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# Cibenzoline Attenuates Coronary Systolic Reversal Flow in a Patient With Hypertrophic Obstructive Cardiomyopathy: A Case Report

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**Abstract**

Effects of cibenzoline on coronary hemodynamics, especially systolic reversal flow, were assessed in a 53-year-old man with hypertrophic obstructive cardiomyopathy by coronary flow study using a Doppler guidewire. Intravenous administration of cibenzoline resulted in decreases in the pressure gradient (60 to 0 mmHg) and systolic left ventricular pressure (162 to 126 mmHg), and an increase in systolic arterial pressure (102 to 132 mmHg). Furthermore, the systolic reversal flow observed at baseline was markedly diminished following administration of cibenzoline. Therefore, we speculate that cibenzoline reduces ventricular wall stress by diminishing the left ventricular obstruction that occurs with compression of the intramyocardial arteries. Cibenzoline-induced attenuation of coronary systolic reversal flow may be associated with the effectiveness of cibenzoline for diminishing the left ventricular obstruction.

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**Key Words**

■**Cardiomyopathies, hypertrophic (obstructive)** ■**Coronary circulation**
■**Doppler ultrasound (guidewire)** ■**Drug administration (cibenzoline)**

## INTRODUCTION

The degree of left ventricular outflow tract obstruction correlates with prognosis in patients with hypertrophic cardiomyopathy (HCM).[1] Cibenzoline administration resulted in attenuation of left ventricular outflow pressure gradients in patients with hypertrophic obstructive cardiomyopathy (HOCM), which, in turn, is related to a decrease in myocardial contractility.[2–4]

Measurement of phasic coronary flow dynamics at baseline shows that compression of the intramural coronary bed, elevated peak diastolic coronary flow velocity, and reduced peak systolic coronary flow velocity are frequently observed in patients with HOCM. Several studies have demonstrated coronary systolic reversal flow in patients with HOCM.[5–8] However, the effects of cibenzoline on coronary hemodynamics and coronary flow velocity pattern have not been characterized.

The present case describes cibenzoline-induced attenuation of systolic reversal flow in a patient

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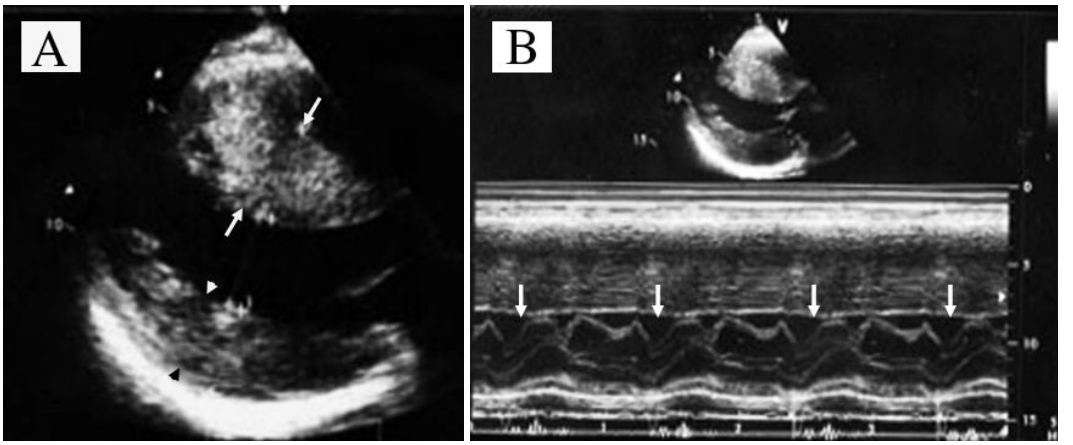


**Fig. 1 Echocardiograms**
*A*: Parasternal long-axis echocardiogram. The interventricular septum thickness (between *arrows*) was 32 mm, and the thickness of the posterior wall was 30 mm (between *arrowheads*). Concentric left ventricular hypertrophy and narrowness of left ventricular dimensions could be detected in this view.
*B*: M-mode echocardiogram of the mitral valve shows systolic anterior motion of the mitral valve (*arrows*).

with HOCM.

## CASE REPORT

A 53-year-old man was hospitalized in November 2004 secondary to rotary vertigo and exertional dyspnea (New York Heart Association functional class II). Blood pressure was 122/62 mmHg, and a systolic ejection murmur (grade 3/6) was heard at the fourth intercostal space at the left sternal border. An S4 heart sound was also appreciated. Chest radiography demonstrated cardiomegaly with a cardiothoracic ratio of 63.5% and prominent right second and left fourth arches. Electrocardiography showed sinus rhythm at 70 beats/min, left axis deviation (−66 °), high voltage in the left side of the heart, a QS pattern in leads $V_3$ to $V_6$, and inverted T-waves in I, $aV_L$, and $V_4$ to $V_6$. Laboratory data were unremarkable except for elevation of brain natriuretic peptide and atrial natriuretic peptide (462 and 160 pg/m*l*, respectively). Echocardiography showed diffuse and severe left ventricular hypertrophy and apical asynergy (ejection fraction of 60%). Thickness of the interventricular septum was 30 mm, and that of the ventricular posterior wall was 32 mm (**Fig. 1−A**). M-mode echocardiography showed systolic anterior movement of the anterior mitral leaflet (**Fig. 1−B**). Continuous wave Doppler echocardiography showed a peak flow velocity of 4.6 m/sec, and the systolic pressure gradient was calculated as 84 mmHg throughout the left ventricular outflow tract. Coronary angiography revealed no significant stenosis.

To assess the hemodynamic impact of the left ventricular pressure gradient, left ventricular and aortic pressures were obtained at baseline and during cibenzoline administration. A 0.014-inch Doppler guidewire was placed in the left anterior descending coronary artery, and average peak velocity was recorded continuously. Intravenous administration of cibenzoline (30 mg) resulted in decreases in the pressure gradient (60 to 0 mmHg) and systolic left ventricular pressure (162 to 126 mmHg) and an increase in systolic arterial pressure (102 to 132 mmHg; **Fig. 2**). Furthermore, the systolic reversal flow observed at baseline was markedly diminished following administration of cibenzoline, whereas average peak velocity decreased from 53 to 32 cm/sec (**Fig. 3**) and coronary artery diameter remained generally unchanged (3.3 vs 3.2 mm). Left anterior descending coronary artery coronary blood flow (CBF = cross-sectional area × average peak velocity × 0.5)[9] also decreased from 107 to 76 m*l*/min.

## DISCUSSION

In this case, administration of cibenzoline induced decreased coronary blood flow, although the aortic diastolic pressure was increased as shown in **Figs. 2** and **3**. There are several reasons for this discrepancy. First, the aortic-left ventricular diastolic pressure and the time spent in diastole are the

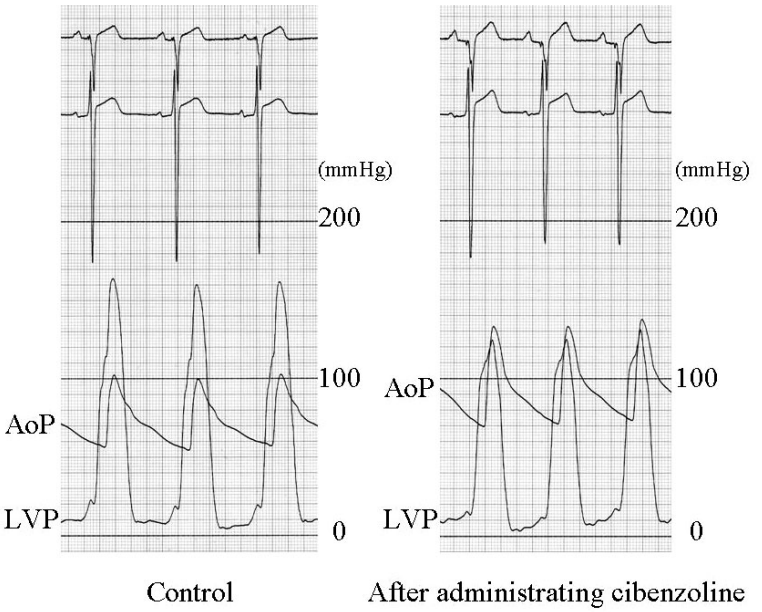


**Fig. 2 Pressure gradient between the left ventricle and the ascending aorta before (*left*) and after administration of cibenzoline (*right*)**
Administration of cibenzoline resulted in decreases in the pressure gradient (60 to 0 mmHg) and systolic left ventricular pressure (162 to 126 mmHg) and an increase in systolic arterial pressure (102 to 132 mmHg). AoP = aortic pressure; LVP = left ventricular pressure.

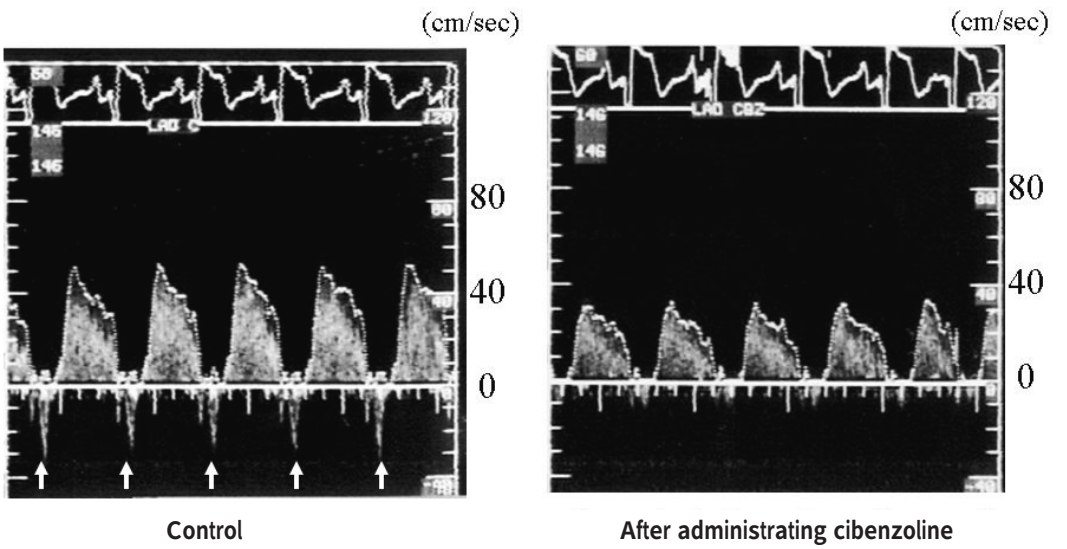


**Fig. 3 Representative coronary flow velocity pattern before (*left*) and after injection of 30 mg of cibenzoline (*right*)**
The systolic reversal flow (*arrows* in *left*) was markedly diminished following administration of cibenzoline (*right*).

major determinants of coronary blood flow. However, elevated diastolic aortic pressure does not result in unneeded perfusion because of autoregulation. Second, myocardial oxygen consumption can be estimated by myocardial mass, wall stress, contractility, and heart rate. Out of these four determinants, wall stress and contractility were markedly diminished immediately after cibenzoline administration, which might reduce coronary blood flow by sparing myocardial oxgen consumption. Third, systolic reversal flow may be associated with this discrepancy. Antegrade diastolic coronary blood flow compensating for systolic reversal flow might be returned to normal by cibenzoline administration.

This is the first case of cibenzoline-induced changes in average coronary artery peak velocity patterns in a patient with HOCM. Systolic reversal

flow in patients with HCM has been reported[5,6,8−10] and was thought to be secondary to an increase in systolic-extravascular coronary bed compression and to increased systolic perivascular resistance caused by differences in cardiac muscle structure.[5,6,11] The present study indicates that the left ventricular outflow gradient magnitude and resultant changes in ventricular wall tension are related to the coronary blood flow velocity pattern.

Cibenzoline has a negative inotropic and chronotropic effect.[12] Left ventricular ejection time correlates with the severity of left ventricular pressure gradient in patients with HOCM.[13]

Differences in left ventricular pressure gradient correlated with left ventricular ejection time index before and after administration of cibenzoline.[2] Thus, the decrease in left ventricular ejection time associated with cibenzoline may be related to decreases in left ventricular outflow obstruction and to changes in left ventricular myocardial contractility.

Angiographic evidence suggests septal perforator artery compression in hypertrophic cardiomyopathy could result in proximal reversal of systolic blood flow.[14] This is consistent with the baseline observations in the present case. The systolic reversal flow may be secondary to increased left ventricular pressure and decreased aortic driving pressure during systolic ejections that encourage retrograde flow from the septum and left anterior descending artery. The release phase during cibenzoline administration was associated with return of the left ventricular pressure to basal levels, abolition of left ventricular-aortic gradient, and normalization of the phasic coronary flow velocity pattern. In the present patient, cibenzoline-induced attenuation of systolic reversal flow resulted in decreases in peak left ventricular pressure, left ventricular external work, and coronary blood flow. Therefore, we speculate that cibenzoline reduces ventricular wall stress by diminishing the left ventricular obstruction that occurs with compression of the intramyocardial arteries.

Cibenzoline-mediated improvement in pressure gradients between the left ventricle and ascending aorta was found in a patient with obstructive hypertrophic cardiomyopathy. Cibenzoline administration also resulted in attenuation of coronary systolic reversal flow in the left anterior descending artery, which may be associated with the responsiveness of cibenzoline for reducing the left ventricular obstruction. Although the mechanism and generalizability of this phenomenon remain unclear, this case demonstrates the profound effects of cibenzoline on coronary regulation and myocardial contractility.


## 要　　約

### シベンゾリンが冠動脈収縮期逆流を減弱させることが検証された閉塞性肥大型心筋症の1症例

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閉塞性肥大型心筋症におけるシベンゾリンの冠血流動態，とくに収縮期逆流に及ぼす影響について検討したところ，興味深い知見を示した症例を経験したので報告する．症例は53歳，男性で，ドップラーガイドワイヤーを用いて冠血流動態の検討を行った．シベンゾリンの静注により左室収縮期圧は162から126 mmHgに減少し，左室と大動脈の収縮期圧較差は60から0 mmHgにまで改善した．その結果，大動脈収縮期圧は102から132 mmHgに増加した．さらに，シベンゾリンの投与により冠血流収縮期逆流は消失した．以上の所見より，シベンゾリンの効果発現の機序として，心室壁張力を軽減させることにより，左室大動脈圧較差を減少させると同時に心筋内動脈の圧排を軽減させることが関与していると考えられた．よってシベンゾリンによる冠動脈収縮期逆流の消失は，圧較差改善効果と関連していることが示唆される．


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