心不全心筋におけるナノオーダーの力学特性とクロスブリッジ動態
Altered nano-order elasticity and crossbridge kinetics in failing myocaridium

中村一文[a]、奥山博司[b]、豊田弘子[b]、毛利聡[b]、三浦大志[a]、清水壽一朗[c]、松尾龍人[d]、八木直人[e]
Kazufumi Nakamura[a], Hiroshi Okuyama[b], Hiroko Toyota[b], Satoshi Mohri[b], Daiji Miura[a], Juichiro Shimizu[c], Tatsuhito Matuo[d], Naoto Yagi[e]

[a]岡山大学循環器内科、[b]川崎医科大学、[c]広島国際大学、[d]大阪大学、[e]高輝度光科学研究センター
[a]Department of Cardiovascular Medicine, Okayama University; [b]Kawasaki Medical University; [c]Hiroshima International University; [d]Osaka University; [e]JASRI, Spring-8

イソプロテレノールによるラット肥大心の心筋細胞の硬さを原子間力顕微鏡で測定したところ、正常対象心に比べ、硬さが増していた。その増加は Butanedione monoxime にて減少した。X 線回折像では弛緩期において BDM 後に(1,0)/(1,1)比の増加を認めた。すなわちアクチンに近接したミオシン頭部が減少した。心筋細胞の硬さは肥大心で増加しており、これは不完全な弛緩が関与することが示唆された。

Elasticity of ten living cardiomyocytes was measured by an atomic force microscope (AFM). Elasticity of cardiomyocytes was significantly higher in ISOPROTELENOLE(ISO) group than in control. X-ray diffraction analysis revealed that intensity ratio ((1,0)/(1,1)) at diastole was significantly increased after BDM in ISO group (P<0.005), indicating that proportion of myosin heads in proximity to actin was reduced by BDM. In conclusion, cardiomyocyte stiffness was increased in hearts with ISO-induced hypertrophy. This was caused by incomplete relaxation.

Background: We hypothesized that cardiomyocyte stiffness in transverse direction is increased in hypertrophied hearts.

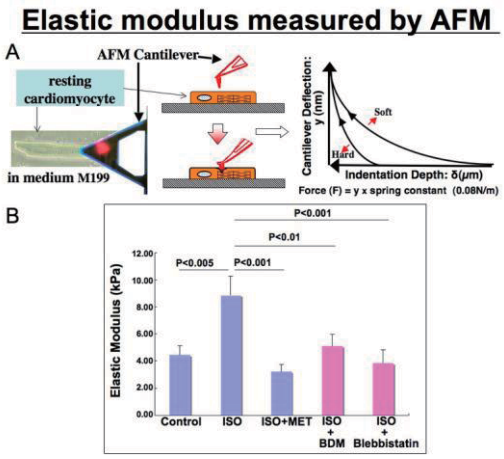
Methods and Results: Male Wistar rats received a vehicle (control), isoproterenol (ISO) or ISO+β1-blocker metoprolol (MET) subcutaneously. After 7 days, compared with those in control and ISO+MET groups, ISO administration had increased left ventricular (LV) wall thickness (P<0.05), and increased LV end-diastolic pressure (*P*<0.05). Elasticity of living cardiomyocytes was measured by an atomic force microscope (AFM) [1] (Fig A). Elasticity of cardiomyocytes was significantly higher in ISO group than in control and ISO + MET groups (Fig B). Butanedione monoxime (BDM), an inhibitor of actin-myosin interaction and blebbistatin, a specific myosin II inhibitor, significantly reduced the elasticity of cardiomyocytes in ISO group (Fig B). X-ray diffraction analysis[2] revealed that intensity ratio ((1,0)/(1,1)) at diastole was significantly increased by BDM in ISO group (P<0.005), indicating that proportion of myosin heads in proximity to actin was reduced by BDM.

Conclusions: Cardiomyocyte stiffness in transverse direction was increased in hearts with ISO-induced hypertrophy. This is caused by incomplete relaxation.

Key words

Beta blocker, diastolic heart failure

Figure



References

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