study was different from that previously reported in other countries [20, 21], suggesting a profound racial difference.

The coexistence of HCM and CSA presents a therapeutic challenge. In general, beta-adrenergic blocking agents or nitrates may potentially be harmful to patients with either CSA or HCM alone. Although calcium channel blockers might provide a more ideal therapeutic approach to this problem, they can exacerbate left ventricular outflow gradients and cause hemodynamic deterioration [22]. Therefore, they are not routinely recommended in patients with severe obstruction and pronounced symptoms [4, 22]. One of the possible treatments for coexistent HCM and CSA may be the class Ia antiarrhythmic agents disopyramide [23] or cibenzoline [24]. These agents can reduce left ventricular obstruction and limit symptoms through their negative inotropic action. In addition, cibenzoline causes calcium channel blockade, which may be an appropriate therapy for CSA (Fig. 1).

Several reports [25–27] have shown the transition from typical HCM to the dilated and hypokinetic left ventricle seen in patients with HCM. This has been observed in 2.4–14% of patients with HCM. The mechanism of the transition to the dilated phase of HCM remains unclear. Massive myocardial fibrosis, disarray of the salvaged myocardial fibers and regional ischemia in the intramyocardial small arteries may relate to this transition [28]. Coronary vasospasm, which induces myocardial ischemia, may affect the transition to dilated phase in patients with HCM.

In this study, HCM patients with CSA were given more drugs than those without CSA. Because the frequency of obstructive HCM in patients with CSA was higher than that in patients without it, more drugs may have been necessary to relieve the symptoms of the patients with CSA. We could not find statistical differences in NYHA functional classification and echocardiographic data between HCM patients with CSA and those without it. However, HCM patients with CSA tended to have more severe forms of HCM and a higher prevalence of NYHA functional classes II, III, and IV (Table 1) than those without it. A recent study showed that patients with essential hypertension and the Asp298 variant are resistant to conventional antihypertensive therapy [29]. In this study, HCM patients with the Asp298 variant were treated with more drugs than patients without it, suggesting that the Asp298 variant might confer resistance to drug therapy.

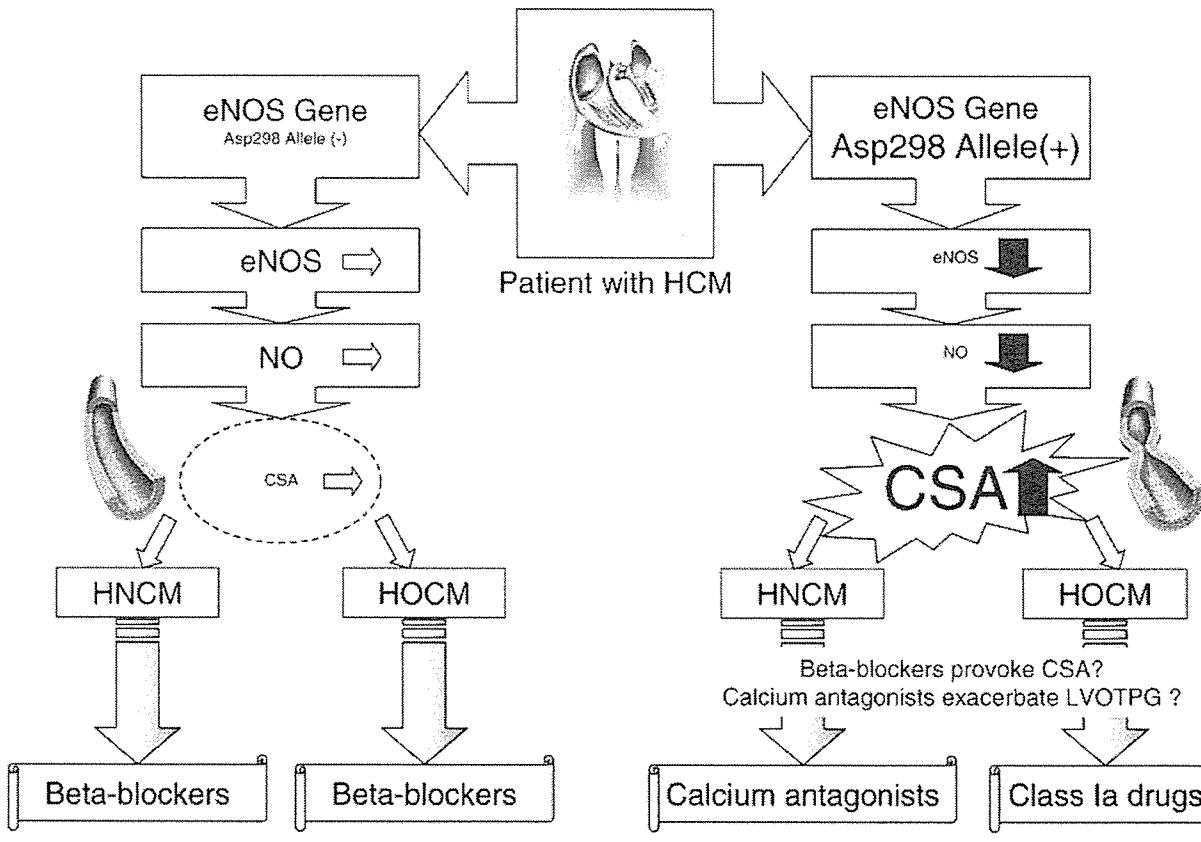

Fig. 1 The *eNOS* gene polymorphism in patients with HCM as a guide to personalized therapy. The *bottom of the figure* shows the possible first-line drugs in each HCM patient, which have not yet been confirmed by large studies. *HCM* Hypertrophic cardiomyopathy, *eNOS* endothelial nitric oxide synthase, *NO* nitric oxide, *CSA* coronary spastic angina, *HNCM* hypertrophic non-obstructive cardiomyopathy, *HOCM* hypertrophic obstructive cardiomyopathy, *LVOTPG* left ventricular outflow tract pressure gradient

Since the number of patients in our study was relatively small, our findings may have resulted from chance association. In addition, our HCM patients may have more symptoms than unselected HCM patients because our hospital is a tertiary referral center for the disease. Therefore, the true frequency of the Asp298 variant in patients with HCM may not have been estimated in our HCM patient population. Our results should be compared with those of longitudinal studies in various countries. Further molecular, biological, and clinical studies are needed to clarify the relation between the *eNOS* gene polymorphism and HCM patients with CSA.

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