Life Sciences 123 (2015) 100–106

Contents lists available at ScienceDirect

Life Sciences

journal homepage: www.elsevier.com/locate/lifescie

Review article

Evidence for distinct effects of exercise in different cardiac hypertrophic disorders

Emily J. Johnson [a], Brad P. Dieter [b,c], Susan A. Marsh [c,*]

[a] Graduate Program in Pharmaceutical Sciences, College of Pharmacy, Washington State University, Spokane, WA, USA
[b] Graduate Program in Movement Sciences, College of Education, University of Idaho, Moscow, ID, USA
[c] Section of Experimental and Systems Pharmacology, College of Pharmacy, Washington State University, Spokane, WA, USA

ARTICLE INFO

Article history:
Received 20 October 2014
Accepted 2 January 2015
Available online 26 January 2015

Keywords:
Aerobic exercise
Cardiac hypertrophy
Exercise prescription
Pathological hypertrophy
Physiological hypertrophy
Myocardial infarction
Diabetic cardiomyopathy

ABSTRACT

Aerobic exercise training (AET) attenuates or reverses pathological cardiac remodeling after insults such as chronic hypertension and myocardial infarction. The phenotype of the pathologically hypertrophied heart depends on the insult; therefore, it is likely that distinct types of pathological hypertrophy require different exercise regimens. However, the mechanisms by which AET improves the structure and function of the pathologically hypertrophied heart are not well understood, and exercise research uses highly inconsistent exercise regimens in diverse patient populations. There is a clear need for systematic research to identify precise exercise prescriptions for different conditions of pathological hypertrophy. Therefore, this review synthesizes existing evidence for the distinct mechanisms by which AET benefits the heart in different pathological hypertrophy conditions, suggests strategic exercise prescriptions for these conditions, and highlights areas for future research.

Contents

Introduction

Cardiac hypertrophy is enlargement of the heart that occurs in response to metabolic stress, hemodynamic insults, or inherent genetic defects. It is characterized by increases in ventricular wall thickness

* Corresponding author at: Section of Experimental and Systems Pharmacology, College of Pharmacy, Washington State Univ., P.O. Box 1495, Spokane, WA 99210-1495, USA.
E-mail address: susan.marsh@wsu.edu (S.A. Marsh).

http://dx.doi.org/10.1016/j.lfs.2015.01.007
0024-3205/

and/or internal chamber dimensions. With the exception of the physiological hypertrophy that occurs in response to pregnancy or exercise, hypertrophic cardiac remodeling is a response to a pathological condition, and precedes or causes impaired cardiac function [10]. However, the prognoses as well as the structural, metabolic, and functional phenotypes of different hypertrophic disorders are distinct, and depend on the initial insult as well as the presence of cardiovascular comorbidities (Fig. 1).

Aerobic exercise training (AET) reduces the risk of cardiac events with an efficacy comparable to pharmacological therapy [81]. Increasingly, AET is prescribed for the prevention, management, or rehabilitation of those cardiovascular diseases that are characterized by cardiac hypertrophy, including hypertension, myocardial infarction (MI), and diabetic cardiomyopathy [55,78]. The rationale for prescribing AET is based on evidence that it reduces cardiovascular mortality and cardiac event recidivism rates, and improves cardiovascular risk factors such as high blood pressure and overweight [18,67,83,110]. Translational studies have shown that improvements in cardiovascular risk factors can be improved by both interval-based and continuous AET [52,112,117]. Therefore, a key question is what modes and intensities of exercise elicit the greatest benefit in individuals with various hypertrophic conditions.

Evidence for the effects of exercise training in humans with cardiovascular disease is mixed, and the exercise programs that have been used to investigate these effects use highly varied methods and outcome measures [80,99]. The Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) Trial is the largest clinical trial to date examining the effects of AET in patients with reduced ejection fraction or New York Heart Association class II-IV heart failure who were normalized to exercise training or usual care [38,84]. Thirty-six weeks of supervised cardiac rehabilitation followed by home-based AET until the median follow-up point of 30 months was associated with modest but significant reductions in rehospitalization and all-cause mortality, after these outcomes were adjusted for key prognostic indicators such as atrial arrhythmias [84]. Similarly, exercise training improved self-reported wellbeing assessed by the Kansas City Cardiomyopathy Questionnaire [38].

These data indicate that AET is an effective therapy for improving outcomes in patients with pathological cardiac remodeling and cardiac dysfunction. However, evidence for the structural and functional effects of aerobic exercise on different types of pathological cardiac hypertrophy is lacking, and the effects may differ depending on the mode or duration of training. Therefore, the purpose of this review is to summarize current evidence for the therapeutic mechanisms and efficacy of AET in different types of cardiac hypertrophy.

Physiological hypertrophy

Chronic AET, such as running, rowing or cycling, is associated with 12-lead electrocardiogram (ECG) changes indicative of increases in ventricular mass [5,114]. Echocardiographic studies unequivocally support the existence of an "athlete's heart" [6], characterized by eccentric ventricular remodeling, an increase in septal thickness and ventricular wall thickness [123,124], and normal or improved ejection fraction (EF) [90]. In male athletes, left ventricular wall thickness may be between 12 and 16 mm in male athletes [94]; in females, this increase is about 23% less [89]. This remodeling is beneficial to cardiac function and is associated with improved oxygen delivery, angiogenesis, and nitric oxide sensitivity [46].

Classic "physiological" hypertrophy results from AET and not from resistance exercise training. Indeed, it is important to clarify that resistance strength training actually results in concentric cardiac hypertrophy, and a reduction in internal ventricular chamber dimensions [8,26]. The resistance-trained heart is therefore morphologically similar

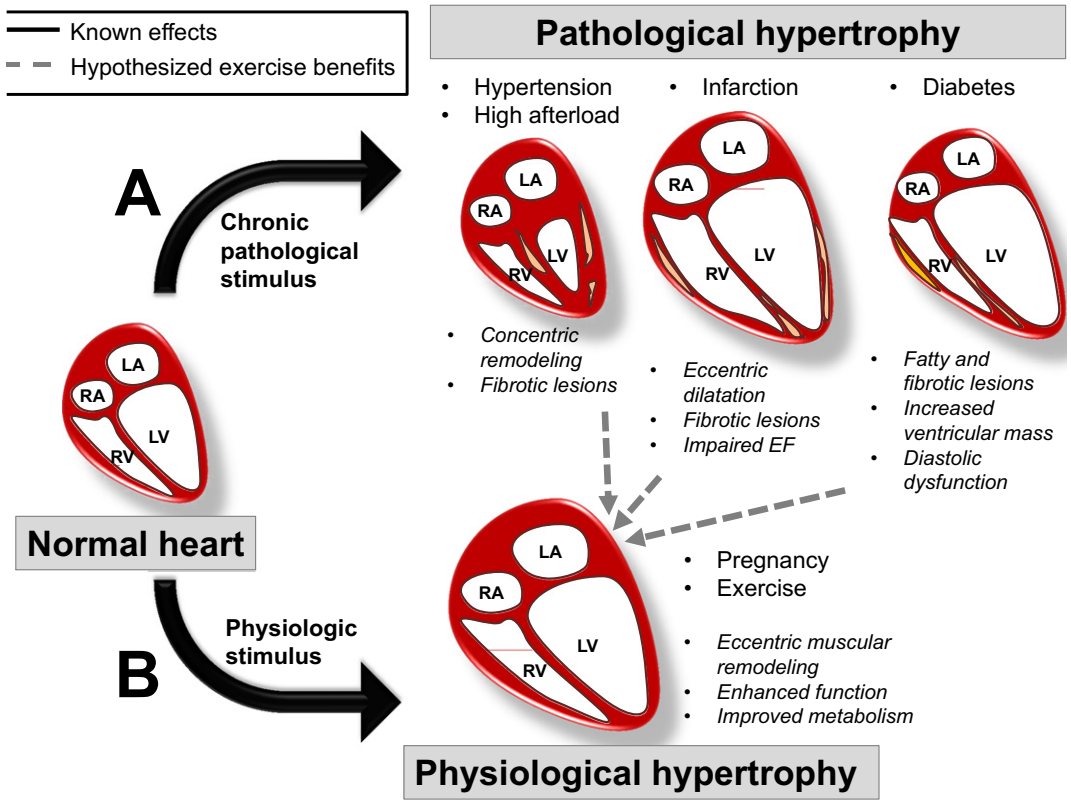

Fig. 1. Phenotypes of physiological and pathological cardiac hypertrophy. (A) Chronic pathological insults such as hypertension, myocardial infarction, and chronic diabetes result in morphologically distinct types of pathological cardiac hypertrophy. (B) Physiological stimuli such as exercise and pregnancy induce physiological cardiac enlargement, or hypertrophy. Tan areas indicate fibrotic lesions. Orange areas indicate fatty streaks.