Association of Serum Omentin-1 Concentrations with the Presence of Atrial Fibrillation

**Background:** Omentin-1 is one of the adipokines associated with obesity, diabetes, and coronary heart disease development. We determined to investigate whether serum omentin-1 concentrations were correlated with the presence of atrial fibrillation (AF).

**Material/Methods:** Serum omentin-1 concentrations were examined in a cross-sectional population that included 220 patients with AF (70 with paroxysmal AF, 78 with persistent AF, and 72 with permanent AF) and 115 healthy controls.

**Results:** Reduced serum omentin-1 concentrations were found in AF patients compared to the controls. In addition, patients with permanent AF had lower serum omentin-1 concentrations compared to patients with persistent AF and patients with paroxysmal AF. Significantly decreased serum omentin-1 concentrations were observed in persistent AF patients compared to paroxysmal AF patients. Spearman correlation analysis suggested that serum omentin-1 concentrations were negatively correlated with left atrial diameter in AF patients.

**Conclusions:** Serum omentin-1 concentrations were correlated with the presence of AF and atrial remodeling.

**MeSH Keywords:** Adipokines • Atrial Fibrillation • Inflammation Mediators • Obesity Hypoventilation Syndrome

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Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice, and contributes to a high prevalence of mortality and morbidity [1]. The exact mechanism underlying AF is complex and unclear. Factors such as aging, obesity, diabetes, hypertension, and cardiovascular diseases are considered to increase the risk of developing AF [2].

Omentin, a novel adipokine, is produced and secreted mainly by visceral adipose tissue. Omentin is codified by two genes named omentin-1 and omentin-2, and the former is the major circulating form [3]. Recombinant omentin-1 results in increased insulin-stimulated glucose uptake and Akt phosphorylation in human adipocytes [4]. Recently, omentin-1 has been shown to be correlated with obesity [5], hypertension [6], diabetes [7], and coronary artery disease (CAD) [8]. Omentin-1 is speculated to mediate the mechanism of AF.

The aim of this study was to determine the correlation between serum omentin-1 concentrations and the presence of AF and atrial remodeling.

Material and Methods

Patients

A cross-sectional study was performed in a consecutive population of 220 patients who were diagnosed with AF. The criteria for a diagnosis of AF were in accordance with the guidelines established by American Heart Association [9]. Patients were excluded from the study if they had valvular heart disease, hyperthyroidism, acute coronary syndrome, previous cardiac surgery, or systemic disease. AF patients were divided into three groups according to American Heart Association guidelines [9]: paroxysmal AF (n=70), persistent AF (n=78), and permanent AF (n=72). Control participants were recruited from individuals presenting for routine checkup in our hospital. Patients with systemic disease were excluded from this study. The study plan was approved by the Research Ethics Committee of our hospital (NO. GDREC2012143H), and all patients provided informed consent.

Measurements

Anthropometric (height, weight, and blood pressure), clinical, and laboratory analysis were performed. Venous blood was collected after a minimum of 10 hours of fasting for further examination. An enzyme-linked immunosorbent assay kit (Cusabio Biotech Corporation, USA) was utilized to evaluate serum omentin-1 concentrations. Transthoracic echocardiography was performed by experienced echocardiologists on all patients to evaluate the characteristics of their left atrial diameter (LAD).

Statistical analysis

The data were exhibited as means ± standard errors (interquartile range). The unpaired t-test, chi-square tests, or the Mann-Whitney U test was utilized to determine the parameter differences between AF patients and control patients. Comparison of the characteristics between the three AF subgroups was performed by chi-square tests, one-way ANOVA, or the Kruskal-Wallis test. The correlation of serum omentin-1 concentrations with LAD were analyzed by Pearson correlation analysis. A value of p less than 0.05 was statistically significant.

Results

Baseline clinical characteristics

AF patients showed higher levels of SBP, DBP, LDL-C, and LAD, as well as statin, aspirin, and warfarin treatment, compared to healthy controls (Table 1).

Serum omentin-1 concentrations in AF patients

AF patients showed significantly reduced serum omentin-1 concentrations compared to healthy controls (Table 1). The characteristics of AF subgroups are shown in Table 2. In AF subgroups, permanent AF patients had lower serum omentin-1 concentrations compared to paroxysmal AF and persistent AF patients (Figure 1). Furthermore, significant decreased serum omentin-1 concentrations were observed in persistent AF patients compared to paroxysmal AF patients (Figure 1).

The correlation of serum omentin-1 with AF

Simple and multiple logistic regressions both showed a significant association of serum omentin-1 with a decreased risk of developing AF (Table 3). The ROC curve of serum omentin-1 concentrations determining AF development are shown in Figure 2.

Serum omentin-1 concentrations with other characteristics

Pearson correlation analysis revealed a negative relationship of serum omentin-1 concentrations with BMI (r=-0.283, p<0.001), TG (r=-0.256, p<0.001), and LAD (r=-0.332, p<0.001).

Discussion

The present study indicated that AF patients had reduced serum omentin-1 concentrations compared to the healthy
### Table 1. Clinical and biochemical characteristics of AF patients and controls.

|                  | The controls | AF patients                  | P value |
|------------------|--------------|------------------------------|---------|
| N                | 115          | 220                          | 0.244   |
| Age (years)      | 58.43±9.55   | 59.75±10.03                  | 0.770   |
| Gender (M/F)     | 61/54        |                              |         |
| BMI (Kg/m²)      | 24.28±2.47   | 24.57±2.99                   | <0.001  |
| SBP (mmHg)       | 123.13±9.12  | 136.09±14.11                 | <0.001  |
| DBP (mmHg)       | 80.11±5.52   | 85.82±10.40                  | 0.210   |
| TC (mmol/L)      | 4.91±0.88    | 5.05±0.99                    | 0.295   |
| TG (mmol/L)      | 1.52±0.47    | 1.60±0.81                    | 0.001   |
| LDL-C (mmol/L)   | 3.19±0.45    | 3.43±0.74                    | 0.126   |
| HDL-C (mmol/L)   | 1.14±0.22    | 1.17±0.23                    | 0.566   |
| Smoking, n (%)   | 25 (21.74%)  | 54 (24.55%)                  | <0.001  |
| Statin treatment, n (%) | 17 (22.86%) | 152 (70.45%)                 | <0.001  |
| aspirin treatment, n (%) | 21 (18.26%) | 115 (52.27%)                | <0.001  |
| warfarin treatment, n (%) | –        | 90 (40.91%)                  |         |
| Omentin-1 (ng/mL)| 203.13 (168.39–245.07) | 156.49 (133.49–187.14) |         |

### Table 2. Clinical and biochemical characteristics of AF subgroups.

|                  | Paroxysmal AF | Persistent AF | Permanent AF | P value |
|------------------|---------------|---------------|--------------|---------|
| N                | 70            | 78            | 72           |         |
| Age (years)      | 59.41±9.87   | 60.90±10.71   | 58.83±9.43   | 0.429   |
| Gender (M/F)     | 33/37         | 41/37         | 39/33        | 0.680   |
| BMI (Kg/m²)      | 24.41±2.89   | 24.74±3.14    | 24.55±2.96   | 0.799   |
| SBP (mmHg)       | 138.21±12.57 | 133.21±13.24 a| 137.15±15.99 | 0.072   |
| DBP (mmHg)       | 85.93±9.49   | 83.85±10.19   | 87.85±11.19 b| 0.062   |
| TC (mmol/L)      | 5.02±0.97    | 4.96±0.97     | 5.17±1.04    | 0.407   |
| TG (mmol/L)      | 1.53±0.65    | 1.49±0.76     | 1.80±0.97 ab | 0.036   |
| LDL-C (mmol/L)   | 3.40±0.71    | 3.41±0.78     | 3.48±0.73    | 0.805   |
| HDL-C (mmol/L)   | 1.16±0.23    | 1.12±0.20a    | 1.11±0.21 b  | 0.285   |
| Smoking, n (%)   | 16 (22.86%)  | 18 (23.08%)   | 20 (27.78%)  | 0.739   |
| Statin treatment, n (%) | 40 (51.14%) | 50 (64.10%)    | 62 (86.11) ab | <0.001 |
| aspirin treatment, n (%) | 57 (81.43%) | 56 (71.79%) | 2 (2.78%) ab | <0.001 |
| warfarin treatment, n (%) | –            | 90 (40.91%)   |             |         |

* P<0.05 vs. paroxysmal AF; † P<0.05 vs. persistent AF.
controls. Serum omentin-1 concentrations were negatively correlated with left atrial diameter in AF patients. In short, this is the first study that has demonstrated the association of serum omentin-1 and AF.

Adipokine is a cytokine produced from adipocytes. Recent studies have demonstrated the important role of adipokines in the mechanism of AF. Some adipokines, such as adiponectin [10] and resistin [11] were reported to be associated with the development of AF. Our results also showed a correlation between omentin-1, another adipokine, and AF development. These results point to an important role for adipose tissue and adipokine in the pathophysiology of AF. Nowadays, serum biomarkers are used in the diagnosis and prediction of cardiovascular disease [12,13]. Therefore, serum omentin-1 may be utilized as a new biomarker to predict and assess the risk of developing AF.

Obesity has been reported to be correlated with the development of AF. Large body size, assessed using body surface area in youth, and weight gain from age 20 to midlife, have both been independently correlated to AF development [14]. During a median time of 12.9 years’ follow-up, BMI was associated with an increased risk of 4.7% with each kilogram per square meter of developing AF [15]. In addition, overweight and obesity were associated with adjusted short-term increased risk of AF development [15]. Omentin-1 is a newly discovered adipokine associated with lipid metabolism and obesity. Plasma

Table 3. Logistic regression analysis for the presence of AF.

| Simple regression | Multiple regression |
|-------------------|---------------------|
| **OR (95%CI)**    | **P**               | **OR (95%CI)** | **P**               |
| Age (years)       | 1.014 (0.991–1.038) | 0.244          | 1.014 (0.991–1.038) | 0.244          |
| Gender (M/F)      | 1.070 (0.681–1.680) | 0.770          | 1.070 (0.681–1.680) | 0.770          |
| BMI (Kg/m²)       | 1.038 (0.957–1.125) | 0.367          | 1.038 (0.957–1.125) | 0.367          |
| SBP (mmHg)        | 1.101 (1.073–1.130) | <0.001         | 1.101 (1.073–1.130) | <0.001         |
| DBP (mmHg)        | 1.087 (1.052–1.123) | <0.001         | 1.087 (1.052–1.123) | <0.001         |
| TC (mmol/L)       | 1.166 (0.917–1.482) | 0.210          | 1.166 (0.917–1.482) | 0.210          |
| TG (mmol/L)       | 1.191 (0.858–1.653) | 0.295          | 1.191 (0.858–1.653) | 0.295          |
| LDL-C (mmol/L)    | 1.794 (1.243–2.591) | 0.002          | 1.794 (1.243–2.591) | 0.002          |
| HDL-C (mmol/L)    | 0.453 (0.164–1.252) | 0.127          | 0.453 (0.164–1.252) | 0.127          |
| Smoking, n (%)    | 1.171 (0.683–2.008) | 0.566          | 1.171 (0.683–2.008) | 0.566          |
| Omentin-1 (ng/mL) | 0.972 (0.965–0.979) | <0.001         | 0.972 (0.965–0.979) | <0.001         |
Omentin-1 concentrations, as well as omentin-1 gene expression levels, were significantly decreased in obese and overweight subjects compared to lean subjects [5]. Furthermore, plasma omentin-1 concentrations were inversely correlated with BMI and waist circumference [5]. Circulating omentin-1 concentrations increased significantly after weight loss [16] and aerobic training [17]. These results point to the important role of omentin-1 in obesity. Therefore, omentin-1 may have a protective effect in AF development and persistence of AF partly by inhibiting obesity or regulating lipid metabolism.

Diabetes, hypertension, and CAD are clear risk factors for developing AF. Serum omentin-1 concentrations were markedly reduced in patients with type 2 diabetes [7]. Omentin inhibited platelet-derived growth factor BB-induced vascular smooth muscle cell migration by reducing oxidative stress [18]. This indicates that omentin-1 may serve as a target for treating hypertension by inhibiting vascular structural remodeling [18]. In addition, omentin treatment inhibited pulmonary arterial hypertension in rats by inhibiting vascular structural remodeling and abnormal contractile reactivity [6]. Furthermore, omentin treatment inhibited contractile dysfunction and insulin resistance in cardiomyocytes. Decreased serum omentin-1 concentrations were found in patients with CAD [8]. The aforementioned results indicate a close correlation between omentin-1 and diabetes, hypertension, and CAD.

Recent evidence has focused on the important role of inflammation in AF development. AF patients have shown elevated circulating inflammatory markers. Those inflammatory markers could predict AF development and AF recurrence [19]. Omentin-1 has been demonstrated to have an anti-inflammatory role. Omentin inhibited tumor necrosis factor (TNF)-induced vascular inflammation in human endothelial cells [20,21]. Furthermore, a negative correlation was found between serum omentin-1 and inflammatory mediators such as TNF-α, interleukin-6 (IL-6), and C-reactive protein [22,23]. Inflammation is a potential mechanism for AF. Omentin-1 is hypothesized to take part in the mechanism of AF by inhibiting inflammation.

The limitations of the present study should be considered. First, this is a cross-sectional study. Therefore, our findings should be validated by further longitudinal studies. Second, the sample of our study is relatively small.

Conclusions

In conclusion, serum omentin-1 concentrations were inversely correlated with the development of AF and atrial remodeling.

Conflict of interests

All authors have no conflict of interests to declare.
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