Association of Serum Myonectin Concentrations With the Presence of Atrial Fibrillation

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Research

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Abstract

Objective: Myonectin, a recently found myokine, has a role of inhibiting inflammation. The aim of this research is to see if myonectin levels are linked to the occurrence of atrial fibrillation (AF).

Methods: We examined serum myonectin in a population of 194 patients with AF who were then classified into three subgroups: paroxysmal AF, persistent AF, and permanent AF. Atrial remodeling was assessed using left atrial diameter (LAD).

Results: Serum myonectin was significantly lower in AF group compared with healthy controls. Logistic regression analysis demonstrated that serum myonectin concentrations were correlated with a decreased risk of AF. Patients with permanent AF displayed decreased serum myonectin than in persistent and paroxysmal AF groups. Serum myonectin was lower in persistent AF group than in paroxysmal AF group. Serum myonectin concentrations in AF patients were negatively associated with body mass index (BMI), systolic blood pressure, diastolic blood pressure, and LAD. BMI and LAD stayed to be correlated with serum myonectin according to multiple stepwise regression analysis.

Conclusion: Our study demonstrated a correlation between serum myonectin and AF.

Introduction

Atrial fibrillation (AF), a common cardiac rhythm disorder, is an important indicator of morbidity and mortality [1]. The incidence of AF increases with aging. The development of AF is correlated with changes in the electrical and structural remodeling of the atria [2]. The potential mechanism of AF is still unclear. Recent studies have highlighted significant connection between AF and aging, obesity, and inflammation [3].

Myonectin, also known as CTRP15—C1q/TNF-related protein, stimulates fatty acid absorption in adipocytes and hepatocytes [4]. The myonectin level dropped dramatically after exercise preparation in females [5]. Myonectin blocked lipopolysaccharide induced inflammatory reaction to in macrophages via the S1P/cAMP/Akt-dependent biochemical pathway [6]. This indicates that myonectin has a role of inhibiting inflammation. Inflammation plays a role in the development of AF. As a result, myonectin is thought to play a protective role in the pathogenesis of AF.

We conducted this cross-sectional study to see whether serum myonectin is linked to the development of AF.

Materials And Methods

Subjects

This research was carried out on a group of 194 patients who had been diagnosed with AF. Valvular heart disease, diabetes, hyperthyroidism, acute coronary syndrome, cardiac surgery, and infection disease
during the past month were all exclusion factors for patients with AF. Patients with AF were then divided into three groups: paroxysmal (n=71), chronic (n=60), and permanent (n=63). The control group consisted of 112 healthy adults. The control group was comparable to the case group in terms of age, gender, and body mass index (BMI). The Human Ethics Review Committee at our hospital gave their approval to the study procedure, and each subject signed a consent document.

**Measurements**

The serum myonectin was estimated using an enzyme-linked immunosorbent assay kit (Aviscera Biosciences, Santa Clara, CA). An experienced echocardiography specialist assessed the left atrial diameter (LAD).

**Statistical analysis**

The data were exhibited as means ± standard errors or median (interquartile range). The differences of clinical characteristics between the case and control groups were determined using unpaired t test, Chi-square tests, or Mann-Whitney U test. Logistic regression analysis was used to determine the risk factor for AF development. Comparison of the characteristics between the three AF subgroups was performed by Chi-square tests, one-way ANOVA, or Kruskal-Wallis test. Linear regression analysis was utilized to see if there was a correlation between serum myonectin and other variables. *P*-value of less than 0.05 was thought to be statistically significant.

**Results**

**Baseline clinical characteristics**

When compared to controls, AF patients had higher systolic blood pressure (SBP), diastolic blood pressure (DBP), low-density lipoprotein cholesterol (LDL-C), and LAD, as well as lower high-density lipoprotein cholesterol (HDL-C).

**Serum myonectin concentrations in AF patients**

In the case group, serum myonectin concentrations were lower than in the control group (*P* < 0.001) (Table 1). SBP, DBP, LDL-C, HDL-C, and serum myonectin were all linked to AF in a univariate logistic regression study (Table 2). After multivariate logistic regression analysis, serum myonectin was still linked to a lower risk of AF (Table 2).

**Table 1** Clinical and biochemical characteristics of the case and control groups
|                  | The controls | AF patients | P value |
|------------------|--------------|-------------|---------|
| N                | 112          | 194         |         |
| Age (years)      | 62.07 ± 10.15| 61.55 ± 9.88| 0.66    |
| Gender (M/F)     | 57/55        | 99/95       | 0.982   |
| BMI (Kg/m²)      | 25.1 ± 2.7   | 25.34 ± 2.94| 0.481   |
| SBP (mmHg)       | 123.84 ± 9.18| 135.02 ± 12.26| < 0.001|
| DBP (mmHg)       | 77.19 ± 7.25 | 83.38 ± 8.98 | < 0.001 |
| TC (mmol/L)      | 4.3 ± 0.84   | 4.45 ± 1.17 | 0.253   |
| TG (mmol/L)      | 1.41 ± 0.52  | 1.5 ± 0.93  | 0.333   |
| LDL-C (mmol/L)   | 2.74 ± 0.47  | 3.05 ± 0.73 | < 0.001 |
| HDL-C (mmol/L)   | 1.16 ± 0.2   | 1.09 ± 0.21 | 0.006   |
| LAD (mm)         | 28.58 ± 3.69 | 40.97 ± 4.27| < 0.001 |
| Myonectin (pg/mL)| 321.65 (256.11-395.66) | 265.81 (222.04-303.63) | < 0.001 |

Table 2 Logistic regression Analysis for the presence of AF
### Differences in clinical characteristics between AF subgroups

Table 3 shows the characteristics of AF subgroups. Permanent AF patients had elevated LAD and decreased serum myonectin than in paroxysmal and persistent AF patients. In addition, relative to paroxysmal AF patients, persistent AF patients had substantially higher LAD and lower serum myonectin.

**Table 3** Clinical and biochemical characteristics of AF subgroups.
The correlation with other variables

Serum myonectin concentrations in AF patients were found to be negatively associated with BMI, SBP, DBP, and LAD in simple linear regression model (Table 4). BMI and LAD are both linked to serum myonectin according to multiple stepwise regression analysis (Table 4).

Table 4 Linear regression analyses between serum myonectin and other clinical parameters

|                      | paroxysmal AF | persistent AF | permanent AF | P value |
|----------------------|---------------|---------------|--------------|---------|
| N                    | 71            | 60            | 63           |         |
| Age (years)          | 61.76 ± 9.61  | 62.05 ± 10.54 | 60.84 ± 9.41 | 0.774   |
| Gender (M/F)         | 35/36         | 30/30         | 34/29        | 0.851   |
| BMI (Kg/m²)          | 25.47 ± 3.17  | 25.26 ± 3.06  | 25.25 ± 2.55 | 0.89    |
| SBP (mmHg)           | 135.32 ± 10.91| 133.58 ± 13.18| 136.03 ± 12.83 | 0.525   |
| DBP (mmHg)           | 82.18 ± 7.5   | 82.67 ± 10.68 | 85.4 ± 8.5³a | 0.089   |
| TC (mmol/L)          | 4.51 ± 1.18   | 4.2 ± 1.16    | 4.61 ± 1.15  | 0.126   |
| TG (mmol/L)          | 1.58 ± 0.9    | 1.34 ± 0.76   | 1.56 ± 1.08  | 0.274   |
| LDL-C (mmol/L)       | 2.97 ± 0.71   | 3.05 ± 0.73   | 3.15 ± 0.77  | 0.39    |
| HDL-C (mmol/L)       | 1.16 ± 0.23   | 1.06 ± 0.21³a| 1.05 ± 0.14³a| 0.004   |
| LAD (mm)             | 38.19 ± 4.07  | 41.7 ± 3.18³a | 43.42 ± 3.6³ab| <0.001  |
| Myonectin (pg/mL)    | 294.15        | 268.07        | 245.25       | <0.001  |
|                      | (241.88–331.4)| (224.38–309.12³a)| (185.74–275.71³ab)|         |

³a P< 0.05 vs paroxysmal AF patients; ³b P< 0.05 vs persistent AF patients
|                        | Simple linear regression | Multiple linear regression |
|------------------------|--------------------------|---------------------------|
|                        | r            | P     | β     | P     |
| Age (years)            | 0.112        | 0.12  |       |       |
| Gender (M/F)           | -0.002       | 0.983 |       |       |
| BMI (Kg/m²)            | -0.288       | <0.001| -0.235| <0.001|
| SBP (mmHg)             | -0.215       | 0.003 | -0.175| 0.053 |
| DBP (mmHg)             | -0.205       | 0.004 | -0.06 | 0.504 |
| TC (mmol/L)            | -0.008       | 0.908 |       |       |
| TG (mmol/L)            | -0.056       | 0.439 |       |       |
| LDL-C (mmol/L)         | -0.046       | 0.523 |       |       |
| HDL-C (mmol/L)         | 0.051        | 0.478 |       |       |
| LAD (mm)               | -0.369       | <0.001| -0.325| <0.001|

**Discussion**

AF is a significant predictor of morbidity and mortality. As a result, it's critical to determine the likelihood of AF earlier and then to devise methods to avoid or handle AF. Serum myonectin concentrations were significantly lower in patients with AF than in the controls according to our findings. Serum myonectin may be used as a new biomarker to predict the existence and intensity of AF.

Recent studies have focused on the important role of inflammation in AF pathogenesis. Atrial biopsy specimens from lone AF patients showed the infiltration of lymphomononuclear cells and necrosis of the adjacent myocytes, while those from subjects with sinus rhythm showed no significant inflammation [7]. Inflammatory activity of epicardial adipose tissue was higher in patients with AF than that in controls [8]. Aviles et al reported that subjects with higher C-reactive protein (CRP) levels showed higher prevalence of AF compared with those with lower CRP levels [9]. In addition, CRP was demonstrated to predict the risk for future development of AF. Baseline higher CRP predicted a higher risk for developing future AF after a follow-up of median 7.8 years [9]. On the other hand, anti-inflammatory therapy had an effect on the development of AF. A meta review including 42 randomized controlled trials demonstrated that glucocorticoids treatment significantly lowered participants' risk of developing perioperative AF compared with placebo [10]. Therefore, inflammation is closely correlated with AF mechanism.
In comparison to wild-type mice, ischemia-reperfusion increased the size of myocardial infarcts, cardiac dysfunction, apoptosis, and proinflammatory gene expression such as TNF-, interleukin-6 (IL-6), and monocyte chemoattractant protein 1 (MCP-1) in myonectin-knockout mice [6]. TNF- and IL-6 expression in the ischemic heart was substantially lower in myonectin-transgenic mice relative to wild-type mice [6]. Myonectin incubation reduced lipopolysaccharide-induced expression of TNF-, IL-6, and MCP-1 in macrophages [6]. In diabetic patients, serum myonectin concentrations were found to be inversely linked to CRP [11]. These results pointed to myonectin's anti-inflammatory properties. As a result, myonectin can interact with inflammatory molecules and play a role in the development of AF by promoting the inflammatory action.

There are some possible drawbacks to this report. First, the sample size is insufficient to draw firm conclusions. More research with a large sample size is needed. Second, our research is of a cross-sectional kind. Future longitudinal research would be required to validate the causal relationship.

Finally, serum myonectin levels are inversely linked to the occurrence of AF and atrial remodeling.

**Declarations**

**Ethics approval and consent to participate**

This study was approved by the Research Ethics Committee of Peking University Shenzhen Hospital. Informed consent was obtained from all participants.

**Consent for publication**

All authors approved the paper publication.

**Availability of data and material**

Data are available upon reasonable request.

**Competing interests**

All authors have no interests to declare.

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**Authors' contributions**

Xiongbiao Chen conceived and designed the research. Chun Wang and Ye Luo collected data and conducted the research. Liangxian Qiu and Xiaosu Li completed the ELISA assay. Chun Wang and Qianwen Huang wrote the initial paper. All authors read and approved the final manuscript.
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