

ORIGINAL ARTICLE

Ageing and plasma adiponectin concentration in apparently healthy males and females

Marcin Adamczak*, Ewa Rzepka†, Jerzy Chudek* and Andrzej Więcek*

*Department of Nephrology, Endocrinology and Metabolic Diseases Medical University of Silesia, Katowice and †Emergency Department, Klimontowicza General Hospital, Gorlice, Poland

Summary

Objective It is well known that ageing is associated with several hormonal alterations. However, the consequence of ageing on the endocrine function of adipose tissue is not fully elucidated. Adiponectin is a new anti-inflammatory protein secreted exclusively by adipocytes and plays a protective role against insulin resistance and atherosclerosis. Therefore, the aim of present study was to estimate plasma adiponectin concentration in apparently healthy elderly subjects.

Subjects Fifty-eight women and 67 men aged 20–93 years were included in this study. Subjects were divided into three groups: younger than 50 years, between 50 and 70 years and older than 70 years of age.

Measurements Plasma adiponectin concentration was estimated by an enzyme-linked immunosorbant assay in blood samples withdrawn in the morning after overnight fasting. In males plasma testosterone and dehydroepiandrosterone sulphate concentrations were assessed by a radioimmunoassay method.

Results Plasma adiponectin concentration only tended to be higher in all elderly subjects (above 70 years) than in the group of all subjects aged between 50 and 70 and the group younger than 50 years of age (12.8 ± 5.7 ; 9.9 ± 5.7 and 10.7 ± 5.4 $\mu\text{g/ml}$, respectively). Plasma adiponectin concentration was of similar magnitude in female subjects of these three groups (11.2 ± 5.7 ; 11.2 ± 6.8 and 11.7 ± 4.9 $\mu\text{g/ml}$, respectively). In contrast, males over 70 years old are characterized by significantly higher plasma adiponectin (14.0 ± 5.4 $\mu\text{g/ml}$) concentration than males between 50 and 70 years of age (8.9 ± 4.7 $\mu\text{g/ml}$, $P < 0.01$) and males younger than 50 years of age (9.6 ± 5.7 $\mu\text{g/ml}$, $P < 0.05$). In the entire studied group a significant but weak, positive correlation was found between plasma adiponectin concentration and age ($\tau = 0.12$; $P = 0.04$). Additionally, significant correlation was found between plasma adiponectin concentration and age in males when analysed separately ($\tau = 0.28$; $P = 0.0007$). Such correlation was not significant in females ($\tau = -0.06$; $P = 0.5$).

Conclusions Plasma adiponectin concentration in females did not change significantly with age. In contrast to females, elderly males over 70 years of age are characterized by significantly higher plasma adiponectin concentration than younger ones.

(Received 29 June 2004; returned for revision 19 July 2004; finally revised 3 August 2004; accepted 30 August 2004)

There is growing evidence that the adipose tissue *per se* is a large endocrine organ secreting several biologically active substances with systemic action.^{1,2} These include leptin, adiponectin, plasminogen activator inhibitor-1 (PAI-1), angiotensin II, tumour necrosis factor- α (TNF- α) and resistin.^{1,2}

Adiponectin is a recently discovered anti-inflammatory protein secreted exclusively by adipocytes.³ Results of animal experiments strongly suggest that adiponectin plays a protective role against insulin resistance and atherosclerosis (see reference⁴ for review). Plasma adiponectin concentrations in humans are lower in obese than in nonobese subjects, in males than in females and in patients with coronary artery disease,⁵ diabetes mellitus Type 2⁶ and essential hypertension⁷ than in healthy subjects.

Normal ageing in humans is associated with several hormonal and metabolic alterations. It is well known that plasma concentrations of gonadal hormones, dehydroepiandrosterone, thyroid hormones and GH gradually decline throughout adult life.⁸ The consequence of ageing on endocrine function of adipose tissue has not been fully examined. However, we⁹ and other authors¹⁰ did not find any significant changes of plasma leptin concentration in very elderly male and female subjects. Ageing is very often accompanied by decreased insulin tolerance⁸ and increased blood pressure.¹¹ Moreover, advanced age is one of the major risk factor of atherosclerosis.¹²

Taking into account the antiatherogenic properties of adiponectin and its beneficial influence on insulin sensitivity, estimation of plasma adiponectin concentration in apparently elderly subjects seems to be fully justified.

Materials and methods

Fifty-eight women and 67 men aged 20–93 years were included in this study after giving informed consent. The study protocol was

No conflict of interest is declared.

Correspondence: Andrzej Więcek, Department of Nephrology, Endocrinology and Metabolic Diseases, Silesian University Medical School, Francuska 20/24 Street, 40–027 Katowice, Poland. Tel: +48 32 2552695; Fax: +48 32 2553726; E-mail: awiecek@spskm.katowice.pl

Table 1. Clinical and biochemical characteristic of female and male subjects from different age groups (mean \pm SD)

	< 50 years		50–70 years		> 70 years	
	Females (<i>n</i> = 18)	Males (<i>n</i> = 17)	Females (<i>n</i> = 17)	Males (<i>n</i> = 24)	Females (<i>n</i> = 23)	Males (<i>n</i> = 26)
Age (years)	36 \pm 9	35 \pm 8	62 \pm 6 ^{†††}	61 \pm 6 ^{†††}	80 \pm 6 ^{†††§§§}	79 \pm 7 ^{†††§§§}
BMI (kg/m ²)	25.3 \pm 3.3	26.6 \pm 3.7	27.5 \pm 2.9	26.0 \pm 3.0	26.6 \pm 3.3	26.0 \pm 3.5
Insulin (μ U/ml)	13.8 \pm 8.00	21.7 \pm 18.4	18.3 \pm 11.0	23.5 \pm 21.7	21.6 \pm 16.2	23.4 \pm 15.5
Glucose (mmol/l)	4.1 \pm 1.0	4.8 \pm 1.5	5.0 \pm 1.6	4.9 \pm 1.4	5.5 \pm 1.6	4.9 \pm 1.4
HOMA IR	2.4 \pm 1.2	4.8 \pm 3.7	4.4 \pm 3.8	5.8 \pm 7.7	5.2 \pm 5.2	5.5 \pm 4.7
Creatinine (mg/dl)	0.74 \pm 0.08 ^{***}	0.87 \pm 0.06	0.83 \pm 0.16 ^{**}	0.95 \pm 0.12	0.89 \pm 0.28 ^{**}	1.03 \pm 0.21 ^{††}
GFR (ml/min)	113 \pm 22 ^{**}	133 \pm 21	86 \pm 24 ^{†††}	89 \pm 18 ^{†††}	58 \pm 15 ^{†††§§§}	62 \pm 21 ^{†††§§§}
MAP (mmHg)	92 \pm 8 [*]	97 \pm 8	106 \pm 13 [†]	103 \pm 9	107 \pm 12 ^{††}	104 \pm 10 [†]
ALT (IU/l)	19 \pm 8	20 \pm 12	22 \pm 13	19 \pm 9	15 \pm 4	17 \pm 7

BMI, body mass index; HOMA IR, homeostasis model assessment insulin resistance index; MAP, mean arterial blood pressure; GFR, calculated glomerular filtration rate; ALT, alanine aminotransferase.

Statistical significance vs. corresponding group of males **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

Statistical significance vs. subjects younger than 50 years †*P* < 0.05, ††*P* < 0.01, †††*P* < 0.001.

Statistical significance vs. subjects aged between 50 and 70 years §§§*P* < 0.001.

approved by the Local Bioethical Committee. Subjects were in good physical health, fully ambulatory and well nourished. None of the subjects had clinical features of endocrine, metabolic, kidney, liver and other intercurrent disease. Subjects were divided into three groups: younger than 50 years, between 50 and 70 years of age and older than 70 years of age. Biochemical parameters were estimated in blood samples withdrawn in the morning after overnight fasting. Clinical and biochemical characteristic of patients from these three groups is given on Table 1. Plasma adiponectin concentration was assessed by an enzyme-linked immunosorbent assay (ELISA) method using kits from B-Bridge International, Inc., San Jose, CA, USA (coefficients of variation were 1.4% for low and 3.4% for high values, respectively). Plasma testosterone and dehydroepiandrosterone sulphate (DHEAS) concentrations were assessed by a radioimmunoassay (RIA) method (Orion Diagnostica, OY, Espoo, Finland). Plasma insulin concentration was assessed by a RIA method previously described.¹³ Other parameters were assessed by routine laboratory methods. Homeostasis model assessment insulin resistance index (HOMA IR) was calculated according to the formula: fasting plasma glucose concentration (mmol/l) \times fasting plasma insulin concentration (μ U/ml)/22.5. Glomerular filtration rate (GFR) was calculated as an endogenous creatinine clearance according to the formula by Cockcroft and Gault: $GFR = [140 - \text{age (years)}] \times \text{body mass (kg)} \times 1$ (for males) or 0.85 (for females)/ $72 \times \text{serum creatinine concentration (mg/dl)}$.

Statistical evaluation of the results obtained was performed using the Mann–Whitney *U*-test (comparison between females and males) and ANOVA test followed by a Sheffé test (comparison between age groups). Correlation coefficient was calculated according the Kendall tau correlation test. Multiple regression analysis in the subjects of the whole studied group with adiponectin as a dependent variable and body mass index (BMI), age, sex, serum creatinine and plasma insulin concentration as independent variables was also performed. Multiple regression analysis in the males with adiponectin as a dependent variable and BMI, age, plasma creatinine, insulin, glucose, testosterone

and DHEAS concentrations as independent variables was also performed. All results are expressed as means \pm SD.

Results

Plasma adiponectin concentration only tended to be higher (not statistically significant) in very elderly subjects than in the group of subjects aged between 50 and 70 and the group younger than 50 years (12.8 \pm 5.7; 9.9 \pm 5.7 and 10.7 \pm 5.4 μ g/ml, respectively). Plasma adiponectin concentration was of similar magnitude in all studied females and males (11.4 \pm 5.7 vs. 11.1 \pm 5.7 μ g/ml, respectively).

In several previously published studies, gender-dependent differences in plasma adiponectin were found.⁴ Comparison among the three groups in this study was also performed separately for female and male subjects. BMI, insulin and glucose concentration, as well as HOMA IR were similar in all age groups of both females and males (Table 1). We have observed slight but significantly higher blood pressure values and serum creatinine concentration in elderly subjects of both gender then in corresponding groups of ones younger than 50 years of age (Table 1). Calculated values of GFR were significantly reduced with the ageing in both males and females (Table 1). As shown in Fig. 1(a), plasma adiponectin concentration was of similar magnitude in all female groups. In contrast, males over 70 years old were characterized by significantly higher plasma adiponectin concentrations than younger ones. To study the possible relationship between plasma adiponectin concentration and androgens we have measured plasma testosterone and DHEAS in male subjects. As shown in Table 2, plasma testosterone concentration in elderly male subjects tended only to be slightly lower than in younger individuals. In contrast, we have observed a significant reduction of plasma DHEAS concentration in ageing males (Table 2).

In the whole group studied, significant negative correlations were found between plasma adiponectin concentration and BMI ($\tau = -0.18$; *P* = 0.004), plasma insulin concentration ($\tau = -0.19$; *P* = 0.002), HOMA IR ($\tau = -0.19$; *P* = 0.002) and calculated GFR

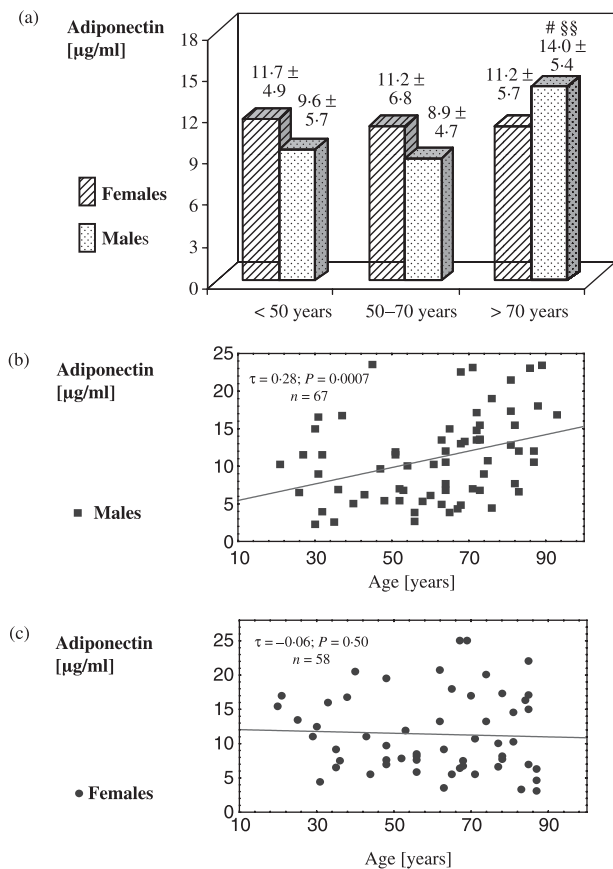


Fig. 1 (a) Plasma adiponectin concentration in different age groups. # $P < 0.05$ vs. males younger than 50 years. §§ $P < 0.01$ vs. males aged between 50 and 70 years. (b) Correlation between plasma adiponectin concentration and age in the group of males. (c) Correlation between plasma adiponectin concentration and age in the group of females.

Table 2. Plasma testosterone and DHEAS concentration of male subjects from different age groups (shown as mean \pm SD)

	< 50 years (n = 17)	50–70 years (n = 24)	> 70 years (n = 26)
Testosterone (ng/ml)	4.1 \pm 1.7	4.4 \pm 1.6	3.8 \pm 2.2
DHAES (μ mol/l)	9.1 \pm 4.2	4.1 \pm 2.0*	2.3 \pm 1.1*†

Statistical significance vs. subjects younger than 50 years, * $P < 0.01$.

Statistical significance vs. subjects aged between 50 and 70 years, † $P < 0.05$.

($\tau = -0.16$; $P = 0.005$). In the entire group studied, a significant, but weak, positive correlation was found between plasma adiponectin concentration and age ($\tau = 0.12$; $P = 0.04$). Additionally, significant positive correlation was found between plasma adiponectin concentration and age in males when analysed separately ($\tau = 0.28$; $P = 0.0007$; Fig. 1b). Such correlation was not significant in females when analysed separately ($\tau = -0.06$; $P = 0.5$; Fig. 1c). No significant correlation was found between plasma testosterone and adiponectin concentration ($\tau = 0.11$; $P = 0.2$) in males (Fig. 2a). In contrast, a significant positive correlation was found between plasma adiponectin

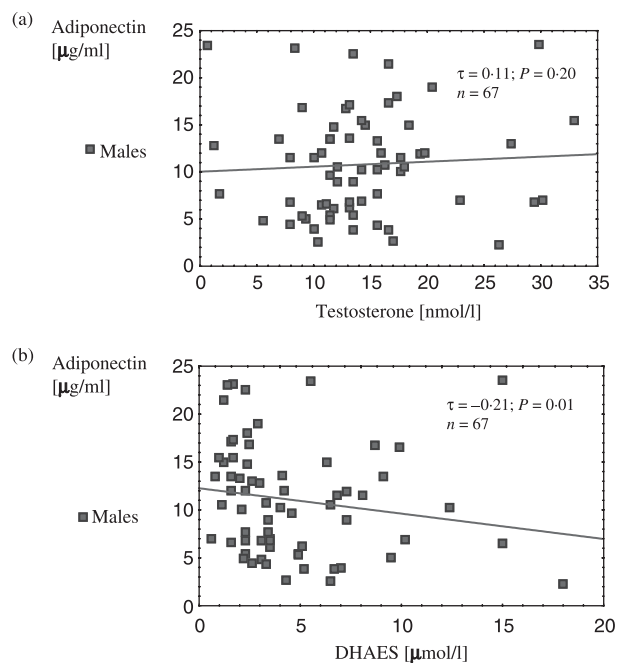


Fig. 2 (a) Correlation between plasma adiponectin and testosterone concentration in the group of males. (b) Correlation between plasma adiponectin and dehydroepiandrosterone sulphate (DHEAS) concentration in the group of males.

concentration and plasma DHEAS concentration in males ($\tau = -0.21$; $P = 0.01$; Fig. 2b).

Multiple regression analysis performed for the entire group, with plasma adiponectin concentration as the dependent variable and BMI, age, gender, plasma insulin and serum creatinine concentration, as independent variables showed that in this model ($R^2 = 0.14$) plasma adiponectin concentration significantly depends only on BMI ($\beta = -0.24$; $P = 0.0001$) and plasma insulin concentration ($\beta = -0.19$; $P = 0.04$). Multiple regression analysis performed for the males, with plasma adiponectin concentration as the dependent variable and BMI, age, plasma insulin, testosterone and DHEAS and serum creatinine concentration as independent variables showed that in this model ($R^2 = 0.27$) plasma adiponectin concentration significantly depends only on BMI ($\beta = -0.27$; $P = 0.03$) and age ($\beta = 0.56$; $P = 0.001$).

Discussion

In the present study we have found a significant positive relationship between plasma adiponectin concentration and age. Such a correlation was recently found by Daimon *et al.*¹⁴ In another study, Yamamoto *et al.*¹⁵ failed to find such correlation. However, both of these studies have not analysed possible gender differences in the relationship between age and plasma adiponectin concentration.

In the current study plasma adiponectin concentration in females did not change significantly with age. Similar results were recently obtained by Nishizawa *et al.*¹⁶ and Ryan *et al.*¹⁷ These authors showed that women of different age groups did not differ with respect to plasma adiponectin concentration. In contrast to female gender we found that males over 70 years of age are characterized by significantly

higher (by about 57%) plasma adiponectin concentration than younger ones. Pathogenesis of higher plasma adiponectin concentration in elderly males remains to be clarified.

Taking into account that ageing is often accompanied by a gradual decrease of plasma testosterone and DHEAS concentrations, one may hypothesize that the andropause participated, at least partially, in the pathogenesis of increased plasma adiponectin concentration in elderly males. In the current study plasma testosterone concentration in elderly males only tended to be lower than in younger ones. Additionally, we did not find any relationship between plasma adiponectin and testosterone concentration in the group of healthy males by univariate (Fig. 2a) and multiple regression analysis. Recently, Lanfranco *et al.*¹⁸ found that hypogonadal males are characterized by significantly elevated plasma adiponectin concentration compared with eugonadal ones. Moreover, testosterone substitution in hypogonadal subjects resulted in the increase, i.e. normalization of plasma adiponectin concentration.¹⁸ Nishizawa *et al.*¹⁶ showed in sham-operated and castrated mice, as well as in cultured adipocytes, that testosterone inhibits adiponectin secretion without affecting adiponectin mRNA. Therefore, an existence of a testosterone-dependent factor regulating adiponectin secretion by adipocytes was postulated.¹⁶ Results of our study do not support this hypothesis. The results above, however, cannot be compared directly with our data, because Lanfranco *et al.*¹⁸ have studied hypogonadal males, whilst we performed our study in subjects characterized by normal plasma testosterone concentrations. In contrast to testosterone, ageing was accompanied in our males by a pronounced, and significant decline of plasma DHEAS concentration. Moreover, we have found by correlation analysis a significant positive relationship between plasma DHEAS and adiponectin concentrations (Fig. 2b). To prove a possible role of DHEAS in regulation of adiponectin secretion further clinical and experimental studies are necessary. It is, however, interesting to stress the negative correlation between adiponectinaemia and plasma DHEAS concentration recently found in haemodialysis uraemic patients.¹⁹

Multiple regression analysis performed for the males failed to show any relationship between plasma adiponectin concentration and each of the androgens studied. Therefore, it seems unlikely that changes in androgen status may play a crucial role in the higher plasma adiponectin concentration in observed elderly males.

Based on correlation analysis performed in this study we have confirmed that, in healthy subjects, plasma adiponectin concentration inversely depends on BMI and insulin concentration and/or markers of insulin sensitivity. In this study subjects from different age groups were carefully matched according to BMI. The limitation of our study is that we did not measure body composition. Therefore, we are unable to exclude the fact that elderly males had lower body fat mass in comparison to younger ones, which can significantly influence plasma adiponectin concentration in elderly males. Recently, Zamboni *et al.*²⁰ showed that body composition in elderly males did not change significantly during ageing. Therefore we speculate that differences in body composition are not related to differences in plasma adiponectin concentration. We did not find any significant differences in plasma insulin concentration and HOMA IR between subjects from different age groups. Therefore, it is unlikely that changes in BMI and/or insulin resistance participate in the higher plasma adiponectin concentration observed in elderly males.

It is also important to emphasize that a significant negative correlation was found between plasma adiponectin concentration and calculated GFR. These results are in line with the recent concept that kidneys are important in the degradation and elimination of adiponectin. Therefore, kidney function, among other factors, strongly determines plasma adiponectin concentration. It was found previously that plasma adiponectin concentration is elevated in haemodialysed patients with chronic renal failure^{21,22} and is reduced after successful renal transplantation.²³ Mallamacci *et al.*²⁴ showed an inverse relationship between GFR and plasma adiponectin concentrations in a group of patients with essential hypertension. As expected we have observed a reduction in calculated GFR with age. The calculated GFR was very similar in elderly males and females. Therefore, it is unlikely that age-related deterioration of kidney function participates in the observed gender differences in plasma adiponectin concentration in elderly subjects.

It should be mentioned that several other factors not investigated here might influence plasma adiponectin concentration and contribute to the observed higher plasma adiponectin concentration seen in elderly males. Tietge *et al.*²⁵ recently found that adiponectin is also cleared by the liver. These authors showed in a small observational study that, in patients with liver cirrhosis, plasma adiponectin concentration is significantly increased. We are unable to exclude formally that minor differences in liver function influence plasma adiponectin concentration in the present study. However, we think that it is unlikely because in our study only healthy individuals without any clinical and biochemical features of liver dysfunction participated. Additionally, all subgroups studied did not differ significantly with respect of alanine aminotransferase activity. Recently, Sierksma *et al.*²⁶ found that moderate alcohol intake is associated with an increase in insulin sensitivity and plasma adiponectin concentration. However, Avogaro *et al.*²⁷ in another study, failed to find an influence of alcohol intake on plasma adiponectin concentration. In the current study we have not estimated alcohol consumption. Therefore we are unable to exclude the possibility that differences in alcohol intake may influence our results. However, it should be stressed that all subjects in this study were characterized by the same cultural and ethnic background. Therefore it seems likely that there was no major differences in alcohol intake between age groups.

A limitation of our study is that it is only an observational study. Therefore, we are not able to follow plasma adiponectin concentrations in ageing individuals. It is possible that due to higher cardiovascular mortality in ageing males the selection bias has occurred. One may speculate that male subjects with higher plasma adiponectin concentration are characterized by longer survival and, therefore, males with high plasma adiponectin concentrations are over-represented in our group of subjects older than 70 years.

What is a biological meaning of these findings? It is possible that due to antiatherogenic and antidiabetic properties of adiponectin an increase in plasma adiponectin in elderly males may be a defence mechanism against atherosclerosis and glucose intolerance; common features in the elderly subjects.

In conclusion, plasma adiponectin concentration in females did not change significantly with age, whilst in contrast elderly males over 70 years of age are characterized by a significantly higher plasma adiponectin concentration than younger ones.

Acknowledgements

This paper was supported by the Polish Committee for Scientific Research.

References

- Diamond, F.B. Jr & Eichler, D.C. (2002) Leptin and the adipocyte endocrine system. *Critical Reviews in Clinical Laboratory Science*, **39**, 499–525.
- Więcek, A., Kokot, F., Chudek, J. & Adamczak, M. (2002) The adipose tissue: a novel endocrine organ of interest to the nephrologist. *Nephrology in Dialysis and Transplantation*, **17**, 191–195.
- Maeda, K., Okubo, K., Shimoura, I., Funahashi, T., Matsuzawa, Y. & Matsubara, K. (1996) cDNA cloning and expression of a novel adipose specific collagen-like factor, apM1 (AdiPose Most abundant Gene transcript 1). *Biochemical and Biophysical Research Communications*, **221**, 286–289.
- Diez, J.J. & Iglesias, P. (2003) The role of the novel adipocyte-derived hormone adiponectin in human disease. *European Journal of Endocrinology*, **148**, 293–300.
- Dzielińska, Z., Januszewicz, A., Więcek, A., et al. (2003) Decreased plasma concentration of a novel anti-inflammatory protein-adiponectin in hypertensive men with coronary artery disease. *Thrombosis Research*, **110**, 365–369.
- Hotta, K., Funahashi, T., Arita, Y., et al. (2000) Plasma concentration of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. *Arteriosclerosis and Thrombosis in Vascular Biology*, **20**, 1595–1599.
- Adamczak, M., Więcek, A., Funahashi, T., Chudek, J., Kokot, F. & Matsuzawa, Y. (2003) Decreased plasma adiponectin concentration in patients with essential hypertension. *American Journal of Hypertension*, **16**, 72–75.
- Lamberts, S.W.J., van den Beld, A. & van der Lely, A. (1997) The endocrinology of aging. *Science*, **278**, 419–424.
- Rzepka, E., Adamczak, M., Kokot, F. & Więcek, A. (2002) Influence of aging on plasma leptin concentration. *Polish Archives of International Medicine*, **107**, 125–133.
- Koistinen, H.A., Koivisto, V.A., Karonen, S.L., Ronnema, T. & Tilvis, R.S. (1998) Serum leptin and longevity. *Aging*, **10**, 449–454.
- Burt, V.L., Whelton, P., Roccella, E.J., et al. (1995) Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988–91. *Hypertension*, **25**, 305–313.
- Hazzard, W.R. & Ettinger, W.H. Jr (1995) Aging and atherosclerosis: Changing considerations in cardiovascular disease prevention as the barrier to immortality is approached in old age. *American Journal of Geriatric Cardiology*, **4**, 16–36.
- Kokot, F. & Stupnicki, R. (1985) *Radioimmunological and Radio-competitive Methods used in the Clinical Practice*. Polish National Publisher, Warsaw.
- Daimon, M., Oizumi, T., Saitoh, T., et al. (2003) Decreased serum levels of adiponectin are a risk factor for the progression to type 2 diabetes in the Japanese population: the Funagata study. *Diabetes Care*, **26**, 2015–2020.
- Yamamoto, Y., Hirose, H., Saito, I., et al. (2002) Correlation of the adipocyte-derived protein adiponectin with insulin resistance index and serum high-density lipoprotein-cholesterol, independent of body mass index, in the Japanese population. *Clinical Science*, **103**, 137–142.
- Nishizawa, H., Shimomura, I., Kishida, K., et al. (2002) Androgens decrease plasma adiponectin, an insulin-sensitizing adipocyte-derived protein. *Diabetes*, **51**, 2734–2741.
- Ryan, A.S., Berman, D.M., Nicklas, B.J., et al. (2003) Plasma adiponectin and leptin levels, body composition, and glucose utilization in adult women with wide ranges of age and obesity. *Diabetes Care*, **26**, 2383–2388.
- Lanfranco, F., Zitzman, M., Simoni, M. & Nieschlag, E. (2004) Serum adiponectin levels in hypogonadal males: influence of testosterone replacement therapy. *Clinical Endocrinology*, **60**, 500–507.
- Wiecek, A., Ignacy, W., Chudek, J., et al. (2003) Plasma adiponectin concentration and survival of haemodialysis patients with end stage kidney diseases. *Nephrology, Dialysis, Transplantation*, **18** (Suppl. 4), 715.
- Zamboni, M., Zoico, E., Scartezzini, T., et al. (2003) Body composition changes in stable-weight elderly subjects: the effect of sex. *Aging Clinical and Experimental Research*, **15**, 321–327.
- Zoccali, C., Mallamaci, F., Tripepi, G., et al. (2002) Adiponectin, metabolic risk factors, and cardiovascular events among patients with end-stage renal disease. *Journal of the American Society of Nephrology*, **13**, 134–141.
- Wiecek, A., Nieszporek, T., Witkiewicz, J. & Nowak, L. (2003) Does relationship exist between plasma adiponectin and dehydroepiandrosterone sulfate concentration in haemodialysis patients? *Journal of the American Society of Nephrology*, **14**, 226A.
- Chudek, J., Adamczak, M., Karkoszka, H., et al. A. (2003) Plasma adiponectin concentration before and after successful kidney transplantation. *Transplantation Proceedings*, **35**, 2186–2189.
- Mallamaci, F., Zoccali, C., Cuzzola, F., et al. (2002) Adiponectin in essential hypertension. *Journal of Nephrology*, **15**, 507–511.
- Tietge, U.J., Boker, K.H., Manns, M.P. & Bahr, M.J. (2004) Elevated circulating adiponectin levels in liver cirrhosis are associated with reduced liver function and altered hepatic hemodynamics. *American Journal of Physiology Endocrinology and Metabolism*, **287**, E82–E89.
- Sierksma, A., Patel, H., Ouchi, N., et al. (2004) Effect of moderate alcohol consumption on adiponectin, tumor necrosis factor-alpha, and insulin sensitivity. *Diabetes Care*, **27**, 184–189.
- Avogaro, A., Sambataro, M., Marangoni, A., et al. (2003) Moderate alcohol consumption, glucose metabolism and lipolysis: the effect on adiponectin and tumor necrosis factor alpha. *Journal of Endocrinological Investigation*, **26**, 1213–1218.