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The effect of overt and subclinical hypothyroidism on the development of non-dipper blood pressure

Wpływ jawnej i subklinicznej niedoczynności tarczycy na rozwój profilu ciśnienia tętniczego typu *non-dipper*

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Abstract

Introduction: 'Non-dippers' are individuals without the anticipated nocturnal decrease in blood pressure. An increased incidence of target organ damage and a worse outcome in terms of cardiovascular events have been reported in this group of people. The pathogenesis of non-dipper hypertension is not clear at present. We aimed to investigate the effects of overt and subclinical hypothyroidism on the development of a non-dipper blood pressure pattern via 24-hour ambulatory blood pressure monitoring.

Material and methods: 109 normotensive patients with overt and subclinical hypothyroidism were evaluated, and 95 of these patients without reverse dipping and masked hypertension were included in the study. The control group consisted of 75 gender- and age-matched, normotensive, euthyroid healthy individuals.

Results: Median serum TSH levels were 7.61 and 1.59 mUmL in patient and control groups, respectively. The number of non-dippers according to systolic, diastolic and mean blood pressure was significantly higher in the patients with hypothyroidism compared to the control group. In linear regression analysis, TSH had a negative effect on the night/day ratio of the systolic, diastolic and mean blood pressures.

Conclusion: Despite the fact that the effect of hypothyroidism on non-dipper blood pressure pattern is not known, the present study has revealed that elevated TSH levels are likely to increase the risk of non-dipping in normotensive patients with either overt or subclinical hypothyroidism. **(Pol J Endocrinol 2012; 63 (2): 97–103)**

Key words: *hypothyroidism, dipping, non-dipper blood pressure, ambulatory blood pressure monitoring, TSH*

Streszczenie

Wstęp: U osób określanych jako *non-dippers* nie występuje fizjologiczne obniżenie ciśnienia tętniczego w godzinach nocnych. Jak wynika z doniesień, w tej grupie chorych częściej dochodzi do zmian narządowych i zdarzeń sercowo-naczyniowych. Patogenezy nadciśnienia tętniczego typu *non-dipper* dotychczas nie wyjaśniono. Celem autorów było zbadanie wpływu jawnej i subklinicznej niedoczynności tarczycy na rozwój profilu dobowej zmienności ciśnienia tętniczego typu *non-dipper* metodą całodobowego automatycznego pomiaru ciśnienia tętniczego.

Materiał i metody: Spośród 109 chorych z prawidłowym ciśnieniem i z jawną lub subkliniczną niedoczynnością tarczycy do analizy włączono 95 osób, u których nie występował nocny wzrost ciśnienia tętniczego (*reverse dipping*) ani utajone nadciśnienie tętnicze. Grupa kontrolna składała się z 75 zdrowych osób z prawidłowym ciśnieniem tętniczym i prawidłową czynnością tarczycy odpowiednio dobranych pod względem płci i wieku.

Wyniki: Mediany stężeń TSH w surowicy w grupach badanej i kontrolnej wynosiły odpowiednio 7,61 i 1,59 mUml. Liczba osób, u których nie występował nocny spadek wartości skurczowego, rozkurczowego i średniego ciśnienia tętniczego, był istotnie wyższy w grupie chorych z niedoczynnością tarczycy niż w grupie kontrolnej. W analizie regresji liniowej wykazano istnienie odwrotnej zależności między stężeniem TSH a stosunkiem między nocnymi i dziennymi wartościami ciśnienia skurczowego, rozkurczowego i średniego ciśnienia tętniczego.

Wnioski: Mimo że nie wiadomo, jaki jest mechanizm oddziaływania niedoczynności tarczycy na rozwój dobowego profilu ciśnienia tętniczego typu *non-dipper*, w niniejszym badaniu wykazano, że podwyższone stężenie TSH może zwiększać ryzyko wystąpienia takiego profilu ciśnienia tętniczego u osób z prawidłowym ciśnieniem tętniczym i jawną lub subkliniczną niedoczynnością tarczycy. **(Endokrynol Pol 2012; 63 (2): 97–103)**

Słowa kluczowe: *niedoczynność tarczycy, nocny spadek ciśnienia tętniczego, profil typu non-dipper, automatyczny całodobowy pomiar ciśnienia tętniczego, TSH*

Introduction

Overt and subclinical hypothyroidism is closely associated with increased cardiovascular morbidity. This increase has been attributed to accelerated atherosclerosis, along with changes in blood pressure [1–5]. However, the relation between thyroid stimulating hormone (TSH) and blood pressure remains unclear [6]. Some recent studies have suggested that the risk of hypertension may increase with hypothyroidism, even with mild

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increases in TSH levels [7–9]. Sympathetic nervous system activation, increased vascular resistance, increased arterial stiffness, and endothelial dysfunction, which are thought to occur in association with hypothyroidism, may lead to an impairment in the regulation of blood pressure [3, 5, 7]. Moreover, it is thought that high TSH levels in such patients may lead to an impairment of the circadian rhythm of blood pressure by means of the changes occurring in the vascular system [10].

Twenty-four hour ambulatory blood pressure monitoring (ABPM) is of great importance in identifying night-time blood pressure changes. A decrease of less than 10% in night-time blood pressure compared to daytime blood pressure is defined as non-dipping. A non-dipping profile is closely associated with cardiovascular morbidity and mortality, cerebrovascular accidents, and target organ damage, both in hypertensive and normotensive subjects. Therefore, early identification of a non-dipping profile is of great importance [11–15]. However, the etiopathogenesis of non-dipping has yet to be fully defined [11–15]. A limited number of studies have shown that a non-dipping profile is commoner in hypertensive patients with increased TSH levels. An increased prevalence of non-dippers after short-term hypothyroidism has been reported in a group of normotensive patients with thyroid carcinomas [10, 16].

The present study aimed to investigate the effect of overt and subclinical hypothyroidism on the development of a non-dipper blood pressure profile, via 24-hour blood pressure monitoring, in normotensive subjects.

Material and methods

109 normotensive patients, who had been diagnosed with overt and subclinical hypothyroidism (TSH ≥ 4.5 mUmL), in the Internal Medicine and Endocrinology outpatient units of Gazi University Hospital between December 2007 and June 2008 were screened, and those who met the eligibility criteria were enrolled. Individuals who had previously received or were currently receiving antihypertensives or hypothyroidism medication, medication with a potential to elevate blood pressure levels (e.g. prednisone), or who had clinical or laboratory evidence of other secondary causes of hypertension, were excluded. Individuals with renal, hepatic (cirrhosis, elevated liver enzymes) dysfunction, cardiac insufficiency, infection and acute inflammatory states were also excluded, along with patients with reverse dipping and masked hypertension. Finally, 95 patients were eligible for the study.

The control group consisted of 75 gender- and age-matched, normotensive, euthyroid healthy individuals out of 83 cases, with reverse dipping and masked hypertension excluded as in the hypothyroid group. In order to rule out selection bias, those healthy individuals who gave informed consent to participate in our study and who were admitted to the internal medicine outpatient clinic over a two month period, were all included in the control group. The institutional review board approved the human research protocol.

Clinic blood pressure measurements

Clinic blood pressure (BP) of each participant was measured three times on the non-dominant arm using a mercury sphygmomanometer with an appropriately-sized cuff. Systolic and diastolic blood pressure values were identified from the first and fifth phase of Korotkoff sounds. During the measurements, the participant remained seated with the arm comfortably placed at heart level.

Ambulatory Blood Pressure Monitoring (ABPM)

All subjects underwent 24-hour ABPM on a normal working day. They were instructed to act and work normally. A Spacelabs 90217 ambulatory blood pressure monitor was used. Each patient used an arm cuff of similar size to the one used for routine office BP measurement in the non-dominant arm. The device was programmed to measure BP every 15 minutes between 6 a.m. and 11 p.m., and every 30 minutes between 11 p.m. and 6 a.m. All subjects were advised to rest or sleep between 10 p.m. and 6 a.m. Shift workers, and patients who could not rest or sleep at night, were not included in the study. 'Dippers' were defined as individuals whose night-time blood pressures dropped by more than 10% compared to their daytime blood pressures [17]. Likewise, a patient whose night-time blood pressure dropped by less than 10% was defined as a 'non-dipper' and one whose night-time blood pressure was greater than the daytime value was defined as a 'reverse dipper'. 'White-coat hypertension' was defined as office hypertension with ambulatory normotension and 'masked hypertension' was defined as office normotension and ambulatory hypertension [17–19]. The study was conducted according to the Helsinki Declaration and approved by the Ethics Committee of the Gazi University School of Medicine.

Clinical information and laboratory data

Clinical information including height, weight, medical history, current medications, laboratory data, and smoking history was recorded. Body weight was measured with the participants in light clothing without shoes. Body mass index (BMI) was calculated as weight in kg divided by height in m^2. Serum

parameters analysed were creatinine, blood glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides, free T3 (FT3), free T4 (FT4) and TSH (normal range 0.35–4.5 mIUmL). Assays were performed centrally in the Laboratory of Gazi University Hospital.

Statistical analysis

Data was shown as mean ± SD or as percentages, where appropriate. Standard descriptive statistics, a two-tailed student's t test and a chi-squared test were used where appropriate to compare characteristics of the groups. Mann-Whitney U test was used for non-normally distributed variables. Univariate correlation was established by the Spearman's correlation coefficient. To assess the influence of tested parameters on BP night/day ratio as the dependent variable, multiple regression analysis was performed. All statistical calculations were performed using the Statistical Package for the Social Sciences (SPSS version 13). A p value of 0.05 was considered as statistically significant.

Results

Comparisons of the anthropometric measurements, demographic information and biochemical analysis results of the hypothyroid patients and the control group are shown in Table I. Serum LDL-C, total cholesterol and TSH levels of hypothyroid patients were significantly higher, and serum fT3 (free T3) and fT4 (free T4) levels were significantly lower, than the control group (Table I).

The readings of clinic blood pressure and 24-hour blood pressure of the participants are shown in Table II. Although all the patients were within the normotensive ranges, the clinic blood pressures of the hypothyroid patients were found to be significantly lower than those of the individuals in the control group. According to the 24-hour ABPM, the dipping ratios (daytime to night-time variation) of the systolic, diastolic and mean blood pressures were significantly lower in the patient group compared to the control group.

The number of non-dippers according to systolic, diastolic and mean blood pressure was significantly higher in the patients with hypothyroidism compared to the control group (Figure 1). The correlation analysis between TSH levels and the study parameters revealed a weak positive correlation between TSH levels and triglyceride and LDL-C levels ($R = 0.303$, $p = 0.000$ and $R = 0.257$, $p = 0.001$ respectively) (Table III). The correlation analysis of ambulatory blood pressure measurements and the clinic blood pressure measurements showed a negative correlation between TSH levels and clinic systolic and diastolic blood pressures as well as with 24-hour systolic, diastolic and mean blood pressures (Table III). In addition, there was a weak negative correlation between TSH levels and the daytime/night-time variations of systolic, diastolic and mean blood pressures ($R = –0.333$, $p = 0.001$, $R = –0.322$, $p = 0.001$, and $R = –0.344$, $p = 0.001$ respectively) (Table III). In linear regression analysis evaluating the independent effect of TSH on the night/day ratios, TSH had a negative effect on the night/day ratio of the systolic and diastolic blood

Table I. *Demographic and laboratory parameters of hypothyroid patients and control group*
Tabela I. *Dane demograficzne i parametry laboratoryjne u chorych z niedoczynnością tarczycy i w grupie kontrolnej*

	Hypothyroid patients (n = 95)	Control group (n = 75)	p
Gender (F/M)	85/10	62/13	0.144
Age (years)	39.78 ± 11.67	39.00 ± 12.25	0.710
BMI [kg/m^2]	27.02 ± 4.50	26.13 ± 4.41	0.203
Smoking (Y/N)	36/59	25/50	0.325
TSH	18.16 ± 26.10	1.77 ± 0.99	0.000
FT3	2.35 ± 0.57	2.63 ± 0.42	0.011
FT4	0.90 ± 0.25	1.11 ± 0.33	0.000
FBG [mg/dL]	88.47 ± 9.59	89.44 ± 8.36	0.542
Cr	0.82 ± 0.14	0.79 ± 0.13	0.172
TG	143.04 ± 74.56	112.23 ± 54.97	0.002
LDL	134.25 ± 46.05	115.12 ± 33.33	0.003

F — female; M — male; Y — yes; N — no

Table II. *Clinical and 24-hour ambulatory blood pressure recordings of hypothyroid patients and control group*

Tabela II. *Zapisy całodobowego automatycznego pomiaru ciśnienia tętniczego u chorych z niedoczynnością tarczycy i w grupie kontrolnej*

	Hypothyroid patients (mean ± SD)	Control group (mean ± SD)	p
Clinic SBP	116.79 ± 9.56	121.60 ± 8.42	0.002
Clinic DBP	74.63 ± 6.15	77.60 ± 5.15	0.001
24-hour SBP	110.04 ± 8.25	111.79 ± 6.87	0.109
24-hour DBP	69.47 ± 6.73	70.21 ± 5.53	0.345
24-hour MAP	83.73 ± 6.49	84.41 ± 5.51	0.443
Daytime SBP	111.93 ± 13.53	114.87 ± 14.29	0.013
Daytime DBP	72.33 ± 7.05	74.39 ± 5.87	0.031
Daytime MAP	86.39 ± 6.81	88.47 ± 5.98	0.042
Night-time MAP	104.42 ± 8.74	104.31 ± 13.03	0.474
Night-time DBP	64.03 ± 7.28	62.43 ± 6.20	0.132
Night-time MAP	78.45 ± 6.82	76.59 ± 5.96	0.057
SBP night/day ratio	7.52 ± 4.64	11.09 ± 4.60	0.000
DBP night/day ratio	11.38 ± 6.24	16.00 ± 6.21	0.000
MAP night/day ratio	9.12 ± 5.21	13.38 ± 5.29	0.000

SD — standard deviation; SBP — systolic blood pressure; DBP — diastolic blood pressure; MAP — mean arterial pressure

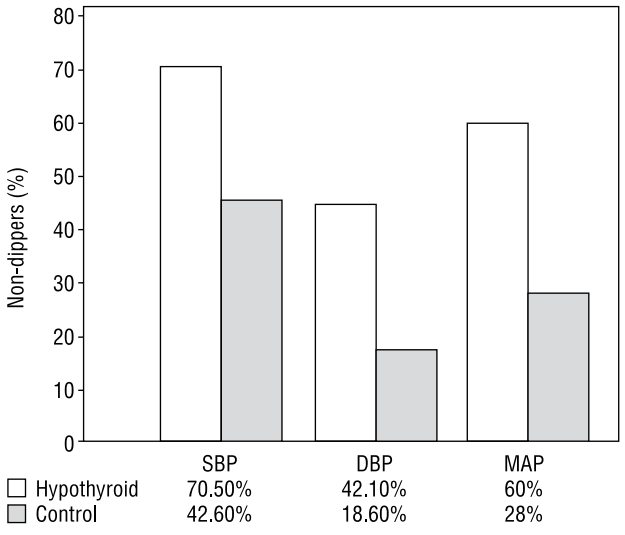

Figure 1. *Percentages of non-dippers in the patients with hypothyroidism and the control group χ^2 test revealed significant differences between the groups in terms of number of dippers ($p = 0.000$, $p = 0.001$, and $p = 0.000$, respectively); MAP — mean arterial pressure*

Rycina 1. *Odsetek osób z profilem typu* non-dipper *w grupie chorych z niedoczynnością tarczycy i w grupie kontrolnej; w teście χ^2 wykazano istotne różnice między grupami pod względem liczby osób z fizjologicznym nocnym spadkiem ciśnienia tętniczego (odpowiednio $p = 0{,}000$; $p = 0{,}001$; $p = 0{,}000$); MAP — średnie ciśnienie tętnicze*

pressures, when the night/day ratio was considered as the dependent variable, and age, BMI, LDL-C and TSH were considered as the independent variables ($\beta = -0.152$, $p = 0.04$; $\beta = -0.158$, $p = 0.03$; $\beta = -0.176$, $p = 0.02$, respectively) (Figure 2).

Discussion

In the present study, the number of non-dippers was found to be significantly higher in the group involving patients with overt and subclinical hypothyroidism compared to healthy euthyroid individuals. And the night/day ratios of blood pressure measurements were significantly lower in the patient group compared to the control group.

Non-dipping profile is important in assessing the cardiovascular prognosis and in determining target organ damage at early stages [11–15]. However, the mechanism of the development of non-dipping remains unknown [11–15]. The imbalance between the sympathetic and parasympathetic nervous systems may be the major effective mechanism. A decrease in the parasympathetic activity and an increase in the sympathetic activity are observed all night long in non-dipping patients [15]. Besides, various hormones (catecholamines, renin, aldosterone and cortisol) are thought to be effective in the development of a non-dipper profile [20]. It has been suggested, in the limited number of recent studies, that TSH is also likely to be among these hormones [7, 10, 16, 20]. However, conflicting results have been obtained from these studies [7, 10, 16]. A TSH-mediated increase in vascular resistance, endothelial dysfunction, and

Table III. *Correlation between TSH levels and study parameters or clinic and 24-hour ambulatory blood pressure readings*
Tabela III. *Korelacja między stężeniami TSH i innymi parametrami analizowanymi w badaniu a wynikami całodobowego automatycznego pomiaru ciśnienia tętniczego*

Blood pressure			Study parameters		
	R	p		R	p
Clinical SBP	–0.249	0.001	FT3	–0.398	0.000
Clinical DBP	–0.261	0.001	FT4	–0.555	0.000
24-hour DBP	–0.073	0.344	Age	0.169	0.102
24-hour SBP	–0.114	0.138	BMI	0.150	0.051
24-hour MAP	–0.067	0.386	FBG	–0.053	0.490
Night-time SBP	0.068	0.381	Creatinine	0.142	0.065
Night-time DBP	0.110	0.155	LDL-C	0.257	0.001
Night-time MAP	0.133	0.084	TG	0.303	0.000
Daytime SBP	–0.178	0.020			
Daytime DBP	–0.156	0.042			
Daytime MAP	–0.154	0.045			
DBP night/day ratio	–0.322	0.000			
SBP night/day ratio	–0.333	0.000			
MAP night/day ratio	–0.344	0.000			

SBP — systolic blood pressure; DBP — diastolic blood pressure; MAP — mean arterial pressure; FT3 — free T3; FT4 — free T4; BMI — body mass index; FBG — fasting blood glucose; LDL-C — low-density lipoprotein cholesterol; TG — triglyceride

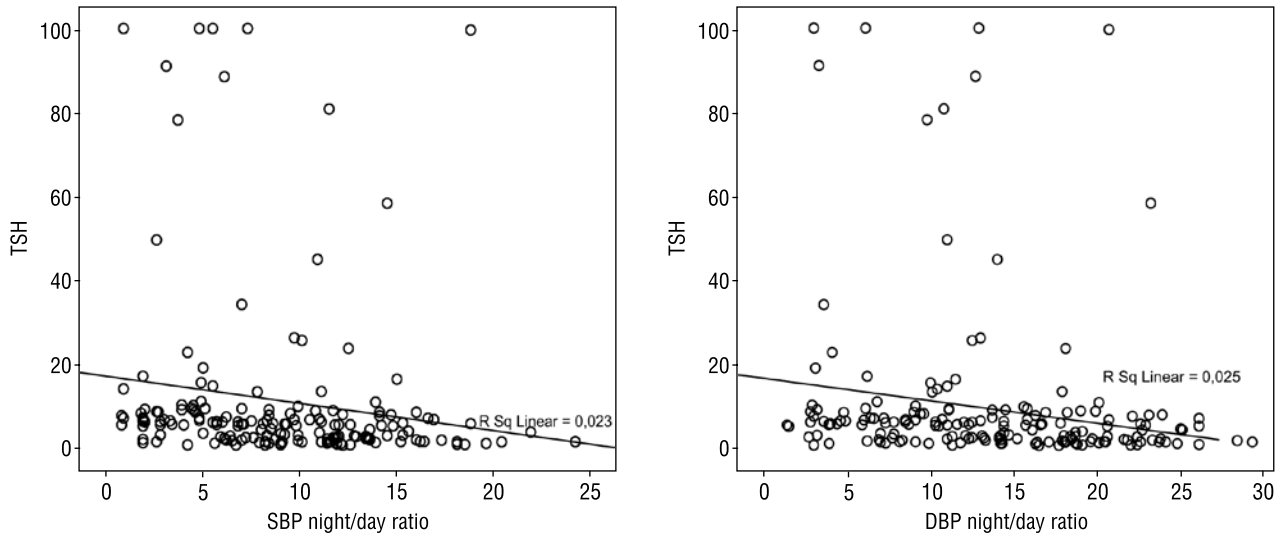

Figure 2. *Relation between TSH levels and dipping ratios of systolic and diastolic blood pressure; TSH — thyroid stimulating hormone; DBP — diastolic blood pressure; SBP — systolic blood pressure*

Rycina 2. *Zależności między stężeniami TSH i częstością nocnych spadków ciśnienia skurczowego i rozkurczowego; TSH — hormon tyreotropowy; DBP — ciśnienie rozkurczowe; SBP — ciśnienie skurczowe*

increased sympathetic nervous system sensitivity, may play a role in this probable association [3, 21–24]. Accordingly, high noradrenalin levels and decreased number of vascular beta-adrenergic receptors may prevent the night-time decrease in blood pressure [15]. Moreover, endothelial dysfunction concurrent with TSH elevation via a decrease in vascular relaxation may be effective in the development of non-dipping [25]. The relation between TSH and renal sodium uptake might be another mechanism considered for the development of

a non-dipping profile in patients with hypothyroidism. According to this mechanism, renal sodium uptake that increases with the increase in TSH levels may play a role in the development of a non-dipping profile, because previous studies have shown that serum Na+ levels are higher in non-dipper patients compared to dippers, and that a non-dipping profile is observed more commonly in Na+-sensitive hypertensives [22, 26].

Moreover, a weak but significant negative correlation was found between TSH levels and the night/day ratio of blood pressure. This indicates that elevated TSH levels are likely to increase the risk of non-dipping. At the very least, we can state that a non-dipping pattern is more prevalent in hypothyroid patients. Furthermore, the independent effect of TSH on night/day ratios, as shown in linear regression analysis, corroborates the hypothesis of increased non-dipping with elevated TSH levels. In the limited studies on this subject in the literature, it has been suggested that TSH elevation and non-dipping occur simultaneously in hypertensive patients [10]. An important element of our present study is the involvement of normotensive patients predominantly with subclinical hypothyroidism, because the necessity for cardiovascular risk assessment and treatment in subjects with subclinical hypothyroidism is still a matter of debate. Precise estimation of cardiovascular risk classification in such patients may help make accurate decisions for both the follow-up and treatment. In normotensive patients, a recent study about the association between TSH and dipping pattern was conducted by Botella-Carretero et al. [16]. It showed that short term hypothyroidism resulted in an increase in night-time systolic, mean and diastolic blood pressure, and was accompanied by an increase in the proportion of non-dippers in normotensive patients with differentiated thyroid carcinoma compared to euthyroid patients [16]. These outcomes parallel our findings.

The other finding of our study was the negative correlation between TSH levels and clinic blood pressure and daytime ABPM measurements. Moreover, these measurements were observed to be significantly lower in the hypothyroid patients compared to the control group, suggesting that elevated TSH levels might lead to a decrease in daytime blood pressures. We attributed this result to the close relation between TSH and the sympathetic and parasympathetic nervous systems. Elevated TSH levels activate the sympathetic nervous system while inhibiting the parasympathetic nervous system [15]. Long term activation of the sympathetic nervous system may further result in insensitivity against sympathetic nervous system stimulations. Such insensitivity may lead to the relatively low activation of the sympathetic nervous system during daytime and high activation during night-time, and consequently to low blood pressures during the day and high blood pressures during the night. The decreased variation between daytime and night-time blood pressures via TSH effect may result in non-dipping. In an ABPM study conducted by Kotsis et al., a negative correlation was found between TSH and the mean systolic and diastolic blood pressures [7]. However, quite different results have been obtained from studies performed on the relation between TSH and blood pressure [6–9, 16]. While it has been suggested in some of the studies that there may be an increase in blood pressure levels by TSH level elevation, others have suggested just the opposite. These differing results may be due to variability in the study population characteristics as well as TSH levels, comorbidities, and the determination of blood pressure using methods other than ABPM [6–9].

The other finding of this present study was the significant positive correlation of TSH levels with cholesterol and triglyceride. There are studies in the literature suggesting that subclinical hypothyroidism, as well as overt hypothyroidism, leads to dyslipidaemia [1, 27]. Such negative effects on the lipid profile may play a role in the development of accelerated atherosclerosis in patients with hypothyroidism.

Our study has several limitations. First, the sample size was rather small; it would need to be larger to be of convincing statistical significance. Second, the subjects in the control group were selected from a clinical practice and not from the general population. Third, the results of the correlation and regression analysis in our study are weak. They only mean an association between TSH and non-dipping, not a causative effect.

Conclusion

This study has revealed that elevated TSH levels are likely to increase the risk of non-dipping in normotensive patients with either overt or subclinical hypothyroidism. In other words, we have found that a non-dipping blood pressure pattern is more prevalent in mild or overt hypothyroid patients. Moreover, it has been determined that elevated TSH levels seem to be associated with a decrease in daytime blood pressure measurements, even though the mechanism is not completely defined. These outcomes suggest that a non-dipping profile, which is associated with cardiovascular morbidity, may present as an additional risk factor in patients with hypothyroidism.

Accordingly, ABPM measurements should be considered in hypothyroid patients to assess the risk factors, even if they are normotensive. Besides, in setting the indications of thyroid hormone replacement therapy in subclinical hypothyroidism, evaluating the dipping pattern via ABPM would play a role in the accurate

estimation of cardiovascular risk factors, even in patients who are clinically normotensive. Further studies are warranted to confirm this association, and to find out the probable mechanisms of this association.

Conflict of interest

The authors have no financial disclosures to declare, and no conflicts of interest to report.

References

1. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women the Rotterdam Study. Ann Intern Med 2000; 132: 270–278.
2. Bernstein R, Müller C, Midtbo K, Smith G, Haug E, Hertzenberg L. Silent myocardial ischemia in hypothyroidism. Thyroid 1995; 5: 443–447.
3. Dagre AG, Lekakis JP, Papaioannou TG et al. Arterial stiffness is increased in subjects with hypothyroidism. Int J Cardiol 2005; 103: 1–6.
4. Biondi B, Palmieri EA, Lombardi G, Fazio S. Effects of subclinical thyroid dysfunction on the heart. Ann Intern Med 2002; 137: 904–914.
5. Fommei E, Iervasi G. The role of thyroid hormone in blood pressure homeostasis evidence from short-term hypothyroidism in humans. J Clin Endocrinol Metab 2002; 87: 1996–2000.
6. Walsh JP, Bremner AP, Bulsara MK et al. Subclinical thyroid dysfunction and blood pressure a community-based study. Clin Endocrinol 2006; 65: 486–491.
7. Kotsis V, Alevizaki M, Stabouli S et al. Hypertension and hypothyroidism results from an ambulatory blood pressure monitoring study. J Hypertens 2007; 25: 993–999.
8. Asvold BO, Bjoro T, Nilsen TI, Vatten LJ. Association between blood pressure and serum thyroid-stimulating hormone concentration within the reference rangea population-based study. J Clin Endocrinol Metab 2007; 92: 841–845.
9. Liu D, Jiang F, Shan Z et al. A cross-sectional survey of relationship between serum TSH level and blood pressure. J Hum Hypertens 2010; 24: 134–138.
10. Kanbay M, Turgut F, Karakurt F et al. Relation between serum thyroid hormone and 'nondipper' circadian blood pressure variability. Kidney Blood Press Res 2007; 30: 416–420.
11. Redon J, Lurbe E. Nocturnal blood pressure versus nondipping pattern what do they mean Hypertension 2008; 51: 41–42.
12. Hansen TW, Jeppesen J, Rasmussen S, Ibsen H, Torp-Pedersen C. Ambulatory blood pressure monitoring and risk of cardiovascular disease a population based study. Am J Hypertens 2006; 19: 243–250.
13. Madin K, Iqbal P. Twenty four hour ambulatory blood pressure monitoring a new tool for determining cardiovascular prognosis. Postgrad Med J 2006; 82: 548–551.
14. Clement DL. Night and day what blood pressure matters Hypertension 2007; 49: 1213–1214.
15. Routledge FS, McFetridge-Durdle JA, Dean CR; Canadian Hypertension Society. Night-time blood pressure patterns and target organ damage a review. Can J Cardiol 2007; 23: 132–138.
16. Botella-Carretero JI, Gómez-Bueno M, Barrios V et al. Chronic thyrotropin-suppressive therapy with levothyroxine and short-term overt hypothyroidism after thyroxine withdrawal are associated with undesirable cardiovascular effects in patients with differentiated thyroid carcinoma. Endocr Relat Cancer 2004; 11: 345–356.
17. O'Brien E, Sheridan J, O'Malley K. Dippers and non-dippers. Lancet 1988; 2: 397.
18. O'Brien E, Asmar R, Beilin L et al. European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003; 21: 821–848.
19. Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. Hypertension 2002; 40: 795–796.
20. Lapiński M, Lewandowski J, Januszewicz A et al. Hormonal profile of dipper and non-dipper patients with essential hypertension. J Hypertens Suppl 1993; 11: 294–295.
21. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med 2001; 344: 501–509.
22. Gumieniak O, Perlstein TS, Hopkins PN et al. Thyroid function and blood pressure homeostasis in euthyroid subjects. J Clin Endocrinol Metab 2004; 89: 3455–3461.
23. Lekakis J, Papamichael C, Alevizaki M et al. Flow-mediated, endothelium-dependent vasodilation is impaired in subjects with hypothyroidism, borderline hypothyroidism, and high-normal serum thyrotropin (TSH) values. Thyroid 1997; 74: 11–14.
24. Taddei S, Caraccio N, Virdis A et al. Impaired endothelium-dependent vasodilatation in subclinical hypothyroidism beneficial effect of levothyroxine therapy. J Clin Endocrinol Metab 2003; 88: 3731–3737.
25. Kohara K, Nishida W, Maguchi M, Hiwada K. Autonomic nervous function in nondipper essential hypertensive subjects. Evaluation by power spectral analysis of heart rate variability. Hypertension 1995; 26: 808–814.
26. Marcisz C, Jonderko G, Kucharz EJ. Influence of short-time application of a low sodium diet on blood pressure in patients with hyperthyroidism or hypothyroidism during therapy. Am J Hypertens 2001; 14: 995–1002.
27. Althaus BU, Staub JJ, Ryff-De Leche A, Oberhänsli A, Stähelin HB. LDL/HDL-changes in subclinical hypothyroidism possible risk factors for coronary heart disease. Clin Endocrinol 1988; 28: 157–163.