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

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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/m^2; ± 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

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 and function 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 1. Anthropometric, body composition and physiological characteristics of the subjects

Variables	Mean	SD
Age (y)	23.0	1.4
Body weight (Kg)	78.3	8.1
BMI ($Kg.m^{-2}$)	24.1	1.4
WHR	0.87	0.04
Body fat (%)	12.0	3.3
Fat mass (kg)	9.5	3.3
Lean body mass (kg)	68.3	5.4

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

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

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

Variables	Galectin-3 (pg/ml)	
	r	P
Cardiac structure variables		
PWTLV	– 0.27	0.3
Interventricular septal	– 0.15	0.9
Aorta diameter	0.12	0.6
Pulmonary artery diameter	0.25	0.3
Cardiac function variables		
LVEF	– 0.12	0.6
LVEDV	0.009	0.9
LVESV	0.24	0.3

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

1. Maron BJ. Structural features of the athlete heart as defined by echocardiography. J Am Coll Cardiol 1986; 7: 190-203.

2. Morganroth J, Maron BJ, Henry WL, Epstein SE. Comparative left ventricular dimensions in trained athletes. Ann Intern Med 1975; 82: 521-524.

3. D'Andrea A, Limongelli G, Caso P, Sarubbi B, Della Pietra A, Brancaccio P, et al. Association between left ventricular structure and cardiac performance during effort in two morphological forms of athletes heart. Int J Cardiol 2002; 86: 177-184.

4. D'Andrea A, Caso P, Scarafile R, Salerno G, De Corato G, Mita C, et al. Biventricular myocardial adaptation to different training protocols in competitive master athletes. Int J Cardiol 2007; 115: 342-349.

5. D'Andrea A, Caso P, Severino S, Galderisi M, Sarubbi B, Limongelli G, et al. Effects of different training protocols on left ventricular myocardial function in competitive athletes: a Doppler tissue imaging study. Ital Heart J 2002; 3: 34-40.

6. Spence AL, Naylor LH, Carter HH, Buck CL, Dembo L, Murray CP, et al. A prospective randomised longitudinal MRI study of left ventricular adaptation to endurance and resistance exercise training in humans. J Physiol 2011; 589(Pt 22): 5443-5452.

7. Barondes SH, Cooper DN, Gitt MA, Leffler H. Galectins. Structure and function of a large family of animal lectins. J Biol Chem 1994; 269: 20807-20810.

8. Rapoport EM, Kurmyshkina OV, Bovin NV. Mammalian galectins: structure, carbohydrate specificity, and functions. Biochemistry (Mosc) 2008; 73: 393-405.

9. Dumic J, Dabelic S, Flogel M. Galectin-3: an open-ended story. Biochim Biophys Acta 2006; 1760: 616-635.

10. Kim H, Lee J, Hyun JW, Park JW, Joo HG, Shin T. Expression and immunohistochemical localization of galectin-3 in various mouse tissues. Cell Biol Int 2007; 31: 655-662.

11. Liu FT, Rabinovich GA. Galectins: regulators of acute and chronic inflammation. Ann N Y Acad Sci 2010; 1183: 158-182.

12. de Boer RA, Voors AA, Muntendam P, van Gilst WH, van Veldhuisen DJ. Galectin-3: a novel mediator of heart failure development and progression. Eur J Heart Fail 2009; 11: 811-817.

13. van der Velde AR, Gullestad L, Ueland T, Aukrust P, Guo Y, Adourian A, et al. Prognostic value of changes in galectin-3 levels over time in patients with heart failure: data from CORONA and COACH. Circ Heart Fail 2013; 6: 219-226.

14. Daniels LB, Clopton P, Laughlin GA, Maisel AS, Barrett-Connor E. Galectin-3 is independently associated with cardiovascular mortality in community-dwelling older adults without known cardiovascular disease: the Rancho Bernardo Study. Am Heart J 2014; 167: 674-682.

15. Chiu CG, Strugnell SS, Griffith OL, Jones SJ, Gown AM, Walker B, et al. Diagnostic utility of galectin-3 in thyroid cancer. Am J Pathol 2010; 176: 2067-2081.

16. Barrow H, Guo X, Wandall HH et al. Serum galectin-2, -4, and -8 are greatly increased in colon and breast cancer patients and promote cancer cell adhesion to blood vascular endothelium. Clin Cancer Res 2011;17:7035–46.

17. Chen C, Duckworth CA, Zhao Q, Pritchard DM, Rhodes JM, Yu LG. Increased circulation of galectin-3 in cancer induces secretion of metastasis-promoting cytokines from blood vascular endothelium. Clin Cancer Res 2013;19:1693–704.

18. Gustafsson F, Badskjær J, Hansen FS, Paulsen AH, Hildebrandt P. Value of N-terminal proBNP in the diagnosis of left ventricular systolic dysfunction in primary care patients referred for echocardiography. Heart Drug 2003; 3: 141-146.

19. Gardner RS, Ozalp F, Murday AJ, Robb SD, McDonagh TA. N-terminal pro-brain natriuretic peptide. A new gold standard in predicting mortality in patients with advanced heart failure. Eur Heart J 2003; 24: 1735-1743.

20. Costello-Boerrigter LC, Boerrigter G, Redfield MM, Rodeheffer RJ, Urban LH, Mahoney DW, et al. Amino-terminal pro-B-type natriuretic peptide and B-type natriuretic peptide in the general community: determinants and detection of left ventricular dysfunction. J Am Coll Cardiol 2006; 47: 345-353.

21. Bordbar S, Bigi MA, Aslani A, Rahimi E, Ahmadi N. Effect of endurance and strength exercise on release of brain natriuretic peptide. J Cardiovasc Dis Res 2012; 3: 22-25.

22. Chen K, Jiang RJ, Wang CQ, Yin ZF, Fan YQ, Cao JT, Han ZH, et al. Predictive value of plasma galectin-3 in patients with chronic heart failure. Eur Rev Med Pharmacol Sci 2013; 17: 1005-1011.

23. Armstrong WF, Feigenbaum H. Echocardiography. In: Braunwald E, Zipes DP, Libby P, eds. Heart disease: a textbook of cardiovascular medicine, 6th ed. Philadelphia: WB Saunders, 2001: 160-228.

24. Kou S, Caballero L, Dulgheru R, Voilliot D, De Sousa C, Kacharava G, et al. Echocardiographic reference ranges for normal cardiac

chamber size: results from the NORRE study. Eur Heart J Cardiovasc Imaging 2014; 15: 680-690.

25. Fagard RH. Impact of different sports and training on cardiac structure and function. Cardiol Clin 1997; 15: 397-412.

26. Haykowsky MJ, Quinney HA, Gillis R, Thompson CR. Left ventricular morphology in junior and master resistance trained athletes. Med Sci Sports Exerc 2000; 32: 349-352.

27. Barauna VG, Rosa KT, Irigoyen MC, de Oliveira EM. Effects of resistance training on ventricular function and hypertrophy in a rat model. Clin Med Res 2007; 5: 114-120.

28. Spirito P, Pelliccia A, Proschan MA, Granata M, Spataro A, Bellone P, et al. Morphology of the "athlete's heart" assessed by echocardiography in 947 elite athletes representing 27 sports. Am J Cardiol 1994; 74: 802-806.

29. Shimizu G, Hirota Y, Kita Y, Kawamura K, Saito T, Gaasch WH. Left ventricular midwall mechanics in systemic arterial hypertension. Myocardial function is depressed in pressure-overload hypertrophy. Circulation 1991; 83: 1676-1684.

30. Hildick-Smith DJ, Shapiro LM. Echocardiographic differentiation of pathological and physiological left ventricular hypertrophy. Heart 2001; 85: 615-619.

31. Nishimura RA, Housmans PR, Hatle LK, Tajik AJ. Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography. Part I. Physiologic and pathophysiologic features. Mayo Clin Proc 1989; 64: 71-81.

32. Colan SD, Sanders SP, Borow KM. Physiologic hypertrophy: effects on left ventricular systolic mechanics in athletes. J Am Coll Cardiol 1987; 9: 776-783.

33. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. JAMA 2002; 287: 1308-1320.

34. Eijsvogels TM, Fernandez AB, Thompson PD. Are there deleterious cardiac effects of acute and chronic endurance exercise? Physiol Rev 2016; 96: 99-125.

35. Hattasch R, Spethmann S, de Boer RA, et al. Galectin-3 increase in endurance athletes. Eur J Prev Cardiol 2014; 21: 1192-1199.

36. Ansari U, Behnes M, Hoffmann J, Natale M, Fastner C, El-Battrawy I, et al. Galectin-3 reflects the echocardiographic grades of left ventricular diastolic dysfunction. Ann Lab Med 2018; 38: 306-315.

37. Sharma UC, Pokharel S, van Brakel TJ, van Berlo JH, Cleutjens JP, Schroen B, et al. Galectin-3 marks activated macrophages in failure-prone hypertrophied hearts and contributes to cardiac dysfunction. Circulation 2004; 110: 3121-3128.

38. Liu YH, d'Ambrosio M, Liu YD, Peng H, Rhaleb NE, Sharma U, et al. Nacetyl-seryl-aspartyl-lysyl-proline prevents cardiac remodeling and dysfunction induced by galectin-3, a mammalian adhesion/growth-regulatory lectin. Am J Physiol Heart Circ Physiol 2009; 296: H404-H412.

39. de Boer RA, Voors AA, Muntendam P, van Gilst WH, van Veldhuisen DJ. Galectin-3: a novel mediator of heart failure development and progression. Eur J Heart Fail 2009; 11: 811-817.

40. Shah RV, Chen-Tournoux AA, Picard MH, van Kimmenade RR, Januzzi JL. Galectin-3, cardiac structure and function, and long-term mortality in patients with acutely decompensated heart failure. Eur J Heart Fail 2010; 12: 826-832.