Objective Cytchrome P450 2E1 (CYP2E1) is an effective generator of reactive oxygen species, such as the superoxide anion radical and hydrogen peroxide. The expression of CYP2E1 varies with the progression of myocardial ischaemia and cardiomyopathy. This paper examined the heart specific CYP2E1 transgenic mice to study the effect of CYP2E1 on DCM.

Methods The expression of CYP2E1 in both hypertrophic cardiomyopathy (HCM) and DCM mice were analysed using RT-PCR and western blot on cTnTR92Q and cTnTR141W transgenic mice. The cDNA of CYP2E1 was amplified by RT-PCR from the mice heart, and del inserted into the downstream of α-MHC promoter to construct the CYP2E1 expression vector. The transgenic mice were created by the method of microinjection. And they were del crossed with cTnTR141W transgenic mice. The cardiac structure and function were analysed with M-mode echocardiography. Survival data of the experimental mice were recorded. Pathologic changes were observed by light microscopy. The contents of hydrogen peroxide (H2O2), malonaldehyde malondialdehyde (MDA), reduced glutathione (GSH) as well as the total anti oxidation capable (T-AOC) were detected by spectrophotometry. Myocyte apoptosis was analysed by in situ terminal dUTP nick end labelling (TUNEL) stain.

Results In the current paper, it was indicated that expression of CYP2E1 was lightly up- regulated in HCM hearts from cTnTR92Q transgenic mice and was strongly down-regulated in DCM hearts from cTnTR141W transgenic mice at 3 months old. The transgenic expression of CYP2E1 reduced mortality of CYP2E1 transgenic mice by 7.5% and increased the mortality of cTnTR141W transgenic mice from 10% to 45% (n=40, p<0.01). The expression of CYP2E1 also brought about increases in left ventricular volumes, diameters, and decreases in left ventricular walls, ejection fraction and fractional shortening, as well as increases in myocyte disarray and interstitial fibrosis for both of CYP2E1 and cTnTR141W transgenic mice. The levels of H2O2 and MDA were increased and the levels of GSH and T-AOC were strongly reduced in both of CYP2E1 and CYP2E1×cTnTR141W transgenic mice. In addition, myocyte apoptosis del increased 7-fold in the CYP2E1 transgenic mice compared with WT mice (n=5, p<0.01) and increased 1.7-fold in the CYP2E1×cTnTR141W transgenic mice compared with cTnTR141W transgenic mice (n=5, p<0.01).

Conclusions Expression of CYP2E1 was regulated in the progression of transgenic cardiomyopathy mice. CYP2E1-mediated oxidative stress and myocyte apoptosis may play an important role in aggravating the DCM phenotype.