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ARAŞTIRMA MAKALESİ

The relationship between arterial stiffness and helicobacter pylori infection

Helicobakter pylori enfeksiyonu ve arteriyel sertlik arasındaki ilişki

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ABSTRACT

Aim: Studies have found the association of Helicobacter Pylori (Hp) seropositivity with cardiovascular diseases and it has been shown that chronic inflammation with Hp may be related to early atherosclerosis. The aim of this study is to evaluate the relationship between Hp positivity detected by endoscopic gastric biopsy and arterial stiffness. **Material and Method:** In this cross-sectional study, patients were divided into 2 groups as Hp positive (n=48) and Hp negative (n=61) according to endoscopic gastric biopsy findings. Augmentation index, arterial stiffness and central blood pressure were measured using Pulse wave velocity analysis/Ambulatory blood pressure monitoring in all patients. **Result:** Augmentation index was significantly higher in the Hp positive group (p=0.020). There was no correlation between central blood pressure and augmentation index and the intensity of Hp colonization (p=0.070, r=0.263). However, logistic regression analysis revealed that positive Hp (OR: 3.593, 95%CI: 1.341-9,629, p=0.011) was the only variable predictive for an augmentation index > 24.9 among variables including, age, BMI, systolic and diastolic blood pressure, central blood pressure, glucose, creatinine, total cholesterol, C-reactive protein, and positive Hp. **Conclusion:** Helicobacter Pylori positive patients with confirmed biopsy have an increased arterial stiffness. Moreover, presence of Hp infection is predictive for an increased arterial stiffness. Regarding the diversity and frequency of Hp worldwide long term follow up studies with larger sample size are needed to elaborate the mechanism of this relationship.

Keywords: helicobacter pylori; vascular stiffness; arteriosclerosis; pulse wave analysis

ÖZ

Amaç: Çalışmalar, Helicobacter Pylori (Hp) seropozitifliğinin kardiyovasküler hastalıklar ile ilişkisini bulmuş ve Hp enfeksiyonu sırasında kronik inflamasyonun erken evre ateroskleroza neden olduğu gösterilmiştir. Bu çalışmanın amacı, endoskopik mide biyopsisi ile saptanan Hp pozitifliği ile ateroskleroz arasındaki ilişkiyi değerlendirmektir. **Gereç ve Yöntem:** Bu kesitsel çalışmada, hastalar endoskopik mide biyopsi bulgularına göre Hp pozitif (n=48) ve Hp negatif (n=61) olmak üzere 2 gruba ayrılmıştır. Tüm hastalarda augmentasyon indeksi, arteriyel sertlik ve santral kan basıncı Nabız dalga hızı analizi/Ambulatuvar kan basıncı izlemi kullanılarak ölçüldü. **Bulgular:** Helicobacter Pylori pozitif grupta augmentasyon indeksi anlamlı olarak daha yüksekti (p=0.020). Santral kan basıncı ve augmentasyon indeksi ile Hp kolonizasyonunun yoğunluğu arasında hiçbir korelasyon yoktu (p=0.070, r=0.263). Ancak yapılan lojistik regresyon analizine göre yaş, BMI, sistolik ve diyastolik kan basıncı, merkezi kan basıncı, glikoz, kreatinin, toplam kolesterol, C-reaktif protein ve pozitif Hp faktörleri arasında pozitif Hp'nin 24.9 üzerinde augmentasyon indeksini tek ön gördürücü faktör olduğu belirlendi (OR: 3.593, 95%CI: 1.341-9,629, p=0.011). **Sonuç:** Helicobacter Pylori pozitif saptanan hastalarda ateroskleroz ve arteriyel sertlik riski artmıştır. Ek olarak Hp pozitifliğinin arteryel sertlik için ön gördürücü olduğu izlenmiştir. Hp ile ateroskleroz ilişkinin mekanizmasını detaylandırmak için daha büyük örneklem büyüklüğünde uzun vadeli takip çalışmalarına ihtiyaç vardır.

Anahtar Kelimeler: helicobacter pylori; damar sertliği; arterioskleroz; nabız dalga analizi

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INTRODUCTION

Helicobacter Pylori (Hp) is highly prevalent among general population.(1) Hp invades the gastric wall and causes various mucosal and systemic diseases.(2) Chronic inflammatory state and inflammatory cytokines throughout the blood stream can lead to development of atherosclerosis.(3,4) However, data concerning the role of Hp infection and atherosclerosis is controversial.(5-7) A few studies have reported that Hp infection with high blood cytokine levels was associated with atherosclerosis.(8,9) This also supports the fact that chronic inflammation during Hp infection may be associated with atherosclerosis. Arterial stiffness is one of the major indicators of atherosclerosis and can act as an independent predictor for cardiovascular disease and all-cause mortality.(10-12) It can be measured non-invasively utilizing Pulse wave velocity (PWV) and Augmentation index (Aix).(13-15)

This study purposed to investigate the association between Hp infection and arterial stiffness, which is a reliable marker of early atherosclerosis, in a study population who underwent upper GIS endoscopy and subsequent endoscopic gastric biopsy.

MATERIAL and METHODS

The study was conducted in Health Sciences University Keçiören Education and Research Hospital between January 2016 and June 2017. Ethics committee approval was obtained from Health Sciences University Keçiören Education and Research Hospital with the date 09.03.2016 and the code number is:1006. Written informed consent was obtained from all participants.

Outpatients with dyspepsia were investigated for having Hp infection and positive cases underwent endoscopy. Patients with positive pathology result were enrolled in the study. Patients under the age of 18, with comorbid diseases such as hypertension, atherosclerotic heart disease, diabetes, chronic kidney disease, peripheral artery disease, cerebrovascular disease, hypothyroidism, hyperthyroidism, hyperlipidemia, malignancy, smoking and/or alcohol use and patients who have recently used antibiotics and proton pump inhibitors were excluded. Both verbal and written informed consent was obtained from the patients who participated in the study.

A control group was also assigned with similar age and baseline demographics. Individuals with no accompanying diabetes mellitus, hypertension, atherosclerotic cardiovascular disease, hypothyroidism, hyperthyroidism, hyperlipidemia, chronic renal failure, cerebrovascular and peripheric arterial disease, no history of smoking and alcohol, no regular usage of any drug and no usage of antibiotics within the last 6 months were assigned to the control group. The endoscopies of all control group subjects were also negative for Hp. Patients were divided into two groups as Hp positive and Hp negative.

The determination of Hp bacteriae on the luminal mucosal epithelial of gastric wall has been conducted via hematoxylin eosin dye on giemza hystochemistry analysis. The gull wing structures were identified as Hp bacteriae on the microscope and recorded according to Sydney Classificiation. Blood pressure and arterial stiffness were calculated by using Pulse wave velocity analysis (PWA)/Ambulatory blood pressure monitoring (ABPM) in all patients. Participants were placed in a quiet room and waited still before the arterial stiffness measurement procedure. Brachial blood pressure measurement was performed with the Mobil-O-Graph PWA/ABPM (I.E.M. GmBH, Stolberg, Germany) device, which was approved by BHS and ESR and whose reliability studies were conducted in terms of Pulse wave analysis (PWA). A total of 4 pulse wave velocity analyzes were performed from the patients. Pulse, pulse pressure (PP), diastolic blood pressure (DBP), systolic blood pressure (SBP), mean blood pressure (MBP), central diastolic blood pressure (c)DBP, central systolic blood pressure (c)SBP, central pulse pressure (c)PP, cardiac output (CO), body surface, peripheral vascular resistance, cardiac index, augmentation pressure (AP), augmentation index (Aix @75) arranged according to the pulse rate of 75 beats/minute and the pulse wave velocity data were obtained. The data have been transferred to the software program for offline analysis.

Statistical analysis

Statistical analyses were conducted via SPSS-15 program. Kolmogorov Smirnov test was performed for compliance with normal distribution. Discrete variables were expressed as % and continuous variables as mean ± standard deviation. Mann Whitney U test was utilized for continuous variables in comparison of groups with and without Hp positivity. Chi-square test was applied to compare discrete variables. Sperman's correlation coefficient was used for correlation comparison of age, BMI, SBP, DBP, OCD, central diastolic blood pressure (c)DBP ve central systolic blood pressure (c)SBP. Logistic regression analysis was performed to identify the contributors for an increased augmentation index. A p value of<0.05 was considered as statistically significant.

RESULTS

A total of 109 patients (n=48 Hp positive and n=61 Hp negative) were enrolled in the study (mean age 36.9 ± 7.5, 39.4 % male). Demographic features of the subjects with and without Hp infection were similar. The (c)SBP and (c)DBP measurements, peripheral resistance, PWV and augmentation pressure values of the two groups were also similar (Table-1).

Table1: Demographic properties of groups with Helicobacter Pylori (+) and Helicobacter Pylori (-), blood pressure values and comparison of arterial stifness parameters

	n=61 Hp (-)	n=48 Hp (+)	p
Age	35(18-63)	39(21-78)	0.363
Body Mass Index	25.6(17.8-34.3)	26.4(15.8-32.9)	0.378
Systolic Blood Pressure	118(96-133)	123(91-135)	0.170
Diastolic Blood Pressure	81(49-92)	85(51-95)	0.060
Mean Blood Pressure	92(72-116)	98(76-129)	0.109
Central Systolic Blood Pressure	109(80-129)	113(85-131)	0.086
Central Diastolic Blood Pressure	74(56-101)	80(62-129)	0.146
Peripheral Resistance	1.18(0.80-1.39)	1.19(0.80-1.42)	0.523
Augmentation Pressure	6(2-80)	5(1-112)	0.709
Augmentation Index	21.5(4-50)	27(1-47)	0.020*
Pulse Wave Velocity	5.6(4.3-9.8)	5.7(4.2-10.5)	0.488
Sex(F,%)	%59.0	%60.4	0.982

The augmentation index of the Hp (+) group was significantly higher than that of the Hp (-) patients (27(1-47) vs. 21.5(4-50, p=0.020). We have elaborated the Hp intensity of the Hp positive group: Hp intensity 1 had a density frequency of 35.4%, Hp intensity 2 had a density frequency of 39.6% and Hp intensity 3 had a density frequency of 25.0%. No significant difference was found between the groups with Hp intensity 1, 2 and 3 in terms of augmentation index (25.9±8.9, 29.2±12.9 and 25.4±10.5, p=0.389).

No significant correlation was found between augmentation index and age, BMI, SBP, DBP, OCD, central SBP and central DBP in the Hp (+) group (p=0.969, r=-0.004, p=0.769, r=0.043, p=0.070, r=0.264, p=0.280, r=0.159, p=0.164, r=0.204, p=0.070, r=0.263, p=0.601, r=0.077, respectively).

The mean augmentation index of the whole study population was 24.9 ± 6.2. 20 of hte study subjects had an augmentation index > 24.9. Logistic regression analysis revealed that positive Hp (OR: 3.593, 95%CI: 1.341-9,629, p=0.011) was the only variable predictive for an augmentation index > 24.9 among variables including, age, BMI, systolic and diastolic blood pressure, central blood pressure, glucose, creatinine, total cholesterol, C-reactive protein, and positive Hp.

DISCUSSION

Helicobacter pylori is a spiral-shaped gram-negative bacteria that naturally colonizes in the gastricepithelial wall. The prevalence of Hp infection rate is relatively high in Turkey as Hp infection is more common in developing countries. (16) The bacteriae is usually acquired during childhood and the infection is generaly asymptomatic. Hp not only results in several gastroduodenal pathologies by producing acute inflammation, but it also causes several systemic diseases by the release of various inflammatory cytokines.(8,17) According to previous data Hp may play a role in the pathogenesis of atherosclerosis. Published data from Japan elaborated that Hp seropositivity has a significant correlation with coronary heart disease.(18) This relationship was more common in patients under 55 years of age. Hp infection may trigger the initiation and progression of atherosclerosis and is a risk factor for cerebrovascular and cardiovascular diseases.(9,19,20) During the brachial-ankle pulse wave velocity (PWV), it was found that Hp seropositivity was associated with high levels of CRP, which is an early marker for atherosclerosis.(21) Adachi et al. showed that carotid-femoral PWV was higher in young people with Hp seropositivity in their study.

The non-invasive evaluation of arterial stiffness measuring the ankle brachial index (ABI) and the brachial-ankle PWV, showed that the degree of arterial stiffness was higher in Hp positive young cases than in Hp negative young cases but no difference was observed in elderly individuals.(21) It was also denoted that there was a significant association between Hp seropositivity and arterial stiffness measured by the cardio-ankle vascular index (CAVI) in healthy asymptomatic individuals. (22) These findings suggest that Hp infection may contribute to the development of early stage of atherosclerosis which is indicated by arterial stiffness.

In this study, our findings indicate that Hp seropositive individuals have increased arterial stiffness compared to Hp seronegative counterparts. Moreover, Hp seropositivity may be a significant predictor for an increased arterial stiffness, which is an indicator for atherosclerotic vascular disease. Although the exact mechanism underlying the role of H Hp infection in the course of arterial stiffness and atherosclerosis is unclear, the inflammatory process contributing in the development of atherosclerotic vascular disease appears the most popular theory. The concentration of certain inflammatory markers such as tumor necrosis factor, interleukin-6, interleukin-8, serum CRP and fibrinogen have been shown to increase in Hp infection. (23,24) In addition to the inflammatory state presenting during the Hp infection, antioxidants are reduced in patients with Hp infection.(25) On the other hand, a number of studies report an association between Hp infection and dyslipidemia, which

can further contribute to the development of atherosclerotic vascular disease. All these data support that Hp infection may precipitate atherosclerosis through inflammatory pathways, reduced antioxidants and dyslipidemia.

Arterial stiffness is defined as the stability, resistance and compliance of the vascular wall. It depends on the balance of collagen and elastin, which are the basic proteins of the vascular wall. Disruption of this balance due to biochemical reasons such as mechanical and inflammatory processes (increased vascular luminal pressure) results in excessive production of collagen and elastin destruction. This situation contributes to arterial stiffness by decreasing the compliance and increasing in vascular resistance.(26)

Increased arterial stiffness is an indicator of both progressive hypertension and future hypertension and at the same time, it is associated with peripheral arterial disease, ischemic or hemorrhagic stroke, impaired cognitive function, renal glomerular damage (increase in proteinuria and loss of kidney function).(27-30) Arterial stiffness, an early marker of systemic atherosclerosis, is an independent indicator of cardiovascular events and all-cause mortality, can be measured in several ways. Pulse wave velocity (PWV) is a simple, non-invasive and easy method used to measure arterial stiffness.(31)

It has been published in many articles that Hp infection is a risk factor for the development of cardiovascular diseases in healthy populations.(5-7,10) According to a study conducted in South Korea, Hp infected(confirmed by biopsy) patients had significantly higher arterial stiffness.(32,33) Multiple linear regression analysis showed that Hp infection was positively correlated with ba PWV. In our study, we have also diagnosed the Hp pathology by gastroduodenal biopsy. However, there was no significant relationship between Hp intensity in biopsy and atherosclerosis. This situation may be related with the low sample size. Serological tests are used frequently in the diagnosis of Hp infection as they are cost-effective and easy to access, but have a high negative predictive value. It may maintain its positivity for a few years after Hp eradication. For this reason, detecting Hp positivity by endoscopic gastric biopsy is a more reliable than serologic way.

The most important limitation of this study is the relatively small patient population. Due to its cross-sectional design, sufficient interpretation cannot be made regarding the mechanism of the relationship between Hp positivity and atherosclerosis. In addition, the fact that various factors that may affect arterial stiffness (such as comorbidities) were not examined in our study may have caused erroneous interpretation of the results.

On the other hand, the strength of this study lies beneath the fact that the patients with Hp positivity had been detected by histologic examination of endoscopic gastric biopsy specimens, not using a serological method.

CONCLUSION

Hp positive patients with confirmed biopsy have increased arterial stiffness. Moreover, Hp seropositivity may predict an increased arterial stiffness. Regarding the diversity and frequency of Hp worldwide long term follow up studies with larger sample size are needed to elaborate the mechanism of this relationship.

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Conflict of Interest: The authors have no conflict of interest to declare.

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Ethics Committee Approval: Health Sciences University Keçiören Education and Research Hospital Ethics Committee Permission was obtained with the letter dated 09.03.2016 and numbered 1006.

REFERENCES

1. Suerbaum S, Michetti P. Helicobacter pylori infection.N Engl J Med. 2002;347:1175-86. DOI: 10.1056/NEJMra020542.

2. Konturek SJ, Konturek PC, Konturek JW, M Plonka, M Czesnikiewicz-Guzik, T Brzozowski et al. Helicobacter pylori and its involvement in gastritis and peptic ulcer formation. J Physiol Pharmacol. 2006;57 Suppl3:29–50.

3. Torisu T, Takata Y, Ansai T,Matsumoto T, Sonoki K, Soh Iet al. Possible association of atrophic gastritis and arterial stiffness in healthy middle-aged Japanese. J Atheroscler Thromb. 2009;16 (5):691-7. DOI: 10.5551/jat.943.

4.Yang YF, Li Y, Liu JH, Wang XM, Wu BH, He CS et al. Relation of Helicobacter pylori infection to peripheral arterial stiffness and 10-year cardiovascular risk in subjects with diabetes mellitus. Diab Vasc Dis Res. 2020 May-Jun;17(5):1479164120953626. DOI: 10.1177/1479164120953626.

5. Xu Z, Li J, Wang H, Xu G Helicobacter pylori infection and atherosclerosis: is there a causal relationship?.Eur J Clin Microbiol Infect Dis. 2017 Dec;36(12):2293-2301. DOI: 10.1007/s10096-017-3054-0.

6. Jafarzadeh A, Nemati M, Tahmasbi M, Ahmadi P, Rezayati MT, Sayadi AR. The association between infection burden in Iranian patients with acute myocardial infarction and unstable angina. Acta Med Indones. 2011;43(2):105–11.

7.Schottker B, Adamu MA, Weck MN, Müller H, Brenner H. Helicobacter pylori infection, chronic atrophic gastritis and major cardiovascular events: a population-based cohort study. Atherosclerosis. 2012;220(2):569–74. DOI:10.1016/j.atherosclerosis.2011.11.029.

8. Franceschi F, Gasbarrini A. Helicobacter pylori and extragastric diseases. Best Pract Res Clin Gastroenterol. 2007;21(2):325-34. DOI:10.1016/j.bpg.2006.10.003.

9.Mendall MA, Patel P, Asante M, L Ballam, J Morris, D P Strachan et al. Relation of serum cytokine concentrations to cardiovascular risk factors and coronary heart disease. Heart. 1997;78(3):273–7. DOI: 10.1136/hrt.78.3.273.

10. Laurent S, Boutouyrie P, Asmar R,Gautier I, Benetos A, Lacolley Pet al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension. 2001;37(5):1236−41. DOI: 10.1161/01.hyp.37.5.1236.

11. Shirai K, Hiruta N, Song M, Kurosu T, Suzuki J, Tomaru Tet al. Cardio-ankle vascular index (CAVI) as a novel indicator of arterial stiffness: theory, evidence and perspectives. J Atheroscler Thromb. 2011;18(11):924–38. DOI: 10.5551/jat.7716.

12. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol. 2010;30;55(13):1318-27. DOI: 10.1016/j.jacc.2009.10.061.

13. Glasser SP, Arnett DK, McVeigh GE, Finkelstein SM, Bank AJ, Morgan DJet al. Vascular compliance and cardiovascular disease: a risk factor or a marker? Am J Hypertens. 1997;10(10 Pt 1):1175-89. DOI: 10.1016/s0895-7061(97)00311-7.

14.Shirai K, Utino J, Otsuka K, Takata M. A novel blood pressure-independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI). J Atheroscler Thromb. 2006; 13(2):101-7. DOI: 10.5551/jat.13.101.

15. Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJet al. Aortic pulse wave velocity improves cardiovascular event prediction: An individual participant metaanalysis of prospective observational data from 17,635 subjects. J Am Coll Cardiol. 2014;63(7):636–46. DOI: 10.1016/j.jacc.2013.09.063.

16.Kadayifci A, Buyukhatipoglu H, Cemil Savas M, Simsek I et al. Eradication of Helicobacter pylori with triple therapy: an epidemiologic analysis of trends in Turkey over 10 years. Clin Ther. 2006;28(11):1960-6. DOI: 10.1016/j.clinthera.2006.11.011.

17. Realdi G, Dore MP, Fastame L. Extradigestive manifestations of Helicobacter pylori infection: fact and fiction. Dig Dis Sci. 1999;44(2):229-36. DOI: 10.1023/a:1026677728175.

18. Yamashina A, Tomiyama H, Takeda K, Tsuda H, Arai T, Hirose Ket al. Validityreproducibilityand clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. Hypertens Res. 2002;25(3):359−64. DOI: 10.1291/hypres.25.359.

19. Markus HS, Mendall MA. Helicobacter pylori infection: a risk factor for ischaemic cerebrovascular disease and carotid atheroma. J Neurol Neurosurg Psychiatry. 1998;64(1):104−7. DOI: 10.1136/jnnp.64.1.104.

20. Osawa H, Kawakami M, Fujii M, Kubo N, Iwanaka H, Yamamoto W et al. Helicobacter pylori infection and coronary heart disease in Japanese patients. Cardiology. 2001;95(1):14−9. DOI: 10.1159/000047337.

21. Adachi K, Arima N, Takashima T, Miyaoka Y, Yuki M, Ono M et al. Pulse-wave velocity and cardiovascular risk factors in subjects with Helicobacter pylori infection. J Gastroenterol Hepatol. 2003;18(7): 771−7. DOI: 10.1046/j.1440-1746.2003.03059.x.

22. Saijo Y, Utsugi M, Yoshioka E, Horikawa N, Sato T, Gong Y et al. Relationship of Helicobacter Pylori Infection to Arterial Stiffness in Japanese Subjects. Hypertens Res. 2005;28(4):283-92. DOI: 10.1291/hypres.28.283.

23. Moss SF, Legon S, Davies J, Calam J. Cytokine gene expression in Helicobacter pylori associated antral gastritis. Gut. 1994;35(11): 1567−70. DOI: 10.1136/gut.35.11.1567.

24. Crabtree JE, Shallcross TM, Heatley RV, Wyatt JI. Mucosal tumour necrosis factor alpha and interleukin-6 inpatients with Helicobacter pyloriassociated gastritis.Gut.1991;32(12):1473-7. DOI: 10.1136/gut.32.12.1473.

25. Zhang ZW, Patchett SE, Perrett D, Domizio P, Farthing MJ.Gastric alpha-tocopherol and beta-carotene concentrationsin association with Helicobacter pylori infection. Eur JGastroenterol Hepatol.2000;12(5):497-503. DOI: 10.1097/00042737-200012050-00004

26. Shirwany NA, Zou MH. Arterial stiffness: a brief review. Acta Pharmacol Sin. 2010;31(10):1267-76. DOI: 10.1038/aps.2010.123.

27. Muiesan ML, Salvetti M, Rizzoni D, Paini A, Agabiti-Rosei C, Aggiusti Cet al. Pulsatile hemodynamics and microcirculation: Evidence for a close relationship in hypertensive patients.Hypertension.2013;61(1):130-6. DOI:10.1161/HYPERTENSIONAHA.111.00006.

28. Laurent S, Katsahian S, Fassot C, Tropeano AI, Gautier I, Laloux B et al. Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. Stroke. 2003;34(5):1203–6. DOI: 10.1161/01.STR.0000065428.03209.64.

29. Scuteri A, Tesauro M, Appolloni S, Preziosi F, Brancati AM, Volpe M. Arterial stiffness as an independent predictor of longitudinal changes in cognitive function in the older individual. J Hypertens. 2007;25(5):1035–40. DOI: 10.1097/HJH.0b013e3280895b55.

30. Hashimoto J, Ito S. Central pulse pressure and aortic stiffness determine renal hemodynamics: Pathophysiological implication for microalbuminuria in hypertension. Hypertension. 2011;58(5):839–46. DOI: 10.1161/HYPERTENSIONAHA.111.177469.

31. Omboni S, Posokhov IN, Kotovskaya YV, Protogerou AD, Blacher J. Twenty-Four-Hour Ambulatory Pulse Wave Analysis in Hypertension Management: Current Evidence and Perspectives. Curr Hypertens Rep. 2016;18(10):72. DOI: 10.1007/s11906-016-0681-2.

32.Sung HR, Cho HC, Sang JH, Park KC, Kim MJ, Park KS et al. The relationship between Helicobacter pylori infection and arterial stiffness in adults with abnormal gastroduodenoscopic findings. Korean J Fam Pract. 2015;5(Suppl 3):43-48.

33. Choi JM, Lim SH, Han YM, Lee H, Seo JY, Park HE et al. Association between Helicobacter pylori infection and arterial stiffness: Results from a large cross-sectional study. PLoS One 2019 Aug 29;14(8):e0221643. DOI: 10.1371/journal.pone.0221643.