

Abstract

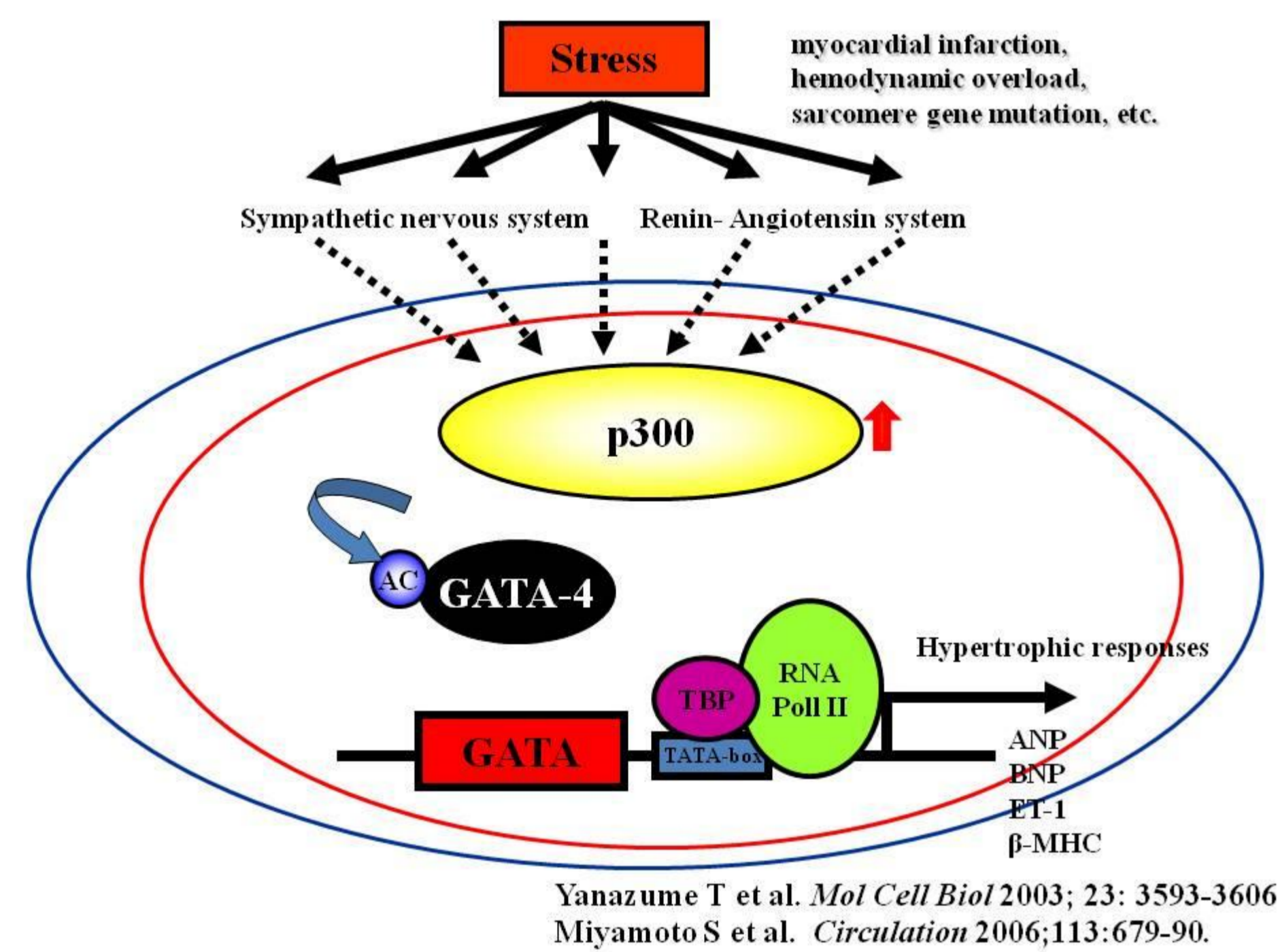
Background: Nuclear acetylation of cardiomyocytes is being recognized as a critical event Purpose: Signals activated by increased hemodynamic overload to the heart finally reach nuclei of cardiomyocytes, change patterns of gene expression and cause their maladaptive hypertrophy. Acetylation of hypertrophy-responsive transcription factors by an intrinsic histone acetyltransferase (HAT), p300, is a critical event during this process. Cardiac p300 activity is increased in common types of heart failure in which pathological cardiomyocyte overgrowth occurs in response to hemodynamic overload. A natural compound, curcumin (Cur), possesses HAT inhibitory activity with specificity for p300. We have demonstrated that Cur treatment prevents the deterioration of systolic function in two different rat models of heart failure, hypertension and myocardial infarction. Recently, by using a novel drug-delivery system, we have developed highly absorptive curcumin (HS-Cur). We hypothesized that HS-Cur improves LV function in hypertensive patients.

Methods and Results: Twenty hypertensive patients received daily HS-Cur (60 mg/day) for 24 weeks. Anti-hypertensive treatment was continued and unchanged during this period. No adverse effects were observed, and all patients completed the 24-week follow-up period. LV function was assessed by two-dimensional and Doppler echocardiography at baseline and at the end of follow-up. The ratio of early diastolic transmitral flow velocity/early diastolic velocity of mitral annulus, a parameter of diastolic function, improved from 12.0 ± 0.58 to 11.3 ± 0.56 ($p=0.097$). Fractional shortening increased from $37 \pm 1.1\%$ to $40 \pm 1.1\%$ ($p=0.066$). However, systolic and diastolic blood pressures did not change during this period (from $130 \pm 3/75 \pm 3$ to $135 \pm 4/78 \pm 2$, $p>0.1$). In a subset of patients with left ventricular hypertrophy (LVH, LV mass index >116 g/m²), LV mass index significantly ($p=0.038$) decreased from 127 ± 9.0 to 115 ± 5.8 .

Conclusion: Treatment of hypertensive patients by 60mg/day of HS-Cur for 24 weeks is safe and well-tolerable. HS-Cur regresses LVH and appears to improve LV systolic function as well as diastolic function independent of blood pressure in hypertensive patients. dietary compound is expected as a novel useful agent for heart failure in humans.

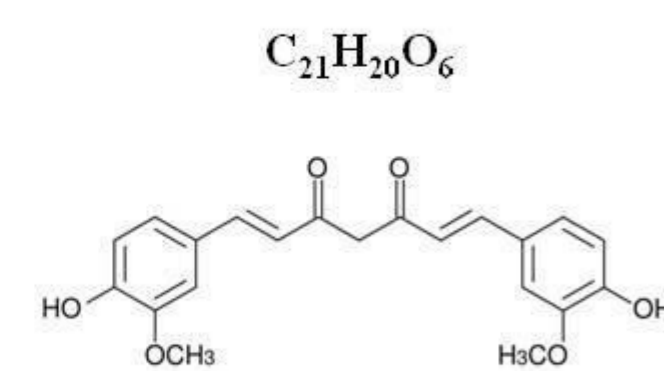
Disclosure of Interest: Non

Background

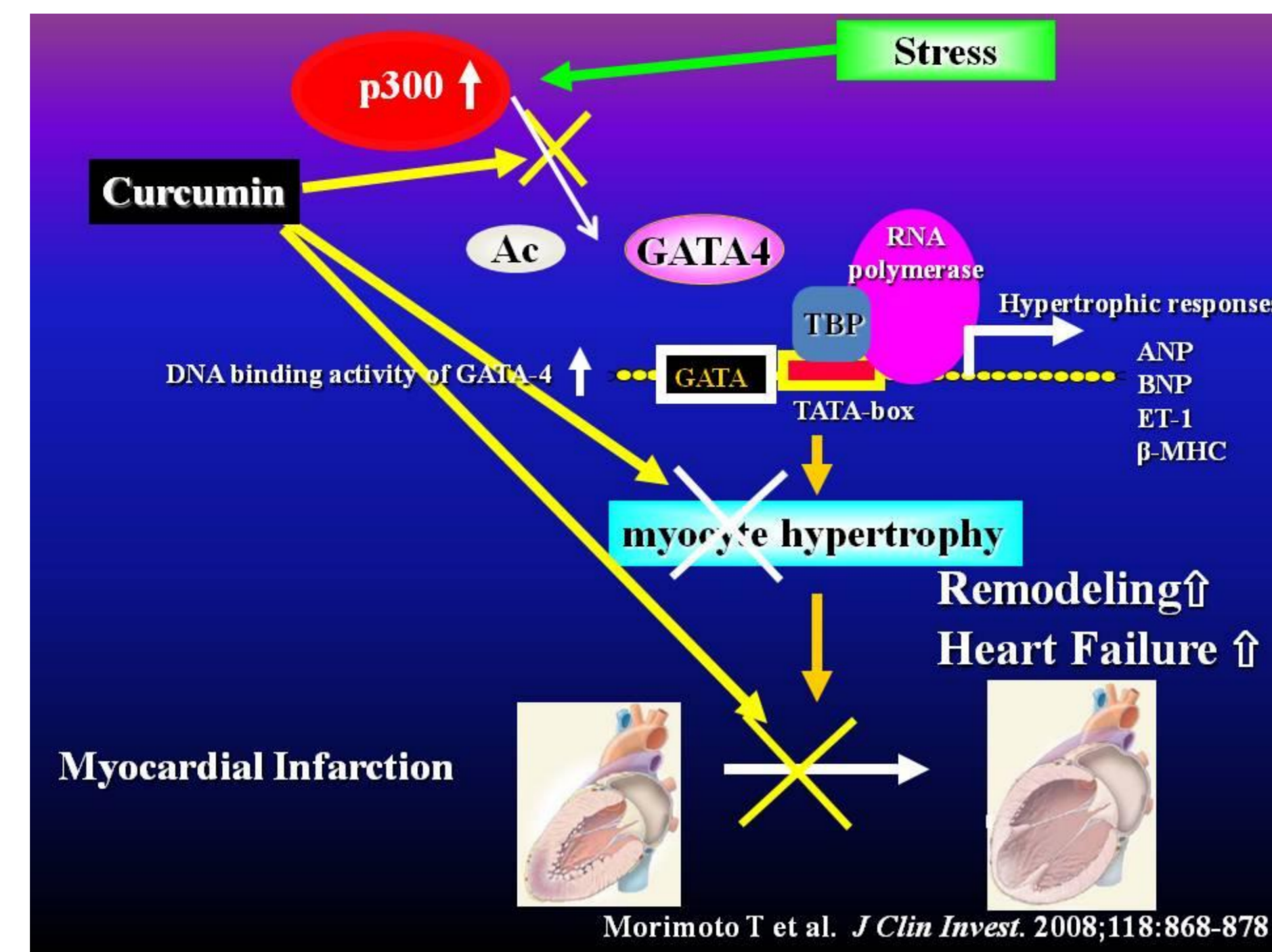


Curcumin

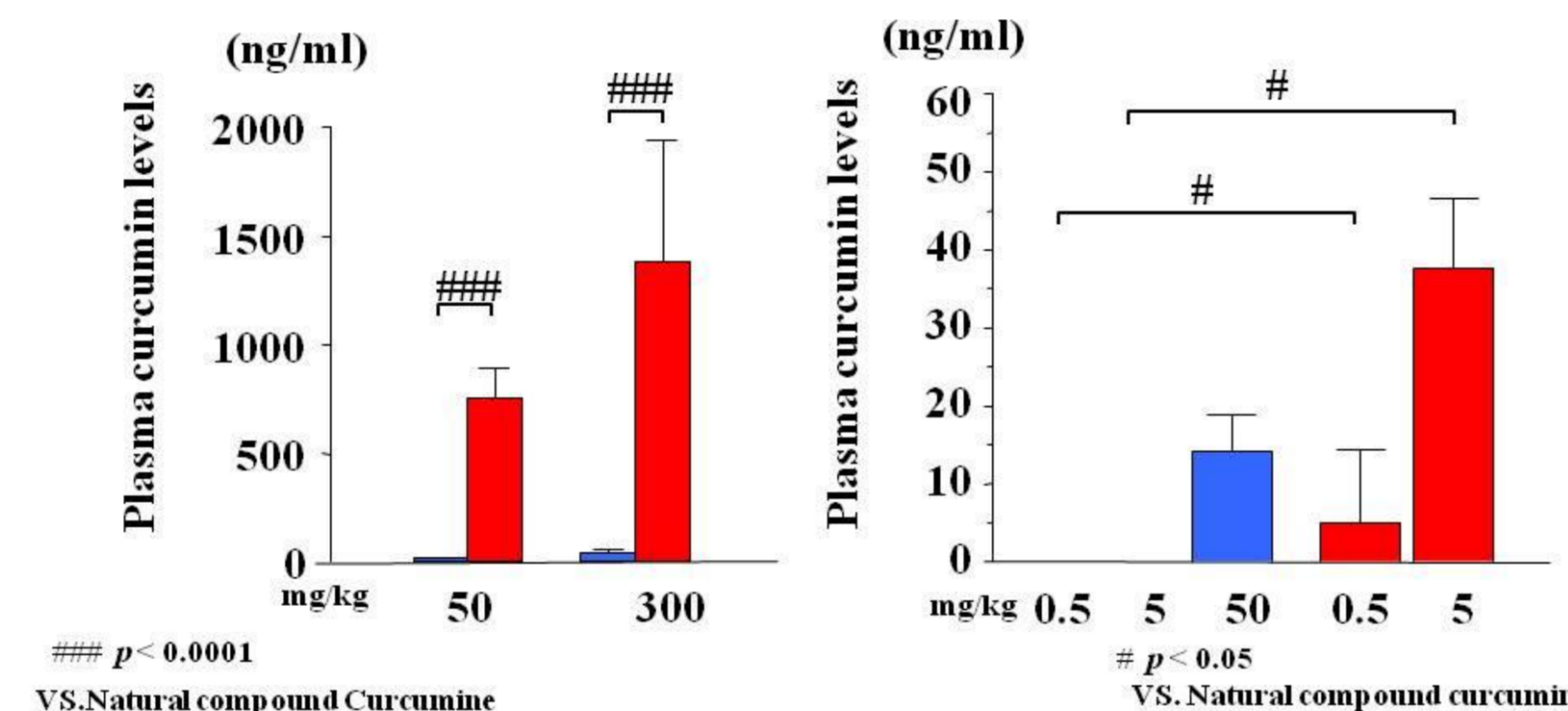
○ Curcumin is a polyphenol that is responsible for the yellow color of Indian curry spice turmeric, and commonly used as a health-food diet.



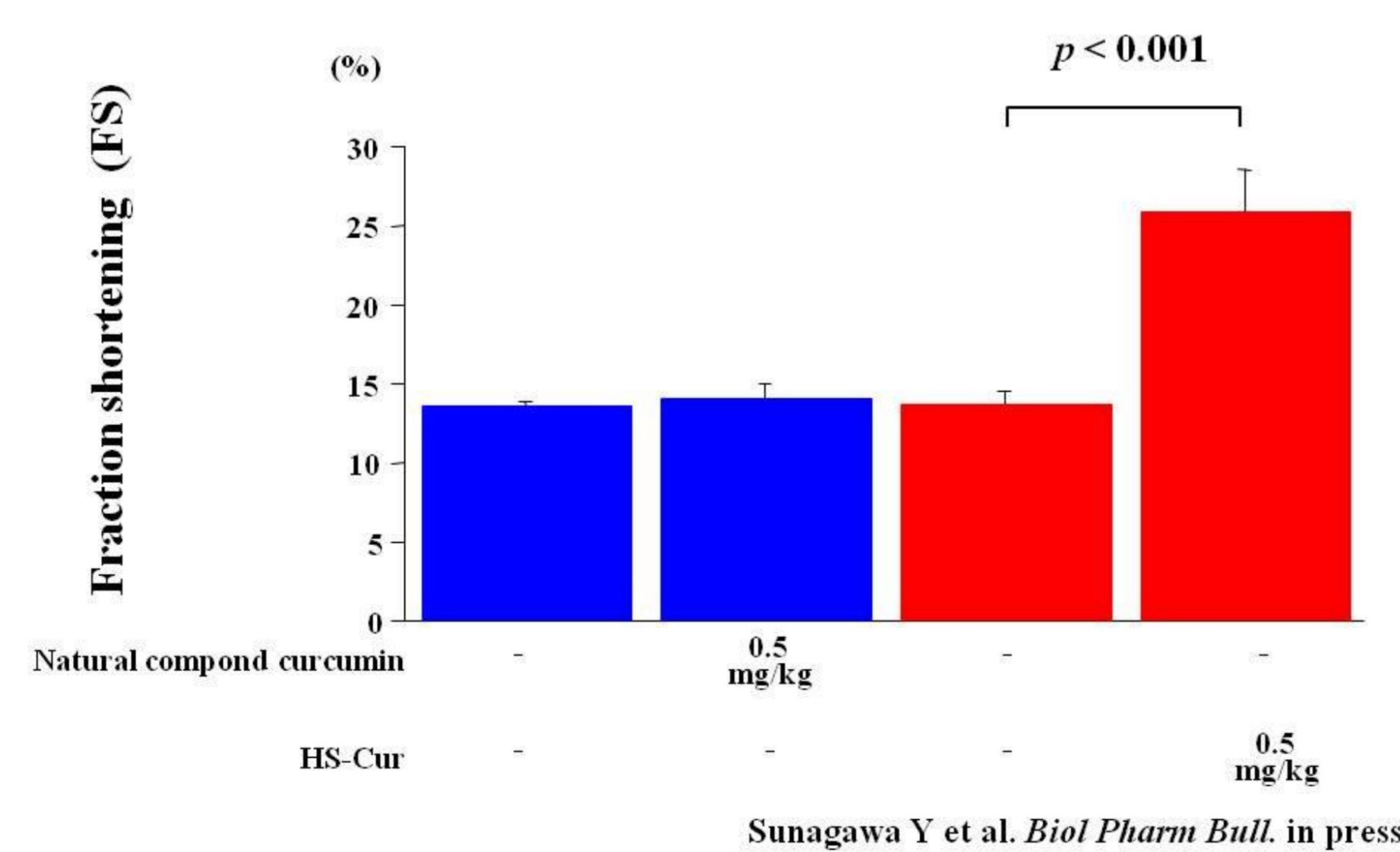
○ Curcumin is known for its antitumor, antioxidant, and anti-inflammatory properties.



Drug delivery system improved plasma curcumin levels in rats



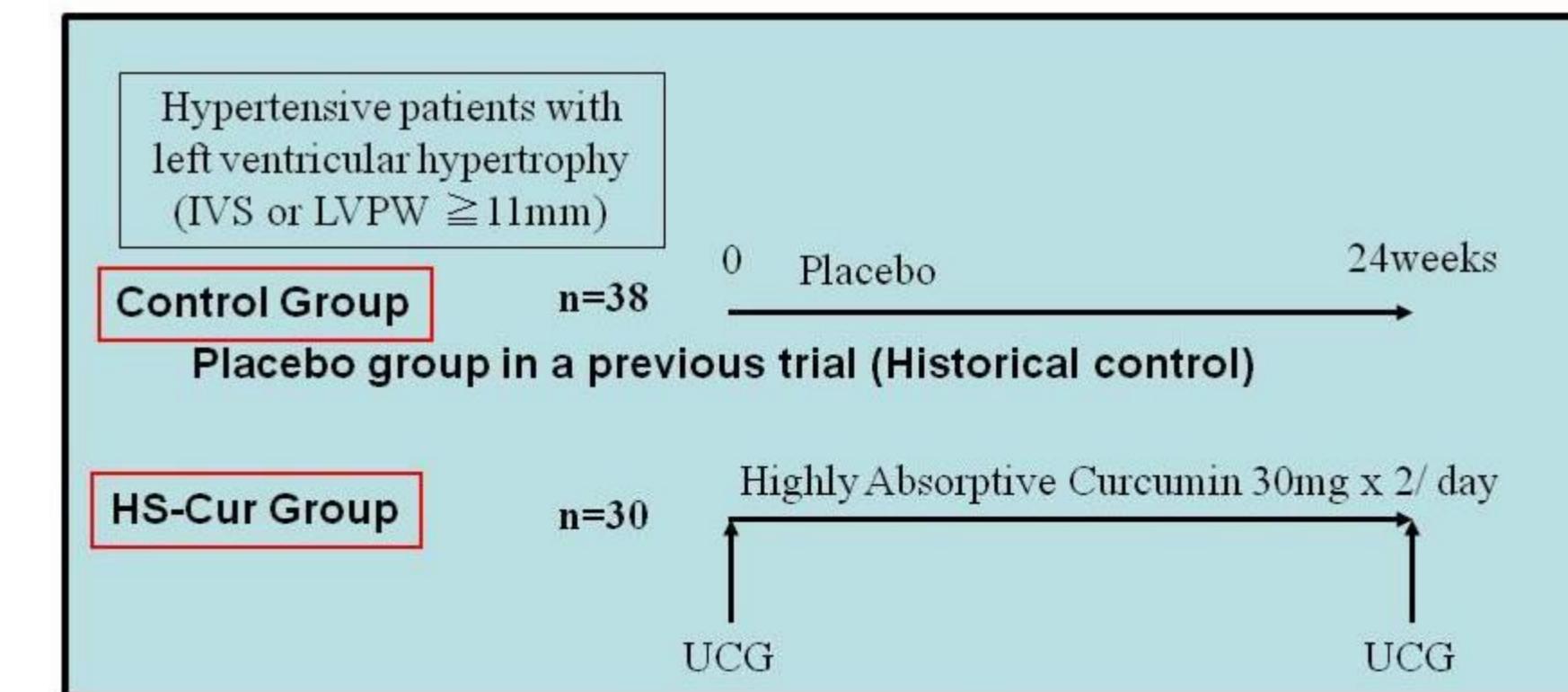
Low dose of DDS curcumin significantly improved LV systolic function after MI in rats



Objective

To examine the effect of highly absorptive curcumin (theracurruin) on diastolic dysfunction in hypertensive left ventricular hypertrophy

Protocol



Primary End Point: Left Ventricular Diastolic Function by Ecocardiography: E/E'

Registration started on July 2010

Hypertension → LV hypertrophy

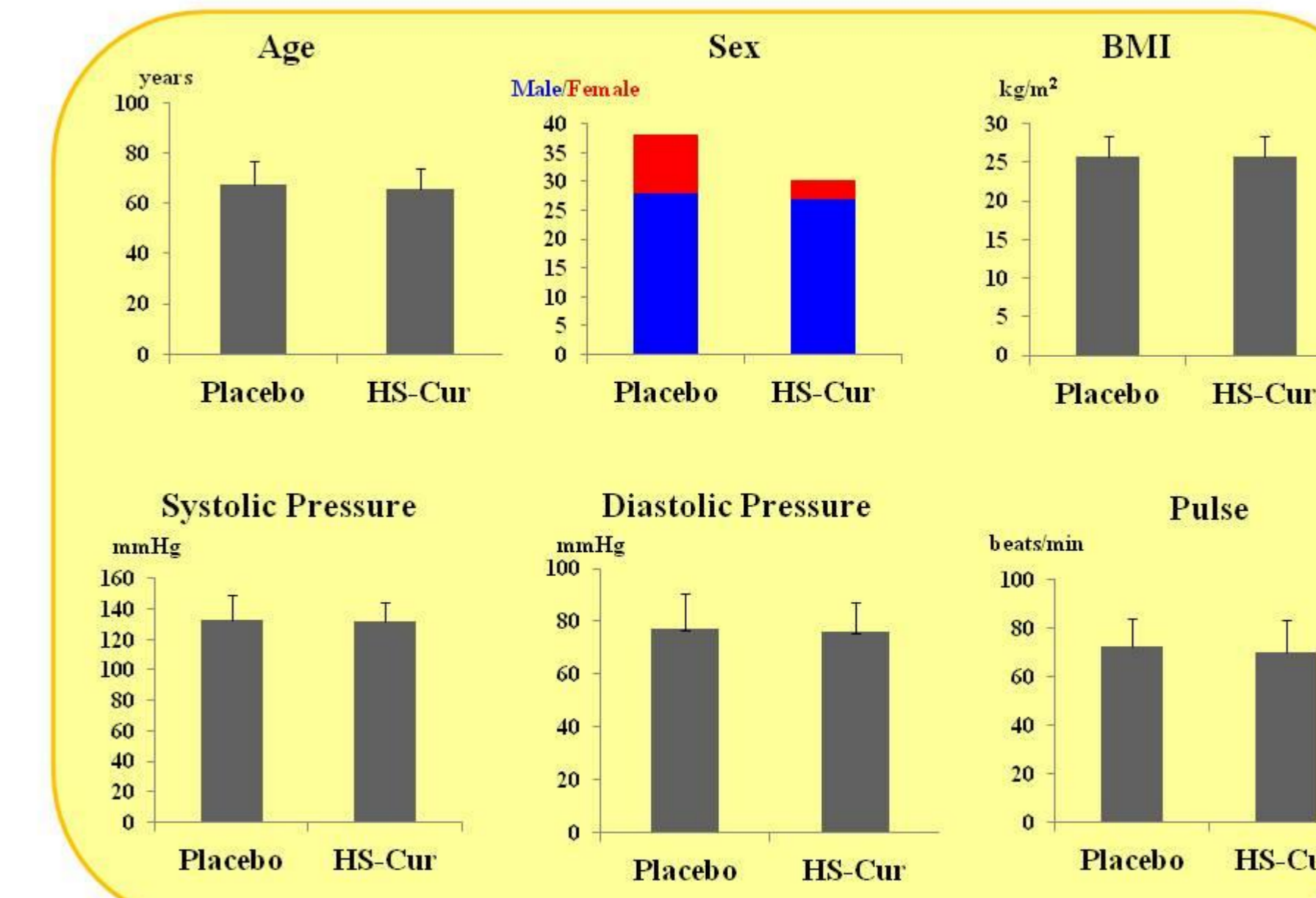


LV diastolic dysfunction

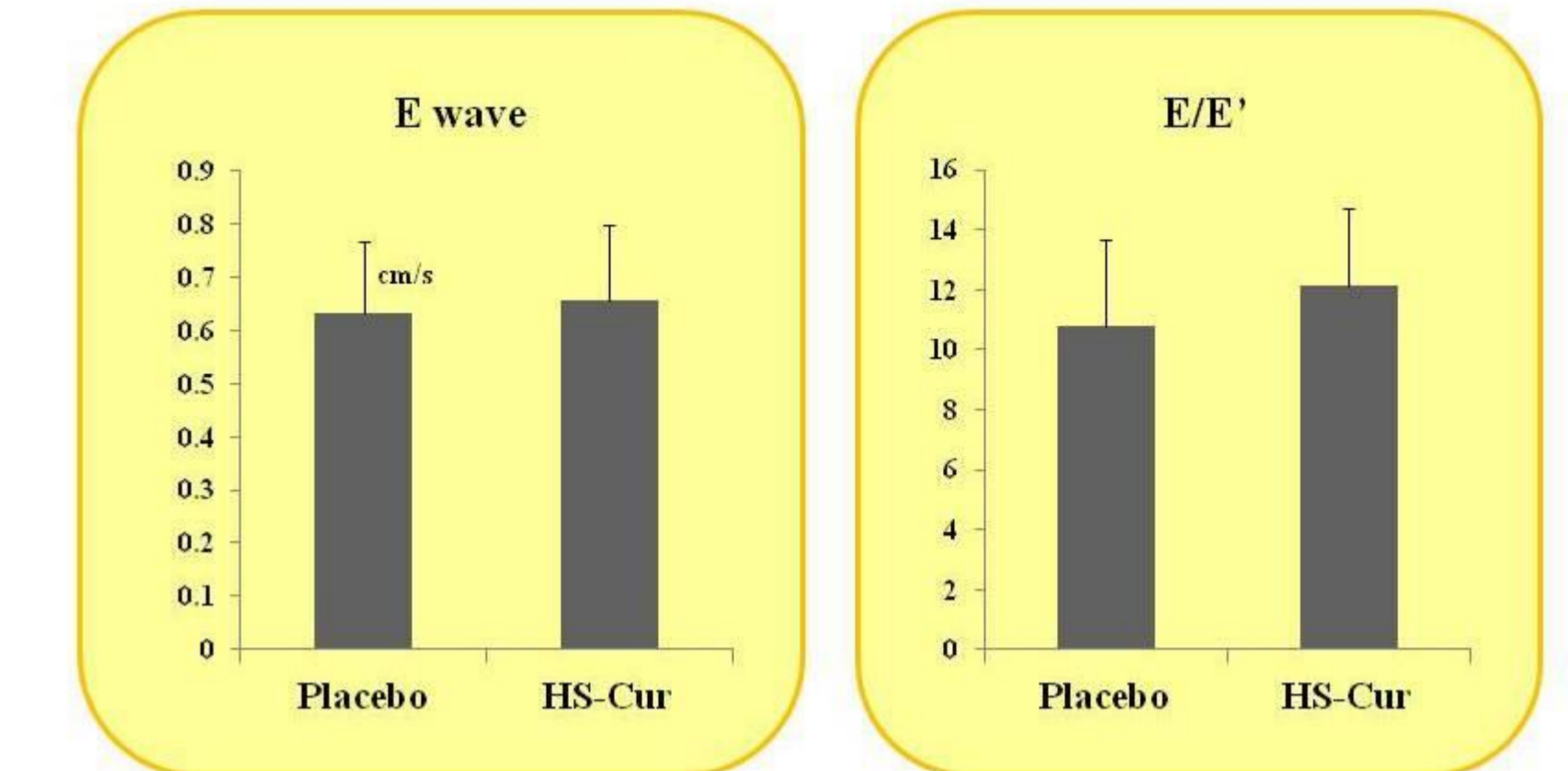
Indicator of LV diastolic dysfunction E/E' ≡ LV stiffness
E = Peak early-diastolic filling velocity
E' = Peak early-diastolic mitral annulus velocity

Results

Patient Background before Administration

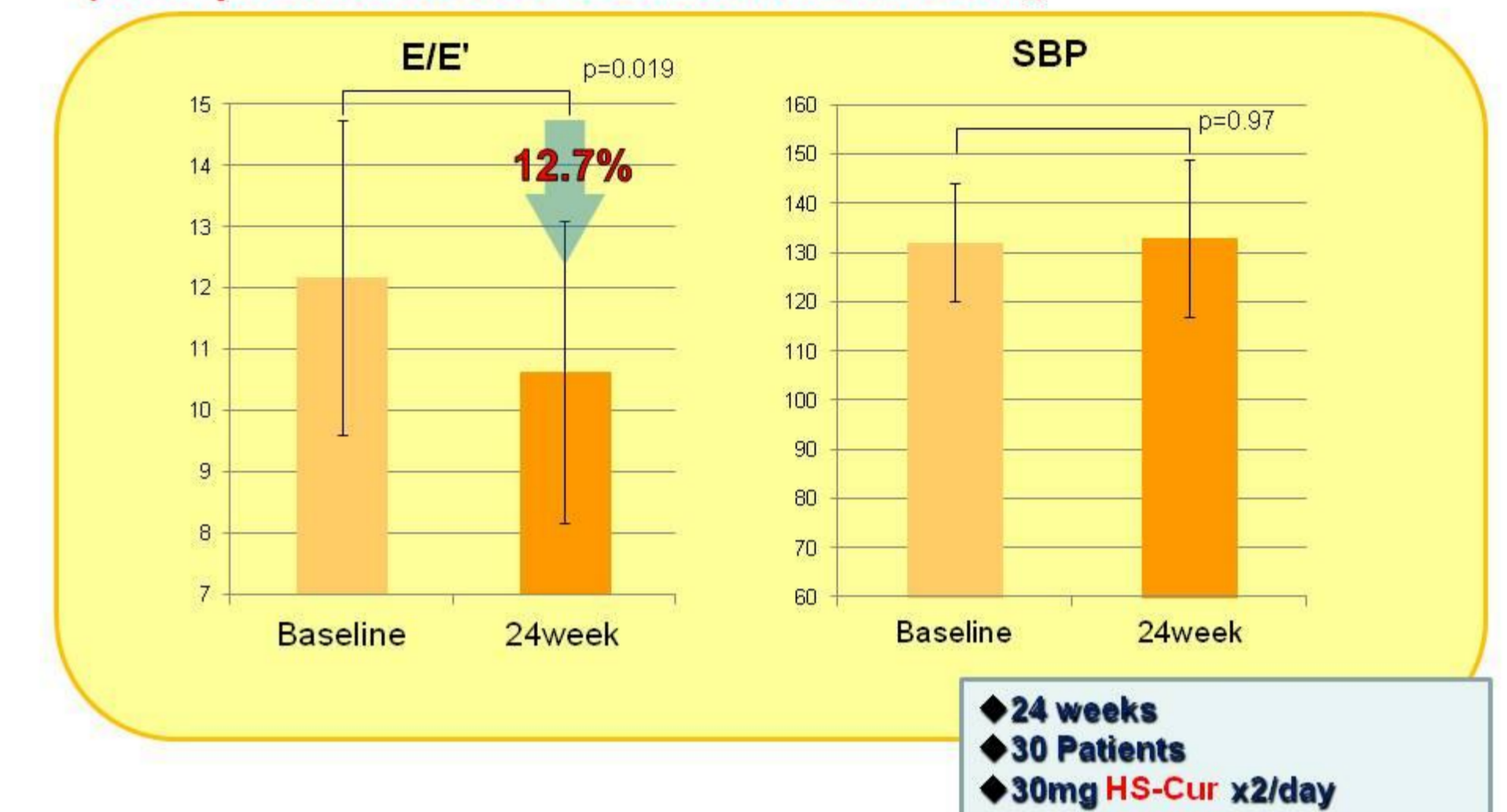


Doppler Ecocardiography before Administration

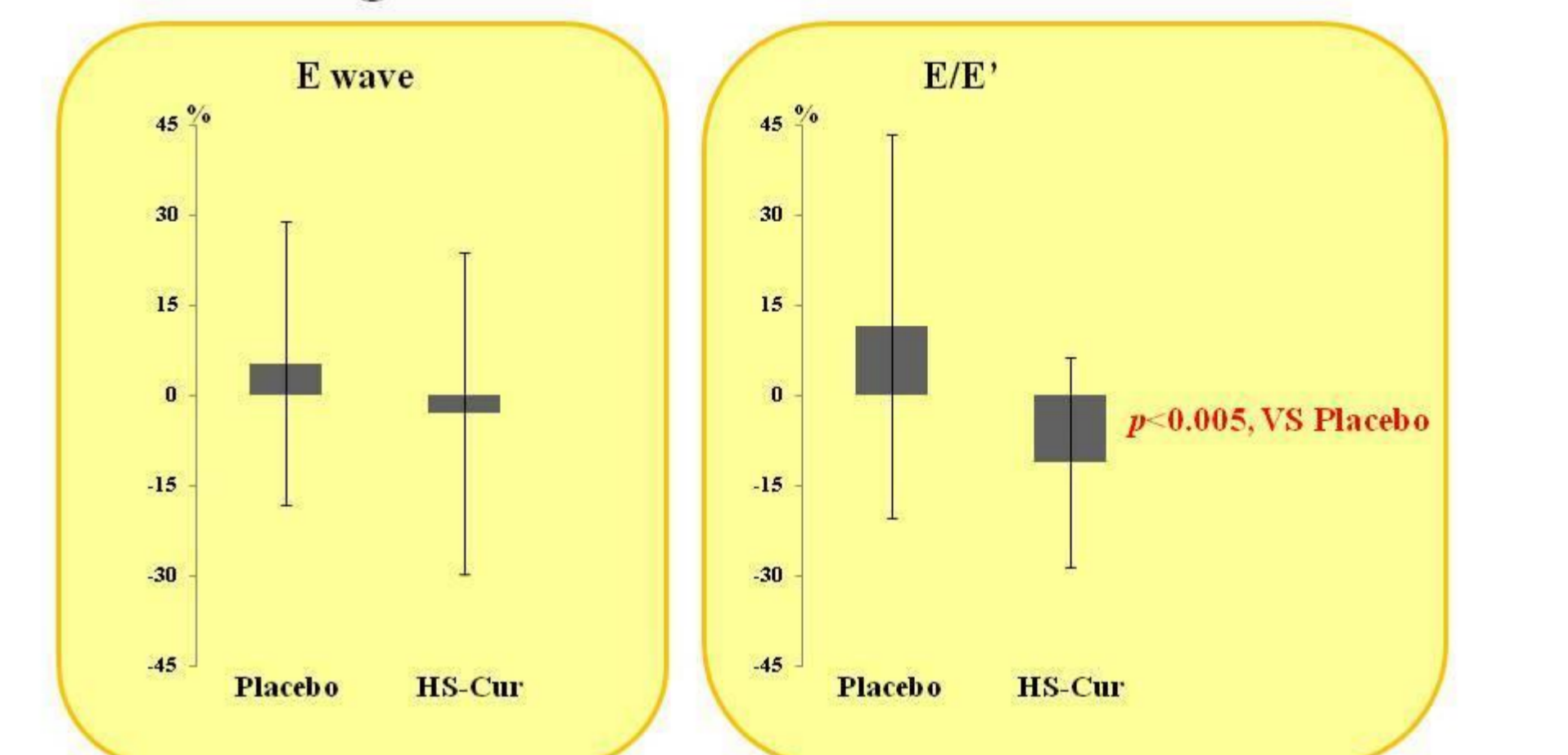


Highly absorptive curcumin improves diastolic function in hypertensive left ventricular hypertrophy

•E/E': Ratio of left ventricular filling velocity vs. mitral annulus velocity (An important indicator of LV diastolic function)



Doppler echocardiography %Change (before→24 weeks after administration)



Hypothesis

We provide the first evidence that highly absorptive curcumin improves diastolic function in hypertensive patients with left ventricular hypertrophy.