Nutrition, Metabolism & Cardiovascular Diseases (2015) **25**, 594–601

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

High circulating adiponectin levels predict decreased muscle strength among older adults aged 70 years and over: A prospective cohort study

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Received 19 January 2015; received in revised form 13 March 2015; accepted 17 March 2015
Available online 27 March 2015

KEYWORDS
Adipokine;
Sarcopenia;
Physical function;
Aging

Abstract *Background and aims:* Population-based researches indicate that circulating adiponectin is inversely associated with muscle strength. However, interpretation of the findings has been limited by the use of a cross-sectional design. This study aimed to examine the prospective relationship between baseline circulating adiponectin concentration and change in muscular function-related physical performance in older adults.
Methods and results: A 1-year prospective cohort study of Japanese community-dwelling elderly was conducted between 2002 and 2003. Four hundred thirty-four older persons participated in the measurements of physical function, including leg extension power, functional reach, timed up-and-go test, and 10-m maximum walking speed, at baseline and follow-up. After adjustment for potential covariates, higher serum adiponectin concentration was found to be significantly associated with poorer physical performance at baseline (leg extension power [watt], $P < 0.001$; functional reach [cm], $P < 0.001$; log timed up-and-go test, $P = 0.007$; log 10-m maximum walking speed, $P < 0.001$). The results of the prospective analysis by analysis of covariance indicated that the elderly with higher serum adiponectin concentrations (tertiles) at baseline tended to have a decreased performance in leg extension power (means [95% confidence interval]: lowest, −105 [−125, −85.7]; middle, −117 [−135, −97.8]; highest, −140 [−160, −120], watt, P for trend = 0.021) and timed up-and-go test (lowest, −0.08 [−0.28, −0.12]; middle, −0.10 [−0.29, 0.10]; highest, 0.28 [0.07, 0.48], s, P for trend = 0.019), but not two other functioning.
Conclusion: High circulating adiponectin concentration may be an indicator of decreased physical performance, especially muscle strength, in older adults.

Introduction

Adiponectin, first identified in 1996, is a 244-amino acid protein that is abundantly expressed in adipose tissue [1]. Having been shown to be related to lower incidence rates of type 2 diabetes and metabolic syndrome [2], this adipocyte-derived hormone is believed to benefit human health. Recently, however, increasing evidence

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http://dx.doi.org/10.1016/j.numecd.2015.03.010
0939-4753/

from population-based studies indicated that circulating adiponectin level is related to cardiovascular events and mortality in older subjects [3,4]. High circulating adiponectin concentration was also reported to be a predictor of bone mineral density loss [5] and lung function decline [6]. Such epidemiological findings indicate the potentially paradoxical involvement of adiponectin in health status.

Most recently, a population-based epidemiological study showed that the elderly with relatively higher circulating adiponectin levels tended to have an increasing number of frailty components compared to the elderly with relatively lower levels [7]. Furthermore, the potential negative effect of adiponectin on physical function is supported by the findings of two population-based prospective cohort studies that concur that relatively higher serum adiponectin concentration contributes to incident physical disability in older subjects from the United States [8] and Japan [9]. Based on these findings, an inverse correlation between adiponectin and skeletal muscle function, an essential component of physical function, has been hypothesized. It is worth to note that muscle strength decreased after the age of 50 and muscle strength loss is most dramatic after 70 years old [10]. Previous study showed that the lower-extremity muscle strength in older adults aged 75 years decreased by 16.5% during 2.8 years follow-up [11]. Thus, decline of muscle strength with age has become a major public health problem since lower muscle strength is a predictor of mortality in the elderly [12].

In a previous study, we identified an inverse association between serum adiponectin concentration and upper- and lower-extremity muscle strength in middle-aged Japanese adults [13]. Similar findings were reported by several other cross-sectional studies in which high circulating adiponectin concentration was found to be associated with poor muscle strength in European adolescents [14] and adults [15,16]. Although an inverse association between adiponectin concentration and muscle strength has been indicated, prospective research on this topic is limited. Therefore, this prospective cohort study aimed to examine the relationship between baseline serum adiponectin concentrations and changes in lower-extremity muscle strength, as well as other components of physical function among community-dwelling elderly adults.

Methods

Study participants

The study participants were the participants of the Tsurugaya Project, a community-based Comprehensive Geriatric Assessment (CGA) of Japanese aged $\geq$70 years who are living in the Tsurugaya area of Sendai City, Japan. In brief, the CGA used a structured approach to measure the physical, mental, and social functionings of older individuals to assess early deterioration in long-term care conditions and promote healthy aging. The methods used in the Tsurugaya Project have been reported in detail elsewhere [9,17].

Among the 2730 elderly inhabitants residing in the Tsurugaya area in 2002, 1198 participated in the health survey, yielding a 43.8% response rate, and 1177 provided written informed consent to be included in the analysis, yielding a 43.1% participation rate. Of the 1177 potential participants, 672 were excluded from the analysis owing to missing data regarding serum adiponectin concentration and 21 were excluded owing to lack of data regarding physical function measurements, yielding a sample of 484 potential participants at baseline. A further 50 participants were excluded because they had not participated in physical function measurement in 2003 or had a measured value of 0 for leg extension power assessment, which was considered as a measurement error. As a result, an analytical sample of 434 participants was used for the prospective research. The study protocol was approved by the institutional review board of Tohoku University Graduate School of Medicine.

Serum adiponectin measurement

In this study, all blood samples were obtained under nonfasting conditions. It is has been that circulating adiponectin did not differ between fasting and nonfasting conditions [18]. Serum adiponectin concentration was determined by enzyme-linked immunosorbent assay (Otsuka Pharmaceutical, Tokyo, Japan) or latex particle-enhanced turbidimetric immunoassay (Mitsubishi Chemical Medience, Tokyo, Japan), the results of which were closely correlated ($r = 0.98$) [19]. The intra-assay and inter-assay coefficients of variation were $<$10% for enzyme-linked immunosorbent assay, and $\leq$2% for latex particle-enhanced turbidimetric immunoassay. All assays were performed at a clinical testing laboratory (SRL, Tokyo, Japan).

Physical function measurement

To assess skeletal muscle strength, maximal bilateral leg extension power was measured using a dynamometer (Anaeropress 3500; Combi Co., Tokyo, Japan). After the subjects sat back on the seat and placed both feet on the sliding footplate with the knee angle adjusted to 90°, a belt was firmly fastened at the waist and the load of the footplate was set to their body weight. The subjects were then instructed to extend their legs as much as possible. Five trials were conducted with 15-s intervals between them, and the average value of the two best measurements (farthest extensions) was recorded as the leg extension power (watt). The validity of the leg extension power measurement is described in detail elsewhere [20]. To assess functional reach, a measure of balance as assessed by measuring the maximal distance that one can reach forward beyond arm's length while standing without losing balance [21], the subjects were asked to place their feet comfortably apart (approximately shoulder width), hold their arms out straight at shoulder height, and then reach as forward as possible while simultaneously maintaining a fixed support in a standing position. The farthest reach in