Acute and chronic changes of myocardial energetics
in the mammalian and human heart*

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Summary

In earlier studies using papillary muscles of the rat left ventricle and highly sensitive thermopiles we demonstrated that the heat liberated per gram of myocardium per unit of developed tension-time integral is decreased when the rats suffered from hypothyroidism or renal hypertension. This increase in economy of force production was shown to be associated with a decrease in myosin-ATPase activity and a change in isomyosin composition. In a recent study we showed an increase in heat per gram of mammalian myocardium per tension-time integral of 70% after application of isoproterenol.

In order to study the relationship between energy costs and developed tension-time integral in the human heart, haemodynamics and myocardial oxygen consumption were measured. The data were obtained using a Millar microtip catheter pressure transducer and the argon method. Haemodynamics and myocardial energetics were analysed in 8 patients without significant heart disease before and after application of isoproterenol and in 10 patients with dilative cardiomyopathy (NYHA II–III). During one cardiac cycle, myocardial oxygen consumption per gram of LV myocardium per beat (MVVO₂/g x beat) is related to LV stress-time integral (ʃσxt). The economy of myocardial contraction (EC) was calculated by

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EC = \frac{ʃσxt}{MVVO₂/g \times \text{beat}}
\]

EC was 11.3 ± 3.2 in normal and 14.3 ± 4.7 dyn × s × g/cm² × μcal in dilative cardiomyopathic hearts (NS). Isoproterenol decreased EC from 11.3 ± 3.2 to 5.5 ± 1.6 dyn × s × g/cm² × μcal in the normal hearts (p < 0.01).

In the rat myocardium, changes in economy of force generation were found due to catecholamines, pressure overload and hypothyroidism. In the human heart, similar energetic changes were observed due to catecholamines. No significant differences in energy of force production were seen between normal and dilative cardiomyopathic hearts.

The effect of catecholamines in the mammalian and human myocardium is explained by changes in activation processes and in chemomechanical energy transduction at the level of the contractile proteins.

Introduction, methods and results

Myocardial energetics may be the key for understanding the fundamental mechanisms involved in cardiac hypertrophy and heart failure. Therefore, we investigated myocardial energetics in experimental animal models as well as in human hearts.

Because it is the aim of our studies to investigate possible energetic changes on the level of the myocardium, the experimental animal studies were performed on left or right

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ventricular papillary muscles in which the energy turnover of an isometric contraction can be measured simultaneously with the force or force-time integral. This type of experiment is not yet possible in the isolated human myocardium. Therefore, myocardial oxygen consumption was measured in the human, and pressure-time, volume-time and pressure-volume data were additionally obtained. Similar to the animal experiments, it was thereby possible to analyse the economy of contraction in terms of force-time integral per myocardial oxygen consumption by normalizing all data for a unit of myocardium.

I. Acute and chronic changes of myocardial energetics in the mammalian heart

Chronic changes of myocardial energetics in the rat are shown to occur in hypothyroidism and pressure-overload hypertrophy [1, 7, 8, 9, 16]. Hypothyroidism was induced by oral application of propylthiouracil (PTU) over a period of 4 weeks. The hypothyrotic myocardium exhibits a slowed contraction phase and a small decrease in peak developed tension (Fig. 1, PTU). Pressure-overload hypertrophy resulted from renal hypertension by narrowing the left renal artery 5 weeks before experimental investigation. The hypertrophied myocardium (GOP means Goldblatt operated) shows a prolongation of the contraction phase and a small increase in peak developed tension (Fig. 1, GOP).

Simultaneously with the tension development we measured liberated initial and total activity-related heat using highly sensitive antimony-bismuth thermopiles [20, 1, 10].

Initial heat is the heat liberated during the contraction period and is therefore a measure of the amount of consumed ATP molecules.

Total activity-related heat is the sum of initial heat and recovery heat. Recovery heat represents the amount of ATP molecules which are resynthesized after the contraction period. Resting heat, which represents basal metabolism, was also measured, but is is not reported in this paper.

As a measure of isometric myocardial contraction economy, we calculated the ratio of developed tension and total activity-related heat or developed tension-time integral and total activity-related heat.

![Fig. 1. Left. Representative isometric mechanograms of control (C) and hypothyrotic (PTU) rat myocardium. Note the increase in time to peak tension and relaxation time. Right. Representative isometric mechanograms of control (C) and pressure-overload (GOP = Goldblatt operated) rat myocardium. Note the increase in peak developed force.](image-url)