Introduction: Hypertrophic cardiomyopathy (HCM) is known to have impaired energy metabolism due to inappropriate myocardial energy demand or decreased mitochondrial ATP production. We speculate that cardiac mitochondrial homeostasis is one of the significant factors affecting prognosis in patients with HCM. Here, we studied cardiac mitochondrial ultrastructure and respiratory chain enzymatic (RC) activities in patients with HCM.

Methods: Five patients with HCM (or HCM/RCM overlap) (Aged 10-28 y/o) were studied retrospectively. Genetic study showed sarcomeric gene mutation (TNNI3, MYL2) in 3 cases and mtDNA mutation (mt.3243 A>G) in 2 cases. Myocardial samples were obtained by right ventricular endomyocardial biopsy (EMB). Mitochondrial ultrastructure and RC activities in EMB samples were studied by transmission electron microscopy (TEM) and RC assay, respectively. One case (mt.3243 A>G) was lost due to heart failure two years after EMB at 12 years old, and another case (TNNI3) was lost suddenly 10 months after EMB at 11 years old.

Results: TEM revealed increased number of mitochondria in all patients. In patients with mt.3243 A>G, mitochondria appeared quite irregular in size and contour with aberrant cristae. RC assay revealed decreased activity of complex I and I+IV, respectively. In patients with sarcomeric gene mutation, mitochondria appear almost regular in size with lamellar cristae, however some swollen mitochondria with a paucity of cristae were found. Notably, a case of sudden death with TNNI3 mutation had increased number of swollen mitochondria and decreased activity of complex IV, while others revealed almost normal lamellar cristae in EM and normal RC activity.

Conclusions: Mitochondrial evaluation in patients with HCM using EMB may be a critical role in not only diagnosis of primary mitochondrial cardiomyopathy, but assessment of secondary mitochondrial dysfunction in HCM with sarcomeric gene mutation.