The relationships between galectin-3 levels with cardiac structure and function in resistance-trained athletes

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Received: 14 November 2018 / Accepted: 23 January 2019

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Abstract

Introduction: Galectin-3 is a new and promising biomarker for heart failure and myocardial fibrosis. Although clinical studies indicated that galectin-3 levels are strongly associated with changes of left ventricular structure and function in patients with chronic heart failure, but these relationships in athletes are not well known. The present study was conducted to examine the relationships between galectin-3 levels with cardiac structure and function in resistance-trained athletes.

Material & Methods: Fifteen resistance-trained male athletes (aged: 23.0 ± 1.4 years and BMI: 24.1 ± 1.4 kg/m²; ± SD) volunteered to participate in this study. Galectin-3 concentrations were assessed by enzyme-linked immunosorbent assay (ELISA) kits and cardiac morphology and function were assessed by echocardiography. Pearson correlation test was used to analyze the relationship between the variables.
Results: The results demonstrated that there were no significant relationships between galectin-3 concentrations with left ventricle ejection fraction (LVEF) \( (r = -0.12 , P = 0.6) \), aorta \( (r = 0.12 , P = 0.6) \) and pulmonary artery diameter \( (r = 0.25 , P = 0.3) \), posterior wall thickness of left ventricle at end diastole (PWTLV) \( (r = -0.27 , P = 0.3) \), interventricular septal \( (r = -0.15 , P = 0.9) \), left ventricle end-diastolic volume (LVEDV) \( (r = 0.009 , P = 0.9) \), and left ventricle end-systolic volume (LVESV) \( (r = 0.24 , P = 0.3) \).

Conclusions: In conclusion, galectin-3 concentration is not a powerful predictor for cardiac structure and function in resistance-trained athletes.

Keywords: Galectin-3, Cardiac structure, Cardiac function, Resistance-trained athletes

1. Introduction
Intense regular physical exercise is often associated with morphologic and physiologic heart modification known as "athlete's heart" (1). Morganroth et al. (1975) were the first to postulate two different morphological forms of athlete's heart: endurance and strength athlete's heart (2). Indeed, cardiovascular response to exercise largely depends on the type of exercise performed. Resistance training (e.g., weight lifting, body building) often determines left ventricular (LV) concentric hypertrophy, characterized by a relative wall thickness > 0.42 and increase in LV mass index (3,4). Resistance-trained athletes undergo static exercise and may develop a concentric hypertrophy secondary to pressure overload; indeed LV chambers in resistance-trained athletes are smaller compared to endurance-trained athletes. (5,6).

Galectin-3 is a 26-kDa beta-galactoside-binding protein belonging to the galectin cluster (7). It consists of one carbohydrate recognition domain (CRD) and one regulatory domain with repeated collagen-like regions (8). Galectin-3 is produced by a variety of cell types including macrophages, mast cells, eosinophils and neutrophils (9). In murine
Galectin-3 and cardiac structure

In tissues, Galectin-3 is amply expressed in, for example, lung and colon, and at lower levels in, for example, heart and liver (10). Many biological activities have been attributed to Galectin-3 depending on cell type including effects on apoptosis, cytokine production, cell migration and adhesion (11). Within recent years, Galectin-3 has been implicated in the pathophysiology of heart failure by modulating cardiac remodelling and fibrosis (12). Moreover, Galectin-3 in serum is increased in patients with heart failure (13), and elevated Galectin-3 is associated with cardiovascular and all-cause mortality in elderly people (14). Galectin-3 levels are also increased in certain malignant tumours, thyroid (15) and colonic (16) in particular, and circulating Galectin-3 holds promise as a useful seromarker of disease dissemination (17).

Although brain natriuretic peptide (BNP) and its N-terminal fragment NT-proBNP are the most commonly used biomarkers in cardiac remodeling in patients with heart failure (HF) (18-20) and in well trained-athletes (21), the association between galectin-3 and heart structure and function are not well known.

Chen et al. (2013) were studied the association among plasma galectin-3 levels and cardiac structure in patients with HF. The results indicated that the level of plasma galectin-3 was positively correlated with diastolic left atrial diameter (DLAD) and left ventricular end-diastolic diameter (LVEDD), but negatively correlated with left ventricular ejection fraction (LVEF) (22). By our knowledge no previous study has investigated the association among plasma galectin-3 levels and cardiac structure in well trained-athletes, thus the present study was conducted to examine the relationships between galectin-3 levels with cardiac structure and function in resistance-trained athletes.

2. Material & Methods

Subjects

The study population comprised of fifteen resistance-trained male athletes with a mean (±SD) age of 23.0 ± 1.4 years and weight of 78.3 ± 8.1 kilogram. Participants were strength trained at least 3 times per week for more than 3 years. The Islamic Azad University, Marvdasht
branch Ethics Committee approved the study and written informed consent was obtained from all subjects.

**Measurements**

*Anthropometric and body composition measurements*

Height and body weight were measured, and body mass index (BMI) was calculated by dividing body mass (kg) by height (m$^2$). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist (cm) by hip circumference (cm). Body fat percentage was assessed by skinfold thickness protocol. Skinfold thickness was measured sequentially, in chest, abdominal, and thigh by the same investigator using a skinfold caliper (Harpenden, HSK-BI, British Indicators, West Sussex, UK) and a standard technique.

*Biochemical measurement*

Blood for measurement of galectin-3 concentrations was collected by venipuncture in Vacuette polyethylene terephthalate glycol EDTA tubes (Greiner Bio-One) on the day of the echocardiographic evaluation. Blood samples were centrifuged at 3500g for 10 min at 4°C immediately after collection. Galectin-3 levels were determined in duplicate via an enzyme-linked immunosorbent assay (ELISA) kits (Hangzhou Eastbiopharm Co., LTD, China) with a sensitivity of 2.49 pg/ml.

*Echocardiography*

M-Mode and 2-dimensional images and spectral and color-flow Doppler recordings were obtained with a single commercially available instrument operating at 2.0 – 3.5 MHz. Two-dimensional imaging examinations were performed in the standard fashion in parasternal long and short-axis views and apical 4- and 2-chamber views. All measurements were performed as recommended (23).

Two-dimensional echocardiograms were subjected to careful visual analyses to detect regional contractile abnormalities. Left ventricular end-systolic and end-diastolic volumes (LVEDV and LVESV) and
ejection fraction (LVEF) were derived from biplane apical (2- and 4-chamber) views with the modified Simpson’s rule algorithm. Left ventricular dimensions were measured from M-mode images by the leading-edge technique, which included interventricular septal thickness at end diastole and posterior wall thickness of left ventricle at end diastole (PWTLV).

**Statistical analysis:**
Data were analyzed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL). Shapiro-wilk t-test was used for normality. Pearson correlation test was used to evaluate the relationship between the variables. The significance level of this study was set at P < 0.05.

3. Results
Personal characteristics of the subjects are presented in the Table 1. As shown in the Table 1, the subjects have the normal weight, WHR and body fat percentage.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>23.0</td>
<td>1.4</td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>78.3</td>
<td>8.1</td>
</tr>
<tr>
<td>BMI (Kg.m^-2)</td>
<td>24.1</td>
<td>1.4</td>
</tr>
<tr>
<td>WHR</td>
<td>0.87</td>
<td>0.04</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>12.0</td>
<td>3.3</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>9.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>68.3</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Galectin-3 level and cardiac structure and function parameters of the subjects are presented in the Table 2 (See the abbreviations below the table).
Table 2. Galectin-3 level and cardiac structure and function parameters of the subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galectin-3 (pg/ml)</td>
<td>782.6</td>
<td>567.9</td>
</tr>
<tr>
<td>PWTLV (mm)</td>
<td>10.6</td>
<td>1.1</td>
</tr>
<tr>
<td>Interventricular septal (mm)</td>
<td>11.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Aorta diameter (mm)</td>
<td>29.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Pulmonary artery diameter (mm)</td>
<td>26.7</td>
<td>2.4</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>53.4</td>
<td>8.3</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>95.5</td>
<td>15.5</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>42.9</td>
<td>9.5</td>
</tr>
</tbody>
</table>

PWTLV: Posterior wall thickness of left ventricle at end diastole; LVEF: left ventricle ejection fraction; LVEDV: left ventricle end-diastolic volume and LVESV: left ventricle end-systolic volume.

The Shapiro-wilk test demonstrated that the data had distribute normal, thus Pearson test was used to evaluate the relationship between galectin-3 levels with cardiac structure and function. The correlation between the variables is presented in the Table 3. The results, demonstrated that there were no significant relationship between galectin-3 levels and cardiac structure including: PWTLV, Interventricular septal, Aorta diameter and Pulmonary artery diameter. As shown in the Table 3, no significant relationship was observed between galectin-3 levels and cardiac function including: LVEF, LVEDV and LVESV.

Table 3. Relationships between galectin-3 an cardiac parameters of the subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Galectin-3 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
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<tr>
<td><strong>Cardiac structure variables</strong></td>
<td></td>
</tr>
<tr>
<td>PWTLV</td>
<td>-0.27</td>
</tr>
<tr>
<td>Interventricular septal (mm)</td>
<td>-0.15</td>
</tr>
<tr>
<td>Aorta diameter (mm)</td>
<td>0.12</td>
</tr>
<tr>
<td>Pulmonary artery diameter (mm)</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>Cardiac function variables</strong></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>-0.12</td>
</tr>
<tr>
<td>LVEDV</td>
<td>0.009</td>
</tr>
<tr>
<td>LVESV</td>
<td>0.24</td>
</tr>
</tbody>
</table>
4. Discussion
Although the relationship between the BNP and echocardiographic measures of cardiac structure and function has been widely explored in healthy people, cardiovascular patients or athletes, there is no study was performed to examine the relationship between galectin-3 concentrations with cardiac structure and function in athletes population. The aim of present study was to examine the relationships between galectin-3 levels with cardiac structure including PWTLV, Interventricular septal, Aorta diameter, Pulmonary artery diameter and the relationships between galectin-3 levels with cardiac function including LVEF, LVEDV and LVESV in resistance-trained athletes.

The results showed that PWTLV and interventricular septal in resistance-trained male athletes are greater than the normal range (10.6 mm vs., 9.3 mm and 11.0 mm vs., 9.2 mm respectively). Kou et al. (2014) reported the reference ranges of PWTLV (9.3 mm for males and 8.5 mm for females) and interventricular septal (9.2 mm for males and 8.2 mm for females) for healthy males and females (24). Previous studies in line with the present study results indicated that resistance-trained individuals have both the PWTLV and interventricular septal greater than average (25-27). Haykowsky et al. (2000) noted three mechanisms for resistance training-induced cardiac hypertrophy: (1) acute cardiopulmonary mechanisms that minimize the increase in transmural pressure and LV wall stress during exercise, (2) the underlying use of anabolic steroids by the athletes, or (3) the specific type of resistance training performed (26).

The results showed that LVEF and LVEDV in resistance-trained male athletes are lower than the normal range (53.4% vs., 63.3% and 95.5 ml vs., 107.1 ml respectively); however, LVESV in resistance-trained male athletes is greater than the normal range (42.9 ml vs., 39.7 ml). The reference ranges of LVEF (63.3% for males and 64.1% for females), LVEDV (107.1 ml for males and 83.8 ml for females) and LVESV (39.7 ml for males and 30.2 ml for females) reported by Kou et al. (2014) previously (24). LV systolic function is generally assessed in echocardiographic studies by measuring the extent of fiber shortening, ejection fraction and velocity of circumferential fiber shortening (28),
while diastolic function is assessed by studying the pattern of ventricular filling through the mitral valve (29). Abnormalities in systolic and diastolic function are generally associated with cardiac hypertrophy induced by pathological conditions, such as hypertension and valvular disease (30,32). The present study results are in agreement with those in the literature where reports demonstrate that cardiac function is not altered in resistance-trained individuals (27,32,33).

Exercise-induced increases in cardiac biomarkers, such as troponin, a marker of cardiomyocyte damage, and BNP, a marker of myocardial stress, are common in athletes after endurance and resistance exercise (21,34). Recent studies explored the impact of endurance exercise on novel cardiac biomarkers, such as galectin-3, a marker of myocardial fibrosis (35). Resting levels of galectin-3 were higher in athletes compared to controls (12.8 ± 3.4 vs. 10.5 ± 3.0), whereas significant increases were observed following a 30-km run (12.8 ± 3.4 to 19.9 ± 3.9 ng/ml, p < 0.001) (35). Increases in cardiac biomarkers are modest and transient, but the clinical implications of these elevations are unknown. Accordingly, long-term exercise training/competition with repetitive exposure to prolonged vigorous exercise may increase cardiac fibrosis. By our knowledge no previous study has investigated the association among plasma galectin-3 levels and cardiac structure in well trained-athletes. The results, demonstrated that there were no significant relationship between galectin-3 levels and cardiac structure including: PWTLV, Interventricular septal, Aorta diameter and Pulmonary artery diameter and no significant relationship was observed between galectin-3 levels and cardiac function including: LVEF, LVEDV and LVESV in resistance-trained male athletes. Chen et al. (2013) were studied the association among plasma galectin-3 levels and cardiac structure and function in patients with HF. The results indicated that the level of plasma galectin-3 was positively correlated with DLAD and LVEDD, but negatively correlated with LVEF (22). Recently, Ansari et al. (2018) mentioned that galectin-3 concentrations were associated with PWTLV, interventricular septal and left atrium area in patients with heart failure with preserved ejection fraction syndrome (36). These discrepant results may be attributed to differences in subject populations because our subjects were well-trained athletes while patients with HF and patients
with heart failure with preserved ejection fraction syndrome were participated in the Chen et al. and Ansari et al. studies respectively. Clinical studies indicated that Galectin-3 is essentially a product of active macrophages with binding sites on cardiac-resident fibroblasts, mechanistically influencing increased myocardial collagen expression, interstitial fibrosis, TGF-β activation, and subsequent LV dysfunction (37-39). Its role in response to injury and inflammation in HF is further supplemented by a significant contribution to ventricular remodeling (40).

5. Conclusion
The results indicated that there were no significant relationship between galectin-3 levels and cardiac structure and function in resistance-trained male athletes, thus galectin-3 concentration is not a powerful predictor for cardiac structure and function in these population.

Reference


