

# Pimobendan in Chronic Right Heart Failure in a Left Ventricular Assist Device Patient

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## Abstract

We report the case of a 76-year-old patient who developed chronic right heart failure 1 year after left ventricular assist device implantation due to ischemic cardiomyopathy. Initial recompensation was achieved through dobutamin, sildenafil, and levosimendan treatment. Yet, discharge was successful only after the off-label use of the oral calcium sensitizer pimobendan. Ten months after discharge, the patient presents with no clinical signs of right heart failure and significantly improved right heart function without any impairment in quality of life.

## Keywords

- ▶ circulatory assist devices
- ▶ heart failure
- ▶ right ventricle

## Introduction

Chronic right heart failure in patients after left ventricular assist device (LVAD) implantation is an increasing problem with limited therapeutic options.<sup>1</sup> When conservative heart failure medication to reduce right ventricular pre- and afterload is exhausted, positive inotropic drugs are the method of choice.<sup>1</sup> However, inotropic therapy usually requires hospitalization of the patients. We report the case of a patient who developed chronic right heart failure 1 year after LVAD implantation. Initial recompensation was achieved, yet discharge was successful only after the off-label use of the oral calcium sensitizer pimobendan. To the best of our knowledge, we hereby present the first case of the successful management of refractory right heart failure in a patient on prolonged LVAD therapy through oral pimobendan therapy.

## Case Report

In this report, a 76-year-old male patient initially presented to our center in 2013 with ischemic cardiomyopathy with highly impaired left ventricular function (left ventricular ejection fraction [EF]: 20% and fractional shortening [FS]: 15%), moderate tricuspid regurgitation, and mildly impaired right ventricular function (tricuspid annular plane systolic excursion [TAPSE]: 14 mm). He was treated in December 2013

with a LVAD Heartmate II and a tricuspid valve annuloplasty with a 32-mm prosthetic ring (Carpentier–Edwards). The postoperative period was uneventful and the patient was discharged afterward. Regular follow-up checkups were organized in our LVAD outpatient clinic. Over the following period, the left ventricle was well unloaded and the LVAD function was uneventful. However, right heart function decreased steadily to a TAPSE of 7 mm despite increased sildenafil, oral diuretic therapy, and no signs of residual tricuspid regurgitation.

In October 2014, the patient routinely presented himself in our clinic, when a mild driveline infection was diagnosed. The patient was admitted and the local infection was successfully treated conservatively. Meanwhile, the patient suffered of recurrent pleural effusion and peripheral edema due to a highly impaired right heart function (TAPSE: 7 mm) significantly limiting his level of physical activity. Treatment consisted of escalated diuretic and sildenafil therapy as well as chest drainage.

Over the next weeks, the patient's condition did not improve through conservative medical treatment and he had to be transmitted to our cardiac intensive care unit when he presented with worsening decompensated right heart failure. At that time, the patient's central venous saturation was 30%. Echocardiographically, the right heart function was significantly impaired (TAPSE: 6–7 mm). Pleural effusions and worse peripheral edema were visible.

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Recompensation was achieved through intravenous furosemide and inotropic therapy (dobutamine). Yet, successful catecholamine weaning was possible not before repeated intravenous levosimendan loading. At that point, all conservative medical heart failure medication including phosphodiesterase inhibitor therapy was exhausted, while levosimendan administration was only possible in an intensive care unit setting in our institution.

To allow the patient to be discharged from our center with refractory right heart failure, we decided on a therapeutic off-label attempt with the oral calcium sensitizer pimobendan. The drug is approved in Japan for terminal heart failure but not within the European Union.

Informed consent was obtained and the patient's condition improved significantly over the next few weeks. We were able to discharge the patient with the oral pimobendan drug therapy (2.5 mg twice a day) in due course with significantly improved right heart function. Pleural effusions were regressive and chest drainage was not necessary anymore. Right heart function was significantly improved echocardiographically before discharge (TAPSE: 15 mm), while there was no difference in left ventricular function. The patient presented regularly in our LVAD clinic afterward at intervals of 4 weeks.

At every single presentation afterward from January to October 2015, no peripheral edema was visible and no pleural effusion was detectable. Echocardiographically, right heart function remained improved (TAPSE: 13–15 mm), while the left ventricle did not present with better contractility (EF: 20–25% and FS: 10–20%). The patient's general condition was significantly improved and he was able to fully participate in his every day live, limited only by his LVAD. There were no clinical signs of right heart failure present over a period of 10 months while the patient was taking pimobendan. Moreover, right heart function was considerably improved and remained comparably well while the patient was taking the calcium sensitizer.

## Discussion

Pimobendan is a positive inotropic calcium sensitizer available in Japan functioning through a combination of cyclic adenosine monophosphate-dependent action and calcium-sensitizing properties.<sup>2–4</sup> In fact, the heart failure guideline in Japan has stated the necessity of investigating the role of oral inotropic agents in patients with chronic heart failure (CHF).<sup>2</sup> Pimobendan, along with doxapamine and denopamine have proven to significantly improve the New York Heart Association functional class, cardiothoracic ratio, and B-type natriuretic peptide levels in elderly patients with CHF<sup>2</sup> through enhance contractility, relaxation, and improved cardiac performance.<sup>5,6</sup> Moreover, the number of emergency room visits and hospitalizations were significantly reduced in patients

taking the oral calcium sensitizers.<sup>2,7</sup> These results were confirmed in another study showing that pimobendan in conjunction with conventional therapy for heart failure decreases the readmission rate in elderly patients with severe heart failure for at least 2 years.<sup>8</sup>

There is only one case report about the use of pimobendan in the setting of a cardiac assist device therapy: Imamura et al were able to successfully prevent the implantation of a right ventricular assist device in a patient with right ventricular dysfunction who was implanted a LVAD through pimobendan and sildenafil therapy.<sup>9</sup>

To the best of our knowledge, we hereby present the first case of the successful management of refractory right heart failure in a patient on prolonged LVAD therapy through oral pimobendan therapy in a dosage of 2.5 mg twice a day. Due to the good experience with the drug, we believe that further research on the therapeutic effects of positive inotropic calcium sensitizers is necessary in patients with right heart failure especially in patients with ongoing LVAD therapy.

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