This document is a case report discussing the failure of disopyramide to improve right ventricular outflow tract obstruction (RVOTO) after living-donor lobar lung transplantation (LDLLT) for patients with primary pulmonary hypertension (PH). The case involves a 28-year-old female patient referred for LDLLT due to primary PH that did not respond to medical treatment. The patient underwent a successful LDLLT, but developed dyspnea and exercise intolerance during rehabilitation. Transthoracic echocardiography revealed RVOTO, which was treated with intravenous disopyramide. However, this led to adverse electrical and hemodynamic effects, and thus, fluid administration and low-dose atenolol were started instead. The symptoms improved, and RVOTO improved on transthoracic echocardiography. The case suggests that disopyramide should be avoided for patients with RVOTO following lung transplantation and that other negative inotropic agents, such as β-blockers, are more effective for relief of RVOTO.

**Key Words:** Disopyramide; Living-donor lobar lung transplantation; Primary pulmonary hypertension; Right ventricular outflow tract obstruction

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**Case Report**

A 28-year-old female patient with shortness of breath on exercise had been diagnosed with primary pulmonary hypertension (PPH) in 1993, at the age of 18 years. Treatment with beraprost sodium and oxygen treatment was started, but she remained in New York Heart Association functional class III and despite initiation of continuous intravenous prostacyclin therapy in 2001, there was little improvement. Cardiac catheterization revealed that the patient’s RV pressure, pulmonary arterial pressure and cardiac index were 114/9 mmHg, 113/36/66 mmHg and 1.7 L·min⁻¹·m⁻², respectively. The patient was referred for LDLLT. Preoperative transthoracic echocardiography showed a dilated and hypertrophied right ventricle with hypertrophied septal and parietal bands, but no obstruction of the RVOT. In December 2002, she underwent LDLLT with a right lower lobe from her father (52 years old) and a left lower lobe from her mother (53 years old). Intraoperative transesophageal echocardiography showed that the RVOT was 1.5 cm in diameter and that there was slight acceleration of its blood flow.

The operation was successful. However, transthoracic echocardiography performed on the fourth postoperative day showed that the velocity of blood flow in the RVOT was 3.1 m/s and it was thought that dehydration and the administration of inotropic agents had augmented the stenosis of the RVOT. Therefore, fluids were administered and the dosages of the inotropic agents were tapered, resulting in slight improvement in peak velocity in the RVOT (2.7 m/s) on the 8th postoperative day.

As her rehabilitation advanced, she developed dyspnea...
and exercise intolerance. Repeated transthoracic echocardiography on the 40th postoperative day showed aggravation of the RVOTO with turbulent flow (Fig 1); the peak velocity of blood flow in the RVOT was 4.0 m/s. Thus, we considered that her symptoms were caused by the worsening of the RVOTO. Cardiac catheterization confirmed the RVOTO (Fig 2), and the pressure gradient through the RV outflow tract was 35 mmHg. Dysopyramide (2 mg/kg) was administered intravenously at the rate of 10 mg/min\(^{10,13}\) and the pressure gradient in the RVOT immediately decreased to 16 mmHg. However, the reduction was achieved only by an increase in pulmonary arterial systolic pressure without a decrease in the RV systolic pressure. Moreover, cardiac output decreased and mechanical and electrical alternans appeared (Table 1, Fig 3). Administration of intravenous disopyramide was not beneficial for this patient.

After cardiac catheterization, fluid administration and treatment with a low dosage of atenolol (12.5 mg/day) were started, and her symptoms improved. Repeated transthoracic echocardiography revealed improvement in the RVOTO, with a reduction in the peak flow velocity to 3.2 m/s and no mechanical alternans in the flow profile of the RVOT.

**Discussion**

This is the first case report of RVOTO after LDLLT. Symptomatic severe RVOTO is an uncommon complication after cadaveric lung transplantation for patients with PH, causing right heart failure\(^5\)\(^\text{-}^8\). Only 8 cases have been reported. Long-standing PH induces significant structural changes in the heart such as marked RV hypertrophy and enlargement\(^16\) and in such patients, lung transplantation causes a rapid reduction in the RV afterload, which in turn

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**Fig 1.** Transthoracic echocardiography shows the right ventricular (RV) outflow tract obstruction (Left) and the marked acceleration flow across the RV outflow tract (Right).

**Fig 2.** End-diastolic (A) and end-systolic (B) images of the patient with RVOTO in the left anterior oblique view. Marked infundibular narrowing can be seen (arrow).

**Table 1** Hemodynamics Before and After Injection of Disopyramide

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>65</td>
<td>60</td>
</tr>
<tr>
<td>PAP (s/d/m) (mmHg)</td>
<td>17/4/10</td>
<td>36/14/23</td>
</tr>
<tr>
<td>RVSP/EDP (mmHg)</td>
<td>52/2</td>
<td>52/4</td>
</tr>
<tr>
<td>CO/CI (L/min/L·min⁻¹·m⁻²)</td>
<td>2.4/2.1</td>
<td>2.0/1.7</td>
</tr>
<tr>
<td>TPR (dyne·s⁻¹·cm⁻⁵·m⁻²)</td>
<td>381</td>
<td>1,082</td>
</tr>
</tbody>
</table>

PASP (s/d/m), pulmonary arterial systolic pressure (systolic/diastolic/mean); RVSP, right ventricular systolic pressure; EDP, end-diastolic pressure; CO, cardiac output; CI, cardiac index; TPR, total pulmonary resistance.
causes a rapid decrease in the size of the hypertrophied right ventricle, resulting in acquired RVOTO. The usefulness of a preoperative echocardiographic study for predicting postoperative RVOTO has not been clarified. Postoperative administration of inotropic agents may also induce RVOTO and in such cases, dramatic improvement occurs when the administration is discontinued.

Once RVOTO occurs, medical treatment, such as a β-blocker or a calcium channel antagonist, is required until RV remodeling and regression of the hypertrophy have been completed. These agents are thought to be effective because they reduce contractility, improve the intrinsic diastolic function and increase the diastolic filling time. Myectomy and outflow tract patching have been performed in 2 patients with RVOTO after cadaveric lung transplantation.

Disopyramide has been reported as effective for reducing the pressure gradient and improving the diastolic properties in patients with hypertrophic cardiomyopathy consequently, reducing the severity of the clinical symptoms. Its effectiveness not only for LV outflow tract obstruction, but also for treatment of RVOTO in a small number of patients with tetralogy of Fallot, has been reported. In the case of hypertrophic cardiomyopathy, the reduction in the pressure gradient is achieved through a decrease in LV systolic pressure and a rise in aortic systolic pressure, which may reflect an increase in systemic vascular resistance. The decrease in the intracellular Ca²⁺ concentration because of inhibition of the Na⁺/Ca²⁺ exchanger would contribute to the negative inotropic effect and increased systemic vascular resistance. The mechanism by which the pressure gradient through the LV outflow tract is reduced by disopyramide is thought to be a negative inotropic effect and increased systemic vascular resistance. It has also been reported that cibenzoline attenuated the biventricular pressure gradients in patient with hypertrophic cardiomyopathy.

Therefore, we expected that disopyramide would also improve the RVOTO after LDLT and indeed, the pressure gradient through the RVOT was reduced immediately after the injection of disopyramide. However, this reduction was achieved only by an increase in pulmonary arterial systolic pressure, and the RV systolic pressure remained high. In other words, disopyramide only increased the pulmonary vascular resistance and had almost no negative inotropic effect on the right ventricle. We do not know why disopyramide failed to improve RVOTO in the present case. Unlike hypertrophic obstructive cardiomyopathy, the RVOTO after LDLT develops because of the rapid decrease in the size of the cavity of the hypertrophied right ventricle. Moreover, in this case the RVOT in diastole was very narrow because of the rapid reduction in preload and afterload of the right ventricle. Therefore, it is possible that disopyramide could not induce a sufficient negative inotropic effect to relieve the mechanical obstruction.

The present results suggest that disopyramide should not be given to patients with RVOTO following lung transplantation and that other negative inotropic agents, such as β-blockers, and adequate fluid therapy will relieve the obstruction.

References
Disopyramide for RVOTO


