Adiponectin in Chronic Thromboembolic Pulmonary Hypertension

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Background: The correlation between serum adiponectin concentration and hemodynamics or certain metabolic markers in patients with chronic thromboembolic pulmonary hypertension (CTEPH) is unknown.

Methods and Results: We enrolled 30 CTEPH patients who underwent interventional therapy of balloon pulmonary angioplasty or pulmonary endarterectomy. Serum adiponectin concentrations positively correlated with B-type natriuretic peptide (BNP) concentrations, pulmonary vascular resistance, and mean pulmonary arterial pressure. After the therapeutic interventions, serum adiponectin concentrations improved and changes in serum adiponectin concentrations significantly correlated with changes in BNP concentrations.

Conclusions: Adiponectin can be a useful marker for the severity of CTEPH.

Key Words: Adiponectin; B-type natriuretic peptide; Chronic thromboembolic pulmonary hypertension
Adiponectin in CTEPH

Figure. Serum adiponectin concentrations in patients with chronic thromboembolic pulmonary hypertension (CTEPH). (A) Serum adiponectin concentrations in 17 patients with World Health Organization functional class (WHO-FC) I or II and 13 patients with WHO-FC III or IV. (B) Correlations between log adiponectin concentrations and different clinical parameters (n=30 patients). (C) Changes in serum adiponectin concentrations in 8 patients who underwent an interventional therapy, such as pulmonary endarterectomy or balloon pulmonary angioplasty, from before to 6 months after therapy. The boxes show the interquartile range, with the median value indicated by the horizontal line; whiskers show the range. Symbols indicate individual data points. (D) Correlation between changes (from before to 6 months after therapy) in serum adiponectin and BNP concentrations. 6MWD, 6-min walk distance; BMI, body mass index; BNP, B-type natriuretic peptide; HDL-C, high-density lipoprotein cholesterol; HOMA-R, homeostasis model assessment of insulin resistance; PAP, pulmonary arterial pressure; PVR, pulmonary vascular resistance; SvO₂, mixed venous oxygen saturation; TAPSE, tricuspid annular plane systolic excursion in echocardiography; TG, triglycerides.
distribution in values of changes of both adiponectin and BNP levels was confirmed by Shapiro-Wilk normality test. The performance of the study using patients’ samples and analysis of data were approved by the institutional review boards of Keio University Hospital, and all the patients provided informed consent.

**Results**

Serum adiponectin concentrations were significantly lower in patients categorized as World Health Organization functional classes (WHO-FC) I and II than in those categorized as WHO-FC III and IV (medium [IQR] 12.7 [8.6–17.1] vs. 21.8 [13.2–34.4] μg/mL, respectively; P=0.022; Figure A). Serum adiponectin concentrations inversely correlated with 6-min walk distance, mixed venous oxygen saturation, body mass index, body weight, insulin levels, TG, TG:HDL-C ratio, HOMA-R, and tricuspid annular plane systolic excursion (Figure B). Furthermore, serum adiponectin concentrations positively correlated with BNP (P=0.034; Figure D), and not with changes in metabolic markers such as insulin concentrations (P=0.236), TG (P=0.517), TG:HDL-C ratio (P=0.727), and body weight (P=0.632), hemodynamic markers such as mean PAP (P=0.801), PVR (P=0.701), and cardiac output (P=0.384), and 6-min walk distance (P=0.941).

**Discussion**

The present study demonstrated that serum adiponectin concentrations in CTEPH patients before intervention correlated with both markers of IR and hemodynamics, suggesting that adiponectin is a useful marker of both IR and the severity of CTEPH. Serum adiponectin concentrations decreased after PEA or BPA. Changes in adiponectin concentrations correlated with changes in BNP concentrations, despite no correlation with metabolic or hemodynamic markers, suggesting that the decrease in serum adiponectin level after the interventions was mainly affected by the improvement in right heart overload, rather than improvement in the pulmonary circulation. Thus, these findings suggest the importance of measuring serum adiponectin level as a biomarker, rather than the pathophysiology in CTEPH.

Adiponectin is primarily expressed in adipose tissue, but recent studies have reported adiponectin expression in cardiomyocytes. In patients with chronic heart failure (CHF), increases in BNP are related to the production of adiponectin. High adiponectin concentrations have been reported as a predictor of death in patients with CHF. These previous findings raise the possibility that, in the case of pulmonary hypertension, pressure- and/or volume-overloaded cardiomyocytes in the right ventricle may produce adiponectin, explaining the relationship between adiponectin and BNP concentrations and raising the possibility of using adiponectin as a biomarker and predictor of death in CTEPH and right heart failure. Furthermore, another study reported that adiponectin has beneficial effects on vascular remodeling in a mouse model of PAH. Thus, there is another possibility that the increase in adiponectin concentration identified in the present study has a protective effect in CTEPH patients, but further studies are needed to clarify all potential roles of adiponectin in CTEPH.

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None.

**Relationship With Industry Policy**

The authors have no relationships with industry relevant to this study.

**References**


