International Journal Of

Recent Scientific Research

ISSN: 0976-3031
Volume: 7(4) April -2016

LEPTIN AND FRAILTY, UNEXPECTED RELATIONSHIP

Randa Ali-Labib., Safaa Hussein Ali., Heba Youssif Kamil., Amal Mansour., Marwa Ali and Ghada Mohamed

THE OFFICIAL PUBLICATION OF
INTERNATIONAL JOURNAL OF RECENT SCIENTIFIC RESEARCH (IJRSR)
http://www.recentscientific.com/ recentscientific@gmail.com

ISSN: 0976-3031

Available Online at http://www.recentscientific.com

International Journal of Recent Scientific Research
Vol. 7, Issue, 4, pp. 10061-10065, April, 2016

International Journal of Recent Scientific Research

RESEARCH ARTICLE

LEPTIN AND FRAILTY, UNEXPECTED RELATIONSHIP

Randa Ali-Labib[1]., Safaa Hussein Ali[2]*., Heba Youssif Kamil[3]., Amal Mansour[4]., Marwa Ali[5] and Ghada Mohamed[6]

[1]Medical Biochemistry and Molecular Biology, Faculty of Medicine, Ain Shams University, Cairo,
[2,3]Geriatrics and Gerontology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[1,4,5,6]Medical Biochemistry and Molecular Biology, Faculty of Medicine,
Ain Shams University, Cairo, Egypt

ARTICLE INFO

Article History:

Received 05th January, 2015
Received in revised form 08th February, 2016
Accepted 10th March, 2016
Published online 28st April, 2016

Keywords:

leptin- sarcopenia- body mass index- age

ABSTRACT

Background: Age-related losses in skeletal muscle mass and function (sarcopenia) present an extremely important current and future public health issue. **Aim:** to assess leptin level in relation to sarcopenia. ***Methodology*:** fifty elderly patients divided into two groups, 25 elderly diagnosed with sarcopenia, and 25 elderly without Sarcopeniarecruited from the Geriatric department, Ain-Shams University Hospital. Leptin level is assessed in each case. ***Results:*** sarcopenic patients are significantly older (P≤ 0.05) and have significantly lower physical activity and lower BMI. Leptin is significantly lower in sarcopenic patients in univariate and multivariate regression (P≤ 0.05). ***Conclusion;*** Our study showed a negative independent association between leptin and sarcopenia irrelevant to BMI.

INTRODUCTION

Aging is associated with a progressive decline of muscle mass, quality, and strength, a condition known as sarcopenia [1]. The term sarcopenia, coined by I. H. Rosenberg, originates from the Greek words sarx (flesh) and penia (loss).Clinically, it denotes loss of muscle mass, it is often used to describe both a set of cellular processes (denervation, mitochondrial dysfunction, inflammatory and hormonal changes) and a set of outcomes such as decreased muscle strength, decreased mobility and function [2], increased fatigue, a greater risk of falls [3], and reduced energy needs [4]. In addition, reduced muscle mass in aged individuals has been associated with decreased survival rates following critical illness [5].

Several possible mechanisms for age-related muscle atrophy have been described; however, the precise contribution of each is unknown. Age-related muscle loss is a result of reductions in the size and number of muscle fibers [6] possibly due to a multifactorial process that involves physical activity, nutritional intake, oxidative stress, and hormonal changes [3, 7]. The specific contribution of each of these factors is unknown, but there is emerging evidence that the disruption of several positive regulators (Akt and serum response factor) of muscle hypertrophy with age is a principal feature in the progression of sarcopenia [8,9].

Another morphologic aspect of sarcopenia is the infiltration of muscle tissue by lipids because of the increased frequency of adipocyte or lipid deposition [10, 11] within muscle fibers. As with precursor cells in bone marrow, liver and kidney, muscle satellite cells that can express an adipocytic phenotype increase with age [12], although this process is still relatively poorly understood in terms of its range and spatial distribution.

Leptin is a central adipokine produced in levels proportional to fat cell mass [13, 14]. Leptin integrates inflammation, metabolism and neuroendocrine signalingthrough regulating energy consumption and storage. Obesity is associated with increased leptin levels, and leptin resistance may be a characteristic of obesity contributing to insulin resistance and lipotoxicity [14].

Is there a relation between leptin and sarcopenia? Interestingly, the proposed mechanism involved in sarcopenic obesity, which combines sarcopenia and increase body mass index(BMI), could be the increased production from adipose tissue of different substances, such as tumor necrosis factor- (TNF-) and leptin, which are known to influence insulin resistance and

Corresponding author:* **Safaa Hussein Ali
Geriatrics and Gerontology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

growth hormone (GH) secretion [15]. This hypothesis has been confirmed by Schrager and his colleagues [16] who observed in a large-scale sample of men and women that the degree of obesity, as evaluated by BMI and its distribution, and by waist circumference, directly affected inflammation which in turn contributed to the development and progression of sarcopenia. Further increases in leptin, at least, partially depending on the age-related fat mass increase, may lead to leptin resistance and thus to a reduction of fatty acid oxidation in muscles, contributing to ectopic fat deposition in organs such as the liver, heart, and muscles [17] and, in turn, to the loss of muscle quality in obese older subjects. So, it is postulated that leptin is positively related to sarcopenia. It is found that increase in leptin is associated with increase adipose tissue and loss of muscle mass. On the contrary, Hubbard *et al*. (2008) [18] reported low leptin levels in frail elderly subjects with reduced mid-arm muscle area, and they speculated it was due to low body fat.

The relation between Leptin and sarcopenia may be confounded by BMI as leptin is directly related to fat tissue. Our aim is to compare level of leptin in sarcopenic and none and to explore whether this relation affected by body mass index (BMI).

METHODOLOGY

Subjects

Fifty subjects were recruited for this study from Ain Shams Universityhospitals. Before any study procedures were initiated for any subject in the study, a written informed consent was properly executed and documented. Participants were divided into two main groups:

Group a (Sarcopenic Group)

This group included 25 sarcopenic patients according to the European Working Group on Sarcopenia in Older People (EWGSOP, the Sarcopenia Working Group) [19]. Diagnosis is based on documentation of criterion 1 plus criterion 2 or criterion 3

1- Low muscle mass
2- Low muscle strength
3- Low physical performance

Group B (Control Group)

This group included 25 non-sarcopenic patients matching the age of group A.

All participants were subjected to the following: Full medical historyof each patient, full clinical physical examination and radiological imaging to exclude any malignant diseases that causing muscle wasting due to malignant cachexia. The exclusion criteria included: pregnant/lactating women; current or recent history of hepatic or renal disease; supplementation of greater than 400 IUs vitamin D_2 or vitamin D_3; current antiepileptic medications or glucocorticoids; history of intestinal malabsorption; and unwillingness to consent to the study.

Anthropometric measurements

Weight and Height Measurement for BMI

Weight and height measurement procedure was done according to the **Frisancho technique** [20].

BMI=weight (kg)/height (m^2)

Mid Upper Arm Circumference (MAC)

Mid upper arm circumference was measured with a non-extensible, flexible tape, the site was located at the midpoint between the lateral edge of the acromion process, and the upper and lateral border of head of the radius [21].

Triceps Skin Fold Thickness (TSF)

The triceps skinfolds thickness was measured in order to evaluate the body composition according to techniques described by a Harpender calibrator (British Indicators Ltd, Luton, UK) with 0.1 mm precision and constant pressure of approximately 10 g/mm^2 was used for the measurement of the skinfolds. All measurements were performed on the right side of the body in three times and the meanvalues used for the calculations [22].

The tricipital skinfolds were obtained by the perpendicular skin pinching through the positioning of the calibrator in the mid-arm, determined by the distance between the acromial process of the shoulder and the olecranon (ulna extremity), on the posterior right arm positions.

Assessment of Muscle State Mass by Mid-Arm Muscle Circumference

The muscle state was evaluated using the mid arm muscle circumference according to the following equation [19].
MAMC = mid-arm circumference-(3.14 × triceps skinfold thickness)

Assessment of Muscle State Strength by Hand Grip Dynamometer

One trial for each hand grip was performed using the dynamometer (North Coast Hydraulic Hand Dynamometer, Morgan Hill, CA, USA) .The result from the strongest hand was used for the present analyses, using the cut-off points according to Barbosa *et al*, 2005 [23].

Assessment of Muscle State Performance by Timed Get Up and Go Test (TUGT)

TUGT requires the subject to stand up from a chair, walk a short distance (3m), turn around, return and sit down again. It thus serves as an assessment of dynamic balance [19].

Blood Sample Collection and Handling

Informed consent was obtained from patients and normal volunteers prior to the study. The study was approved by Ethics Committees of the Ain Shams University Hospitals. 10ml fresh venous blood treated with EDTA anticoagulant was taken from each subject.

To obtain and clarify plasma, samples were centrifuged at 2000 RPM for 15 min and the plasma was separated and aliquoted. All samples were stored at −80 °C until assay.

Plasma Leptin measurements were conducted according to manufacturer's protocols of DRG Leptin ELIZA Kits supplied from Diagnostic Biochem Canada Incorporation, were used for the measurement of human **leptin**(sensitivity was up to 1 ng/mL) and some samples that exceeded the reading of highest standard were further diluted 2 times.

The samples that exceeded the reading of highest standard were further diluted 2 times; absorbance value was read at 450 nm for all.

RESULTS

Age and physical inactivity were significantly higher among sarcopenic group. BMI and leptin were significantly lower among sarcopenic group. As indicated in **Table .1 & figure 1** **Table 2** indicated that Age increases the likelihood of being sarcopenic while leptin decrease it.

Table 3 Correlation between leptin other variables. In Sarcopenic: There were significant positive correlations between leptin and BMI. In non-sarcopenic: There were significant positive correlations between leptin and age&BMI.

Variables		Sarcopenic (N=25)	Non (N=25)
Age	**R**	-0.226	0.718
	P	0.277	**<0.001***
BMI	**R**	0.538	0.660
	p	**0.006***	**<0.001***

Spearman correlation, *Significant

DISCUSSION

In the current case control study, we investigated the relationship between Leptin and sarcopenia. Sarcopenic group are significantly older.

Table 1 Comparison between sarcopenic and non-sarcopenic groups regarding demographic and risk factors.Age and physical inactivity were significantly higher among sarcopenic group. BMI and leptin were significantly lower among sarcopenic group.

Variables		Sarcopenic (N=25)	Non (N=25)	P	OR (95% CI)
Age (years)	**Mean±SD**	68.6±5.7	45.3±14.6	^ **<0.001***	--
	Range	60.0–84.0	30.0–73.0		
	≥60.0	25 (100.0%)	6 (24.0%)	# **<0.001***	--
Sex (number, %)	**Male**	13 (52.0%)	14 (56.0%)	# 0.777	0.851 (0.280–2.591)
	Female	12 (48.0%)	11 (44.0%)		
BMI (kg/m^2)	**Mean±SD**	23.3±2.3	25.7±3.8	^ **0.009***	--
	Range	20.0–27.8	20.9–37.8		
Physical activity	**Active**	10 (40.0%)	18 (72.0%)	# **0.023***	0.259 (0.079–0.847)
	Inactive	15 (60.0%)	7 (28.0%)		
Leptin (ng/ml)	**Median (IQR)**	8.0 (3.5–21.0)	15.0 (4.7–59.5)	**0.048***	
	Range	1.1–52.0	1.1–104.0		

^Independent t-test, #Chi square test***: p<0.05 is significant**

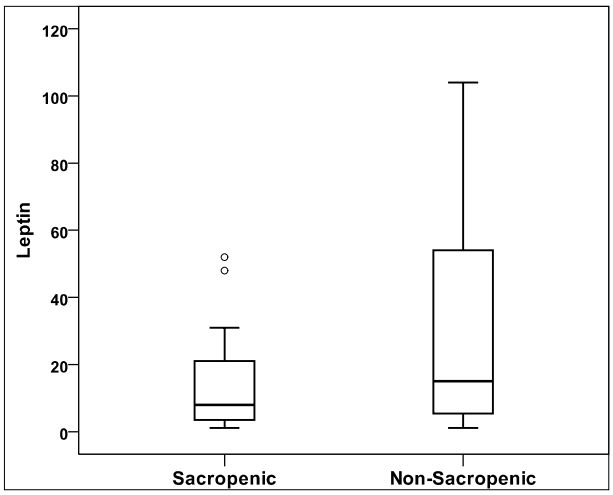

Figure 1 Comparison between sarcopenic and non-sarcopenic groups regarding leptin

Table 2 Regression model for factors affecting being a sarcopenic. Age increases the likelihood of being sarcopenic while leptin decrease it.

Variables	β	SE	P	OR (95% CI)
Age	0.048	0.014	**<0.001***	1.049 (1.021–1.077)
Leptin	-0.055	0.021	**0.009***	0.946 (0.908–0.986)

β: Regression coefficient, SE: Standard error, *Significant, OR: Odd ratio, CI: Confidence interval

Gender is not different between the two groups. Sarcopenic patients have significantly lower BMI and are less active as expected. Leptin is significantly and independent lower in sarcopenic group.

In the present study, sarcopenia is highly significantly related to aging (p<0.001); this is consistent with the findings of previous studies [24-26]. The relation of sarcopenia to aging may be due to the age associated altered central and peripheral nervous system innervations, altered hormonal status, inflammatory effects, and altered caloric and protein intake [27,28]. In addition to this, Cesari *et al*. (2006) [29] also reported that sarcopenia is usually accompanied by physical inactivity, decreased mobility, slow gait, and poor physical endurance which are also common features of the frailty syndrome which associated with aging.

In the present study, BMI was significantly lower among sarcopenic group and this is agree with Iannuzzi-Sucich *et al*. (2002) [30] and Yu *et al*. (2014) [31] and this is explained by exploration of nutritional factors such as protein intake or the inflammatory process associated with cachexia which may assist in understanding the components of sarcopenia[30, 32]. And that fat free mass (FFM) constitutes part of the weight of the body so when the FFM decrease in sarcopenia patients the body weight tends to decrease which will be reflected on BMI [32]. Also the current study revealed a positive correlation between BMI and leptin but this relation is not apparent in

multiregression analysis which point to unknown mechanism of connection between Leptin and sarcopenia.

Concerning physical inactivity, Physical inactivity is significantly higher among sarcopenic patients in this study. Physical exercise is able to increase in skeletal muscle fiber size (both type I and II) [32], capillary density and the number of myonuclei per fiber and myonuclei per unit length of muscle fiber [33]. Physical activity also stimulates the muscle protein synthesis, independent of age [34, 35]. In particular, this increase in muscle protein synthesis seems to occur in specific muscle proteins (i.e. myosin heavy chain) that are crucial for the fiber contraction [34, 35].

Previous studies investigating the association between leptin and sarcopenia have been inconclusive. This current study shows a significant lower level of leptin in sarcopenic patients. Similarly, Gómez *et al*. (2003) [36] noted a positive relationship between serum levels of leptin and fat-free mass in both men and women. Also, Hubbard *et al*. (2008) [18] reported low leptin levels in frail elderly subjects with reduced mid-arm muscle area, and they speculated it was due to low body fat. In contrast, in their study involving 45 healthy elderly subjects, Waters *et al*. (2008) [37] reported a negative correlation between appendicular skeletal muscle mass as measured using a dual energy X-ray absorptiometer and leptin levels after correction with body fat.

However, leptin is known to stimulate inflammation [38], and serum leptin levels have also been shown to be negatively correlated with insulin growth factor I(IGF-1) levels and testosterone [39]. Given that these factors are known to play roles in development of sarcopenia [40], leptin may also play a causative role in development of sarcopenia. Exogenous leptin has also been shown to reduce protein synthesis in myocytes [41]. In contrast, a recent study demonstrated that leptin treatment significantly increased hind limb muscle mass and extensor digitorum longus fiber size in aged mice [42]. Given that obesity is associated with reduced number and function of leptin receptors in leg muscle [43]. These present and previous findings suggest that impaired action of leptin in skeletal muscle may also induce development of sarcopenia.

In Conclusion, we found that leptin is negatively related to sarcopenia irrelevant to BMI. This means a hidden mechanism between Leptin and sarcopenia or may be a u shape relationship.

Authors' contributions

GhadaMohamed conceived the study, recruited the patients and prepared the scientific material. Randa Ali Labib anticipated in the conception and design of the study. Safaa Hussein Alianticipated in the design of the study, prepared the scientific material and wrote the manuscript. Heba Youssif prepared the scientific material and wrote the manuscript. Amal Mansour anticipated in the design of the study and contributed in lab work. Marwa Ali contributed in lab work. All authors discussed the results and read and approved the final manuscript.

Acknowledgments

We acknowledge the study participants for their gracious help.

Disclosure statement

All authors declare that there is no financial support or relationship that may pose conflicts of interest.

References

1. Candow DG and Chilibeck PD, "Differences in size, strength, and power of upper and lower body muscle groups in young and older men," *The Journals of Gerontology A*, vol. 60, no. 2, pp. 148–156, 2005.
2. Melton LJ III, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, and Riggs BL, "Epidemiology of sarcopenia," *Journal of the American Geriatrics Society*, vol. 48, no. 6, pp. 625–630, 2000.
3. Baumgartner RN, Waters DL, Gallagher D, Morley JE, and Garry PJ, "Predictors of skeletal muscle mass in elderly men and women," Mechanisms of Ageing and Development, vol. 107, no. 2, pp. 123–136, 1999.
4. Poehlman ET, Toth MJ, and Fonong T, "Exercise, substrate utilization and energy requirements in the elderly," *International Journal of Obesity, vol. 19, supplement* 4, pp. S93–S96, 1995.
5. Griffiths RD, "Muscle mass, survival, and the elderly ICU patient," Nutrition, vol. 12, no. 6, pp. 456–458, 1996.
6. Lexell J, "Ageing and human muscle: observations from Sweden," *Canadian Journal of Applied Physiology*, vol. 18, no. 1, pp. 2–18, 1993.
7. Roubenoff R and Hughes VA. "Sarcopenia: current concepts," *The Journals of Gerontology A*, vol. 55, no. 12, pp. M716–M724, 2000.
8. Sakuma K and Yamaguchi A. "Inhibitors of myostatin- and proteasome-dependent signaling for attenuating muscle wasting," Recent Patent of Regenerative Medicine, vol. 1, no. 3, pp. 284–298, 2011.
9. Sakuma K and Yamaguchi A, "Sarcopenia: molecular mechanisms and current therapeutic strategy," in Cell Aging, J. W. Perloft and A. H. Wong, Eds., pp. 93–152, Nova Science, New York, NY, USA, 2011.
10. Dubé and B. H. Goodpaster BH. "Assessment of intramuscular triglycerides: contribution to metabolic abnormalities," Current Opinion in Clinical Nutrition and Metabolic Care, vol. 9, no. 5, pp. 553–559, 2006.
11. Kraegen EW and Cooney GJ. "Free fatty acids and skeletal muscle insulin resistance," Current Opinion in Lipidology, vol. 19, no. 3, pp. 235–241, 2008.
12. Shefer G, Wleklinski-Lee M, and Yablonka-Reuveni Z. "Skeletal muscle satellite cells can spontaneously enter an alternative mesenchymal pathway," Journal of Cell Science, vol. 117, no. 22, pp. 5393–5404, 2004.
13. Schautz B, Later W, Heller M, Peters A, Müller MJ, Bosy-Westphal A. Impact of age on leptin and adiponectin independent of adiposity. Br J Nutr. 2012; 108(2):363–70.
14. Moon HS, Dalamaga M, Kim SY, Polyzos SA, Hamnvik OP, Magkos F, *et al*. Leptin's Role in Lipodystrophic and Nonlipodystrophic Insulin-Resistant and Diabetic Individuals. Endocr Rev. 2013; 34(3):377–12.

15. Roubenoff R. Sarcopenic obesity: the confluence of two epidemics. *Obesity Research*. 2004; 12(6):887–888.
16. Schrager MA, Metter EJ, Simonsick E, *et al*. Sarcopenic obesity and inflammation in the InCHIANTI study. *Journal of Applied Physiology*. 2007; 102(3):919–925.
17. Unger RH. Longevity, lipotoxicity and leptin: the adipocyte defense against feasting and famine. *Biochimie*. 2005; 87(1):57–64.
18. Hubbard RE, O'Mahony MS, Calver BL, Woodhouse KW. Nutrition, inflammation, and leptin levels in aging and frailty. J Am GeriatrSoc 2008; 56: 279–84.
19. *Cruz-Jentoft A, Landi F, Topinková E, Michel JP:* Understanding sarcopenia as a geriatric syndrome. *Curr Opin Clin Nutr Metab Care. 2010*; 13 *(1):* 1–7.
20. *Frisancho AR.* New standards of weight and body composition by frame size and height for assessment of nutritional status of adults and the elderly. Am J ClinNutr. ***1984***; 40(4):808-19.
21. *Craig P, Halavatau V, Comino E, Caterson I.* Differences in body composition between Tongans and Australians: time to rethink the healthy weight ranges?. Int J Obes Relat Metab Disord. 2001; 25(12):1806-14.
22. *Lohman RF, Nabawi AS, Reece GP, Pollock RE, Evans GR.:* Soft tissue sarcoma of the upper extremity: a 5-year experience at two institutions emphasizing the role of soft tissue flap reconstruction. Cancer. 1992; 94(8):2256-64.
23. *Barbosa AR, Souza JM, Lebrão ML, Laurenti R, MarucciMde F.* Anthropometry of elderly residents in the city of São Paulo, Brazil. Cad Saude Publica. ***2005***; 21(6):1929-38.
24. Shaver HJ., Loper JA. and Lutes RA. Nutritional Status of Nursing Home Patients. Journal of Parenteral and Enteral Nutrition. 1980 4(4):367-70.
25. Morley JE. Sarcopenia: Diagnosis and Treatment. The Journal of Nutrition Health and Aging. 2008; 12(7):452-6.
26. Landi, F, Liperoti, R, Fusco D, Mastropaolo S, Quattrociocchi A, Tosato M, Bernabei R, Onder, G. Sarcopenia and Mortality among Older Nursing Home Residents. *Journal of the American Medical Directors Association* 2012; 13(2):121-6.
27. Roubenoff R. Origins and clinical relevance of sarcopenia. Can J Appl Physiol. 2001; 26(1): 78–89.
28. Boirie Y. Physiopathological mechanism of sarcopenia. J Nutr Health Aging. 2009; 13(8):717-23.
29. Cesari M, Leeuwenburgh C, Lauretani F, Onder G, Bandinelli S, Maraldi C, Guralnik JM, Pahor M, Ferrucci L. Frailty syndrome and skeletal muscle: results from the Invecchiare in Chianti study. Am J Clin Nutr.2006; 83(5):1142-8.
30. Iannuzzi-Sucich M, Prestwood KM, Kenny AM. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. J Gerontol A BiolSci Med Sci. 2002; 57(12): 772-7.
31. Yu R, Wong M, Leung J *et al*. Incidence, reversibility, risk factors and the protective effect of high body mass index against sarcopenia in community-dwelling older Chinese adults. Geriatr Gerontol Int. 2014 Feb; 14Suppl 1:15-28.
32. Alva MDCV, Camacho MEI, Velázquez JD, Lazarevich I. The Relationship between Sarcopenia, under Nutrition, Physical Mobility and Basic Activities of Daily Living in a Group of Elderly Women of Mexico City. Nutricion Hospitalaria. 2013; 28(2):514-21.
33. Hikida RS, Staron RS, Hagerman FC, Walsh SJ, Kaiser E, Shell S, *et al*. Effects of high-intensity resistance training on untrained older men. II - Muscle fiber characteristics and nucleo-cytoplasmatic relationships. J Gerontol A BiolSci Med Sci. 2000; 55(7):B347–B354.
34. Balagopal P, Schimke JC, Ades P, Nair KS. Age effect on transcript levels and synthesis rate of muscle MHC and response to resistance exercise. Am J Physiol Endocrinol Metab. 2001; 280:E203–E208.
35. Hasten DL, Pak-Loduca J, Obert KA, Yarasheski KE. Resistance exercise acutely increases MHC and mixed muscle protein synthesis rates in 78–84 and 23–32 yr olds. Am J Physiol Endocrinol Metab.2000; 278(4):E620–E626.
36. Gómez JM, Maravall FJ, Gómez N, Navarro MA, Casamitjana R, *et al*.: Interactions between serum leptin, the insulin-like growth factor-I system, and sex, age, anthropometric and body composition variables in a healthy population randomly selected. Clin Endocrinol. 2003; 58: 213–9.
37. Waters DL, Qualls CR, Dorin RI, Veldhuis JD, Baumgartner RN. Altered growth hormone, cortisol, and leptin secretion in healthy elderly persons with sarcopenia and mixed body composition phenotypes. J Gerontol A BiolSci Med Sci. 2008; 63: 536–41.
38. Dyck DJ Adipokines as regulators of muscle metabolism and insulin sensitivity. ApplPhysiolNutrMetab. 2009; 34: 396–402.
39. Proctor DN, Balagopal P, Nair KS. Age-related sarcopenia in humans is associated with reduced synthetic rates of specific muscle proteins. J Nutr 1998; 128: (2 Suppl) 351S–355S.
40. Stenholm S, Harris TB, Rantanen T, Visser M, Kritchevsky SB, *et al*. Sarcopenic obesity: definition, cause and consequences. CurrOpinClinNutrMetab Care 2008; 11: 693–700.
41. Argilés JM, López-Soriano J, Almendro V, Busquets S, López-Soriano FJ. Cross-talk between skeletal muscle and adipose tissue: a link with obesity? Med Res Rev 2005; 25: 49–65.
42. Hamrick MW, Herberg S, Arounleut P, He HZ, Shiver A, *et al*. The adipokine leptin increases skeletal muscle mass and significantly alters skeletal muscle miRNA expression profile in aged mice. Biochem Biophys Res Commun 2010; 400: 379–83.
43. Fuentes T, Ara I, Guadalupe-Grau A, Larsen S, Stallknecht B, *et al*. Leptin receptor 170 kDa (OB-R170) protein expression is reduced in obese human skeletal muscle: a potential mechanism of leptin resistance. ExpPhysiol 2010; 95: 160–71.

TSSN 0976-3031