

# Increased level of serum irisin concentration and its regulation by hyperinsulinemia in women with polycystic ovary syndrome

<sup>1</sup>Agnieszka Adamska, <sup>2,3</sup>Monika Karczewska-Kupczewska, <sup>1</sup>Agnieszka Łebkowska, <sup>4</sup>Robert Milewski, <sup>1</sup>Maria Górka, <sup>3</sup>Elżbieta Otziomek, <sup>2,3</sup>Agnieszka Nikolajuk, <sup>5</sup>Sławomir Wolczyński, <sup>2,3</sup>Marek Strączkowski, <sup>1</sup>Irina Kowalska



<sup>1</sup>Department of the Endocrinology, Diabetology and Internal Medicine, Medical University of Białystok, Poland

<sup>2</sup>Department of Metabolic Diseases, Medical University of Białystok, Poland

<sup>3</sup>Department of Prophylaxis of Metabolic Diseases, Institute of Animal Reproduction and Food Research, Polish Academy of Sciences, Olsztyn, Poland

<sup>4</sup>Department of Statistics and Medical Informatics, Medical University of Białystok, Poland

<sup>5</sup>Department of Reproduction and Gynecological Endocrinology, Medical University of Białystok, Poland

Boström P et al. *Nature* 2012, 481: 463-468.  
Diamanti-Kandarakis and E, Dunaif A. *Endocr Rev* 2012, 33: 981-1030.  
Chang CL et al. *JCEM* 2015, 99: E2539-2548.

## Background

Irisin is an adipokine/myokine which could be connected with insulin sensitivity. It has been shown that irisin induces glucose uptake in differentiated skeletal muscle cells by stimulating the translocation of GLUT4 to the plasma membrane. Elevated serum irisin concentration has been found to be related to an increase in energy expenditure and weight loss. Additionally, irisin improved diet-induced insulin resistance in mice.

Polycystic ovary syndrome (PCOS) affects about 5-10% of reproductive-aged women and is characterized by oligo- or anovulation, polycystic ovary, and hyperandrogenism. Insulin resistance occurs in approximately 50–70% of women with PCOS. It has been shown that serum irisin concentration is elevated in PCOS women.

## Aim

The aim of the present study was to determine the relationship between serum irisin concentration and insulin sensitivity as well as the effect of insulin infusion on circulating irisin in PCOS women as compared with healthy controls.

## Subjects and methods

Seventy seven women were enrolled in the study - 57 with PCOS and 20 healthy controls matched for BMI and age. The diagnosis of PCOS was made according to the 2003 Rotterdam ESHRE/ASRM PCOS Consensus Workshop Group diagnostic criteria. Clinical examination, anthropometric measurements, body fat assessment by bioelectric impedance analysis, and the oral glucose tolerance test (OGTT) has been performed in all study participants. Insulin sensitivity was measured using the euglycemic hyperinsulinemic clamp technique. Serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and estradiol were measured using the chemiluminescence method (ACS Chiron 180), and serum sex hormone-binding globulin (SHBG) was measured by the IRMA method (ZenTech, Angleur, Belgium). Free androgen index was calculated as serum testosterone (nmol/L) × 100/SHBG (nmol/L) ratio. Serum irisin concentration was measured using an enzyme immunoassay (Phoenix Pharmaceuticals, Inc., CA, Cat. No. EK-067-29) with a minimal detectable concentration of 1.1 ng/ml and intra- and inter-assay coefficients of variation less than 10% and 15%, respectively. Absorbance at 450 nm was measured using an mQuant microtiter plate reader (BIOTEK Instruments Inc., Winooski, VT). The serum concentrations of irisin at baseline and after the clamp, as well as changes of serum irisin concentration in response to insulin supplied during the clamp ( $\Delta$  irisin), were estimated.

## Results

Table 1. Clinical and biochemical characteristics of the studied groups

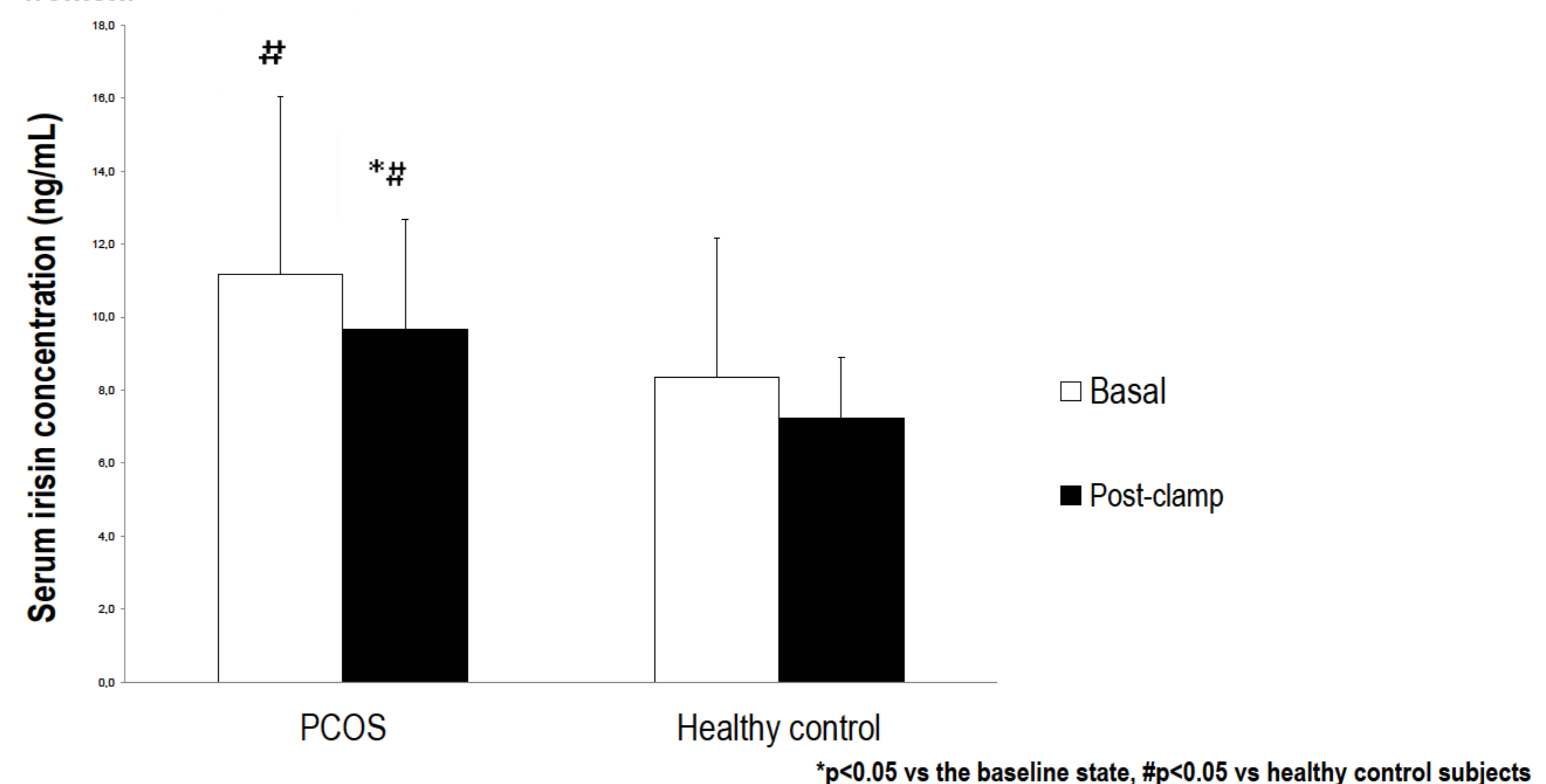
	Control group (n=20)	PCOS (n=57)
Age (year)	27.3±7.1	26.0±5.7
BMI (kg/m <sup>2</sup> )	27.3±7.0	26.7±6.4
Waist circumference (cm)	86.8±17.4	84.4±16.4
FFM (kg)	51.2±5.6	47.2±6.0*
FM (kg)	26.4±15.6	26.2±14.4
Fasting glucose (mg/dL)	83.1±5.3	81.9±10.6
Fasting insulin (μIU/mL)	12.6±5.5	14.5±8.7
Follicle-stimulating hormone (IU/L)	5.3±1.8	5.6±1.8
Luteinizing hormone (IU/L)	4.9±2.0	7.6±4.0*
Testosterone (nmol/L)	1.5±0.6	2.3±1.1*
SHBG (nmol/L)	55.5±35.6	47.4±33.8
Free androgen index	3.8±3.0	7.5±7.6*
M/FFM (mg x kg <sub>ffm</sub> <sup>-1</sup> x min <sup>-1</sup> )	10.1±3.5	8.2±3.3*
$\Delta$ irisin	1.1±2.7	1.5±3.4

Data are presented as mean ± SD. Differences between the groups are derived from the non-parametric Mann-Whitney U test. \*p<0.05 in PCOS women vs the control group

Table 2. Correlation between  $\Delta$  irisin and anthropometric parameters and insulin sensitivity in the studied groups

	Control group (n=20)	PCOS (n=57)
	$\Delta$ irisin	
BMI (kg/m <sup>2</sup> )	r=-0.61, p=0.004	r=0.01, p=0.91
Hip circumference (cm)	r=-0.62, p=0.003	r=0.02, p=0.82
FFM (kg)	r=-0.47, p=0.03	r=0.13, p=0.29
FM (kg)	r=-0.49, p=0.02	r=-0.003, p=0.98
M/FFM (mg x kg <sub>ffm</sub> <sup>-1</sup> x min <sup>-1</sup> )	r=0.56, p=0.009	r=-0.01, p=0.90

Figure 1. Fasting and post-clamp serum irisin concentrations in the PCOS and healthy control group women.



## Conclusions

An increase in serum irisin concentration at baseline and an inappropriate change in response to insulin infusion might be secondary to insulin resistant conditions in PCOS women.

This work was supported by grant No 143-50634L from the Medical University of Białystok