

Apelin levels in men with metabolic syndrome with or without late-onset hypogonadism

Angelova P, Kamenov Z, Tsakova A*

Clinic of endocrinology and *Central clinical laboratory, Alexandrovska University Hospital, Medical University – Sofia, Bulgaria

Introduction

The metabolic syndrome (MS) is a cluster of risk factors: diabetes and prediabetes, abdominal obesity, dyslipidemia and high blood pressure [1].

Late-onset hypogonadism (LOH) in men is clinical and biochemical age-related syndrome that is characterised by a number of clinical symptoms and low testosterone levels [2]. The symptoms are not specific: low activity and depression, decreased fat-free mass, increase of the fat mass, reduced muscle strength, reduced bone density and osteoporosis, etc. Sexual disturbances such as low libido and/or erectile dysfunction are common. Serum total testosterone (TT) is measured in the morning between 7 and 11h. The cut-off point of TT < 10.4 nmol/l is often used to determine biochemically the hypogonadal state [3].

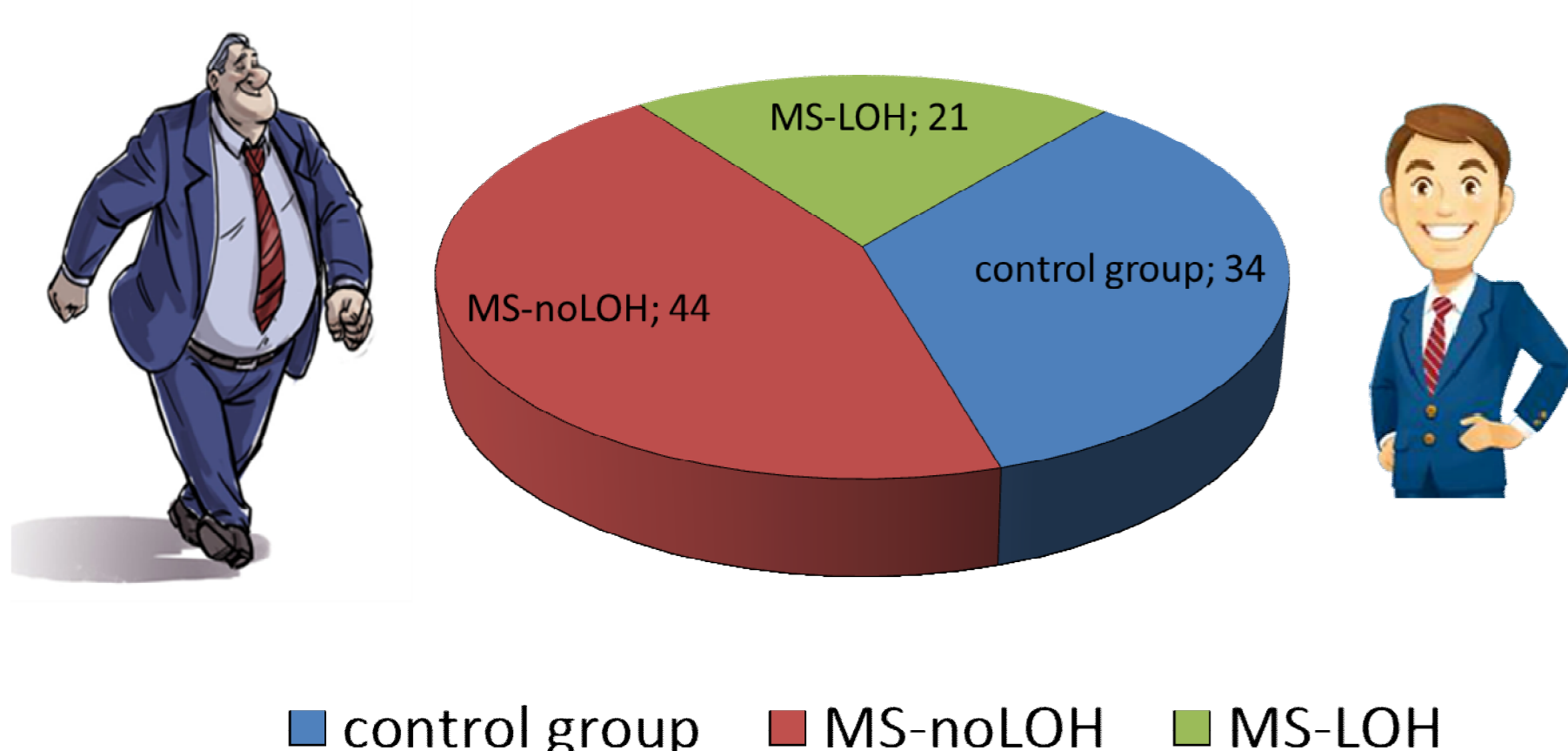
Apelin was isolated in 1998 by Tatemoto et al. [4] as an endogenous ligand for an orphan APJ-receptor. In 2005, Boucher et al. demonstrated that apelin was a new endocrine adipokine produced of mature adipocytes [5]. Apelin was shown to affect many biological functions such as adjusting the neuroendocrine, cardiovascular, and immune systems [6]. Experimental research supports the suppressive effects on insulin resistance [7] but there are also the opposite data [8]. Data about the relationship of apelin to the metabolic syndrome (MS) are still scarce and controversial. LOH is common in men with MS, but we did not find data about the levels of apelin in men with LOH.

The aim of this study was to determine the levels of apelin in men with MS with or without LOH.

Patients and methods

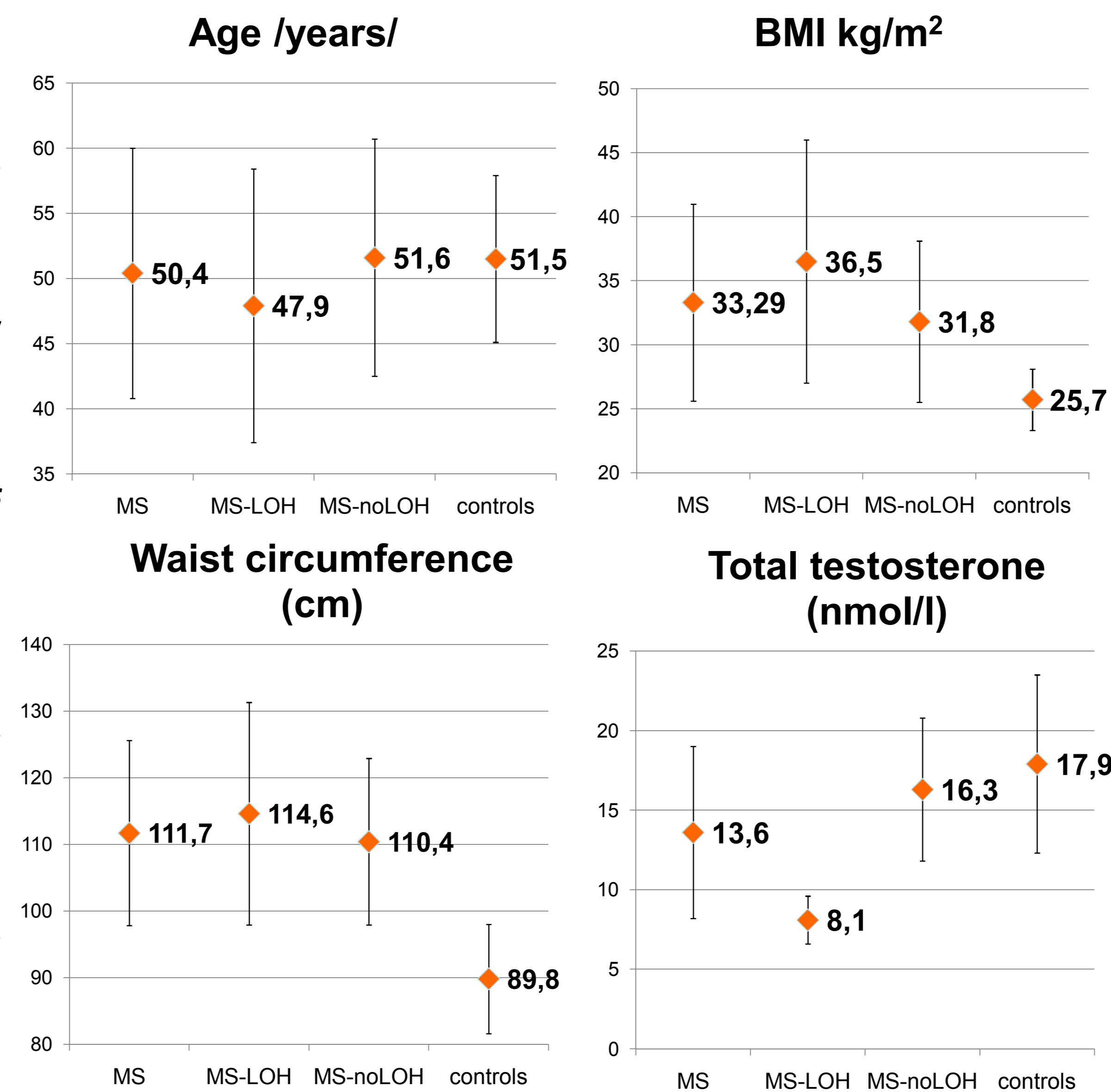
99 men were included in the study. Of them 65 had MS (IDF 2005) and they were divided according to their morning total testosterone (TT) level (cutoff 10.4 nmol/l) into two groups: MS-LOH (N=21) and MS-noLOH (N=44). The control group consisted of 34 age-matched men without MS and LOH. Apelin was determined in serum using enzymelinked immunosorbent assay.

Study design



Results

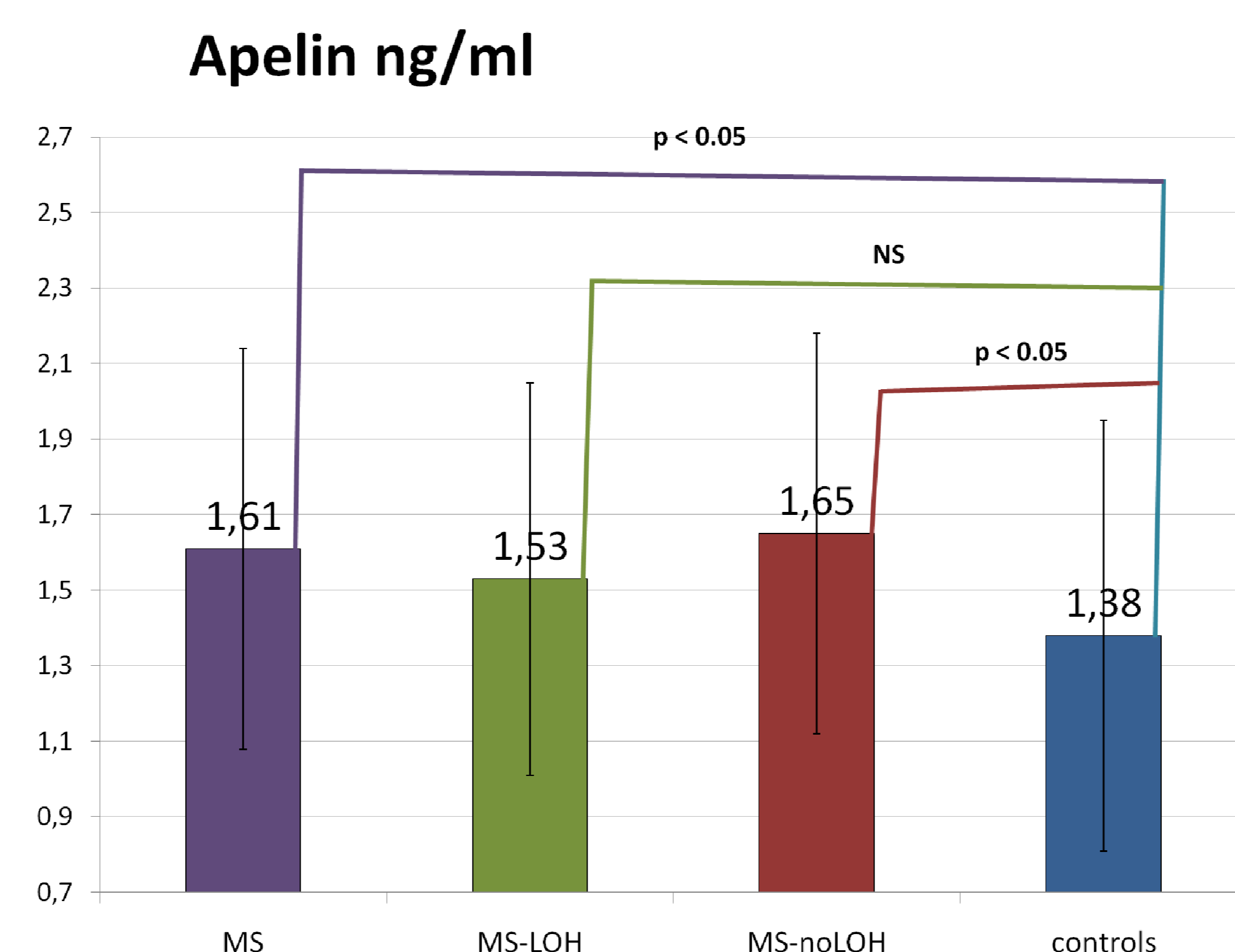
The MS and the control groups were similar in age and height but consistently differed by their weight ($p < 0.001$), BMI ($p < 0.001$), waist circumference ($p < 0.001$) and hip circumference ($p < 0.001$), waist-to-hip ratio ($p < 0.001$). Defining the subgroups by TT-levels, more than 30% of the MS patients were hypogonadal.



74% of the men in the MS group had diabetes mellitus type 2 (DM2) and their mean HbA1c was $7.6 \pm 1.2\%$. The diagnose was established 6 years ago (average). Additionally complications were diagnosed: neuropathy had 77.5%; retinopathy - 26.5% (30% of them- proliferative) and only 2% had nephropathy.

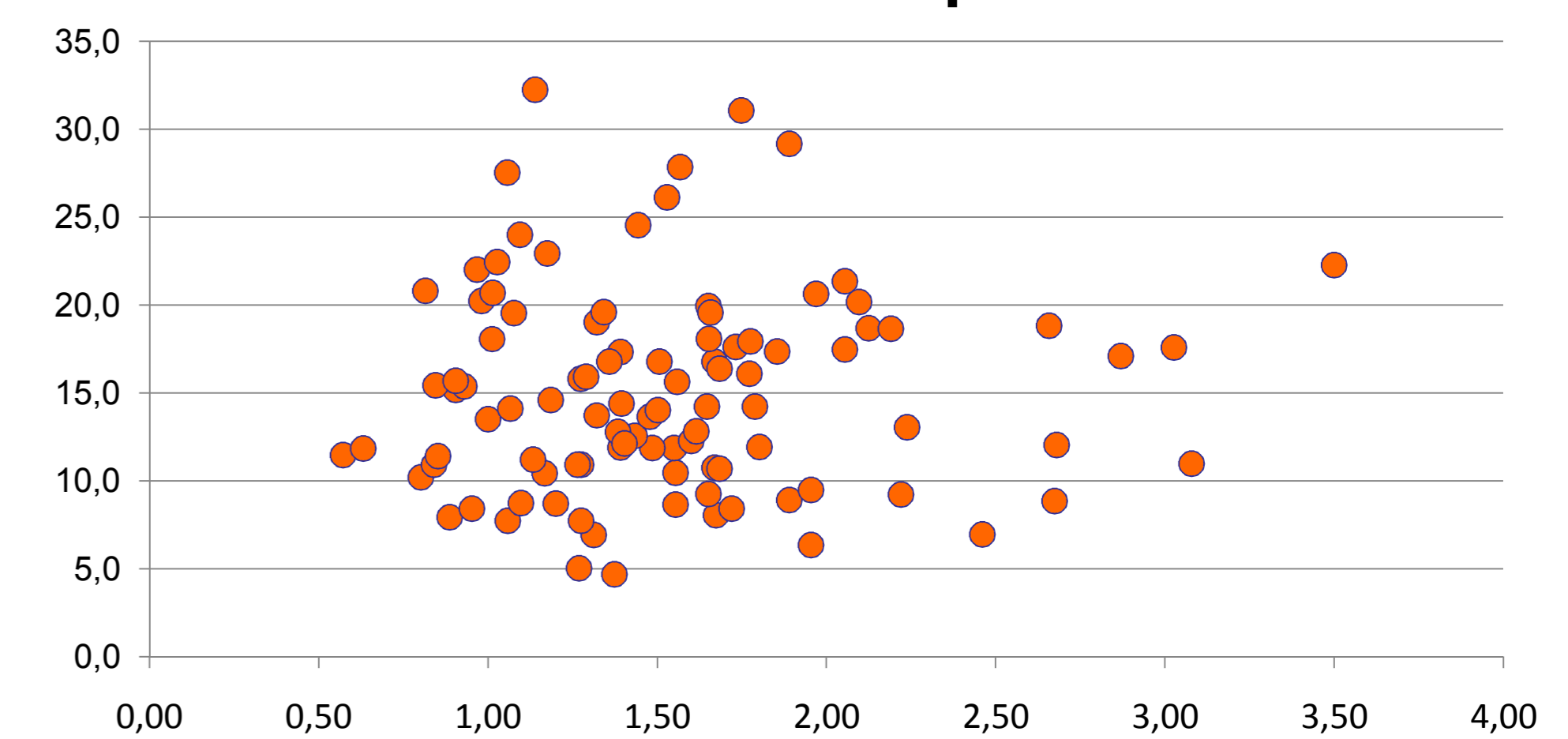
Hypertension was part of the MS in 71% of the patients and almost all of them had already been assigned to antihypertensive medication. 32% of the controls were also hypertensive.

Lipid-lowering medication had already been prescribed to 25% of the MS-patients. After laboratory evaluation more than 50% had low HDL, in more than 50% high triglycerides were established, and 27% had both lipid abnormalities.



The levels of apelin were higher in the MS group compared to the control one ($p < 0.05$). There was no difference between MS-LOH and MS-NoLOH sub-groups. The MS-NoLOH differed from the control group ($p < 0.05$).

Apelin/TT



We found no correlation between the serum apelin and TT-levels for all groups of patients in this study.

Discussion

Significantly higher apelin levels in MS confirm similar data in the literature [9]. On the other hand no significant correlation with the BMI was found. The reason might be that adipose tissue isn't the only source of apelin synthesis and other sources like the endothelia could mask this effect [10].

The role of the sex hormones in apelin regulation has been supposed by others [10]. As far as we know this is the first study investigating that relation. Even though the MS and the control groups differ significantly both by their apelin and TT-levels, there's no correlation between them. Our data show that LOH, although tightly related to MS, doesn't contribute to the apelin alterations that are seen in the insulin-resistant state.

Conclusions

In this study the difference in apelin levels was related to the presence of the MS, but not to the TT status

References

1. The IDF consensus worldwide definition of the metabolic syndrome. 2005. http://www.idf.org/webdata/docs/Metac_syndrome_def.pdf
2. Wang C, Nieschlag E, Swerdloff R, Behre HM, et al. Investigation, treatment and monitoring of late-onset hypogonadism in males: ISA, ISSAM, and EAU recommendations. *Int J Androl* 2005; 28:125–127.
3. Mulligan T, Frick MF, Zuraw QC, Stemhagen A, McWhirter C. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract.* 2006 Jul;60(7):762-9.
4. Tatemoto K, Hosoya M, Habata Y, Fujii R, Kakegawa T, Zou MX, et al. Isolation and characterization of a novel endogenous peptide ligand for the human APJ receptor. *Biochem Biophys Res Commun.* 1998; 251 (2): 471-6
5. Boucher J, Masri B, Daviaud D, Gesta S, Guigne C, Mazzucotelli A, et al. Apelin, a newly identified adipokine up-regulated by insulin and obesity. *Endocrinology.* 2005; 146 (4): 1764-71.
6. Sorli SC, van den Berghe L, Masri B, et al. Therapeutic potential of interfering with apelin signalling. *Drug Discov Today.* 2006;11: 1100–6110.
7. Higuchi K, Masaki T, Gotoh K, Chiba S, Katsuragi I, Tanaka K, et al. Apelin, an APJ receptor ligand, regulates body adiposity and favors the messenger ribonucleic acid expression of uncoupling proteins in mice. *Endocrinology* 2007;148:2690-7.
8. Li L, Yang G, Li Q, Tang Y, Yang M, Yang H, et al. Changes and relations of circulating visfatin, apelin, and resistin levels in normal, impaired glucose tolerance, and type 2 diabetic subjects. *Exp Clin Endocrinol Diabetes* 2006;114:544-8.
9. Yu Shan, Zhang Y, Li M. et al. Chemerin and apelin are positively correlated with inflammation in obese type 2 diabetic patients; *Chin Med J* 2012;125(19):3440-3444
10. Reinehr T, Woelfle J, Roth CL. Lack of association between apelin, insulin resistance, cardiovascular risk factors, and obesity in children: a longitudinal analysis. *Metab Clin and Exp* 60(2011)1349-1354

Acknowledgments

This research was sponsored by Medical University – Sofia, grant № 27-D/2011 according to contract № 25-D

