Importance of Cardiac Reserve for Evaluation and Prediction of Cardiac Function and Morbidity assessed by low-dose dobutamine stress echocardiography

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet offentligen kommer att försvaras i hörsalen Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg fredagen den 1 juni 2007, kl. 9.00

av

Margareta Scharin Tång

Fakultetsopponent: Professor Anders Waldenström
Norrlands Universitetssjukhus, Umeå

Avhandlingen baseras på följande delarbeten:

I. The function of left ventricular basal segments is most important for long-term recovery. M Scharin Tång, F Waagstein, B Andersson. Int J Cardiology 2007 doi:10.1016/j.ijcard.2006.11.014


IV. Cardiac reserve in the transplanted heart: effect of a graft polymorfism in the β1-adrenoceptor. M Scharin Tång, E Lindberg, B Grünner Svädb, Y Magnusson, B Andersson. Submitted
Importance of Cardiac Reserve for Evaluation and Prediction of Cardiac Function and Morbidity assessed by low-dose dobutamine stress echocardiography

Margareta Scharin Täng

Department of Molecular and Clinical Medicine/Cardiology, Wallenberg Laboratory, Institute of Medicine, the Sahlgrenska Academy at Göteborgs University, Göteborg, Sweden

2007

Abstract

This thesis aimed to evaluate the cardiac reserve’s capacity to be used to predict treatment effects, subclinical heart disease and to evaluate β₁-adrenoceptor (AR) gene polymorphism (Ser49Gly).

Studies were performed in patients with dilated cardiomyopathy, in rats (young, healthy, diabetic and hypertensive), in mice (immunized against the β₁AR) and in heart-transplanted patients.

The cardiac reserve was assessed by low-dose dobutamine stress echocardiography. In both patient studies by dobutamine infusion until an increased baseline heart rate with ~20 bpm, in rats at doses of 10 µg/kg/min and 20 µg/kg/min dobutamine and in mice after an intraperitoneally injection of 1 µg dobutamine/g of body weight.

Both global and regional cardiac reserve can be used to predict treatment effect of metoprolol in dilated cardiomyopathy patients. However, only cardiac reserve in the basal segments of the heart was independently associated with recovery. In heart transplanted patients a gene-polymorphism in the β₁AR in the graft affects cardiac reserve. Patients having the β₁AR Gly49 variants had a lower resting heart rate, a better stress endurance and chronotropic reserve than patients homozygous for Ser49. They also had better diastolic function shown as better lusitropic capacity. Cardiac reserve can also be used to investigate subclinical heart disease in β₁AR immunized mice and to predict heart disease development in these animals. Furthermore, cardiac reserve decreases with age and is depressed both in hypertension and in diabetes rat model.

We conclude that cardiac reserve can predict left ventricular recovery during beta-blocker treatment and that β₁AR polymorphism affects cardiac reserve in humans. Cardiac reserve decreases with age and is impaired both in severe heart disease and during progression of myocardial dysfunction in rats. Furthermore, cardiac reserve can be used to predict cardiomyopathy development after β₁AR immunization in mice.

Keywords: Stress echocardiography, Heart failure, Beta-1-adrenoceptor, Cardiac reserve.