association and European Heart Rhythm Association of the European Society of Cardiology. European Heart Journal: Acute Cardiovascular Care.

Hindricks G, Potpara T, Dagres N et al. (2021) 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 42(5):373-498.

Iwahashi N, Takahashi H, Abe T et al. (2019) Urgent Control of Rapid Atrial Fibrillation by Landiolol in Patients With Acute Decompensated Heart Failure With Severely Reduced Ejection Fraction. Circ Rep. 1(10):422-430.

Kobayashi S, Susa T, Tanaka T et al. (2012) Low-dose ß-blocker in combination with milrinone safely improves cardiac function and eliminates pulsus alternans in patients with acute decompensated heart failure. Circ J. 76(7):1646-53.

Nagai R, Kinugawa K, Inoue H et al. (2013) Urgent management of rapid heart rate in patients with atrial fibrillation/flutter and left ventricular dysfunction: comparison of the ultra-short-acting ß1-selective blocker landiolol with digoxin (J-Land Study). Circ J. 77(4):908-16.

Okajima M, Takamura M, Taniguchi T (2015) Landiolol, an ultra-short-acting ß1-blocker, is useful for managing supraventricular tachyarrhythmias in sepsis. World J Crit Care Med. 4;4(3):251-7.

Unger M, Morelli A, Singer M et al. (2018) Landiolol in patients with septic shock resident in an intensive care unit (LANDI-SEP): study protocol for a randomized controlled trial. Trials. 19(1):637.

Yamashita T, Nakasu Y, Mizutani H, Sumitani K (2019) A prospective observational survey on landiolol in atrial fibrillation/atrial flutter patients with chronic heart failure - AF-CHF landiolol survey. J Cardiol. 74(5):418-425.

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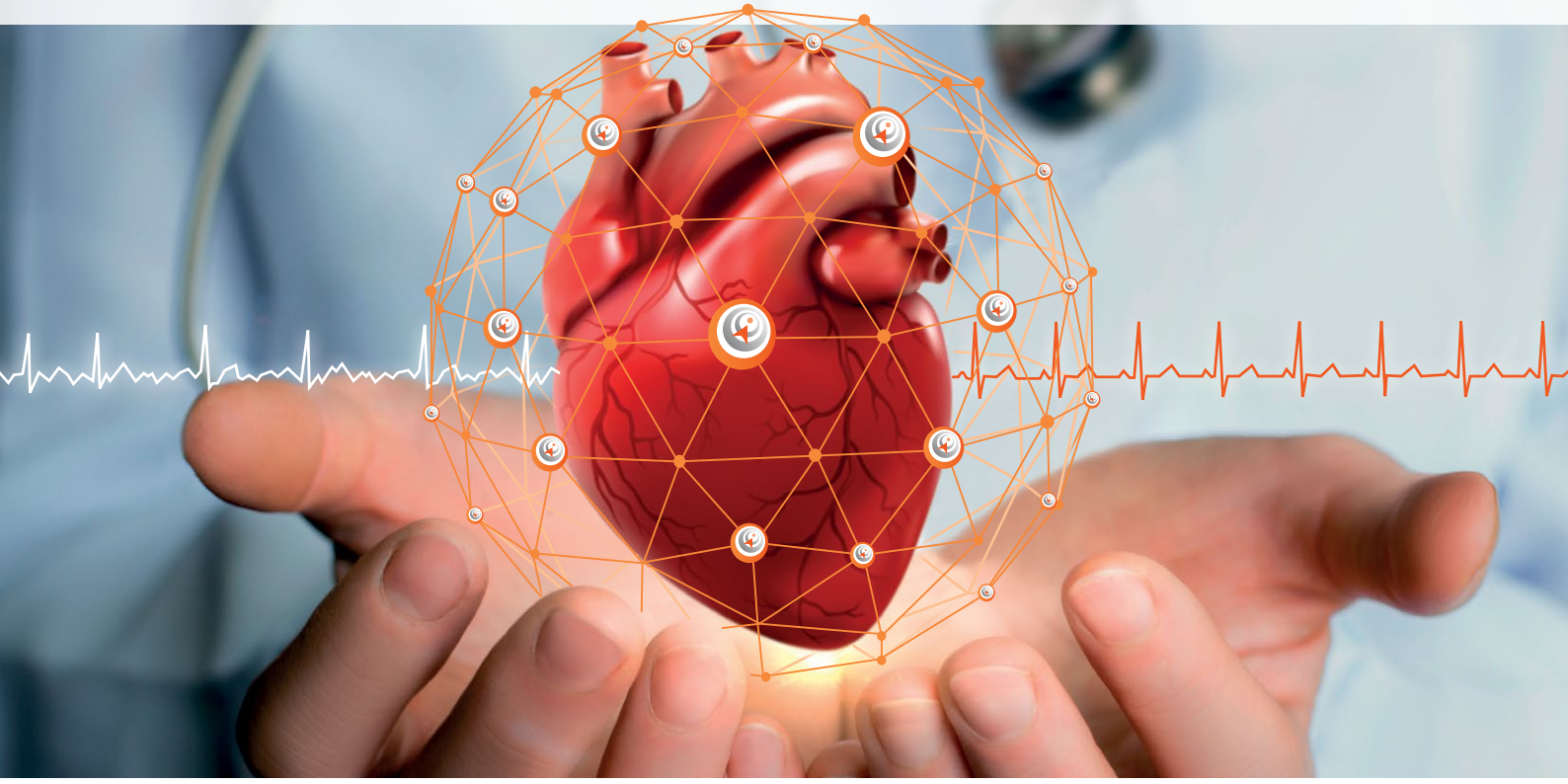
Rapid Rate Control with Myocardial Protection.[1]



Rapid control of ventricular rate in patients with SVTs and AF[1]

First-line for patients with cardiac dysfunction[2]

- **Limited effect** on blood pressure and inotropy[3]
- **Favourable safety profile for patients with renal and hepatic comorbidities** due to inactive metabolites and hydrolysis by plasma esterases[1,4]
- **Compatible with pulmonary disorder patients** due to highest cardioselectivity (β1/β2-selectivity = 255:1) among β1-blockers[5]
- **Limited rebound and tolerance effect** due to lack of pharmacochaperoning activity[6]

1 Summary of Rapibloc® Product Characteristics, current version. – **2** Hindriks G., et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). European Heart Journal (2020) 00, 1-126. – **3** Shibata et al. Direct Effects of Esmolol and Landiolol on Cardiac Function, Coronary Vasoactivity, and Ventricular Electrophysiology in Guinea-Pig Hearts. J Pharmacol Sci 118, 255 – 265 (2012). – **4** Yokoyama H. (2016) Stabilization in Off-Pump Coronary Artety Bypass. Springer Tokyo Heidelberg New York Dordrecht London © Springer Japan. – **5** European Heart Journal Supplements (2018) 20 (Supplement A), A1-A24. – **6** Nasrollahi-Shirazi S et al. Comparison of the b-adrenergic receptor antagonists landiolol and esmolol: receptor selectivity, partial agonism, and pharmacochaperoning actions. J Pharmacol Exp Ther 2016; 359:73–81

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