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Serum Heart Type Fatty Acid Binding Protein Levels in Primary Hyperparathyroidism

Primer Hiperparatiroidizmde Serum Kalp Tipi Yağ Asidi Bağlayıcı Protein Düzeyleri

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Abstract

Purpose: Recent studies indicate that plasma heart-type fatty acid binding-protein (H-FABP) concentration can be used as an early biochemical marker for macrovascular diseases. Patients with primary hyperparathyroidism (PHT) reportedly display an increase in cardiovascular (CV) risk factors. Our aim was to evaluate plasma H-FABP concentration in these subjects with primary hyperparathyroidism, by comparing them with healthy controls.

Material and Method: Anthropometric parameters, serum H-FABP, serum lipid, serum calcium, phosphorus, parathormone (PTH), insulin resistance (HOMA-IR), high sensitive C-reactive protein (h-CRP), 24-hour urine microalbumin excretion and carotid intima-media thickness (CIMT) were evaluated among primary hyperparathyroidism patients (8 males, 80 females) and 87 healthy subjects (12 males, 75 females).

Results: No significant difference was seen in the levels of H-FABP between patients [1086.07 (298-3744)] and controls [1113.36 (263.27-3510)]. The average values of PTH, HOMA-IR, total cholesterol, LDL cholesterol, triglycerides and calcium and mean CIMT were found to be significantly higher in patients with primary hyperparathyroidism ($p<0.05$). H-FABP was positively correlated with age, fasting blood glucose, BMI, and HsCRP.

Discussion: H-FABP levels correlated with some of the CV risk factors like age, fasting blood glucose, BMI, and h-CRP, moreover no difference in H-FABP levels was seen among patients of primary hyperparathyroidism having no cardiac disease.

Keywords: Hyperparathyroidism; H-FABP; cardiovascular risk

Özet

Amaç: Son dönem yapılan çalışmalar, plazma kalp tipi yağ asidi bağlayıcı protein (H-FABP) konsantrasyonunun makrovasküler hastalıklar için erken biyokimyasal bir belirteç olarak kullanılabileceğini göstermektedir. Primer hiperparatiroidizmli hastalarda kardiyovasküler risk faktörlerinin arttığı bildirilmektedir. Bu çalışmada amacımız primer hiperparatiroidizmli hastalarda plazma H-FABP düzeylerini sağlıklı kontrollerle karşılaştırarak değerlendirmektir.

Gereç ve Yöntemler: Primer hiperparatiroidizmli 88 (8 erkek, 80 kadın) hasta ve 87 sağlıklı olguda (12 erkek, 75 kadın) antropometrik parametreler, serum H-FABP, serum lipid, serum kalsiyum, fosfor, parathormon, insulin direnci (HOMA-IR), yüksek-hassasiyetli CRP (hs-CRP), 24 saatlik idrarda mikroalbumin atılımı, karotis intima-media kalınlığı (KIMK) ölçümü yapıldı.

Bulgular: Hasta [1086.07 (298–3744)] ve kontrol grubunda [1113.36 (263.27–3510)] H-FABP düzeyleri arasında anlamlı farklılık bulunmamıştır. Primer hiperparatiroidizmli hastalarda PTH, HOMA-IR, total kolesterol, LDL kolesterol, trigliserid ve kalsiyum ve ortalama KİMK düzeyleri anlamlı olarak yüksek bulunmuştur ($p<0.05$). H-FABP ile yaş, açlık kan glukozu, vücut kitle indeksi (VKİ) ve Hs-CRP arasında anlamlı pozitif korelasyon bulunmuştur.

Tartışma: H-FABP düzeyleri yaş, açlık kan glukozu, VKİ ve hs-CRP gibi bazı kardiyovasküler risk faktörleriyle korele olmakla birlikte kardiyak hastalığı olmayan primer hiperparatiroidizmli hastalarda sağlıklı olgulara kıyasla anlamlı farklılık görülmemiştir.

Anahtar kelimeler: Hiperparatiroidizm; H-FABP; kardiyovasküler risk

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Introduction

Primary hyperparathyroidism (PHT) is one of the most common endocrine disorders, resulting most commonly from parathyroid adenomas. Multiple observational studies indicate that primary hyperparathyroidism might be associated with cardiovascular diseases (1). Hypertension is commonly reported among patients with mild PHT (2–4), while other observational studies also suggest a correlation between left ventricular hypertrophy/diastolic dysfunction and PHT (5,6). The mean carotid intima-media thickness (CIMT) is significantly higher in patients with PHPT and significantly higher levels of parathormone (PTH) are associated with the thickness of aortic and carotid artery (7,8). These results suggested that arteriosclerosis might be associated with the severity of hyperparathyroidism.

Heart-type fatty acid binding-protein (H-FABP) is a low molecular weight, cytoplasmic and non-enzymatic protein that provides the transport of long-chain fatty acids to cardiomyocytes (9).

We have previously demonstrated the presence of elevated levels of H-FABP in various endocrinological and metabolic disorders including acromegaly, prediabetes and metabolic syndrome (10–12). However, these levels were not affected in hyperprolactinemia and hyperthyroidism (13,14).

The kinetics and release of this protein are similar to that of myoglobin, but unlike the latter, it is available at a higher concentration in the heart than the skeletal muscle. Thus making H-FABP more specific than myoglobin for heart tissue (15). Various studies have indicated that H-FABP is closely related to the cardiovascular risk factors, and is an independent risk factor for cardiovascular mortality (16,17). H-FABP is an excellent early marker for cardiac injury in acute coronary syndromes, providing early diagnosis of minor myocardial injury in heart failure and unstable angina (18–20). Moreover, elevated levels of serum H-FABP is also seen in myocardial injuries such as heart failure, hypertrophic and dilated cardiomyopathy, and pulmonary embolism (21–23).

Carotid intima-media thickness is an important marker of early changes in the atherosclerotic process and an indicator for the development of cardiovascular events. The most critical changes seen during the early, subclinical stage of atherosclerotic disease are endothelial dysfunction in the entire arterial system and increased intima-media thickness (IMC). The carotid intima-media thickness is frequently used as a strong predictor of cardiovascular events (myocardial infarction, stroke, and transient ischemic attack) (24).

The purpose of this study is to determine the level of H-FABP in primary hyperparathyroidism and also to evaluate the possible relationship of plasma H-FABP levels with CIMT, serum lipid, HOMA-IR, HsCRP, and microalbuminuria.

Material and Methods

About 88 patients with primary hyperparathyroidism and 87 control subjects in the study were enrolled in this study. Ethical committee approval and written informed consent of participants were obtained before the commencement of the study. After overnight fasting, blood samples were collected from all of the subjects to check the levels of parathormone (PTH), glucose, insulin, free T_4, thyroid-stimulating hormone (TSH), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, total cholesterol, high sensitive C-reactive protein (h-CRP), and H-FABP. Excretion of 24-hour urine microalbumin was assessed in the patient and control group. Weight, height, and waist and hip circumference were measured and the BMI and homeostasis model assessment of insulin resistance (HOMA-IR) were also calculated for both the groups. Additionally, all the patients underwent high-resolution B-mode ultrasonography to measure the carotid artery intima-media thickness (CIMT), wherein the same investigator carried out all the scans and image measurements. Furthermore, all the study participants were interviewed using a standard questionnaire that included information about their demographic characteristics, concomitant disease, use of medications that could affect H-FABP levels and smoking history. Afterward, the patients underwent a physical examination, and those with a history of the acute coronary syndrome (ACS), pulmonary embolism, stroke and heart failure or with immunological or renal diseases were excluded from the study. A control group, comprising of volunteers who had no history of ACS, heart failure, cardiomyopathy, pulmonary embolism, renal diseases, immunological diseases and diabetes mellitus, was also used in this study.

Heart-type fatty acid-binding protein

The H-FABP measurements were performed with the Epoch micro-volume spectrophotometer system (BioTek, Inc., Winooski, VT, USA) using a commercially available enzyme-linked immunosorbent assay ELISA kit (Hycult Biotech,

Uden, The Netherlands). The assay range of the H-FABP ELISA kit was 102 to 25000 pg/mL and the measurements were calculated simultaneously during the same experiment.

The ready-to-use solid-phase human H-FABP ELISA is based on the sandwich principle. Samples and standards were incubated together with a peroxidase-conjugated secondary antibody in microtiter wells coated with a primary antibody that recognizes human H-FABP. During incubation, the solid bound primary antibody captures the human H-FABP and the secondary antibody then binds to the captured human H-FABP, following which, the peroxidase-conjugated antibody reacts with the substrate tetramethylbenzidine (TMB; this reaction was stopped by the addition of oxalic acid). The absorbance at 450 nm was measured with a spectrophotometer.

Statistical Analysis

The statistical analysis was performed using SPSS 11.5 (SPSS, Inc) software. The presentation of the variables that were normally distributed was as mean ±standard deviation (SD) and of those that were non normally distributed was as median (min-max). Categorical variables are presented as case number and percentage (%). Student's *t*-test was used to analyze normally distributed continuous variables. The significance of the difference between medians was compared by the Mann-Whitney U test and categorical variables were compared using the Pearson's chi-square or Fisher's exact test. Correlations were analyzed using Pearson's and Spearman's correlation and a p-value of <0.05 was considered to be statistically Significant for all analyses.

Results

Mean age (49.01±13.08 to 46.06±10.93, p=0.111), sex distribution and BMI were found to be similar between groups (Table 1). The prevalence of hypertension (HT) was significantly higher in the patients as compared to healthy individuals (18% to 0%, p=0.004), but the frequency of smoking was significantly lower in the patients (11% to 20%, p<0.0001). Additionally, no significant dif-

Table 1. Demographic characteristics and biochemical data for the patients with primary hyperparathyroidism and the control subjects.

	Patients (n=89)	Control (n=87)	p
Male/Female	8/81	12/75	0.315
*Age (years)	50.5 (18-73)	46 (23-68)	0.099
*BMI (kg/m^2)	28.39 (19.40-42.91)	27 (20.1-42)	0.065
*Waist/hip ratio	0.90 (0.76-1.20)	0.91 (0.81-1.05)	0.213
*Parathormone (pg/mL)	212 (92-896)	57 (26-133)	<0.001*
*Free T4 (ng/dL)	0.99 (0.52-1.46)	0.97 (0.64-1.40)	0.211
*TSH (µIU/mL)	1.5 (0.52-4.34)	1.63 (0.46-4.1)	0.534
*Fasting blood glucose (mg/dL)	88 (66-138)	86 (71-104)	0.878
*HOMA-IR	2.62 (0.49-11.6)	1.94 (0.27-5)	0.017
*Total cholesterol (mg/dL)	201 (127-382)	186 (17-293)	0.121
*LDL cholesterol (mg/dL)	114 (63.5-225.8)	109 (30.7-160)	0.025
*HDL cholesterol (mg/dL)	49 (26.8-99)	47 (24-83)	0.880
*Triglycerides (mg/dL)	117 (48-1585)	106 (40-290)	0.019
*Microalbuminuria (mg/g)	4.3 (0.1-79)	3.8 (2.7-21.3)	0.723
*HsCRP (mg/L)	2 (0.3-18)	2 (0.68-8)	0.706
*H-FABP (pg/mL)	1086.07 (298-3744)	1113.36 (263.27-3510)	0.374
*Mean CIMT (mm)	0.53 (0.33-0.695)	0.48 (0.4-0.595)	0.018
*Calcium (mg/dL)	10.7 (9.1-13.8)	9.4 (8.6-10.1)	<0.0001
*Vitamin D	12 (4-118)	12 (4-59)	0.537
*Creatinine	0.8 (0.4-1.12)	0.7 (0.6-1)	0.182

* Values are median (minimum-maximum).
Abbreviations: BMI: Body mass index; TSH: Thyroid-stimulating hormone; HOMA-IR: Homeostasis model assessment of insulin resistance; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; H-FABP: Heart-type fatty acid-binding protein; CIMT: Carotid intima-media thickness, HsCRP: High sensitive C-reactive protein.

ference was observed between the patients and controls with respect to the prevalence of diabetes mellitus (DM) (4% to 0%, p=0.351). Coronary artery disease (CAD) was not seen in the patients enrolled in the study and there was no significant difference in average H-FABP value between the patients with or without HT ((1126 (819) to 1059 (956), p=0.218). The average values of PTH, HOMA-IR, total cholesterol, LDL cholesterol, triglycerides, and calcium levels and mean CIMT were significantly higher in patients with primary hyperparathyroidism (p<0.05) (Table 1). Some patients from the control group had secondary hyperparathyroidism due to vitamin D deficiency. No significant change was identified between these two groups with respect to other values (Table 1) and no significant difference was found in H-FABP levels between patients [1078.13 (298-3744)] and controls [1049.91 (263.27-4403.02)] (Figure 1).

There was a positive correlation between age, fasting blood glucose, BMI, HsCRP levels and H-FABP levels (Table 2).

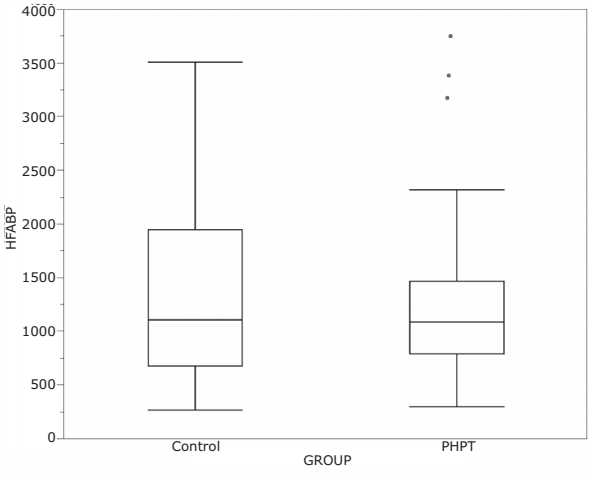

Figure 1: H-FABP levels in patients and control group.

Table 2. Correlation analyses between H-FABP and demographics, metabolic parameters, and cardiovascular risk factors in patients with primary hyperparathyroidism.

	R	P
Age (Years)	0.507	<0.001
Fasting blood glucose (mg/dL)	0.352	0.002
BMI (kg/m^2)	0.312	0.007
HsCRP (mg/L)	0.311	0.028

Discussion

Hyperparathyroidism is known to be associated with cardiovascular mortality and morbidity and with cardiomyopathy, arrhythmia, myocardial hypertrophy, as well as atherosclerosis, and valve and cardiac calcification (8,25,26). In vivo studies have demonstrated the vascular remodeling and vascular calcification effects of the parathormone through atherogenesis, as well as its prosclerotic effects on the vascular smooth muscle cells (27). In addition to these direct effects, hyperparathyroidism has indirect effects on the cardiovascular disease because of its assumed positive correlation to hypertension (28-30). H-FABP is a protein present in the cytosol of cardiomyocytes that is rapidly released into circulation during the event of myocardial tissue damage. H-FABP has been indicated as a more accurate and early marker in the identification of acute myocardial damage (31,32). Several studies have indicated a positive correlation between H-FABP and cardiometabolic risk factors (2–8) Therefore, we investigated whether H-FABP level is increased in patients with PHT. We demonstrated that H-FABP levels did not differ between patients and controls. We further investigated H-FABP levels with various CV risk factors.

Age of the individual also appears to contribute to the development of CVD. In a cohort of more than 3.6 million individuals, aged 40 years or older, who underwent self-referred screening for cardiovascular disease (ankle-brachial index, carotid duplex ultrasound, and abdominal ultrasound), the prevalence of any type of vascular disease increased significantly with each decade of life (33). In addition, h-CRP measurement is also considered to be a useful and independent marker for cardiovascular risk assessment (34). In our study, H-FABP levels showed a positive correlation with age, fasting blood glucose, BMI, and h-CRP.

American Heart Association has identified obesity as an independent risk factor (35). In a meta-analysis of studies assessing the impact of body weight on CHD, there was a 29 percent increase in CHD for every five-unit increase in body mass index (BMI) (36). Similarly, we also found a positive correlation between H-FABP levels and BMI in our study.

In one study with a large group of volunteers, serum H-FABP levels were found to be affected by age, gender, obesity, renal function, and ECG abnormality (37). Another study demonstrated that concentrations of H-FABP and h-CRP corre-

lated positively (38). Taken together these studies suggest that H-FABP levels could be influenced by some CV risk factors and/or markers, such as age, HsCRP, and BMI.

The design of our study excluded patients with overt cardiovascular or cerebrovascular disorder, although, there was an evidence of subclinical atherosclerosis in our patient group. Early atherosclerosis can be detected by CIMT and measured easily in a non-invasive manner. From the ultrasonographic point of view, CIMT measurements represent a good correlation with histology (40) where increased CIMT is associated with vascular risk factors and the presence of severe atherosclerosis (35–38), thus making CIMT level a widely accepted sign of early atherosclerosis. In our study, CIMT levels in patient group were higher than controls, suggesting that the patients with PHPT are at a higher risk for CV diseases. However, probably because of the exclusion of patients with overt CV, no correlation was found between the levels of CIMT and H-FABP.

To the best of our knowledge, this is the first study that evaluates the importance of H-FABP in patients with primary hyperparathyroidism in the literature. The findings of our study reinstate that cardiovascular risk factors such as hyperlipidemia and CIMT are higher in patients with primary hyperparathyroidism. In addition, we found a positive correlation between H-FABP and age, fasting blood glucose, BMI and h-CRP and similar H-FABP levels between groups, which necessitates comprehensive studies including larger populations to enlighten the relationship between H-FABP and primary hyperparathyroidism.

The limitations of this study are its relatively small sample size and it being a single center study.

Conclusion

In the present study, H-FABP levels were seen to correlate with some CV risk factors such as age, fasting blood glucose, BMI and h-CRP; however, these levels did not differ in primary hyperparathyroidism patients who had no cardiac disease.

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Conflict of Interest: No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Author Contributions

Idea/Concept: Bekir Uçan, Mustafa Şahin, Mustafa Özbek; Design: Bekir Uçan, Mustafa Şahin, Mustafa Özbek; Control/Supervision: Bekir Uçan, Mustafa Çalışkan, Muhammed Kızılgül; Data Collection and/or Processing: Bekir Uçan, Mustafa Çalışkan; Analysis and/or Interpretation: Bekir Uçan, Muhammed Kızılgül; Literature Review: Bekir Uçan, Muhammed Kızılgül; Writing The Article: Bekir Uçan, Mustafa Şahin, Güler Öztürk, Mehmet Akif Öztürk; Critical Review: Bekir Uçan, Mehmet Akif Öztürk, Erman Çakal; References and Fundings: Bekir Uçan, Muhammed Kızılgül, Mehmet Akif Öztürk, Erman Çakal; Materials: Bekir Uçan, Güler Öztürk, Mehmet Akif Öztürk, Erman Çakal.

References

1. Andersson P, Rydberg E, Willenheimer R. Primary hyperparathyroidism and heart disease--a review. Eur Heart J. 2004;25:1776-1787.
2. Lind L, Hvarfner A, Palmér M, Grimelius L, Akerström G, Ljunghall S. Hypertension in primary hyperparathyroidism in relation to histopathology. Eur J Surg. 1991;157:457-459.
3. Lind L, Ljunghall S. Pre-operative evaluation of risk factors for complications in patients with primary hyperparathyroidism. Eur J Clin Invest. 1995;25:955-958.
4. Lind L, Jacobsson S, Palmér M, Lithell H, Wengle B, Ljunghall S. Cardiovascular risk factors in primary hyperparathyroidism: a 15-year follow-up of operated and unoperated cases. J Intern Med. 1991;230:29-35.
5. Stefenelli T, Abela C, Frank H, Koller-Strametz J, Globits S, Bergler-Klein J, Niederle B. Cardiac abnormalities in patients with primary hyperparathyroidism: implications for follow-up. J Clin Endocrinol Metab. 1997;82:106-112.
6. Näppi S, Saha H, Virtanen V, Limnell V, Sand J, Salmi J, Pasternack A. Left ventricular structure and function in primary hyperparathyroidism before and after parathyroidectomy. Cardiology. 2000;93:229-233.
7. Rubin MR, Maurer MS, McMahon DJ, Bilezikian JP, Silverberg SJ. Arterial stiffness in mild primary hyperparathyroidism. J Clin Endocrinol Metab. 2005;90:3326-3330.
8. Walker MD, Fleischer J, Rundek T, McMahon DJ, Homma S, Sacco R, Silverberg SJ. Carotid vascular abnormalities in primary hyperparathyroidism. J Clin Endocrinol Metab. 2009;94:3849- 3856.
9. Glatz JF, van Bilsen M, Paulussen RJ, Veerkamp JH, van der Vusse GJ, Reneman RS. Release of fatty acid-binding protein from isolated rat heart subjected to ischemia and reperfusion or to the calcium paradox. Biochim Biophys Acta. 1988;961:148-152.
10. Ozbek M, Erdogan M, Dogan M, Akbal E, Ozturk MA, Ureten K. Serum heart-type fatty acid binding protein (H-FABP) levels in acromegaly patients. J Endocrinol Invest. 2011;34:576-579.

11. Akbal E, Özbek M, Güneş F, Akyürek Ö, Ureten K, Delibaşı T. Serum heart type fatty acid binding protein levels in metabolic syndrome. Endocrine. 2009;36:433-437.
12. Karbek B, Özbek M, Bozkurt NC, Ginis Z, Güngünes A, Ünsal IÖ, Cakal E, Delibası T. Heart-type fatty acid binding protein (H-FABP): relationship with arterial intima-media thickness and role as diagnostic marker for atherosclerosis in patients with impaired glucose metabolism. Cardiovasc Diabetol. 2011;10: 37.
13. Arslan MS, Topaloglu O, Sahin M, Tutal E, Gungunes A, Cakir E, Ozturk IU, Karbek B, Ucan B, Ginis Z, Cakal E, Ozbek M, Delibasi T. Preclinical atherosclerosis in patients with prolactinoma. Endocr Pract. 2014;20:447-451.
14. Ozbek M, Gungunes A, Sahin M, Ginis Z, Ucan B, Sayki M, Tutal E, Cakal E, Kuşkonmaz SM, Öztürk MA, Delibasi T. Serum heart type fatty acid binding protein levels are not changed in hyperthyroidism. Minerva Endocrinol. 2016;41:298-301.
15. Bilezikian JP, Silverberg SJ, Shane E, Parisien M, Dempster DW. Characterization and evaluation of asymptomatic primary hyperparathyroidism. J Bone Miner Res. 1991;6:S85-89.
16. Tso AW, Xu A, Sham PC, Wat NM, Wang Y, Fong CH, Cheung BM, Janus ED, Lam KS. Serum adipocyte fatty acid binding protein as a new biomarker predicting the development of type 2 diabetes: a 10-year prospective study in a Chinese cohort. Diabetes Care. 2007;30: 2667-2672.
17. Xu A, Tso AW, Cheung BM, Wang Y, Wat NM, Fong CH, Yeung DC, Janus ED, Sham PC, Lam KS. Circulating adipocyte-fatty acid binding protein levels predict the development of the metabolic syndrome: a 5-year prospective study. Circulation. 2007;115:1537-1543.
18. Pelsers MM, Hermens WT, Glatz JF. Fatty acid-binding proteins as plasma markers of tissue injury. Clin Chim Acta. 2005;352:15-35.
19. Figiel Ł, Wraga M, Bednarkiewicz Z, Lipiec P, Smigielski J, Krzemińska-Pakuła M, Kasprzak JD. Direct comparison of the diagnostic value of point-of-care tests detecting heart-type fatty acid binding protein or glycogen phosphorylase isoenzyme BB in patients with acute coronary syndromes with persistent ST-segment elevation. Kardiol Pol. 2011;69:1-6.
20. Boscheri A, Wunderlich C, Langer M, Schoen S, Wiedemann B, Stolte D, Elmer G, Barthel P, Strasser RH. Correlation of heart-type fatty acid-binding protein with mortality and echocardiographic data in patients with pulmonary embolism at intermediate risk. Am Heart J. 2010;160:294-300.
21. Arimoto T, Takeishi Y, Niizeki T, Nozaki N, Hirono O, Watanabe T, Nitobe J, Tsunoda Y, Suzuki S, Koyama Y, Kitahara T, Okada A, Takahashi K, Kubota I. Cardiac sympathetic denervation and ongoing myocardial damage for prognosis in early stages of heart failure. J Card Fail. 2007;13:34-41.
22. Komamura K, Sasaki T, Hanatani A, Kim J, Hashimura K, Ishida Y, Ohkaru Y, Asayama K, Tanaka T, Ogai A, Nakatani T, Kitamura S, Kangawa K, Miyatake K, Kitakaze M. Heart-type fatty acid binding protein is a novel prognostic marker in patients with non-ischaemic dilated cardiomyopathy. Heart. 2006;92:615-618.
23. Renaud B, Ngako A. Heart-type fatty acid-binding proteins (H-FABP): a reliable tool for initial risk stratification of pulmonary embolism? Eur Heart J. 2007;28:146-147.
24. Delibasi T, Emral R, Erdogan MF, Kamel N. Effects of alendronate sodium therapy on carotid intima media thickness in postmenopausal women with osteoporosis. Adv Ther. 2007;24:319-325.
25. Walker MD, Silverberg SJ. Cardiovascular aspects of primary hyperparathyroidism. J Endocrinol Invest. 2008; 31:925-931.
26. Saleh FN, Schirmer H, Sundsfjord J, Jorde R. Parathyroid hormone and left ventricular hypertrophy. Eur Heart J. 2003;24:2054-2060.
27. Rashid G, Bernheim J, Green J, Benchetrit S. Parathyroid hormone stimulates endothelial expression of atherosclerotic parameters through protein kinase pathways. Am J Physiol Renal Physiol. 2007;292:F1215-F1218.
28. Jorde R, Svartberg J, Sundsfjord J. Serum parathyroid hormone as a predictor of increase in systolic blood pressure in men. J Hypertens. 2005;23:1639-1644.
29. Snijder MB, Lips P, Seidell JC, Visser M, Deeg DJ, Dekker JM, van Dam RM. Vitamin D status and parathyroid hormone levels in relation to blood pressure: a population-based study in older men and women. J Intern Med. 2007;261:558-565.
30. Taylor EN, Curhan GC, Forman JP. Parathyroid hormone and the risk of incident hypertension. J Hypertens. 2008;26:1390-1394.
31. Ozdemir L, Elonu OH, Gocmen AY. Heart type fatty acid binding protein is more sensitive than troponin I and creatine kinase myocardial band at early stage in determining myocardial injury caused by percutaneous coronary intervention. Int Heart J. 2011;52:143-145.
32. McMahon CG, Lamont JV, Curtin E, McConnell RI, Crockard M, Kurth MJ, Crean P, Fitzgerald SP. Diagnostic accuracy of heart-type fatty acid-binding protein for the early diagnosis of acute myocardial infarction. Am J Emerg Med. 2012;30: 267-274.
33. Savji N, Rockman CB, Skolnick AH, Guo Y, Adelman MA, Riles T, Berger JS. Association between advanced age and vascular disease in different arterial territories: a population database of over 3.6 million subjects. J Am Coll Cardiol. 2013;61:1736-1743.
34. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO 3rd, Criqui M, Fadl YY, Fortmann SP, Hong Y, Myers GL, Rifai N, Smith SC Jr, Taubert K, Tracy RP, Vinicor F; Centers for Disease Control and Prevention, American Heart Association. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: a statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003;107: 499-511.
35. Eckel RH. Obesity and heart disease: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. Circulation. 1997;96:3248-3250.
36. Bogers RP, Bemelmans WJ, Hoogenveen RT, Boshuizen HC, Woodward M, Knekt P, van Dam RM, Hu FB, Visscher TL, Menotti A, Thorpe RJ Jr, Jamrozik K, Calling S, Strand BH, Shipley MJ; for the BMI-CHD Collaboration Investigators. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300 000 persons. Arch Intern Med. 2007;167:1720-1728.
37. Niizeki T, Takeishi Y, Takabatake N, Shibata Y, Konta T, Kato T, Kawata S, Kubota I. Circulating levels of heart-type fatty acid-binding protein in a general Japanese population: effects of age, gender, and physiologic characteristics. Circ J. 2007;71:1452-1457.
38. Jeong JH, Seo YH, Ahn JY, Kim KH, Seo JY, Kim MJ, Lee HT, Park PW. The prognostic value of serum levels of heart-type fatty acid binding protein and high sensitivity C-reactive protein in patients with increased levels of amino-terminal pro-b type natriuretic peptide. Ann Lab Med. 2016;36(5):420-426.
39. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. Circulation. 1986;74: 1399-1406.