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# Case Series Review on Landiolol in Acute Decompensated Heart Failure Secondary to Tachyarrhythmias

*New Drug Applications for an Unmet Medical Need in Critically Ill Patients*

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**Research Letter**

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## Abstract

**Introduction:** Landiolol (Rapibloc, AOP Orphan Pharmaceuticals, Vienna, Austria) is an ultra-short-acting beta-blocker that has a half-life of 2.3–4 min. Landiolol has been used safely and successfully in patients with septic shock and atrial fibrillation and in sepsis-induced tachycardia.

Current evidence regarding the possible application of Landiolol in ADHF (Acute Decompensated Heart Failure) is very limited and confined to case reports.

**Methods:** We reviewed the case reports of the literature of ADHF patients treated off-label with Landiolol.

Only 11 clinical cases of Landiolol administration in ADHF were identified and reviewed in the present research.

Results and conclusions: In 11 clinically complex patients affected by ADHF, the administration of Landiolol was found to be safe and effective and favoured the restoration of a normo-frequent sinus rhythm with an improved pressure profile.

The potential therapeutic effect of Landiolol in patients with acute heart failure is under study.

New clinical uses and further clinical trials led by cardiologists and intensivists will be needed to prove the safety and efficacy of this drug.

**Keywords:** Landiolol; Acute Heart Failure; Sepsis-Induced Cardiac Dysfunction; Tachyarrhythmias.

## Introduction:

Landiolol is a recently innovated ultra-short-acting, highly adjustable and easily titratable β1-blocker. Landiolol hydrochloride has a β1/β2 ratio of 255 and, compared to propranolol, its β1-selectivity is 74–380 times greater while it has a 33–263 times greater β1 affinity than esmolol [1,2].

Landiolol is the only beta-blocker with a specific dose recommendation for patients with cardiac dysfunction and acute atrial fibrillation (Class I recommendation according to the ESC guidelines) [3].

Like other β-blockers, Landiolol is thought to reduce the sympathetic drive and decrease the spontaneous firing of ectopic pacemakers with antiarrhythmic and anti-ischemic effects.

In contrast to esmolol, Landiolol neither blocks Na, Ca and K channels nor decreases plasma renin levels and thus exerts less effect on left ventricular function and blood pressure. In clinical trials, Landiolol reduced heart rate within 1–6 min of administration to patients with tachyarrhythmia during or after surgery, as well as in non-perioperative settings [4].

Landiolol has a shorter elimination half-life than any other beta-blocker, and it can be administered safely to patients with various tachyarrhythmias [5]. The short duration of action and titratability of Landiolol makes it ideal for use in critically ill patients, especially in elderly patients with Sepsis-induced cardiogenic shock.

From the pathophysiological standpoint, the concept of

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"inappropriate tachycardia" is emerging which worsens the outcome of septic shock patients by increasing myocardial workload and oxygen demand.

The presence of a continuous rapid ventricular response can induce left ventricular systolic dysfunction (i.e. tachycardia-induced cardiomyopathy). Furthermore, the takeover of atrial fibrillation with rapid ventricular response further impairs left ventricular filling through loss of active atrial contraction and shortening of diastole, leading to hypotension, which can in turn lead to patient discomfort and organ dysfunction [6].

**Purpose of the Study and Methods:**

We conducted a review of case reports in the literature on the administration of Landiolol in critically ill patients with acute decompensated heart failure (ADHF) secondary to tachyarrhythmias.

Due to off-label use, only 11 case reports/case series have been identified in this clinical setting.

11 cases have been identified [7,8,9,10,11] and all available data are reported in table 1. In addition to the clinical anamnestic data (Figure 1), a plot with the variations of the hemodynamic parameters over time is reported in figure 1. The heart rate and systolic pressure values e before and after the administration of Landiolol were plotted in the same summary in figure 1.

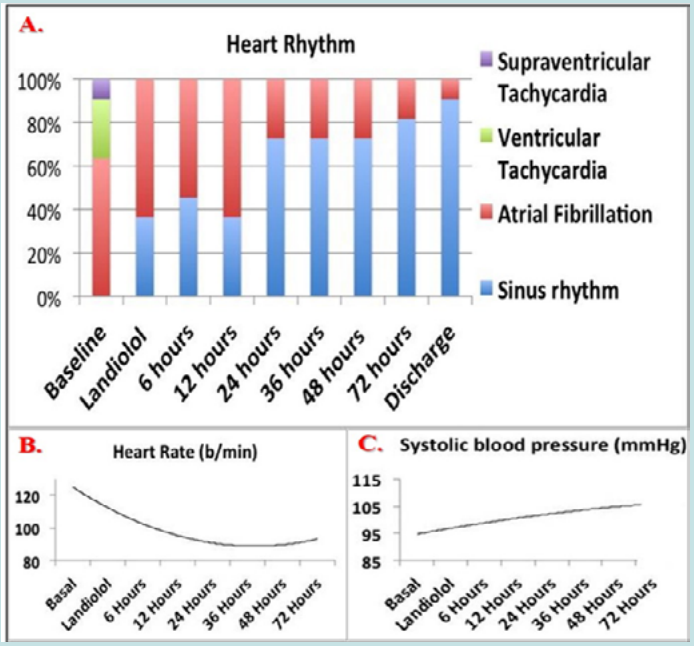


**Figure 1:** Hemodynamic trend of patients included in the case series review. Panel A: Arrhythmic profile over time and restoration of sinus rhythm. Box B: frequency trend line at baseline and after Landiolol infusion. Box C: trend line of systolic blood pressure over time (baseline, after infusion of Landiolol and up to 72 hours after the start of intravenous administration).

**Results:**

The mean age of the 11 patients was 55 years old with high proBNP values at admission.

The etiological diagnosis of heart failure was heterogeneous but tachyarrhythmia was the trigger event in all patients.

Patients were critically ill with a mean EF of 26 ± 16%. Were. ADHF was associated with septic shock in 4 of 11 patients, in 4 of 11 patients the clinical profile evolved into cardiogenic shock; 3 of 11 patients required intubation, 9 of 11 aminic inotropic support, and 3 of 11 required mechanical circulatory support.

Patients had a complex clinical profile, with depressed ejection fraction, hypotensive pressure profile, and non-sinus tachycardia. Landiolol administered together with other antiarrhythmic drugs (amiodarone in 4/11 patients), epinephrine/norepinephrine (9/11) and levosimendan (4/11) favoured heart rate lowering and an increase in systolic blood pressure.

At discharge, 4/11 had improved EF, in 10/11 sinus rhythm was restored, and all patients recovered hemodynamic stability without adverse events related to Landiolol).

All 11 patients survived with the restoration of hemodynamic stability (Table 1, Figure 1).

**Table-1:** Clinical profile, comorbidities, haemodynamic parameters, adverse events and clinical outcomes of the 11 patients included in the case-series review. Quantitative data are reported with +/- standard deviation. The qualitative data of the 11 patients are reported in fractions (n/N).

| **Clinical Profile of ADHF Patients Treated with Landiolol** | |
|---|---|
| Age, (years±SD) | 55,5±21 |
| Sex | 11-May |
| Weight, (kg±SD) | 82±27 |
| **Cardiovascolar Profile** | |
| Hypertension | 11-May |
| Diabetes | 11-Feb |
| History of Atrial Fibrillation | 11-Aug |
| History of Ventricular Arrhythmias | 11-Mar |
| Chronic Kidney Disease | 11-Apr |
| Mean pro-BNP at admission (pg/mL±SD) | 13500±9900 |
| Acute Decompensated Heart Failure | 11-Nov |
| **Heart Failure Aetiologies** | |
| Ischemic Cardiomyopathy | 11-Apr |
| End-stage idiopathic dilated cardiomyopathy | 11-Mar |
| Hypertrofic Cardiomyopathy | 11-Feb |
| Tachycardiomyopathy | 11-Mar |
| **Clinical Status** | |
| NYHA II | 11-Mar |
| NYHA III-IV | 11-Aug |
| Mean Ejection fraction at admission (%±SD) | 26±16 |
| Acute Pulmonary Edema | 11-May |
| Septic Shock | 11-Apr |
| Cardiogenic Shock | 11-Apr |
| Orotracheal Intubation | 11-Mar |
| **Hemodynamic Profile at Admission** | |
| Systolic blood pressure (mmHg±SD) | 95±16 |
| Mean blood pressure (mmHg±SD) | 51±13 |

| | |
|---|---|
| Heart rate (b/min±SD) | 127±36 |
| HEMODYNAMIC PROFILE AT DISCHARGE | |
| Systolic blood pressure (mmHg±SD) | 104±20 |
| Heart rate (b/min±SD) | 87±33 |
| **Cardiovascular Drugs** | |
| Landiolol | 11-Nov |
| Median Duration of Landiolol Infusion (24-72 hours), (hours) | 72 |
| Mean Landiolol dosage, (mg/kg/min±SD) | 9±5 |
| Amiodarone | 11-Apr |
| Other oral beta blockers | 11-Sep |
| Calcium Channel blockers | 11-Jan |
| Dobutamine | 11-Apr |
| Epinephrine / Norepinephrine | 11-Sep |
| Levosimendan | 11-Apr |
| Need for mechanical support (IABP, LVAD) | 11-Mar |
| Need for renal replacement therapy | 11-Feb |
| **Adverse Events from Antiarrhythmics** | |
| Amiodarone toxicity (qt prolongation, torsades de pointes) | 11-Jan |
| Hemodynamic instability from calcium channel blockers | 11-Jan |
| **Clinical Outcomes** | |
| Improved Ejection fraction at discharge | 11-Apr |
| Mean ejection fraction at discharge | 33±15 |
| Sinus rhythm restoration | 11-Oct |
| Hemodynamic stability at discharge | 11-Nov |
| Hospital survival | 11-Nov |

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